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Advances in Precision Medicine

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Effect of Ambroxol Hydrochloride Combined with Pulmonary Rehabilitation on Elderly Patients with COPD and Pulmonary Infection

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Abstract:

Objective: To analyze the effect of ambroxol hydrochloride combined with pulmonary rehabilitation in elderly patients with chronic obstructive pulmonary disease (COPD) and pulmonary infection. *Methods:* A total of 80 elderly patients with COPD combined with pulmonary infection, admitted between January 2022 and December 2023, were randomly divided into an observation group and a control group. The observation group received ambroxol hydrochloride combined with pulmonary rehabilitation, while the control group was treated with ambroxol hydrochloride alone. The efficacy of the two treatments was evaluated. *Results:* The observation group exhibited a shorter clinical symptom resolution time ($P < 0.05$). Following treatment, the observation group demonstrated higher oxygen saturation levels and lower levels of inflammatory factors, including interleukin-6 ($P < 0.05$). Additionally, the lung function index in the observation group improved significantly ($P < 0.05$). *Conclusion:* For elderly patients with COPD and pulmonary infection, pulmonary rehabilitation training effectively enhances the resolution rate of clinical symptoms, reduces inflammatory factor levels, improves oxygen saturation, and facilitates pulmonary function recovery.

Keywords:

Ambroxol hydrochloride
Pulmonary rehabilitation
Elderly COPD
Pulmonary infection

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1. Introduction

In recent years, the prevalence of chronic obstructive pulmonary disease (COPD) in China has been steadily increasing, with middle-aged and elderly populations constituting the primary affected groups. COPD patients often experience symptoms such as persistent cough and

dyspnea, which significantly impact their daily lives. Despite advancements in medical treatments, there remains no specific cure for COPD, and the disease is often complicated by conditions such as pulmonary infections. The treatment of COPD in clinical practice typically involves bronchodilator medications, oxygen

therapy, and anti-infection measures to alleviate symptoms, although the outcomes are often limited.

Elderly patients, due to age-related declines in organ function and weakened immune responses, face an elevated risk of infection, necessitating more comprehensive and tailored treatment strategies. Ambroxol hydrochloride, a mucolytic agent, activates airway ciliary function, reduces mucus viscosity, enhances pulmonary surfactant synthesis, and alleviates respiratory symptoms^[1,2]. Pulmonary rehabilitation, on the other hand, involves customized training programs designed to strengthen respiratory muscles, improve exercise tolerance, and reduce dyspnea.

This study focuses on the combined application of ambroxol hydrochloride and pulmonary rehabilitation to address the treatment challenges in elderly patients with COPD complicated by pulmonary infection, aiming to optimize therapeutic strategies and improve clinical outcomes.

2. Materials and methods

2.1. General information

The subjects in this study were patients diagnosed with COPD, aged over 60 years, with 80 cases complicated by pulmonary infection. The patients were randomly divided into an observation group and a control group. In the observation group, there were 23 males and 17 females, aged between 60 and 75 years, with a mean age of 69.53 ± 3.47 years. In the control group, there were 24 males and 16 females, aged between 61 and 76 years, with a mean age of 69.63 ± 3.51 years. A comparative analysis of the two groups revealed no significant differences ($P > 0.05$).

Inclusion criteria: (1) Patients meeting the diagnostic criteria for COPD; (2) Patients aged over 60 years with a confirmed pulmonary infection.

Exclusion criteria: (1) Patients with known allergies to ambroxol hydrochloride; (2) Patients with comorbid tuberculosis.

2.2. Methods

All patients received conventional treatment based on symptomatic management, including measures such as spasmolysis, oxygen therapy, and anti-infection treatment

to alleviate clinical symptoms.

2.2.1. Treatment methods in the control group

Patients in the control group received ambroxol hydrochloride treatment. The drug, manufactured by Shantou Jinshi Pharmaceutical Factory Co., LTD. (National Medicine Approval Number: H20083547), was administered via intravenous infusion. The medication was prepared by mixing the drug solution with sodium chloride solution in a 30 mg:100 mL ratio and was administered twice daily.

2.2.2. Treatment methods in the observation group

In addition to the treatment provided to the control group, the observation group underwent pulmonary rehabilitation.

- (1) Promotion and education on rehabilitation training: Medical staff analyzed the patients' physical examination results to assess their physiological condition, confirm disease severity, and determine the key points of rehabilitation training. Educational content was optimized to deepen patients' understanding of disease-related knowledge and enhance their cooperation^[3]. Efforts were made to develop a multi-channel health education system, integrating new media (e.g., WeChat) with traditional media. The use of visual aids improved comprehension and promoted self-care. Psychological support was also provided to address any negative emotions, ensuring patient compliance with pulmonary rehabilitation training. Regular thematic lectures allowed patients to demonstrate their rehabilitation training, enabling timely correction of mistakes and improving training enthusiasm.
- (2) Enhancement of pulmonary rehabilitation training programs: Patients were guided through diaphragmatic breathing exercises. This involved positioning one hand on the chest and the other on the abdomen, maintaining an immobile upper body while exhaling and compressing the abdomen, and allowing abdominal expansion during inhalation. Inhalation was performed through

the nose, and exhalation through pursed lips. Lip-pursed breathing exercises were also introduced, with nasal inhalation followed by slow, controlled exhalation through pursed lips, akin to whistling. Each training session lasted approximately 20 minutes ^[4]. Upper limb and thoracic exercises were implemented, including upward stretches, arm extensions, and movements to enhance thoracic expansion. Patients performed coordinated movements such as bending the elbows, spreading the arms, bending the knees, and raising the back of the feet. Training plans were adjusted according to patient progress to ensure appropriate intensity and frequency, promoting optimal recovery of pulmonary function ^[5].

2.3. Observation indicators

The clinical symptoms, such as cough, were analyzed in both groups. Oxygen saturation and levels of inflammatory factors, including interleukin-6, were measured using an automatic biochemical analyzer. Pulmonary function indices, such as forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and the FVC/FEV1 ratio, were assessed using a pulmonary function detector.

2.4. Statistical analysis

Data were processed using SPSS 23.0. The χ^2 test was applied to count data, while the *t*-test was used for measurement data. A *P*-value < 0.05 indicated a statistically significant difference.

3. Results

3.1. Clinical symptoms

As shown in **Table 1**, the resolution time for clinical symptoms in the observation group was significantly shorter compared to the control group, with *P* < 0.05.

3.2. Oxygen saturation and inflammatory factors

Following treatment, the observation group demonstrated higher oxygen saturation and significantly lower levels of inflammatory factors, including interleukin-6, compared to the control group (*P* < 0.05), as shown in **Table 2**.

3.3. Pulmonary function

As shown in **Table 3**, the pulmonary function indices, including FVC, FEV1, and the FVC/FEV1 ratio, showed significant improvement in the observation group after treatment (*P* < 0.05).

Table 1. Time to resolution of clinical symptoms in the two groups (mean \pm SD, days)

Group	<i>n</i>	Pulmonary moist rales	Cough	Expectoration	Shortness of breath	Fever
Observation group	40	4.53 \pm 0.39	4.15 \pm 0.43	5.32 \pm 1.01	5.68 \pm 0.42	1.56 \pm 0.21
Control group	40	6.58 \pm 0.24	6.02 \pm 0.52	8.16 \pm 1.37	7.91 \pm 0.29	2.86 \pm 0.37
<i>t</i>	-	10.352	11.415	12.312	9.839	10.237
<i>P</i>	-	0.001	0.001	0.001	0.001	0.001

Table 2. Oxygen saturation and inflammatory factor levels before and after treatment in both groups (mean \pm SD)

Group	<i>n</i>	Blood oxygen saturation (%)		Interleukin-6 (ng/mL)		Interleukin-8 (ng/mL)	
		Before	After	Before	After	Before	After
Observation group	40	82.34 \pm 6.86	94.02 \pm 2.47	3.35 \pm 0.34	1.89 \pm 0.31	6.02 \pm 1.15	2.27 \pm 0.84
Control group	40	82.41 \pm 6.71	85.64 \pm 2.54	3.41 \pm 0.28	2.57 \pm 0.34	6.08 \pm 1.11	3.45 \pm 0.34
<i>t</i>	-	0.739	9.584	1.126	10.851	0.183	10.352
<i>P</i>	-	0.464	0.001	0.264	0.001	0.854	0.001

Table 3. Pulmonary function indices before and after treatment in both groups (mean \pm SD)

Group	<i>n</i>	FVC (L)		FEV1 (L)		FVC/FEV1 (%)	
		Before	After	Before	After	Before	After
Observation group	40	1.47 \pm 0.38	2.56 \pm 0.43	0.95 \pm 0.21	1.69 \pm 0.24	51.43 \pm 3.47	62.24 \pm 3.48
Control group	40	1.49 \pm 0.35	1.86 \pm 0.45	0.94 \pm 0.18	1.21 \pm 0.23	51.39 \pm 3.52	53.26 \pm 2.65
<i>t</i>	-	0.318	8.957	0.412	8.124	0.328	9.524
<i>P</i>	-	0.778	0.003	0.821	0.011	0.739	0.001

4. Discussion

In general, the physiological characteristics of elderly individuals, coupled with reduced immunity and impaired defense mechanisms, increase the risk of developing COPD and predispose these patients to pulmonary infections. In severe cases, the condition may progress to pulmonary heart disease and eventually cause respiratory failure, posing significant risks to the patients' lives [6,7]. Standard treatment for this condition typically includes oxygen therapy, bronchodilators, and anti-infection measures to alleviate symptoms. However, the efficacy of such treatments is often suboptimal. Studies have reported that symptomatic treatment in elderly patients with COPD and pulmonary infection achieves an effectiveness rate of approximately 70%, which is attributed to the reduced immunity of elderly patients that delays recovery [8]. Additionally, prolonged use of antibiotics may impair infection resistance, increase bacterial resistance, and complicate treatment.

Pulmonary rehabilitation has been shown to improve lung function in such patients. However, certain studies suggest that conventional rehabilitation methods may fall short of achieving optimal outcomes, limiting their effectiveness in improving lung function [9]. Respiratory rehabilitation training has been reported to enhance tidal volume, slow expiratory rates, stabilize airway pressure, and improve exercise tolerance in patients [10]. Nonetheless, the accumulation of sputum can exacerbate disease control challenges, emphasizing the importance of effective drainage to alleviate infection symptoms.

The application of ambroxol hydrochloride stimulates the bronchial mucous glands, increasing neutral mucopolysaccharide secretion, reducing

acidic mucopolysaccharide levels, and enhancing metabolic activity. These effects facilitate respiratory mucus clearance. Research indicates that ambroxol hydrochloride has a relatively long half-life of approximately seven hours, is primarily metabolized by the liver, and avoids significant drug accumulation, reducing the risk of adverse effects [11].

The findings of this study revealed that clinical symptoms resolved more quickly in the observation group. This outcome may be attributed to the combined use of ambroxol hydrochloride and pulmonary rehabilitation training. While ambroxol hydrochloride effectively alleviates lung infection to some extent, its standalone therapeutic effect is limited. When complemented by pulmonary rehabilitation, incorporating respiratory and physical training ensures correct breathing techniques, enhances respiratory tidal volume, facilitates sputum clearance, and expedites symptom resolution.

This study also demonstrated higher oxygen saturation levels and lower inflammatory factor levels in the observation group after treatment. The increased oxygen saturation may result from the stimulation of alveolar function by ambroxol hydrochloride, which enhances the production of active substances, prevents alveolar atrophy, reduces alveolar collapse, improves lung compliance, and alleviates airway hyperresponsiveness and inflammation. Concurrently, pulmonary rehabilitation training improves immune function through respiratory and limb exercises, enhances muscle oxygen-carrying capacity, and further reduces inflammatory factor levels [12,13].

Moreover, significant improvements in lung function were observed in the observation group. This

result can likely be attributed to the integration of pulmonary rehabilitation training tailored to the patient's conditions. By addressing psychological needs, adjusting health education pathways, and increasing awareness of rehabilitation techniques and key measures, patients were guided to adopt correct breathing techniques, enhancing airway compliance, lung ventilation, and overall pulmonary function recovery^[14,15].

5. Conclusion

In conclusion, the treatment of elderly patients with COPD and pulmonary infection through a combination of ambroxol hydrochloride and pulmonary rehabilitation effectively improves pulmonary function, alleviates clinical symptoms, and reduces inflammatory responses.

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Disclosure statement

The author declares no conflict of interest.

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Assessment of Clinical Oncology Nurses' Recognition and Management of Cancer-Induced Fatigue in Patients: A Questionnaire-Based Study

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Abstract:

Objective: To investigate the status of clinical oncology nurses' identification and management of cancer-induced fatigue in cancer patients. *Methods:* A total of 231 clinical oncology nurses in a hospital were surveyed using a self-compiled questionnaire for the identification and management of cancer-related fatigue. The recognition, management, and influencing factors of cancer-related fatigue were analyzed using percentage calculations and single-factor and multi-factor analyses. *Results:* Clinical oncology nurses demonstrated poor recognition of cancer-induced fatigue. The identification accuracy, ranked from highest to lowest, was as follows: influence of cancer fatigue (98.27%), risk factors (97.84%), clinical manifestations (97.40%), characteristics (94.37%), incidence (89.18%), mitigation measures (61.90%), progression (54.11%), evaluation indexes (16.88%), and diagnostic criteria (8.23%). Management was similarly inadequate, with an average implementation rate of 68.01%, falling short of guideline recommendations. Age and years of experience were identified as influencing factors. *Conclusions:* The identification and management of cancer-related fatigue by clinical oncology nurses require improvement. Hospital administrators should actively respond to guideline recommendations by enhancing the construction of cancer fatigue management systems and emphasizing theoretical and practical education on cancer fatigue for nurses. These measures would facilitate improved patient care and quality of life.

Keywords:

Tumor
Nurse
Cancer-related fatigue; Management
Symptom management

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1. Introduction

According to the latest global cancer burden data from 2020, China recorded 4.57 million new cancer cases and 3 million cancer-related deaths, ranking first worldwide and accounting for 23.7% and 30.0% of global cases and deaths, respectively ^[1]. Cancer-related fatigue, which is associated with both the disease and its treatment, is a distressing and persistent subjective sensation of physical and psychological exhaustion. It has been recognized as the sixth vital sign in cancer care ^[2].

In patients newly diagnosed with cancer, the incidence of fatigue symptoms is approximately 40%. Among those undergoing active treatments such as radiotherapy, chemotherapy, and biological therapy, this proportion rises to 62%–85%. Furthermore, even during long-term follow-up, approximately 30% of cancer patients continue to experience moderate to severe fatigue ^[3,4]. Fatigue is therefore a common and significant symptom in cancer patients and, compared to other symptoms such as pain, nausea, and vomiting, it causes greater disruption to daily life ^[5].

With the advent of the “human-centered” nursing philosophy and the evolution of the “bio-psycho-social” medical model, cancer care now focuses not only on extending life expectancy but also on improving the quality of life. Clinical oncology nurses, who maintain close contact with patients, play a crucial role in recognizing fatigue states during daily care and implementing timely and effective management strategies. This approach is essential for enhancing the patient’s quality of life.

This study investigates the current state of symptom recognition and management of cancer-related fatigue by oncology nurses, aiming to provide a robust foundation for subsequent clinical and management practices.

2. Materials and methods

2.1. Research object

Convenient sampling was employed to select nurses directly involved in the care of cancer patients at our hospital from October to November 2023 as the study population. Inclusion criteria included nurses with more than six months of experience in cancer nursing who were familiar with cancer-related work. Exclusion

criteria included nurses absent during the survey period due to illness, maternity leave, or personal leave.

2.2. Survey methods

2.2.1. Survey tools

The questionnaire was compiled by three oncology nursing specialists and two experienced clinical care management experts, referencing the Guidelines for Clinical Care of Adult Cancer-Related Fatigue ^[6] and related literature ^[7,8]. The questionnaire consisted of three sections:

(1) General information questionnaire: This section collected data on gender, age, highest educational qualification, department, title, and years of professional experience.

(2) Cancer-related fatigue identification questionnaire: This section focused on topics such as the occurrence of cancer-related fatigue, clinical manifestations, risk factors, characteristics, duration, and impact. It contained 10 items, with responses recorded as “yes” or “no.” Correct answers were awarded 1 point, while incorrect answers were scored 0. Four items (questions 4, 5, 7, and 8) were reverse-scored. The total possible score was 10 points, with higher scores reflecting better recognition of cancer-related fatigue by nurses. The Cronbach’s alpha coefficient for this questionnaire was 0.855, indicating high reliability. Recognition accuracy for cancer-related fatigue was calculated as follows:

Cancer – related fatigue recognition accuracy

$$= \left(\frac{\text{Number of correct answers}}{\text{Total number of questions}} \right) \times 100\%$$

(3) Cancer-related fatigue management questionnaire: This section included three dimensions—symptom screening (4 items), symptom assessment (7 items), and symptom management (10 items)—for a total of 21 items. Responses were recorded as “yes” or “no,” with positive answers scored as 1 point and negative answers as 0 points. The total possible score was 21, with higher scores indicating better management of cancer-related fatigue. The Cronbach’s alpha coefficient for this questionnaire was 0.867, demonstrating high reliability.

The implementation rate of cancer-related fatigue management was calculated as follows:

Cancer – related fatigue management

implementation rate =

$$\left(\frac{\text{Number of yesresponses}}{\text{Total number of questions}} \right) \times 100\%$$

2.2.2. Data collection methods

Data were collected using the “Questionnaire Star” electronic platform. Tumor nursing managers in the hospital distributed the QR code for the electronic questionnaire to all unit nurses, inviting them to complete the survey. The questionnaire was completed anonymously, with assurances of privacy protection and informed consent obtained from participants. If the completeness of the questionnaire responses reached only 20% of the total questions and did not provide sufficient data to support analysis, those responses were excluded during data analysis.

2.3. Statistical methods

The collected data were analyzed using SPSS 21.0 statistical software. General data were expressed as frequency and percentage, while measurement data were represented by mean and standard deviation. Univariate analysis was conducted using independent sample t-tests or ANOVA, and multivariate analysis was performed through regression analysis. A *P*-value of < 0.05 was considered statistically significant.

3. Results

3.1. General information

A total of 238 nurses participated in the survey. Based on the exclusion criteria, 231 questionnaires were deemed valid. The majority of respondents were female (97.40%), aged 26–35 years (63.64%), and

held undergraduate degrees (93.94%). Slightly more participants were surgical nurses (58.01%) than internal medicine nurses (41.99%). Most nurses (53.68%) had been in practice for more than five years, and a similar proportion held the title of nurse (53.68%).

3.2. Status quo of identification and management of cancer-related fatigue

The clinical oncology nurses exhibited varying levels of recognition of cancer-related fatigue, with an average score of 8.28 ± 1.41 . Recognition accuracy ranged as follows, from highest to lowest: impact of cancer-related fatigue (98.27%), risk factors (97.84%), clinical manifestations (97.40%), characteristics (94.37%), incidence (89.18%), mitigation measures (61.90%), progression (54.11%), evaluation indicators (16.88%), and diagnostic criteria (8.23%) (**Table 1**).

The management of cancer-related fatigue was not optimal, with an average score of 14.73 ± 6.17 and an implementation rate of 68.01%. Implementation rates for each dimension were as follows: symptom screening (60.93%), symptom assessment (67.41%), symptom management (individual) (88.87%), and symptom management (department) (54.81%). Detailed implementation rates for each item are presented in **Table 2**.

3.3. Factors affecting the identification and management of cancer-related fatigue

3.3.1. Single-factor analysis

Univariate analysis identified four variables significantly associated with cancer-related fatigue recognition ($P < 0.05$) and five variables significantly associated with management ($P < 0.05$). Results are summarized in **Table 3**.

3.3.2. Multi-factor analysis

Multiple regression analysis was conducted, with cancer-related fatigue recognition and management as dependent variables and significant general data variables as independent variables. **Table 4** outlines variable assignments and **Table 5** presents the results.

Table 1. Recognition of cancer-related fatigue among clinical oncology nurses ($n = 231$)

Item		Response [n (%)]	Recognition accuracy rank
1. Fatigue is a common symptom of cancer and cancer treatment.	Yes	206 (89.18)	5
	No	25 (10.82)	
2. Fatigue symptoms include lack of energy, weakness, laziness, poor concentration, and memory loss.	Yes	225 (97.40)	3
	No	6 (2.60)	
3. Causes include direct effects of cancer, treatments, comorbidities, and psychosocial factors.	Yes	226 (97.84)	2
	No	5 (2.16)	
4. Diagnostic criteria include fatigue lasting over one week.	Yes	212 (91.77)	10
	No	19 (8.23)	
5. Fatigue, being multifactorial, cannot be measured.	Yes	192 (83.12)	9
	No	39 (16.88)	
6. Cancer-related fatigue is faster, more severe, and less predictable than general fatigue.	Yes	218 (94.37)	4
	No	13 (5.63)	
7. Cancer-related fatigue can be alleviated with regular rest.	Yes	88 (38.10)	7
	No	143 (61.90)	
8. Cancer-related fatigue resolves after treatment completion.	Yes	106 (45.89)	8
	No	125 (54.11)	
9. Fatigue trajectories align with disease or treatment progression.	Yes	213 (92.21)	6
	No	18 (7.79)	
10. Fatigue affects physical, mental, psychological, and emotional aspects.	Yes	227 (98.27)	1
	No	4 (1.73)	

Table 2. Management of cancer-related fatigue by clinical oncology nurses ($n = 231$)

Item	Symptom management implementation rate [n (%)]
Symptom screening	Initial visit
	During treatment
	Follow-up period
	When clinically necessary
	Patient self-assessment
Symptom assessment	Medical team evaluation
	History evaluation
	Evaluation frequency
	Choice of tools
	Assessment of relevant factors
Symptom management (individual)	Assessment of treatable factors
	Daily attention to patient fatigue
	Communicate about fatigue
	Health guidance for patients/families
	Provision of nursing interventions
Symptom management (department)	Timely communication with doctors
	Management by guidelines
	Evaluation norms and processes
	Clinical management pathway
	Structured intervention
	Education and training on fatigue

Table 3. Single-factor analysis of cancer-related fatigue recognition and management

	Item	Number of people [<i>n</i> (%)]	Symptom recognition	Symptom management
Gender	Male	6 (2.60)	7.50 ± 1.87	14.69±6.27
	Female	225 (97.40)	8.30 ± 1.39	16.33±7.42
	Test value		1.043	0.631
	<i>P</i>		0.344	0.528
Age (years)	≤ 25	22 (9.52)	8.86 ± 1.04	17.41 ± 4.73
	26–30	75 (32.47)	8.36 ± 1.26	16.11 ± 6.09
	31–35	72 (31.17)	8.35 ± 1.46	14.22 ± 6.46
	36–40	40 (17.32)	8.18 ± 1.11	13.55 ± 6.22
	≥ 40	22 (9.52)	7.41 ± 2.09	11.18 ± 6.00
	Test value		3.331	4.358
	<i>P</i>		0.011	0.002
Highest educational degree	Junior college	13 (6.06)	8.62 ± 1.39	14.57 ± 6.32
	Bachelor's degree or above	218 (93.94)	8.76 ± 1.41	18.23 ± 3.88
	Test value		0.523	3.620
	<i>P</i>		0.594	0.028
Department	Internal medicine	97 (41.99)	8.42 ± 1.29	15.05 ± 6.00
	Surgery	134 (58.01)	8.18 ± 1.49	14.50 ± 6.50
	Test value		1.328	0.657
	<i>P</i>		0.015	0.021
Position title	Nurse	50 (21.65)	7.33 ± 1.51	14.36 ± 5.63
	Nurse practitioner	124 (53.68)	8.88 ± 0.99	16.49 ± 7.23
	Supervisor nurse	57 (24.67)	8.28 ± 1.41	15.38 ± 5.25
	Test value		2.088	2.312
	<i>P</i>		0.026	0.021
Working years	≤ 1 year	52 (22.51)	8.33 ± 1.13	16.27±5.21
	1–3 years	26 (11.26)	8.42 ± 1.27	16.31 ± 5.54
	3–5 years	29 (12.55)	7.97 ± 1.27	15.97 ± 5.61
	≥ 5 years	124 (53.68)	8.31 ± 1.41	13.47 ± 6.77
	Test value		0.601	3.753
	<i>P</i>		0.025	0.012

Table 4. Assignment of argument variables

Independent variable	Assignment mode
Age (years)	≤ 25 = 1; 26–30 = 2; 31–35 = 3; 36–40 = 4; ≥ 40 = 5
Highest educational degree	College = 1; Bachelor degree or above = 2
Department	Internal medicine = 1; Surgery = 2
Position title	Nurse = 1; Nurse practitioner = 2; Supervisor nurse = 3
Working years	≤ 1 year = 1; 1–3 years = 2; 3–5 years = 3; ≥ 5 years = 4

Table 5. Multi-factor analysis of the status quo of recognition and management of cancer-related fatigue

Variable	Partial regression coefficient	Standard error	Normalized regression coefficient	<i>t</i>	<i>P</i>
Recognition of cancer-related fatigue					
Constant term	9.008	0.249	-	6.108	0.000
Age	3.145	0.203	0.082	0.257	0.002
Working years	2.584	1.133	0.135	1.534	0.023
Management of cancer-related fatigue					
Constant term	20.612	1.315	-	15.676	0.000
Age	3.543	0.366	0.230	1.298	0.000
Working years	2.244	0.327	0.146	0.734	0.026

4. Discussion

4.1. Clinical cancer nurses' recognition and management of cancer-related fatigue

Clinical oncology nurses demonstrate a strong understanding of the influence, risk factors, clinical manifestations, characteristics, and incidence of cancer-related fatigue. This level of understanding may be attributed to their frequent and prolonged contact with patients, leading to a deeper awareness of patients' physical and emotional conditions. However, their ability to identify mitigation measures, progression status, evaluation tools, and diagnostic criteria—elements requiring more specialized knowledge—remains inadequate. This gap may stem from the reliance on clinical practice guidelines for cancer-related fatigue that are predominantly derived from international studies^[2], while evidence-based guidelines tailored to China are still limited. As a result, the application of such guidelines in frontline clinical practice has not yet achieved widespread adoption.

In the absence of standardized nursing protocols, clinical oncology nurses often rely on their personal care experiences or general knowledge to alleviate patients' distress. Consequently, symptoms of cancer-related fatigue may not be effectively addressed, posing a potential risk to patients' comfort and safety. Previous studies have primarily focused on nurses managing specific disease types or those with specialized training, such as in gynecological oncology, which limits direct comparisons with this study^[9,10]. Nonetheless, the

findings indicate that clinical oncology nurses require further training to enhance their recognition of cancer-related fatigue, thereby improving patients' quality of life and ensuring safer nursing practices.

The management of cancer-related fatigue among clinical oncology nurses is similarly suboptimal. Screening and assessment of fatigue symptoms are not comprehensively implemented according to recommended guidelines^[2]. While individual nurses exhibit a more proactive approach to addressing fatigue symptoms, departmental management efforts remain inadequate. The absence of institutionalized processes and quality control measures limits the ability to meet patient needs effectively. These findings suggest that clinical managers should prioritize the standardization of fatigue management practices by developing training programs and supporting the implementation of evidence-based diagnosis and treatment protocols to deliver higher-quality patient care.

4.2. Analysis of factors influencing the identification and management of cancer-related fatigue

Cancer-related fatigue is a prevalent condition among cancer patients, manifesting as disruptions in physiological functions, diminished social behaviors, and intensified role conflicts, all of which severely affect patients' physical and psychological well-being. Patients experiencing these symptoms also demonstrate significant informational and emotional needs^[12]. This

study identified a low recognition rate of cancer-related fatigue among clinical oncology nurses and analyzed contributing factors.

The findings suggest that nurses' recognition of fatigue symptoms improves with age, years of work experience, professional competence, and clinical teaching involvement. These factors equip nurses with the knowledge and skills required to identify and manage fatigue symptoms effectively ^[11]. Similarly, the management of cancer-related fatigue is influenced by age and work experience. Nurses with more extensive experience are better positioned to provide timely and effective care, supported by advanced technical expertise and emotional maturity.

5. Conclusion

In conclusion, the study underscores the need to prioritize

cancer-related fatigue management by establishing comprehensive fatigue management mechanisms and improving nurses' recognition rates. A combination of institutional framework development and targeted nurse training can facilitate systematic and practical learning on cancer-related fatigue. Such initiatives are expected to enhance symptom recognition and reduce pathological fatigue in patients, ultimately promoting their comfort.

This study employed convenience sampling and relied on subjective questionnaire responses, which may limit the representation of cancer-related fatigue management practices in the region. The findings' comprehensiveness and objectivity require further validation. Future research should explore specific aspects of cancer-related fatigue management, such as nutritional and sleep interventions, in accordance with clinical guidelines. Such research can contribute to the refinement of clinical procedures, ensuring improved patient safety and care quality.

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Executive Function and Brain Region Development in ADHD: Mechanisms and Interventions in the Prefrontal Cortex and Related Circuits

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Abstract:

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in children and adolescents, significantly impacting academic performance, emotional regulation, and social adaptation. Executive function, a higher-order cognitive ability that governs cognition, emotion, and behavior, is a core symptom of ADHD. This article examines executive function deficits in ADHD, focusing on the roles of brain regions such as the prefrontal cortex, parietal lobe, and basal ganglia, and how developmental abnormalities in these areas contribute to the disorder. Research shows that deficits in attention control, impulse inhibition, and working memory are linked to structural and functional abnormalities in these brain regions. By integrating neuroimaging and biological research, this article explores how delays or dysregulations in brain development led to executive function impairments, shedding light on the neurobiological mechanisms involved. Furthermore, the paper evaluates the potential of cognitive training, pharmacological treatments, and behavioral therapies in improving these deficits, particularly by enhancing the function of the prefrontal cortex and other key regions, thus boosting cognitive and behavioral outcomes for ADHD patients.

Keywords:

ADHD
Executive function
Prefrontal cortex and other related brain areas
Neuroplasticity
Intervention strategies

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1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder in children and adolescents, with a prevalence of 6.4% among school-age children in China ^[1]. Approximately 65%

of ADHD cases persist into adulthood ^[2], affecting learning, emotional regulation, and social adaptation. Executive function (EF), which includes working memory, inhibitory control, and attention regulation, is often impaired in ADHD patients, leading to significant

difficulties in attention control, impulse inhibition, and working memory ^[3]. These deficits severely impact daily life, including academic performance, work, and social interactions.

Recent studies have shown that executive function deficits in ADHD patients are closely linked to developmental abnormalities in multiple brain regions, particularly the prefrontal cortex, as well as the parietal lobe, basal ganglia, and thalamus ^[4,5]. These dysfunctions contribute to impairments in attention control, impulse inhibition, and working memory in ADHD patients ^[6]. In response, various intervention strategies, such as cognitive training, pharmacological treatments, and behavioral therapies, have been proposed to enhance the function of these brain regions and promote neuroplasticity, ultimately improving executive function in ADHD patients ^[7]. This paper further evaluates the effectiveness of these interventions in enhancing cognitive and behavioral performance.

2. Executive function

Executive function, which regulates behavior, emotions, and cognitive processes such as attention control, working memory, and emotional regulation, enables goal-setting, planning, problem-solving, and decision-making in complex situations ^[8,9]. Its development during childhood and adolescence is critical for academic success, social interactions, emotional regulation, and mental health ^[10]. As individuals transition into adulthood, executive function continues to impact daily life, career development, and mental well-being, making it central to cognitive, behavioral, and emotional growth.

2.1. Executive function deficits in individuals with ADHD

Individuals with ADHD often exhibit varying degrees of deficits in executive functions, with the most prominent symptoms being attention control deficits, poor impulse control, and insufficient working memory.

- (1) **Attention control deficits:** Attention control deficits: ADHD patients struggle with sustained attention and are prone to distractions ^[11]. Studies show lower performance on tasks requiring attention, with frequent distractions ^[12]. These

deficits affect academic performance, decision-making, and adaptation in daily life ^[13], impairing learning and problem-solving.

- (2) **Impulse control deficits:** Impulse control deficits: ADHD patients often struggle with inhibiting impulsive behaviors, such as making quick decisions or reacting emotionally ^[11]. This deficit hampers emotional regulation and causes interpersonal conflicts. Research shows that ADHD children exhibit stronger impulsive behaviors, leading to unstable social interactions ^[14].
- (3) **Working memory deficits:** Working memory deficits: ADHD patients struggle with holding and manipulating information over short periods, impairing their ability to multitask and complete long-term tasks ^[15]. Children with ADHD often fail to integrate information for multi-step instructions, affecting both academic performance and daily planning. These deficits are linked to academic failure, emotional distress, and behavioral issues ^[16].

3. Impact of executive function deficits on daily life

Executive function deficits in ADHD patients significantly impact their academic, social, and emotional functioning, leading to a range of negative outcomes. Due to attention and impulse control issues, they often struggle with poor academic performance, especially in tasks requiring sustained focus, such as mathematics and language arts ^[13]. Additionally, deficiencies in working memory hinder their ability to organize information effectively, reducing task efficiency and quality. In social and emotional domains, ADHD patients frequently experience conflicts with others due to impaired impulse control and emotional regulation, which can strain interpersonal relationships. Research shows that children and adolescents with ADHD are more prone to aggressive behaviors, emotional instability, and antisocial conduct, further complicating their social adaptation ^[14]. The cumulative effects of these deficits not only create academic and social challenges but also carry long-term risks for career success and mental health in adulthood.

4. Neurobiological mechanisms of executive function deficits in ADHD: Functional and developmental abnormalities in brain regions

Recent studies have found that executive function deficits in ADHD patients are closely related to structural and functional abnormalities in specific brain regions, especially the prefrontal cortex (PFC) and its associated neural circuits. Neuroimaging analysis of the brains of ADHD patients has revealed that during tasks requiring executive functions, the relevant brain regions typically exhibit inefficient activity patterns, providing important clues for uncovering the neurobiological mechanisms of ADHD.

4.1. Structural abnormalities

Neuroimaging studies show that ADHD patients often have structural abnormalities in the prefrontal cortex (PFC), including volume reduction and developmental delays^[17]. These patients also exhibit lower gray matter density in the PFC, which is linked to their executive function deficits. Inefficient activation of the PFC during tasks requiring impulse inhibition and sustained attention suggests limited regulatory function. These abnormalities impair the PFC's role in attention control, impulse regulation, working memory, and emotional regulation, leading to difficulties in social interactions and daily behavior^[18]. Additionally, other brain regions, such as the parietal lobe, basal ganglia, cerebellum, and thalamus, also show structural changes that contribute to ADHD symptoms.

4.2. Functional abnormalities

In addition to structural abnormalities, ADHD patients also show significant functional dysfunctions during executive function tasks. Research indicates inefficient brain activity patterns that are closely linked to ADHD's core symptoms. For example, the functional connectivity between the PFC and basal ganglia often exhibits abnormal low- or high-frequency activity, disrupting their coordinated function^[19]. Furthermore, ADHD patients' brain network activity lacks flexibility, leading to ineffective regulation across various tasks. Studies have found inefficient activation in the dorsolateral prefrontal cortex-dorsal striatum-thalamus pathway during "cold"

executive tasks, while "hot" executive tasks may involve abnormalities in the orbitofrontal cortex-limbic system circuit^[20]. These functional impairments suggest that ADHD is not just due to structural damage in specific regions but also to dysregulation in complex brain networks.

4.3. Relationship between developmental abnormalities and executive function deficits in ADHD

Neuroanatomical studies suggest that delays in prefrontal cortex (PFC) development are key to executive function deficits in ADHD. The PFC, which matures later in life, undergoes rapid changes during childhood and adolescence. In ADHD, these developmental delays hinder both structural and functional maturation, leading to ongoing difficulties in cognitive control and emotional regulation^[17]. Limited neuroplasticity in the PFC, influenced by genetic, environmental, and early developmental factors, prevents full maturation of neural circuits, impairing attention control, impulse inhibition, and working memory^[21]. This contributes to the persistence of ADHD symptoms into adulthood.

5. Brain networks and ADHD executive function deficits

ADHD involves abnormalities not only in the prefrontal cortex (PFC) but also in multiple brain regions, including the dorsal prefrontal cortex, orbitofrontal cortex, basal ganglia, thalamus, and parietal cortex^[22]. The executive function relies on a network of interconnected regions, including the cortical-striatal-thalamic-cortical loop for cold executive function and the orbitofrontal cortex-limbic system loop for hot executive function. These networks support functions such as decision-making, working memory, emotional regulation, and impulse control, essential for maintaining executive function integrity^[23].

In addition to the PFC, ADHD involves abnormalities in multiple brain regions, particularly the dorsal prefrontal cortex, orbitofrontal cortex, basal ganglia, thalamus, and parietal cortex. Extensive research indicates that the brain networks supporting executive functions are not limited to the prefrontal cortex; in

fact, they involve multiple brain regions with complex interconnections between them ^[22]. The executive function relies not only on the prefrontal cortex but also on the cortical-striatal-thalamic-cortical loop, which together forms the neural network for executive function. For example, the neural pathways for cold executive function mainly involve the dorsal prefrontal cortex-dorsal striatum-thalamus, while the pathways for hot executive function are formed by the orbitofrontal cortex-limbic system loop. The interaction of these brain networks determines the integrity of an individual's executive function. The dorsal prefrontal cortex-dorsal striatum-thalamus loop primarily supports rational decision-making, working memory, and task planning, which are associated with cold executive function, while the orbitofrontal cortex-limbic system loop is more closely related to emotional regulation, impulse control, and social behavior regulation, which are key aspects of hot executive function ^[24].

ADHD patients exhibit significant abnormalities in the functional connectivity of brain networks during executive function tasks. Specifically, during cognitive tasks, the coordination between the Default Mode Network (DMN) and Task Positive Network (TPN) is impaired. The DMN, involved in decision-making, working memory, and social cognition, fails to be suppressed during task execution in ADHD patients, leading to its persistent activity, which disrupts TPN function. This inability to downregulate the DMN may contribute to attention deficits and executive dysfunction in ADHD ^[21].

The abnormal functioning of brain networks in ADHD involves not only the PFC but also altered connectivity between regions like the basal ganglia and thalamus, which are crucial for motor and cognitive regulation. These dysfunctions disrupt executive function, impairing attention, impulse control, and working memory, and affecting daily life and social adaptation.

6. Intervention strategies for ADHD

An increasing number of studies show that intervention strategies targeting executive function deficits in ADHD patients are becoming more diversified and show great

potential. Research indicates that through a combination of cognitive training, pharmacological treatment, and behavioral therapy, the executive function of ADHD patients can be effectively improved. These interventions focus not only on enhancing the function of the prefrontal cortex (PFC) but also on optimizing the development and function of other relevant brain areas, aiming to promote the overall cognitive ability of the brain ^[22,24]. As the understanding of the neurobiological mechanisms of ADHD deepens, more interventions based on the principles of neuroplasticity are continuously emerging, with the expectation of providing more personalized and precise treatment for individual cognitive deficits.

6.1. Cognitive training and the improvement of executive function

Cognitive training, a non-pharmacological treatment, aims to enhance ADHD patients' core executive functions, such as working memory, attention control, and cognitive flexibility. ADHD patients often struggle with working memory, exhibiting limited capacity and slower processing speeds, which impair task execution and decision-making. Cognitive training, particularly focusing on working memory, helps improve the ability to retain and process information ^[25]. Attention control, another key deficit in ADHD, can also be enhanced through training, improving the ability to sustain focus and resist distractions, thus boosting performance in complex environments ^[26]. Additionally, cognitive flexibility training helps ADHD patients switch between tasks and adapt to unexpected situations, enhancing problem-solving abilities ^[27]. Long-term, diverse cognitive training promotes overall executive function improvements by enhancing brain plasticity and the coordination and efficiency of information processing.

7. Pharmacological treatment and regulation of neurotransmitter systems

Medication remains one of the main treatment approaches for ADHD, particularly stimulant medications.

Stimulant medications improve cognitive performance in ADHD patients by regulating neurotransmitter systems in the brain that are related to executive functions. The

most used medications are methylphenidate (Ritalin) and amphetamines (Adderall), which enhance the activity of norepinephrine and dopamine to improve executive functions such as attention control, impulse inhibition, and working memory^[28].

Research shows that the mechanisms of these medications are not limited to the PFC but also regulate multiple neural circuits in the brain, particularly the cortical-striatal-thalamic pathway^[29]. These pathways typically exhibit inefficient neural activity in ADHD patients, and medication treatment improves the functional connectivity of these brain regions by enhancing neurotransmitter activity, thereby restoring executive functions. Medication treatment can significantly improve task performance in ADHD patients in the short term, but long-term effects and dependence remain important issues in both research and clinical practice.

8. Future research directions and personalized interventions

As our understanding of ADHD's neurobiological mechanisms advances, personalized intervention strategies are becoming increasingly promising. Future treatments will be tailored to each patient's unique neurobiological characteristics, such as the PFC's

developmental status, brain region connectivity patterns, genetic factors, and cognitive-behavioral performance^[17]. Advances in big data, genomics, and neuroimaging will allow for more precise treatment matching. For instance, genomic data can identify genetic markers associated with ADHD symptoms, guiding personalized treatments^[28]. Brain imaging can reveal structural or functional changes in areas like the PFC or basal ganglia, linking these alterations to symptom expression^[22]. This individualized approach aims to maximize treatment effectiveness while minimizing side effects.

With the continuous advancement of neuroscience and intervention methods, the treatment outlook for ADHD is promising. From the perspective of neuroplasticity, cognitive training, medication, and behavioral therapies can all improve the execution functions and neural circuitry connectivity of patients to varying extents. In the future, with the progress of neuroimaging technology, genomics, and interdisciplinary research, personalized interventions will become possible, offering more precise and effective treatment options for ADHD patients. More importantly, future research will not only focus on the prefrontal cortex (PFC) but also consider the functional changes in other relevant brain areas, aiming to provide comprehensive scientific evidence and clinical support for ADHD treatment.

Disclosure statement

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The Effect of Exercise-Psychology-Sleep Intervention on the Psychological State and Sleep Quality in Breast Cancer Patients

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Abstract:

Objective: To explore the specific situation of different intervention programs in patients with breast cancer. **Methods:** 60 cases of breast cancer patients admitted to the hospital from January 2024 to September 2024 were divided into control groups and observation groups by random number table method, with 30 cases in each group. The control group received routine intervention, and the observation group received exercise-psychology-sleep intervention. The psychological state, sleep quality and quality of life of the two groups were compared. **Results:** After intervention, the scores of depression, anxiety, extroversion irritability and introversion irritability were significantly reduced in 2 groups, and the improvement was more prominent in the observation group. In PSQI scores, sleep quality, sleep time, sleep efficiency, hypnotic drugs, daytime dysfunction and sleep disorder scores in the observation group were significantly lower than those in the control group. The scores of social function, emotional function, cognitive function, role function, and physical function of the two groups were significantly improved, and the improvement of the observation group was more prominent. Compared with the above different indexes, the observation group was better than the control group, and the difference was statistically significant ($P < 0.05$). **Conclusion:** The application of exercise-psychology-sleep intervention in breast cancer patients is effective and valuable.

Keywords:

Exercise-psychology-sleep intervention
Breast cancer
Mental state
Sleep quality
Quality of life

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1. Introduction

Breast cancer is a clinical multiple malignant tumor, the lesion location is usually breast epithelium or duct epithelium. Clinical data show that the incidence of breast cancer accounts for 11.9% of the global cancer incidence and the case fatality rate is 6.4%^[1]. The cause of the disease is not clear, and may be directly related to breast cancer genes, sex hormones and other factors, especially for women with a family history of breast cancer, the probability of disease is significantly higher. At the same time, adverse lifestyle and environmental factors may also have a certain impact on the incidence of breast cancer. The progression of breast cancer is mainly divided into four stages: early stage (stage I), middle stage (stage II), locally advanced stage (stage III), and advanced stage (stage IV)^[2]. Among them, early breast cancer patients usually have a high cure rate, but as the disease progresses to the middle and late stages, the difficulty of treatment increases significantly, which causes the psychological state and sleep quality of patients to be generally poor, and thus poses a serious threat to the physical and mental health of patients. At present, the treatment of breast cancer focuses on surgery, chemotherapy, radiotherapy and other means, but due to the long treatment time, high cost, many side effects and other factors, aggravate the patients' anxiety, fear and other negative emotions, resulting in a greatly reduced prognosis of patients. Therefore, it is important to integrate scientifically feasible nursing interventions into the treatment of breast cancer patients. Routine nursing is a single intervention mode, it is difficult to take comprehensive and effective physical and mental care of patients, and may cause poor nursing effect and low patient satisfaction. As for the exercise-psychology-sleep intervention, it is a comprehensive nursing mode,

which has played multiple positive roles by integrating it into modern clinical practice, truly realizing the simultaneous treatment of body and mind, and promoting the comprehensive recovery of patients. Based on this, in order to explore the clinical effects of different intervention schemes for breast cancer patients, a total of 60 patients eligible for the study were included for corresponding analysis, as detailed below.

2. Data and methods

2.1. General information

Sixty patients with breast cancer admitted to our hospital were retrospectively analyzed and divided into 2 groups by random number table method, namely the control group (routine intervention) and observation group (exercise-psychological-sleep intervention). The baseline data corresponding to age, disease course and body mass index of the two groups are shown in **Table 1** below.

Inclusion criteria: (1) Meet the diagnostic criteria of breast cancer in the Guidelines and Norms for Diagnosis and Treatment of Breast Cancer of the Chinese Anti-Cancer Association (2021 edition)^[3]; (2) Willing to accept the intervention plan, sign the informed consent; (3) No other serious organic diseases, such as cardiovascular disease, diabetes, etc.; (4) No history of mental illness or serious mental disorder; (5) No obvious contraindications to exercise.

Exclusion conditions: (1) Advanced breast cancer with short expected survival; (2) Have received other psychological or exercise interventions for breast cancer; (3) Poor compliance, there are language communication barriers; (4) Have other malignant tumors or are receiving other anti-tumor therapy; (5) Be blind in both eyes or deaf in both ears.

Table 1. Comparison of baseline data between the two groups ($n = 30$), (mean \pm standard deviation)

Group	Age (year)	Course of disease (year)	Body mass index (kg/m ²)	Tumor body diameter (cm)
Observation group	50.15 \pm 1.22	2.28 \pm 0.36	22.66 \pm 1.05	4.10 \pm 1.15
Control group	50.00 \pm 1.16	2.30 \pm 0.29	22.52 \pm 1.02	4.21 \pm 1.09
<i>t</i> value	0.488	0.237	0.524	0.380
<i>P</i> value	0.627	0.814	0.602	0.705

2.2. Methods

The control group was subjected to routine intervention, specifically as follows: Professionals explained the disease knowledge of breast cancer to patients, including the pathogenesis, treatment process, possible side effects and coping strategies, so as to strengthen patients' disease cognition. Guide patients to use the drug correctly, explain in detail the time, dosage and possible side effects of each drug, and mobilize patients' compliance with treatment. The importance of maintaining regular work and rest is emphasized, and patients are advised to follow scientific work and rest time to avoid overwork affecting the treatment effect. The observation group was given exercise-psychological-sleep intervention, specifically as follows.

2.2.1. Exercise nursing

(1) Hand training

On the premise of maintaining the stability of the shoulder joint, the patient first performs mindfulness meditation for 5 minutes, closes the eyes, takes a deep breath, focuses on the breath, feels the feeling of air entering and leaving the nasal cavity, and gradually relaxes the muscles of the whole body. Then, the affected hand was used to grip the colored clay ball, and the movements of clenching and releasing were performed successively. At the same time, the state of mindfulness was continued, focusing on the movements and feelings of the hand, such as the texture of the colored clay ball in the hand, the changes in the strength of the finger joints during flexion and extension, and the feeling of muscle stretching when the wrist was bent and extended. Each training consists of 20 clench-release cycles, as well as the same number of finger extension and wrist flexion exercises, 3 sets a day, each set of 1-minute interval rest. During the break, the patient again performed a short mindfulness meditation to refocus and prepare for the next round of training.

(2) Forearm training

The patient remained in a seated or semi-recumbent position and first performed mindful breathing exercises for 3 minutes, focusing on the rise and fall of the abdomen and feeling the physical relaxation brought about by each breath. Then, pass the colored clay ball alternately through the left and right hands, each passing

distance of 30 cm, to enhance the muscle strength of the forearm and hand-eye coordination. During the transmission process, the patient continues to be mindful, focusing on the movements and feelings of the arm, such as the power of the muscles, the movement of the joints, and the transmission sensation of the colored clay ball in the hand. Then, holding a color brush in hand, the forearm was extended on the drawing paper to draw and fill in the outline and color of the pattern, each training lasted 10 min, twice a day.

(3) Elbow training

Start with a 2-minute mindful body scan, starting with the head and gradually moving your attention downward to feel the tension and relaxation in various parts of the body, especially the feeling of the elbows and arms. Then, the affected hand holds the colored clay ball, and with the assistance of the healthy arm, the colored clay ball is slowly lifted to the opposite shoulder for 30 seconds to exercise the stability of the elbow joint. Continue to be mindful, focusing on the stability of your elbow and the sensation of power in your muscles. Next, gently touch the colored clay ball to the same side ear lobe, stretch the elbow muscles and ligaments, and feel the stretching sensation. Five times each time, two sets a day, with a 2-minute rest between each set.

(4) Shoulder training

Start with 4 min of mindful walking exercises, focusing on the lifting, moving and lowering of your feet, and feeling the balance of your body and the shift of your weight. Hold the pen in the affected hand to raise the shoulder joint, straighten and bend the arm to 90°. Continue to be mindful and focus on shoulder movements and feelings, such as the range of motion of the shoulder joint, the contraction and relaxation of the muscles, and the balance and coordination of the body. Each training consisted of 20 extension-flexion cycles, 3 sets per day, with each set spaced 1 minute apart. During the interval, patients perform short mindfulness standing exercises to feel their body's contact with the ground, adjust their breathing, relax and prepare for the next round of training.

2.2.2. Psychological nursing

(1) Emotional release

Emotional release activities were held once a week,

each time lasting 90 min. Through guided meditation, emotional diary sharing and other links, help patients to identify and express their inner fear, anxiety and other negative emotions. Subsequently, cognitive behavioral therapy is used to guide patients to re-evaluate and adjust their cognition of the disease, and establish a positive attitude towards the disease.

(2) Personalized psychological counseling services

The duration of each consultation is 50 minutes. For the questions or concerns of patients, the nursing staff will patiently answer them to relieve the bad emotions of patients. Share successful recovery cases, encourage patients to keep a recovery journal, and teach relaxation techniques such as deep breathing and progressive muscle relaxation to relieve tension and improve mental resilience.

(3) Family support and education

Organize a family support and education activity once a week, each activity lasts 2 hours. Psychological counselors, breast doctors and rehabilitation patients are invited to share the experience of psychological adjustment in the course of disease treatment and promote communication and understanding between patients and their families. Through group discussion, role play and other forms, enhance the sensitivity and support ability of family members to the psychological needs of patients. In the activity, a “voice exchange” link was set up, and each group of families had 15 minutes to play roles so that patients and family members could exchange roles, simulate each other’s daily experiences and feelings, and enhance mutual understanding and empathy.

2.2.3. Sleep care

The root causes of poor sleep quality of patients were analyzed, and targeted sleep intervention programs were formulated according to patients’ personal preferences.

(1) Music therapy

30 minutes before going to bed every night, play soothing music for 15 minutes, such as classical music or natural sounds (such as rain, and waves), and control the volume at about 40 decibels to reduce the difficulty of falling asleep.

(2) Acupressure therapy

At 1 hour before going to bed every night, guide patients to soak their feet, control the water temperature at 40–45 °C, and add an appropriate amount of mugwort or lavender essential oil (about 10 drops) to the water to promote blood circulation and relieve fatigue. After foot soaking, the patient was subjected to acupressure on the head, neck and feet, each massage lasting 15 minutes to improve sleep quality.

(3) Diet therapy

Explain to the patient the benefits of drinking hot milk before going to bed, and advise the patient to avoid eating too much greasy and spicy food at dinner.

(4) Drug therapy

For people with poor sleep quality, it is necessary to take an appropriate amount of sleeping drugs, such as zolpidem, esazolam, etc., but it should be used under the guidance of a doctor to avoid drug dependence. The intervention time of 2 groups was 1 month.

2.3. Observation indicators

- (1) Psychological state: The Irritability, Depression and Anxiety Scale (IDA) was used to evaluate the four dimensions, including depression, anxiety, extroversion irritability and introversion irritability. The total score was 15 points, 15 points, 12 points and 12 points, and the score was negatively correlated with the psychological state.
- (2) Sleep quality score: 7 dimensions of sleep quality, sleep time, sleep time, sleep efficiency, hypnotic drugs, daytime dysfunction and sleep disorders, assessed by the Pittsburgh Sleep Index Scale (PSQI), the total score of each dimension was 3 points, and the total score of sleep quality was 21 points, and the score was negatively correlated with the sleep quality of patients.
- (3) Quality of life: Social function, emotional function, cognitive function, role function, physical function 5 dimensions, the evaluation of the quality of life scale (EORTCQLQ-C30), the total score of each dimension is 100 points, the score is positively correlated with the quality of life of patients.

2.4. Statistical processing

SPSS 23.0 statistical software was used to analyze the study data. Measurement data conforming to normal distribution were expressed as (mean \pm standard deviation), and a comparison of differences between groups was conducted by *t*-test. The count data were expressed as frequency and percentage (%), and the difference between groups was compared by χ^2 test, and $P < 0.05$ was statistically significant.

3. Results

3.1. Compare the psychological state of the two groups before and after the intervention

After the intervention, the psychological status of the observation group was significantly lower than that of

the control group in all dimensions, and the comparison was statistically significant, as shown in **Table 2** below.

3.2. Compare PSQI scores of group 2 patients

After the intervention, the score of sleep quality in the observation group was significantly lower than that of the control group, and the comparative statistical significance was true, as shown in **Table 3** below.

3.3. Compare the quality of life score before and after the intervention

After the intervention, the score of QoL in the observation group was significantly higher than that of the control group, and the comparative statistical significance was true, as shown in **Table 4** below.

Table 2. Comparison of the psychological state of the two groups of patients before and after intervention ($n = 30$), (mean \pm standard deviation)

Project	Time	Observation group	Control group	<i>t</i> value	<i>P</i> value
Depressed	Before the intervention	8.20 \pm 0.22	8.18 \pm 0.17	0.394	0.695
	After the intervention	4.50 \pm 0.11	5.06 \pm 0.15	16.490	0.000
Anxious	Before the intervention	9.02 \pm 0.31	9.11 \pm 0.22	1.297	0.200
	After the intervention	4.50 \pm 0.21	5.26 \pm 0.18	15.050	0.000
Extravagance provoked	Before the intervention	6.70 \pm 0.32	6.68 \pm 0.29	0.254	0.801
	After the intervention	4.31 \pm 0.17	5.25 \pm 0.23	18.002	0.000
Introverted provoke	Before the intervention	6.88 \pm 0.36	6.97 \pm 0.29	1.066	0.291
	After the intervention	4.12 \pm 0.20	5.25 \pm 0.30	17.166	0.000

Table 3. Comparison of the PSQI scores ($n = 30$), (mean \pm standard deviation)

Project	Observation group	Control group	<i>t</i> value	<i>P</i> value
Sleep quality	1.22 \pm 0.21	2.05 \pm 0.52	8.106	0.000
Sleep time	0.98 \pm 0.15	1.57 \pm 0.26	10.766	0.000
hour of sleep	0.80 \pm 0.30	1.52 \pm 0.51	6.665	0.000
Sleep efficiency	0.92 \pm 0.26	1.85 \pm 0.37	11.264	0.000
Hypnotic drugs	0.82 \pm 0.32	1.88 \pm 0.40	11.334	0.000
Day dysfunction	0.85 \pm 0.21	1.69 \pm 0.30	12.564	0.000
Dyssomnia	1.05 \pm 0.50	1.90 \pm 0.39	7.342	0.000

Table 4. Comparison of the quality of life score ($n = 30$), (mean \pm standard deviation)

Project	Time	Observation group	Control group	<i>t</i> value	<i>P</i> value
Social function	Before the intervention	38.05 \pm 2.21	38.20 \pm 2.19	0.264	0.793
	After the intervention	55.60 \pm 2.80	45.72 \pm 2.51	14.391	0.000
Emotional function	Before the intervention	59.12 \pm 2.02	59.10 \pm 2.00	0.039	0.969
	After the intervention	75.77 \pm 2.52	65.76 \pm 2.26	16.197	0.000
Cognitive function	Before the intervention	60.70 \pm 1.85	60.75 \pm 1.82	0.106	0.916
	After the intervention	75.80 \pm 1.99	70.12 \pm 1.86	11.421	0.000
Role function	Before the intervention	46.60 \pm 1.80	46.55 \pm 1.82	0.107	0.915
	After the intervention	60.50 \pm 2.08	52.59 \pm 1.96	15.159	0.000
Somatic function	Before the intervention	55.02 \pm 2.09	55.10 \pm 2.05	0.150	0.882
	After the intervention	72.68 \pm 2.66	65.71 \pm 2.70	10.072	0.000

4. Discussion

In recent years, with the acceleration of the pace of life, more and more people suffering from breast cancer disease, coupled with staying up late, unbalanced diet and other factors, the incidence of the disease group is becoming younger and younger. Once sick, in addition to physical pain, such as breast pain, swelling, skin changes, etc., patients will also face multiple psychological troubles, such as fear, anxiety, depression and other emotional problems. In the long run, patients' sleep and quality of life will be deeply affected^[4]. Taking the decline in sleep quality as an example, the main manifestations are prolonged sleep time, easy to wake up at night, and reduced total sleep time, which virtually aggravates the clinical symptoms of patients, resulting in unsatisfactory treatment effects patients and a blocked rehabilitation process.

Previous studies have pointed out that the effect of simple routine nursing in the clinical treatment of breast cancer patients is not significant, and it is easy to ignore the individual needs and psychological state of patients, resulting in insufficient comprehensive and in-depth nursing, which only increases the helplessness of patients in the face of the disease^[5]. Exercise-psychology-sleep nursing has been a common intervention in clinical practice in recent years. It emphasizes individualized intervention for patients from three levels: movement, psychology and sleep. Taking sports nursing as an example, it emphasizes making exercise plans according

to patients' physical conditions, such as hand training, forearm training, etc., to enhance patients' physical fitness and alleviate the side effects of treatment. Taking psychological care as an example emphasizes listening to the psychological demands of patients, providing psychological counseling and support, and then helping patients to establish a positive attitude. Especially in the aspect of sleep care, the application of music, acupuncture, diet, and other therapies has improved the sleep quality of patients from many aspects. For example, by playing soft music to reduce anxiety. Through acupuncture, relieve patients' physical tension, promote blood circulation, etc., reflects the full respect for patients' individual differences, and undoubtedly provides strong support for patients' road to recovery.

With breast cancer patients as the main body, Wang *et al.* (2023)^[6] focused on the psychological state of patients before and after intervention and the results showed that: The observation group of exercise-psychology-sleep nursing had a more prominent improvement in mental state ($P < 0.05$). In this study, the mental state indicators of patients were also analyzed to verify the researcher's research results, indicating that the clinical application of exercise-psychology-sleep nursing in breast cancer patients is feasible. It has a great relationship with the more comprehensive intervention mode covered by exercise-psychology-sleep care, which meets the disease needs of patients, and promotes the improvement of patients' anxiety,

depression and other adverse emotions. Sleep quality is an important index to evaluate patients' sleep condition. Through the implementation of different intervention methods, the sleep conditions of patients in the observation group were improved more significantly ($P < 0.05$), which was consistent with the research of scholar He (2022) [7], highlighting the self-evident application value of exercise-psycho-sleep care. The reason for the analysis is that this intervention can directly affect patients' daily sleep conditions by improving their daily rest habits. Adjusting the mental state and increasing the appropriate amount of physical activity has directly improved the quality of sleep for patients. This study also found that by implementing different interventions, the quality of life score of the

observation group was significantly higher than that of the control group ($P < 0.05$), which had something in common with the research of Yang *et al.* (2020) [8]. It can be seen that in the nursing of breast cancer patients, the combined intervention mode not only optimized the psychological state and sleep quality but also significantly improved the overall quality of life of patients. It provides strong support for the comprehensive recovery of breast cancer patients. In conclusion, the application of exercise-psycho-sleep intervention to breast cancer patients can help improve their psychological state, sleep quality and quality of life, and is worth promoting.

Disclosure statement

The authors declare no conflict of interest.

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Research Progress on Pathogenesis and Drug Therapy of Atopic Dermatitis in Children

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Abstract:

Children with atopic dermatitis (AD) are a chronic inflammatory skin disease with obvious itching symptoms and high recurrence rate in clinical practice. Under the clinical research of atopic dermatitis in children, the clinical treatment plan has increased significantly. This article reviews the research progress of drug treatment of atopic dermatitis in children.

Keywords:

Children atopic dermatitis
Pathogenesis
Medication
Research progress

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1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease with a high clinical incidence, which has severe itching symptoms and a high recurrence rate. The clinical treatment options are diluted bleaching bath, corticosteroids, and antibiotics to carry out systematic or local treatment. In the study report, it was pointed out that the prevalence of the disease showed an increasing trend year by year. At present, the clinical understanding of AD is relatively shallow, and the understanding of the pathogenesis of the disease is proposed under the research of clinical medicine, epidemiology, molecular biology and genetics. This article reviews the pathogenesis and treatment of atopic dermatitis.

2. Pathogenesis of AD in children

2.1. Autoimmune diseases

In the study, 24 autoimmune diseases in children were investigated, and 13 diseases were associated with AD in children ^[1]. Children with atopic dermatitis have a higher incidence of autoimmune diseases in the musculoskeletal system, blood system, gastrointestinal system, endocrine system and skin tissue. At the same time, there is a strong correlation between AD and atopic diseases, and the relationship between AD and autoimmune diseases needs further analysis, mainly because the prevalence of autoimmune diseases is significantly lower than that of AD and asthma ^[2]. The disease is mostly related to the skin tissue factors of children, and it is necessary to pay attention to the screening of children with autoimmune diseases during treatment.

2.2. Skin microecology

There is a certain relationship between atopic dermatitis in children and abnormal skin microflora ^[3]. Symbiotic bacteria exist in the skin, with the assistance of IL-1, improve the cellular capacity of Th1 and inhibit the function of Th2 cells, thus inhibiting Th2-related allergic diseases and regulating the developmental system of children. During the onset of the disease, the amount of *Staphylococcus aureus* on the surface of the skin tissue of the child varies, and the level varies as the disease progresses ^[4].

2.3. Skin infection

Patients with atopic dermatitis are at risk of skin infection, and the specific influencing factors include immunosuppressive agents, increased infection, bacterial values, decreased antimicrobial peptides, immune disorders, and skin barrier dysfunction. At the same time, the use of systemic immunosuppressive drugs during treatment for disease can lead to an increased risk of infection ^[5]. Other studies have shown that patients with atopic dermatitis are closely related to skin infections at other locations, urinary tract infections, pharyngitis, and infections, and can also change under the influence of diseases such as bone and joint infections, meningitis, endocarditis, and septicemia ^[6].

2.4. Environmental and genetic factors

Genetic studies have shown that there is a certain relationship between disease persistence and skin barrier changes in atopic dermatitis ^[7]. In particular, FLG mutation in serogan protein coding can lead to the onset of AD disease, which is a genetic factor with a high risk of occurrence. Family inheritance is one of the major disease-causing mechanisms that cannot be changed during a child's illness ^[8]. Since the 20th century, the incidence of atopic dermatitis has increased significantly worldwide, affecting up to one in five children worldwide, especially as environmental changes have also led to an increase in the disease. Other studies have shown that in the daily environment, precipitation, ultraviolet exposure, humidity, temperature and other factors also have a certain impact on the disease, increasing the prevalence of AD ^[9]. Through the analysis of the severity of the disease and the degree of air pollution, it can be seen that

the more serious the environmental pollution, the more serious the condition of the patients. It can be seen that there are adverse effects on children's skin health under the change of the earth's climate.

2.5. Allergic contact dermatitis

This disease refers to the delayed allergic skin reaction in children to allergens in the surrounding environment. The incidence of this disease is similar to that of the adult population, and it is rarely detected in pediatric diagnosis, even less than one-tenth of all patch tests. Most children with allergic contact dermatitis are missed. In daily life, emollients, preservatives, topical drugs, perfumes, metals, etc., can affect the onset of disease. In the study report, allergic contact dermatitis and AD disease can occur simultaneously, which makes the diagnosis of atopic dermatitis more difficult. The acute phase of the disease includes erythema plaques, eczematous papules, pruritus, etc. Chronic phase may present pigmentation, skin cracks or lichenization ^[10].

2.6. Food impact

Food allergy is a target factor for accurate treatment of all allergic diseases. Under the influence of food pathophysiological characteristics, the allergy of biomarkers can be defined to ensure clinical effects and diagnostic results. According to the research report ^[11], foods such as shrimp, hazelnuts, peanuts, eggs and milk have high specificity in allergy diagnosis. During the diagnosis of AD disease, it is known that the defective skin barrier is more allergic after contact with food, which is also related to the genetic action of skin tissue and immunoglobulin-mediated food. At present, during the treatment of children with AD disease, it is necessary to understand the treatment and prevention measures of food allergy, and give certain early diagnosis and evaluation and treatment of psychological disorders ^[12].

The skin barrier function can inhibit the entry of sunlight, microorganisms, antigens, etc., and has the inherent function of shrinking and preventing water loss. The skin barrier function can maintain the normal operation of the human body, regulate the absorption of foreign substances through the skin, and regulate the evaporation of skin water. Abnormal lipid composition and sebum moisture in human skin will damage skin

barrier function, lead to abnormal PH value of skin tissue, and affect the integrity of the stratum corneum. Studies have shown that childhood AD is one of the inflammatory diseases with obvious skin barrier function impairment.

3. Drug treatment research

3.1. TCM treatment

Chinese medicine is selected for the local treatment of AD disease in children, and the prescription includes the mixed treatment of chestnut, platycypress, leshu, wild rose and dogwood in a ratio of 1:1:1:1:4^[13]. The drug can inhibit NO and IL-4 in children and reduce the release of mast cell degranulation markers. At the same time, enhancing drug concentration can reduce the release of DPPH free radicals. Studies have reported that providing Ziyun cream treatment for children is ideal for the control of inflammatory response, and can also improve the state of local skin damage, and the actual effect is similar to tacrolimus. At the same time, it can be seen from biological activity studies that traditional Chinese medicine has obvious effects of inhibiting angiogenesis, anti-oxidation, anti-allergy and anti-inflammatory. After medication, children with AD can improve skin barrier function in time, inhibit discomfort symptoms, and have high safety.

3.2. Crenoral

Creborol is a PDE4 inhibitor, which can reduce the level of cyclic adenosine phosphate and reduce the inflammatory response in children with AD. According to the study report, through the overall static test of children, it can be seen that the use of clariborol in the treatment of AD children is ideal. In addition, the use of the drug in the US Food and Drug Administration has been extended to infants aged 3 months and older, with gradual approval in China in 2020.

3.3. Depruliumab

The drug is a common monoclonal antibody biologic in clinical practice and has inhibitory effects on IL-3 and IL-4, the signal transduction. In the report, it was shown that the efficacy of dupriuzumab in the treatment of children with AD aged 6-11 years was ideal. The adverse reactions after treatment only appeared at the injection site,

including eosinophil increase, conjunctivitis, etc. Most of them were mild and could be resolved by themselves.

3.4. Tapinaro

The drug is a therapeutic aromatic pidgin receptor modulator, which can raise the expression of skin barrier genes and adjust the expression of Th2 cytokines after administration to avoid inflammatory oxidative damage in children. Some studies have proposed that medication in children with AD can improve their discomfort symptoms in time, with ideal improvement efficiency and fewer adverse reactions^[14].

3.5. Targeted therapy

Childhood AD involves multiple immune modes in clinical practice, the main mechanism of which is type 2 natural lymphocytes, TH2 cells and related factors driving immune response. Therefore, the targeted therapy of type 2 pathway should be emphasized during clinical treatment. At present, there have been a variety of targeted therapies for children with AD disease in clinical practice.

3.6. Wet wrap treatment and emollients

Studies in China have shown that the use of emollients can be used as adjuvant therapy for children with moderate and severe AD, thereby avoiding excessive use of glucocorticoid drugs and helping children repair skin barrier function. At the same time, with the progress of medical research, it is clinically proposed to take wet wrap treatment for severe refractory children, and select gauze wrap treatment based on local drug use and skin moisturization, which can significantly improve the discomfort symptoms of patients and restore the skin barrier function of patients.

3.7. Oral JAK inhibitors

A variety of cytokines participate in the inflammatory process of AD disease, indicating that JAK inhibitors have a better oral effect. The drug can inhibit the proliferation of some growth factors and cytokines. In the study report, it was pointed out that the disease improvement rate of AD children after medication is as high as more than 90%. At the same time, the drug has good tolerance, no obvious adverse reactions in children, and the drug safety is high.

3.8. Remote diagnosis and treatment of diseases

At present, telemedicine plays an important role in the treatment of AD disease. With the help of telemedicine, the diagnosis of children's AD disease is evaluated, and the appropriate treatment plan is selected according to the actual condition of the patient. Some data suggest that remote diagnosis and treatment can ensure the diagnosis accuracy of about 85%^[15]. Children with mild AD can improve their disease under the management of health care doctors, and children with severe AD can be guided to the hospital for treatment in time.

4. Summary

The pathogenesis of childhood AD is diverse and complex, and with the deepening of clinical understanding of the pathogenesis of childhood AD, the treatment methods will be more diversified. Although the treatment of moderate and severe AD in children is still a great challenge, with various new therapeutic methods, especially the use of targeted therapy for moderate and severe AD in children, doctors and patients are full of hope for the treatment of the disease.

Disclosure statement

The authors declare no conflict of interest.

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Advances in the Investigation of the Oncological Functions and its Target Therapy of Interleukin-1 Receptor-associated Kinase 1 (IRAK1)

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Abstract:

Interleukin-1 receptor-associated kinase 1 (IRAK1) plays as a pivotal regulator within the innate immune signaling and inflammatory processes. Being a critical component in many signaling pathways, emerging evidence strongly suggests the involvement of IRAK1 in the pathophysiology of cancers, thereby rendering it an attractive target for therapeutic intervention. Notably, selective IRAK1-inhibitory molecules have been identified, opening promising avenues for the therapy of tumor. In this review, we also delve into the challenges and future prospects in this field, emphasizing the importance of gaining a deeper understanding of IRAK1 regulation in tumors and the potential of combination therapies targeting IRAK1.

Keywords:

Interleukin-1 receptor-associated kinase 1 (IRAK1)
Tumor progression
Tumor immunity
IRAK1 inhibitors

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1. Introduction

Nowadays, it is increasingly evident that immune system not only comes into play in tumor suppression, known as cancer immunosurveillance, but also contributes to tumorigenesis and tumor progression ^[1]. Accumulating evidence highlights the pivotal function of interleukin-1 receptor-associated kinases (IRAKs) family in immune responses as well as its altered expression in different

types of cancer. Within the IRAKs, a serine/threonine kinases family, four distinct members are identifiable: IRAK1, IRAK2, IRAK3 (also recognized as IRAK-M), and IRAK4 ^[2]. It's important to note that among these, only IRAK1 and IRAK4 exhibit kinase activity ^[3,4]. This review concentrates on the latest progress made in comprehending the significance of IRAK1 in the advancement of tumors as well as potential therapeutic interventions.

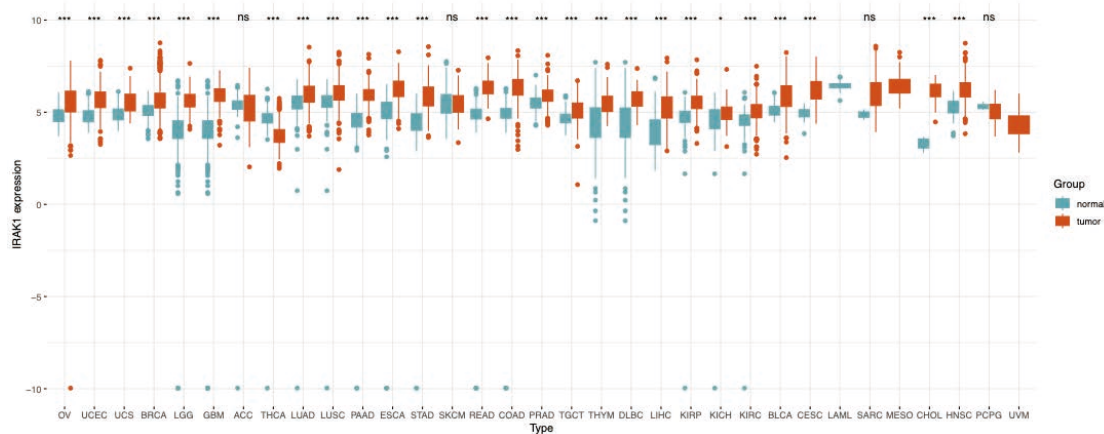


Figure 1. The expression of IRAK1 in different tumors and their paired normal tissues. The dysregulation and aberrant expression of IRAK1 have been subject to analysis across diverse cancer types. Utilizing data from the Cancer Genome Atlas (TCGA) database, it aimed to elucidate IRAK1's potential involvement in various malignancies compared with their corresponding normal tissues. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

2. The expression of IRAK1 and its effects in different cancers

Dysregulation and aberrant activation of IRAK1 have been associated with various effects on tumors (**Figure 1**). The role of IRAK1 in tumor includes promoting tumor growth, survival, inflammation, immune evasion, therapeutic resistance, angiogenesis, and metastasis. Here are some of the effects of IRAK1 in specific tumors.

2.1. Hepatocellular carcinoma

IRAK1 exhibits significant expression in hepatocellular carcinoma (HCC) cell lines and tumor tissues, indicating its feasible involvement in HCC development, which contributes to cancer cell proliferation and the inflammatory tumor microenvironment^[5]. The tumor suppressor serine/threonine-protein kinase 4 (STK4) enhances TLR3/4-activated IFN- β production through IRAK1 binding and phosphorylation^[6]. This leads to IRAK1 degradation and prevents the development of inflammation-related HCC. Furthermore, Cheng and colleagues pinpointed AKR1B10 as a fresh downstream target of IRAK1, and AKR1B10 is usually used as a biomarker of HCC, underscoring a previously unrecognized relationship between these molecules^[7].

2.2. Nasopharyngeal carcinoma

In the context of Nasopharyngeal carcinoma (NPC) metastasis, S100 calcium-binding protein A14 (S100A14)

exhibits a suppressive effect on metastasis by facilitating the ubiquitin-mediated degradation of IRAK1, which blocks cellular migration in NPC^[8]. Additionally, Liu *et al.* discovered that IRAK1 has potential function in drug resistance and poor prognosis in NPC. Specifically, IRAK1 is essential to the expression of S100A9, and the IRAK1/S100A9 axis contributes to drug resistance and unfavorable outcomes in NPC^[9].

2.3. Low-grade glioma

Notably, comprehensive studies have substantiated that the high level of IRAK1 in LGG exerts an oncogenic function by inhibiting cell apoptosis and promoting LGG malignancy^[10]. IRAK1 is warranted to enhance the prognosis and treatment outcomes for LGG patients.

2.4. Colorectal cancer

Aberrant expression of IRAK1 in colorectal cancer (CRC) is linked to malignant phenotypes, and targeting its expression could mitigate the inflammatory process and modulate the downregulation of epithelial-mesenchymal transition (EMT) in mice^[11,12]. Furthermore, scientists have discovered that the loss of heterogeneous nuclear ribonucleoprotein I (hnRNRI) within the intestinal epithelial cells undermines the immune adaption process in newborns, ultimately leading to colitis and colorectal cancer^[13].

2.5. Breast cancer

Research has revealed a substantial decrease in the expression of IRAK1 following neoadjuvant chemotherapy, which aligns with a noticeable reduction in tumor size ^[13]. In the context of triple-negative breast cancer (TNBC), IRAK1 upregulation confers a growth advantage and contributes to acquired resistance to paclitaxel treatment ^[14]. Restraining the phosphorylation of IRAK1 has demonstrated increased apoptosis and reduced migration in TNBC ^[15].

2.6. Prostate cancer

IRAK1 exhibits significant overexpression specifically in prostate cancer (PCa) compared to normal tissues. This overexpression is particularly observed in luminal epithelial cells of Pca ^[16]. Moreover, IRAK1 is found to exhibit varying expression levels between benign and malignant samples within a patient cohort ^[17].

2.7. Non-small cell lung cancer

IRAK1 is highly expressed in non-small cell lung cancer (NSCLC) and is considered a new inflammation-related marker ^[18]. In NSCLC with epidermal growth factor receptor (EGFR) mutation, the IRAK1/NF- κ B axis demonstrates a significant role in standing up to EGFR tyrosine kinase inhibitors (TKIs) ^[19]. Additionally, the expression of IRAK1 in non-tumor cells, such as tumor-associated macrophages (TAMs), can negatively impact the anti-tumor activity against tumor cells ^[20].

2.8. Endometrial carcinoma

The reduction of IRAK1 expression in endometrial carcinoma (EC) cells led to distinct outcomes: it prompted cell cycle arrest and apoptosis while concurrently restraining cell migration and invasion ^[21]. Another study uncovered that the transfer of miR-192-5p via specific exosomes derived from TAMs could inhibit the IRAK1/NF- κ B signaling pathway, leading to the suppression of tumor formation, inhibition of EMT in EC cells, and promotion of EC cell apoptosis ^[22].

2.9. Squamous cell carcinomas

Within squamous cell carcinoma (SCC), the pro-oncogenic impact and tumorigenic properties of Desmoglein 2 (Dsg2) are achieved through the alteration

of IRAK1 and its downstream target IL-8 ^[23]. Furthermore, in Oral SCC, miR-146 is up-regulated and acts as an oncogenic molecule ^[24]. Another significant finding reveals that IRAK1 is transcriptionally upregulated by the chromatin-binding DEK protein, promoting cell survival ^[25]. In an effort to heighten the sensitivity of chemotherapy-resistant cells to chemotherapy, inhibiting IRAK1 pharmacologically can consider as a potentially effective cytostatic method ^[26].

2.10. Melanoma

Within melanoma cells, the expression of chemokines and cytokines associated with cancer cell survival, division, and the promotion of angiogenesis strongly correlates with the activation of IRAK1/IRAK4 signaling ^[27]. Melanoma and its stem cells could respond to the aurora kinase inhibitor CCT137690 because of its effect on a significant decrease in the expression of IRAK1 ^[28].

2.11. Activated B-cell-like diffuse large B-cell lymphoma

In activated B-cell-like diffuse large B-cell lymphoma (ABC DLBCL) with MyD88 mutation, IRAK1 functions as a scaffold protein, facilitating tumor cell proliferation and apoptosis ^[29].

2.12. Stem cell leukemia/lymphoma syndrome

IRAK1 regulates the activity of interferon-gamma (IFN- γ), which facilitates the accumulation of myeloid-derived suppressor cells. These cells inhibit the T-cell response to leukemic cells, contributing to the progression of stem cell leukemia/lymphoma syndrome (SCLL) ^[30].

2.13. Acute myeloid leukemia

IRAK1 is implicated as an oncotarget in acute myeloid leukemia (AML). Targeting IRAK1 has shown promising results in reducing AML progenitors in vitro and decreasing the leukemia burden in xenograft model ^[31]. Moreover, IRAK1 has been identified as a viable target to overcome adaptive resistance in the FLT3-mutant subtype ^[32].

2.14. T-cell acute lymphoblastic leukemia

IRAK1 plays a critical role in T-cell acute lymphoblastic leukemia (T-ALL) cell proliferation and survival through

the stabilization of the antiapoptotic protein MCL1^[33]. Additionally, the DNA methylation of miR-204 has been shown to promote cell proliferation and enhance apoptosis through IRAK1^[34].

2.15. Mixed lineage leukemias

In mixed lineage leukemias (MLL), the inhibition of IRAK1/4 has been shown to delay leukemia progression and improve survival in murine models by stabilizing the normal MLL protein^[35].

2.16. Waldenström macroglobulinemia

Waldenström macroglobulinemia (WM) typically manifests with the presence of a MYD88 mutation. In WM cells, inhibiting the kinase activity of IRAK1/4 leads to apoptosis in WM cells^[37].

3. Application of irak1 inhibitor in tumor therapy

3.1. IRAK1/4 inhibitor

The IRAK1/4 inhibitor shows potential in weakening the stability of the antiapoptotic protein MCL1, demonstrating promising potency in combination treatment for T-ALL with ABT-737 or vincristine^[36]. In the context of anaplastic thyroid cancer (ATC), inhibition of IRAK1 exhibits anti-proliferation and anti-tumor effects its cell lines^[37]. Moreover, combining IRAK-1/4 Inhibitor with ABT-737 proves more effective in restoring white blood cell count in peripheral blood and reducing mortality in a T-ALL mouse model^[38]. Additionally, this inhibitor sensitizes the curative effect of methotrexate chemotherapy in breast cancer cell lines^[39]. In TNBC, the IRAK1/4 inhibitor induces massive apoptosis to reverse paclitaxel resistance^[16]. To address MDS and eliminate MDS-initiating clones, an IRAK1/4 inhibitor is employed to impair MDS cells while preserving normal CD34 positive cells^[40]. Furthermore, the IRAK1/4 inhibitor decreases the expression of inflammatory cytokines and prevents tumor growth in colorectal cancer. Notably, it also inhibits EMT, effectively slowing down colitis-induced tumorigenesis^[12].

3.2. NCGC1481

NCGC1481 demonstrates a novel strategy to overcome

adaptive resistance via inhibiting IRAK1 and its associated signaling^[34]. This approach holds great promise in enhancing treatment outcomes and addressing the challenge of adaptive resistance in AML.

3.3. JH-X-119-01

JH-X-119-01 has been published as a highly potent and selective covalent inhibitor of IRAK1. In the MYD88-mutated B-cell lymphomas, JH-X-119-01 acts as a potent antiproliferative effector, offering a potential therapeutic approach^[41]. Moreover, JH-X-119-01 shows favorable outcomes in LPS-induced septic mice. It not only improves the survival of septic mice but also protects macrophages with reduced toxicity when compared to non-selective IRAK1/4 inhibitors^[42].

3.4. Pacritinib

Recent evidence has shown that pacritinib also acts as a specific inhibitor of IRAK1. Building on this, pacritinib exerts a dual effect on the immune system and tumors by restraining IRAK1. It attenuates leukemogenesis through the suppression of CD4+/CD8+ T-cells and myeloid-derived suppressor cells. Furthermore, pacritinib demonstrates potential as an anti-pan cancer inhibitor by effectively inhibiting tumor proliferation via impacting the PD-1/PD-L1 axis and mediating immunosuppression^[33,43].

3.5. HS-243

HS-243, a takinib analog, is used to suppress IRAK1 in human rheumatoid arthritis, it exhibits a notable responsiveness to cytokine/chemokine signaling in fibroblast-like synoviocytes^[44].

3.6. Takinib

Takinib was developed as a selective inhibitor of TAK1, but because of the similar ATP-binding pocket, takinib could also be used as the inhibitor of IRAK1^[45,46].

3.7. JNJ-1013

Recognizing the significance of IRAK1's scaffolding function, which is crucial for tumor cell survival and distinct from its kinase activity, an IRAK1 degrader Degradar-3 (JNJ-1013) specifically aims to disrupt this function. JNJ-1013 displays valid anti-proliferative

properties in ABC DLBCL cells possessing MyD88 mutation^[30].

4. Conclusion

Amid its functions, IRAK1's involvement in cancer

emerges especially. This association emphasizes the potential of IRAK1 as a valuable target for therapeutic intervention, with selective IRAK1 inhibitors garnering attention. In the broader context, our comprehensive review unveils IRAK1's multifaceted contributions to tumorigenesis, tumor immunity, and progression.

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Disclosure statement

The authors declare no conflict of interest.

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Diagnosis and Treatment of Appendicitis Combined with Delayed Egerter Blood Infection

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Abstract:

Objective: To summarize the effective diagnosis and treatment methods for appendicitis complicated with delayed Escherichia coli blood infection.

Methods: A retrospective analysis of the medical course of one patient with appendicitis complicated with delayed E. coli blood infection was conducted.

Results: The main clinical symptom of appendicitis complicated with delayed E. coli blood infection is high fever. Due to the long culture time of delayed E. coli, early empirical antimicrobial therapy is extremely important. Cefoperazone-sulbactam is one of the effective drugs for treating appendicitis complicated with delayed E. coli blood infection.

Keywords:

Slow Egerterella
Blood infection
Appendicitis

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1. Data analysis

The patient, male, 52 years old, visited the hospital emergency department at around 10:06 AM on October 30, 2022, due to “fever for one day.” The patient developed a fever without any obvious cause about one day prior, with the highest temperature reaching 41°C. He experienced chills, shivering, headache, and dizziness, but had no nausea, vomiting, sore throat, coughing, sputum production, abdominal pain, diarrhea, frequent urination, urgency, or dysuria. After self-administering medication,

his symptoms did not improve. The specific medications taken are unknown. Following an investigation by the fever clinic, he was admitted to the department’s intensive care unit. After symptomatic treatment for fever reduction, he broke out in a heavy sweat. The hospital administered cefmetazole for infection control and fluid replacement. Currently, his blood pressure is lower than baseline. For further diagnosis and treatment, he was admitted to the department with “undetermined fever.” Throughout the course of the illness, the patient has been

in good spirits, able to eat, and has normal bowel and bladder function. Past medical history includes over 10 years of hypertension, regularly taking Lopressor and Irbesartan for antihypertensive treatment, which has controlled his blood pressure. One year ago, he underwent coronary stenting after a myocardial infarction and now takes aspirin, clopidogrel, and rosuvastatin regularly. On admission, physical examination revealed: temperature 39°C, pulse rate 88 beats per minute, respiratory rate 20 breaths per minute, blood pressure 137/63 mmHg. He was wheeled into the ward, conscious and cooperative during the examination. His lips were not cyanotic, and there were no rashes, jaundice, or petechiae on the skin or mucous membranes. Physical examination of the heart and nervous system showed no abnormalities, and auscultation of the lungs revealed normal breath sounds coarse, wet rales heard at the right lung base. Abdomen soft, mild tenderness below the xiphoid process, no rebound tenderness or muscle rigidity, liver and spleen not palpable, shifting dullness (-), normal bowel sounds, no water-hammer sound, positive percussion pain in both renal areas. Ancillary tests: Complete blood count: White blood cells: $4.70 \times 10^9/L$; Neutrophil ratio: 77.20%; Red blood cells: $4.17 \times 10^9/L$; Hemoglobin: 131.00 g/L; Platelets: $120 \times 10^9/L$; Urine routine: Ketones 1+. Electrolytes and kidney function showed no significant abnormalities.

2. Medical treatment process

After admission to the emergency internal medicine department, active treatment was provided with intravenous administration of cefoperazone and tazobactam sodium for anti-infection, oral administration of ibuprofen suspension, and intramuscular injection of paracetamol for fever reduction and other symptomatic supportive treatments. On the day of admission, the patient developed a high fever with a peak temperature reaching 41°C. An enhanced abdominal CT scan indicated peri-appendiceal exudation. The general surgeon was consulted, and the initial diagnosis was appendicitis with exudation. Due to the presence of peri-appendiceal exudation, surgical resection was not suitable. It was recommended to complete relevant examinations to determine the cause of the fever, provide

symptomatic supportive anti-inflammatory treatment, and closely monitor the patient's condition changes. Continued symptomatic supportive treatments such as anti-infection were provided. On the second day of admission, follow-up tests included routine blood tests, liver function, kidney function, electrolytes, C-reactive protein, procalcitonin, 11 respiratory virus tests, blood culture, coagulation profile, D-dimer, myocardial enzymes, infectious disease screening, peripheral blood morphology analysis, and bedside electrocardiogram. On the second day of admission, outpatient blood culture results showed: aerobic bottle initial report: Gram-negative bacilli; anaerobic bacteria initial report: Gram-positive bacilli. The current diagnosis is "fever of unknown origin, bacteremia, appendicitis with exudation, hypertension, coronary artery atherosclerotic heart disease, post-coronary stent surgery, hypokalemia, multiple cysts in both kidneys." Further relevant auxiliary examinations were actively completed, and the results of the enhanced abdominal CT scan are currently available. No specific infection site was indicated, but blood culture reported the presence of bacteria. The specific results will be reported later. Currently, the antibiotics used are cefoperazone and sulbactam, which can cover infections of abdominal organs. Although the patient has been feverish since admission, there has been no recurrence of chills, indicating effective anti-infection treatment. Treatment will continue as is for now, with close monitoring of the patient's abdominal condition. If necessary, follow-up abdominal CT scans or other relevant examinations may be required. On the third day of hospitalization, C-reactive protein: 119 mg/L, Procalcitonin: 2.330 ng/mL; Complete blood count: White blood cells: $4.70 \times 10^9/L$, Neutrophil ratio: 77.20%, Red blood cells: $4.17 \times 10^9/L$, Hemoglobin: 131.00 g/L, Platelets: $120 \times 10^9/L$; Urinalysis: Ketones 1+. No significant abnormalities were found in electrolytes or renal function. Based on the patient's medical history, physical examination, and auxiliary tests, the following considerations are made:

- (1) Blood cultures indicate Gram positive bacilli and Gram negative bacilli. Temporary administration of cefoperazone and sulbactam for anti-infection treatment. The peak temperature and related inflammatory indicators have both decreased, suggesting effective anti-infection treatment.

There is currently no evidence of urinary tract infection, so continue current anti-infection treatment and schedule a follow-up abdominal CT scan.

- (2) The patient has diarrhea without significant abdominal pain. Please consult the gastroenterology department for assistance in diagnosing and adjusting medication. Oral administration of *Bifidobacterium trilactis* enteric-coated capsules is recommended.

On the fifth day of hospitalization, physical examination of the heart, lungs, and abdomen showed no abnormalities. Rechecked C-reactive protein: 7.25 mg/L, procalcitonin: 0.387 ng/mL; blood culture for five days showed no growth of bacteria or anaerobes. The patient had not been feverish in the past three days, and routine blood tests, white blood cell count, and neutrophil ratio were significantly lower than before. It is considered that the anti-infection treatment has been effective, and further consolidation therapy is recommended. During the five-day hospital stay, the patient's vital signs remained stable, with no fever, abdominal pain, diarrhea, or significant discomfort. After communicating with the patient and their family, they requested discharge to continue treatment at a local hospital. It was informed that anti-infection treatment may still lead to perforation, abscess formation, peritonitis, or septic shock. The patient and their family expressed understanding but insisted on discharge. A higher-level doctor was consulted to approve the discharge. On November 10th, the blood culture returned a slow-growing *Escherichia coli*.

3. Discussion

Cheratococcus elegans is an obligate anaerobic gram-positive bacillus that grows slowly and forms visible colonies within five days. It was first isolated from human feces by scientist Ernst Egerth in 1935 and initially classified as an anaerobic bacillus. After sequencing in 1999, it was subdivided into the Ernst Egerth genus [1]. This bacterium is mainly found in the digestive tract and is a rare pathogen of appendicitis, liver abscess and renal abscess. Slow-growing bacteria can enter the blood with primary diseases and form bacteremia [2]. At present, there are few reports on the blood infection

caused by slow Egerteria both at home and abroad. This study summarizes the effective diagnosis and treatment of appendicitis combined with slow Egerteria blood infection based on the diagnosis and treatment process of one patient with appendicitis combined with slow Egerteria blood infection.

Infections caused by slow Egerterella include blood infection, myelitis, liver abscess, kidney abscess, etc., and are also related to appendicitis in adults and children. Blood infection is rarely reported, and if not treated effectively in time, it will endanger the life safety of patients [3,4]. According to the latest literature at home and abroad, when slow Egerterella causes blood infection, the average time of positive blood culture is about one week [5]. The time of blood culture positivity in this study was similar to that of the patients, mainly because of the slow growth of the bacteria. Therefore, empirical antibiotic therapy is particularly important. Summarizing the clinical characteristics and antibiotics used for delayed *Escherichia coli* bloodstream infection can provide reference for empirical clinical treatment.

A clinical study of a case of slow Egerterella bloodstream infection abroad found that the main symptoms of patients at admission were fever, nausea and vomiting, and abdominal pain and diarrhea [6]. Most of the clinical symptoms of patients in this study were consistent. Although the number of cases observed in this study was limited, it cannot be ruled out that gastrointestinal diseases are a high-risk factor for delayed *E. coli* bacteremia. The reason may be that delayed *E. coli* can colonize the normal gastrointestinal mucosa, and when the gastrointestinal mucosa is damaged or the body's immune function declines, this bacterium can invade the bloodstream, leading to bacteremia. In a clinical study of cases in Canada, it was found that almost all patients with delayed *E. coli* bacteremia had underlying gastrointestinal diseases, with adult appendicitis accounting for the highest proportion at 32.8% [7,8]. Because of the few clinical reports on this bacterium, there is no unified drug guide for the selection of antibiotics. Many domestic and foreign literature reports have proved that slow Egerter bacteria are resistant to penicillin, but highly sensitive to amoxicillin, metronidazole and vancomycin [9,10].

4. Conclusion

In short, the main clinical symptoms of appendicitis combined with delayed Egerter blood infection are high fever and mild right lower abdominal pain, which often leads to missed diagnosis by clinicians. Blood culture and 16sRNA gene sequence analysis can be used to identify

delayed Egerter^[11,12]. However, the cultivation time is long, so it is necessary to apply empirical antibiotics in advance. This study proved that cefoperazone-sulbactam sodium was one of the effective antibiotics for the treatment of appendicitis combined with delayed Egerter blood infection.

Disclosure statement

The authors declare no conflict of interest.

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Advancements in Molecular Detection Technology of Senecavirus A: A Comprehensive Review

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Abstract:

In recent years, the *Seneca Valley virus* (SVV) has impeded the sustainable development of the swine industry, posing a major challenge to disease prevention and control in swine populations. The emergence of *Seneca Valley virus* (SVV) presents twofold challenges for swine production systems: it not only significantly interferes with routine farm management protocols, but also substantially complicates clinical differentiation due to its pathognomonic similarity to foot-and-mouth disease (FMD) and swine vesicular disease (SVD). To effectively control the spread of the virus, developing a more convenient and user-friendly rapid detection scheme has become the key focus of disease diagnosis innovation. This paper collected reports on the innovation and application of molecular detection technology of the *Seneca virus*, and sorted out these methods, to provide some scientific basis for the prevention and control of the SVV epidemic in the future, reduce economic losses, and prevent further spread of the virus.

Keywords:

Seneca virus A
Molecular detection
Rapid detection
RPA

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1. Introduction

Seneca Valley virus (SVV), also known as *Seneca Virus A* (SVA), is classified as the sole species within the genus *Senecavirus* (family *Picornaviridae*)^[1]. The clinical manifestations of SVV infection in swine populations closely resemble those induced by vesicular diseases, particularly *Foot-and-mouth disease virus* (FMDV) and

Swine vesicular disease virus (SVDV), as evidenced by comparative histopathological analyses. SVV can cause vesicular lesions on the mouth, nose, and hoof crown of adult pigs, with occasional symptoms such as fever and diarrhea, and increase the mortality of newborn piglets. This makes clinical diagnosis difficult. Also, there is currently no commercially available SVV vaccine. This

has caused a lot of economic losses to the pig breeding industry.

Early diagnosis through validated assays represents a pivotal strategy to control epidemic transmission of SVV in swine populations. The timeliness and accuracy of detection are key determinants for interrupting viral spread, especially within intensive production systems where rapid pathogen transmission occurs via direct contact or fomites. Molecular diagnosis has quickly become a popular pathogen detection method because of its fast detection speed and high sensitivity. Recent advancements in diagnostic technologies have substantially enhanced assay performance, with notable improvements in processing efficiency and analytical sensitivity across multiple detection platforms. In this paper, the molecular detection methods of SVV reported in recent years are sorted out, which provides more choices for the detection methods of this pathogen and also provides a reference for the development of rapid detection technology.

2. Introduction of SVV

Seneca Valley virus (SVV) was incidentally isolated in 2002 from the PER.C6 (transformed fetal retinoblast) cell line [2]. In 2015, Brazil first reported an outbreak of SVV in pigs [3]. Subsequently, the United States [4], Thailand [5], Vietnam [6], Colombia [7], and other countries reported that SVV broke out in their country.

The susceptible animals of *Seneca virus* are pigs, and pigs of all ages are susceptible. Viruses can spread through direct and indirect contact with viral pollutants or aerosols. The pathogenicity and fatality rate of the virus are related to the age, breed, and geographical factors of pigs, and generally occur in spring and autumn [8]. Current epidemiological studies have demonstrated a significant association between SVV infection and elevated mortality rates in neonatal piglets during perinatal stages. The mortality rate of adult pigs is extremely low, usually subclinical infection or recessive infection. The mortality rate of piglets is higher than that of adult pigs, and the incidence rate of sows is as high as 70–90% [9].

3. SVV detection methods

3.1. Pathogenic detection

Virus isolation is the most accurate method to identify and diagnose SVV. It has been found that cells that can be used to isolate the *Seneca virus* include PER.C6 [10], NCI-H1299 [11], HEK293T [12], ST [13], PK-15 [14], and so on. While virus isolation-based detection protocols for SVV demonstrate high diagnostic specificity, their technical complexity, requiring specialized biosafety containment facilities (BSL-2+), and prolonged turnaround time (> 48 hours post-sample collection) render these methods suboptimal for field applications requiring expedited diagnostics during outbreak investigations. The clinical similarity between SVV and FMDV infections in swine poses significant diagnostic challenges. Given that FMDV is a zoonotic pathogen, virus isolation protocols for differential diagnosis necessitate stringent biosafety containment measures (BSL-3), particularly during epizootic investigations where misidentification could amplify public health risks.

3.2. Antibody detection

Antibody detection methods are suitable for handling a large number of samples in epidemiological surveillance or mass diagnostic programs [15]. Serodiagnostic approaches currently implemented for SVV surveillance in swine populations encompass indirect enzyme-linked immunosorbent assay (iELISA) [16], competitive ELISA (cELISA), indirect fluorescent antibody (IFA) testing, and virus neutralization test (VNT) [17,18]. Compared with other Antibody detection assays, ELISA is famous for its high sensitivity, specificity, convenience, rapid, and cost-effectiveness. SVV ELISAs have been developed to detect IgG antibodies against non-structural proteins such as 2C, 3C, 3D, L, and 3AB proteins and Virus-like particles (VLPs) [19,20]. However, serological detection needs a period after virus infection to produce a reliable antibody reaction, so it cannot meet the requirements of rapid detection in the early stage of the epidemic.

3.3. Molecular biological detection

Nucleic acid-based detection methodologies in molecular diagnostics primarily involve polymerase chain reaction (PCR) and its advanced derivative, real-time quantitative reverse transcription PCR (qRT-PCR)

^[21]. Currently, these techniques serve as the primary standard for diagnosing animal vesicular diseases due to their rapidity, sensitivity, and strong specificity in pathogen identification. Conventional PCR relies on agarose gel electrophoresis for result analysis. While cost-effective, this method involves biohazard risks from nucleic acid dyes and requires both thermal cyclers and horizontal electrophoresis units, limiting its application in settings with unstable power supply. Moreover, PCR detection requires not only a precise thermal cycler but also a horizontal electrophoresis instrument, which is very inconvenient when there are not enough electricity resources. qRT-PCR detection methods have high sensitivity and can detect rare targets, which is a very mature detection method. However, this method requires professional laboratory equipment and operators. Meanwhile, to ensure accurate temperature control, it is necessary to supply power to the fluorescence quantitative PCR instrument continuously. A multiplex real-time RT-PCR assay for detecting and distinguishing FMDV from SVV was also recently developed and evaluated ^[22]. The method can identify FMDV and SVV at the same time, aiming at improving the efficiency of disease detection.

3.4. Development of molecular detection technology

3.4.1. Molecular detection method based on polymerase chain reaction technology

Insulated isothermal PCR (iiPCR), a fluorescent probe-mediated nucleic acid amplification system under constant temperature conditions ^[23]. iiPCR technique achieves nucleic acid amplification through sequential thermal cycling across distinct temperature phases (denaturation, annealing, and elongation) within a microfluidic capillary, facilitated by a portable thermal control system. This approach employs an integrated nucleic acid processing system capable of executing automated PCR amplification and result interpretation within approximately one to one and a half hours. Nucleic acid amplification can be completed in 30–40 minutes. Two molecular assays targeting conserved SVV genomic regions were established for viral RNA detection: a reverse transcription PCR (RT-PCR) assay specific to the 5'UTR and a reverse transcription insulated isothermal PCR (RT-iiPCR) method focusing on the 3D gene, with

inter-assay consistency reaching 98.4% ^[24].

Reverse transcription droplet digital PCR (RT-ddPCR) is considered to be an accurate and sensitive technique, showing good sensitivity and specificity in SVV detection. Beyond diagnostic applications, RT-ddPCR facilitates absolute SVV RNA quantification independent of calibration curve construction ^[25]. However, this method requires high personnel operation, and it still can't get rid of expensive precision instrument detection, which can't meet the requirements of on-site rapid detection ^[26].

3.4.2. Molecular detection method based on constant temperature amplification technique

Constant temperature amplification technology is a kind of molecular biological detection method at constant temperature. This methodology demonstrates operational simplicity, minimal instrumentation requirements, and rapid processing timelines when contrasted with standard PCR protocols. At present, this technology is mainly divided into LAMP ^[27], RCA ^[28], RAA ^[29], and RPA. Through the engineering of sequence-specific primers and enzyme systems, the exponential amplification of target DNA or RNA can be realized at constant temperature.

Loop-mediated isothermal amplification (LAMP) is an efficient DNA amplification method, which can rapidly amplify the target DNA sequence at constant temperature. LAMP technology uses multiple primers and DNA polymerase to realize continuous amplification of target DNA. LAMP technology shows good sensitivity and specificity in SVV detection, and its operation is relatively simple, so it is a potential rapid detection method.

Recombinant enzyme polymerase amplification (RPA) is a new isothermal amplification technology, that can rapidly amplify the target nucleic acid sequence at low temperature (37–42 °C) ^[30]. At present, RPA technology can be divided into three categories, including basic RPA, fluorescent RPA, and lateral flow RPA ^[31]. The fundamental RPA system comprises four core components: recombinase, ssDNA-binding protein, DNA polymerase, and amplification-optimized buffer formulation. After adding templates and primers, it can react quickly at room temperature, and the results can be judged within 30 minutes by gel electrophoresis.

The principle of fluorescent RPA is similar to that of fluorescent quantitative PCR. During the amplification reaction, this RPA can cut the recognition sites of special fluorescent probes through the nucleic acid exonuclease in the reagent and release fluorescent signals, which can be combined with a fluorometer for real-time quantitative detection. In response to the lack of professional detection equipment in some areas, some companies have developed portable fluorescence meters that can even be powered by solar energy. These portable fluorescence meters are small in size and light in weight, and nucleic acid amplification can be observed in real-time on the spot through RPA fluorescence meters ^[32].

4. Application of isothermal amplification technology in SVV detection

Recently, isothermal amplification technology has been widely used in the rapid detection of SVV ^[33]. The researchers designed primers and probes for isothermal amplification of SVV-conserved regions, which showed good sensitivity and specificity in detection. Some researchers combined RPA technology with the CRISPR/Cas12a system to develop an accurate and sensitive diagnosis and detection platform for SVV. This methodology demonstrated an analytical sensitivity threshold of 10 copies per reaction ^[34]. This method integrates RPA reaction and CRISPR/Cas system in a centrifuge tube, which reduces the risk of sample pollution and has great practical application potential in an environment with limited resources.

5. Summary

At present, most molecular detection technologies need harsh laboratory environments and professional detection personnel. Infectious diseases are more likely to spread in areas with difficult conditions or poor sanitation.

Therefore, developing more convenient, sensitive, and fast on-site detection methods is the direction of future research. By sorting out the main molecular detection methods at present, RPA has shown its unique advantages in the field of rapid on-site detection because of its characteristics of rapidity, simplicity, and convenience, and has been gradually paid attention to and applied to the detection of zoonotic pathogens. The reaction temperature of RPA is close to human body temperature and its reaction time is short (5–20 min), which makes it more suitable for on-site rapid detection. In recent years, scholars have been trying to combine RPA with LFD, CRISPR/ Cas system, and other diagnostic techniques to develop more sensitive and convenient molecular diagnostic methods. It has been reported that a nucleic acid detection method without RNA is described, which greatly improves the detection speed ^[35]. Another multienzyme isothermal amplification technique used by some scholars is called multienzyme isothermal rapid amplification (Mira), which uses a recombinant enzyme named *Streptomyces azure* recA (SC-recA) to improve the reaction stability and anti-interference ability ^[36]. Researchers have engineered a regenerable dual-channel fiber-optic immunosensing platform (DOFIS) for enhanced diagnostic applications. The detection can be completed in 10 min with low cost and simple operation ^[37]. All the above rapid detection methods can provide some reference for the development of SVV rapid detection.

In addition, using freeze-drying technology, lateral chromatography test strips, and other technical means, developing portable detection reagents or consumables that are easy to carry and use can better meet the needs of grassroots veterinarians for on-site detection. Future research should further improve the detection sensitivity and specificity, and develop portable detection equipment to provide more powerful support for the prevention and control of SVV. In the future, we will continue to pay attention to and explore the research progress in this field, and make greater contributions to the rapid detection of SVV and the prevention and control of diseases.

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Disclosure statement

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Research Progress on Pathogenesis and Drug Therapy of Atopic Dermatitis in Children

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Abstract:

Children with atopic dermatitis (AD) are a chronic inflammatory skin disease with obvious itching symptoms and high recurrence rate in clinical practice. Under the clinical research of atopic dermatitis in children, the clinical treatment plan has increased significantly. This article reviews the research progress of drug treatment of atopic dermatitis in children.

Keywords:

Children atopic dermatitis
Pathogenesis
Medication
Research progress

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1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease with a high clinical incidence, which has severe itching symptoms and a high recurrence rate. The clinical treatment options are diluted bleaching bath, corticosteroids, and antibiotics to carry out systematic or local treatment. In the study report, it was pointed out that the prevalence of the disease showed an increasing trend year by year. At present, the clinical understanding of AD is relatively shallow, and the understanding of the pathogenesis of the disease is proposed under the research of clinical medicine, epidemiology, molecular biology and genetics. This article reviews the pathogenesis and treatment of atopic dermatitis.

2. Pathogenesis of AD in children

2.1. Autoimmune diseases

In the study, 24 autoimmune diseases in children were investigated, and 13 diseases were associated with AD in children ^[1]. Children with atopic dermatitis have a higher incidence of autoimmune diseases in the musculoskeletal system, blood system, gastrointestinal system, endocrine system and skin tissue. At the same time, there is a strong correlation between AD and atopic diseases, and the relationship between AD and autoimmune diseases needs further analysis, mainly because the prevalence of autoimmune diseases is significantly lower than that of AD and asthma ^[2]. The disease is mostly related to the skin tissue factors of children, and it is necessary to pay attention to the screening of children with autoimmune diseases during treatment.

2.2. Skin microecology

There is a certain relationship between atopic dermatitis in children and abnormal skin microflora^[3]. Symbiotic bacteria exist in the skin, with the assistance of IL-1, improve the cellular capacity of Th1 and inhibit the function of Th2 cells, thus inhibiting Th2-related allergic diseases and regulating the developmental system of children. During the onset of the disease, the amount of *Staphylococcus aureus* on the surface of the skin tissue of the child varies, and the level varies as the disease progresses^[4].

2.3. Skin infection

Patients with atopic dermatitis are at risk of skin infection, and the specific influencing factors include immunosuppressive agents, increased infection, bacterial values, decreased antimicrobial peptides, immune disorders, and skin barrier dysfunction. At the same time, the use of systemic immunosuppressive drugs during treatment for disease can lead to an increased risk of infection^[5]. Other studies have shown that patients with atopic dermatitis are closely related to skin infections at other locations, urinary tract infections, pharyngitis, and infections, and can also change under the influence of diseases such as bone and joint infections, meningitis, endocarditis, and septicemia^[6].

2.4. Environmental and genetic factors

Genetic studies have shown that there is a certain relationship between disease persistence and skin barrier changes in atopic dermatitis^[7]. In particular, FLG mutation in sergan protein coding can lead to the onset of AD disease, which is a genetic factor with a high risk of occurrence. Family inheritance is one of the major disease-causing mechanisms that cannot be changed during a child's illness^[8]. Since the 20th century, the incidence of atopic dermatitis has increased significantly worldwide, affecting up to one in five children worldwide, especially as environmental changes have also led to an increase in the disease. Other studies have shown that in the daily environment, precipitation, ultraviolet exposure, humidity, temperature and other factors also have a certain impact on the disease, increasing the prevalence of AD^[9]. Through the analysis of the severity of the disease and the degree of air pollution, it can be seen that

the more serious the environmental pollution, the more serious the condition of the patients. It can be seen that there are adverse effects on children's skin health under the change of the earth's climate.

2.5. Allergic contact dermatitis

This disease refers to the delayed allergic skin reaction in children to allergens in the surrounding environment. The incidence of this disease is similar to that of the adult population, and it is rarely detected in pediatric diagnosis, even less than one-tenth of all patch tests. Most children with allergic contact dermatitis are missed. In daily life, emollients, preservatives, topical drugs, perfumes, metals, etc., can affect the onset of disease. In the study report, allergic contact dermatitis and AD disease can occur simultaneously, which makes the diagnosis of atopic dermatitis more difficult. The acute phase of the disease includes erythema plaques, eczematous papules, pruritus, etc. Chronic phase may present pigmentation, skin cracks or lichenization^[10].

2.6. Food impact

Food allergy is a target factor for accurate treatment of all allergic diseases. Under the influence of food pathophysiological characteristics, the allergy of biomarkers can be defined to ensure clinical effects and diagnostic results. According to the research report^[11], foods such as shrimp, hazelnuts, peanuts, eggs and milk have high specificity in allergy diagnosis. During the diagnosis of AD disease, it is known that the defective skin barrier is more allergic after contact with food, which is also related to the genetic action of skin tissue and immunoglobulin-mediated food. At present, during the treatment of children with AD disease, it is necessary to understand the treatment and prevention measures of food allergy, and give certain early diagnosis and evaluation and treatment of psychological disorders^[12].

The skin barrier function can inhibit the entry of sunlight, microorganisms, antigens, etc., and has the inherent function of shrinking and preventing water loss. The skin barrier function can maintain the normal operation of the human body, regulate the absorption of foreign substances through the skin, and regulate the evaporation of skin water. Abnormal lipid composition and sebum moisture in human skin will damage skin

barrier function, lead to abnormal PH value of skin tissue, and affect the integrity of the stratum corneum. Studies have shown that childhood AD is one of the inflammatory diseases with obvious skin barrier function impairment.

3. Drug treatment research

3.1. TCM treatment

Chinese medicine is selected for the local treatment of AD disease in children, and the prescription includes the mixed treatment of chestnut, platycypress, leshu, wild rose and dogwood in a ratio of 1:1:1:1:4^[13]. The drug can inhibit NO and IL-4 in children and reduce the release of mast cell degranulation markers. At the same time, enhancing drug concentration can reduce the release of DPPH free radicals. Studies have reported that providing Ziyun cream treatment for children is ideal for the control of inflammatory response, and can also improve the state of local skin damage, and the actual effect is similar to tacrolimus. At the same time, it can be seen from biological activity studies that traditional Chinese medicine has obvious effects of inhibiting angiogenesis, anti-oxidation, anti-allergy and anti-inflammatory. After medication, children with AD can improve skin barrier function in time, inhibit discomfort symptoms, and have high safety.

3.2. Crenoral

Creborol is a PDE4 inhibitor, which can reduce the level of cyclic adenosine phosphate and reduce the inflammatory response in children with AD. According to the study report, through the overall static test of children, it can be seen that the use of clariborol in the treatment of AD children is ideal. In addition, the use of the drug in the US Food and Drug Administration has been extended to infants aged 3 months and older, with gradual approval in China in 2020.

3.3. Depruliumab

The drug is a common monoclonal antibody biologic in clinical practice and has inhibitory effects on IL-3 and IL-4, the signal transduction. In the report, it was shown that the efficacy of dupriuzumab in the treatment of children with AD aged 6-11 years was ideal. The adverse reactions after treatment only appeared at the injection site,

including eosinophil increase, conjunctivitis, etc. Most of them were mild and could be resolved by themselves.

3.4. Tapinaro

The drug is a therapeutic aromatic pidgin receptor modulator, which can raise the expression of skin barrier genes and adjust the expression of Th2 cytokines after administration to avoid inflammatory oxidative damage in children. Some studies have proposed that medication in children with AD can improve their discomfort symptoms in time, with ideal improvement efficiency and fewer adverse reactions^[14].

3.5. Targeted therapy

Childhood AD involves multiple immune modes in clinical practice, the main mechanism of which is type 2 natural lymphocytes, TH2 cells and related factors driving immune response. Therefore, the targeted therapy of type 2 pathway should be emphasized during clinical treatment. At present, there have been a variety of targeted therapies for children with AD disease in clinical practice.

3.6. Wet wrap treatment and emollients

Studies in China have shown that the use of emollients can be used as adjuvant therapy for children with moderate and severe AD, thereby avoiding excessive use of glucocorticoid drugs and helping children repair skin barrier function. At the same time, with the progress of medical research, it is clinically proposed to take wet wrap treatment for severe refractory children, and select gauze wrap treatment based on local drug use and skin moisturization, which can significantly improve the discomfort symptoms of patients and restore the skin barrier function of patients.

3.7. Oral JAK inhibitors

A variety of cytokines participate in the inflammatory process of AD disease, indicating that JAK inhibitors have a better oral effect. The drug can inhibit the proliferation of some growth factors and cytokines. In the study report, it was pointed out that the disease improvement rate of AD children after medication is as high as more than 90%. At the same time, the drug has good tolerance, no obvious adverse reactions in children, and the drug safety is high.

3.8. Remote diagnosis and treatment of diseases

At present, telemedicine plays an important role in the treatment of AD disease. With the help of telemedicine, the diagnosis of children's AD disease is evaluated, and the appropriate treatment plan is selected according to the actual condition of the patient. Some data suggest that remote diagnosis and treatment can ensure the diagnosis accuracy of about 85%^[15]. Children with mild AD can improve their disease under the management of health care doctors, and children with severe AD can be guided to the hospital for treatment in time.

4. Summary

The pathogenesis of childhood AD is diverse and complex, and with the deepening of clinical understanding of the pathogenesis of childhood AD, the treatment methods will be more diversified. Although the treatment of moderate and severe AD in children is still a great challenge, with various new therapeutic methods, especially the use of targeted therapy for moderate and severe AD in children, doctors and patients are full of hope for the treatment of the disease.

Disclosure statement

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Advances in the Investigation of the Oncological Functions and its Target Therapy of Interleukin-1 Receptor-associated Kinase 1 (IRAK1)

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Abstract:

Interleukin-1 receptor-associated kinase 1 (IRAK1) plays as a pivotal regulator within the innate immune signaling and inflammatory processes. Being a critical component in many signaling pathways, emerging evidence strongly suggests the involvement of IRAK1 in the pathophysiology of cancers, thereby rendering it an attractive target for therapeutic intervention. Notably, selective IRAK1-inhibitory molecules have been identified, opening promising avenues for the therapy of tumor. In this review, we also delve into the challenges and future prospects in this field, emphasizing the importance of gaining a deeper understanding of IRAK1 regulation in tumors and the potential of combination therapies targeting IRAK1.

Keywords:

Interleukin-1 receptor-associated kinase 1 (IRAK1)
Tumor progression
Tumor immunity
IRAK1 inhibitors

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1. Introduction

Nowadays, it is increasingly evident that immune system not only comes into play in tumor suppression, known as cancer immunosurveillance, but also contributes to tumorigenesis and tumor progression ^[1]. Accumulating evidence highlights the pivotal function of interleukin-1 receptor-associated kinases (IRAKs) family in immune responses as well as its altered expression in different

types of cancer. Within the IRAKs, a serine/threonine kinases family, four distinct members are identifiable: IRAK1, IRAK2, IRAK3 (also recognized as IRAK-M), and IRAK4 ^[2]. It's important to note that among these, only IRAK1 and IRAK4 exhibit kinase activity ^[3,4]. This review concentrates on the latest progress made in comprehending the significance of IRAK1 in the advancement of tumors as well as potential therapeutic interventions.

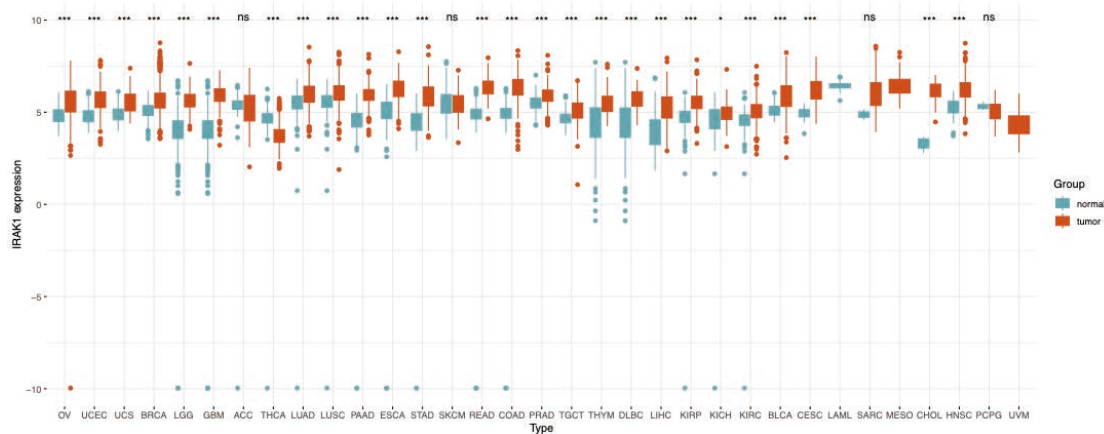


Figure 1. The expression of IRAK1 in different tumors and their paired normal tissues. The dysregulation and aberrant expression of IRAK1 have been subject to analysis across diverse cancer types. Utilizing data from the Cancer Genome Atlas (TCGA) database, it aimed to elucidate IRAK1's potential involvement in various malignancies compared with their corresponding normal tissues. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

2. The expression of IRAK1 and its effects in different cancers

Dysregulation and aberrant activation of IRAK1 have been associated with various effects on tumors (**Figure 1**). The role of IRAK1 in tumor includes promoting tumor growth, survival, inflammation, immune evasion, therapeutic resistance, angiogenesis, and metastasis. Here are some of the effects of IRAK1 in specific tumors.

2.1. Hepatocellular carcinoma

IRAK1 exhibits significant expression in hepatocellular carcinoma (HCC) cell lines and tumor tissues, indicating its feasible involvement in HCC development, which contributes to cancer cell proliferation and the inflammatory tumor microenvironment^[5]. The tumor suppressor serine/threonine-protein kinase 4 (STK4) enhances TLR3/4-activated IFN- β production through IRAK1 binding and phosphorylation^[6]. This leads to IRAK1 degradation and prevents the development of inflammation-related HCC. Furthermore, Cheng and colleagues pinpointed AKR1B10 as a fresh downstream target of IRAK1, and AKR1B10 is usually used as a biomarker of HCC, underscoring a previously unrecognized relationship between these molecules^[7].

2.2. Nasopharyngeal carcinoma

In the context of Nasopharyngeal carcinoma (NPC) metastasis, S100 calcium-binding protein A14 (S100A14)

exhibits a suppressive effect on metastasis by facilitating the ubiquitin-mediated degradation of IRAK1, which blocks cellular migration in NPC^[8]. Additionally, Liu *et al.* discovered that IRAK1 has potential function in drug resistance and poor prognosis in NPC. Specifically, IRAK1 is essential to the expression of S100A9, and the IRAK1/S100A9 axis contributes to drug resistance and unfavorable outcomes in NPC^[9].

2.3. Low-grade glioma

Notably, comprehensive studies have substantiated that the high level of IRAK1 in LGG exerts an oncogenic function by inhibiting cell apoptosis and promoting LGG malignancy^[10]. IRAK1 is warranted to enhance the prognosis and treatment outcomes for LGG patients.

2.4. Colorectal cancer

Aberrant expression of IRAK1 in colorectal cancer (CRC) is linked to malignant phenotypes, and targeting its expression could mitigate the inflammatory process and modulate the downregulation of epithelial-mesenchymal transition (EMT) in mice^[11,12]. Furthermore, scientists have discovered that the loss of heterogeneous nuclear ribonucleoprotein I (hnRNRI) within the intestinal epithelial cells undermines the immune adaption process in newborns, ultimately leading to colitis and colorectal cancer^[13].

2.5. Breast cancer

Research has revealed a substantial decrease in the expression of IRAK1 following neoadjuvant chemotherapy, which aligns with a noticeable reduction in tumor size ^[13]. In the context of triple-negative breast cancer (TNBC), IRAK1 upregulation confers a growth advantage and contributes to acquired resistance to paclitaxel treatment ^[14]. Restraining the phosphorylation of IRAK1 has demonstrated increased apoptosis and reduced migration in TNBC ^[15].

2.6. Prostate cancer

IRAK1 exhibits significant overexpression specifically in prostate cancer (PCa) compared to normal tissues. This overexpression is particularly observed in luminal epithelial cells of Pca ^[16]. Moreover, IRAK1 is found to exhibit varying expression levels between benign and malignant samples within a patient cohort ^[17].

2.7. Non-small cell lung cancer

IRAK1 is highly expressed in non-small cell lung cancer (NSCLC) and is considered a new inflammation-related marker ^[18]. In NSCLC with epidermal growth factor receptor (EGFR) mutation, the IRAK1/NF- κ B axis demonstrates a significant role in standing up to EGFR tyrosine kinase inhibitors (TKIs) ^[19]. Additionally, the expression of IRAK1 in non-tumor cells, such as tumor-associated macrophages (TAMs), can negatively impact the anti-tumor activity against tumor cells ^[20].

2.8. Endometrial carcinoma

The reduction of IRAK1 expression in endometrial carcinoma (EC) cells led to distinct outcomes: it prompted cell cycle arrest and apoptosis while concurrently restraining cell migration and invasion ^[21]. Another study uncovered that the transfer of miR-192-5p via specific exosomes derived from TAMs could inhibit the IRAK1/NF- κ B signaling pathway, leading to the suppression of tumor formation, inhibition of EMT in EC cells, and promotion of EC cell apoptosis ^[22].

2.9. Squamous cell carcinomas

Within squamous cell carcinoma (SCC), the pro-oncogenic impact and tumorigenic properties of Desmoglein 2 (Dsg2) are achieved through the alteration

of IRAK1 and its downstream target IL-8 ^[23]. Furthermore, in Oral SCC, miR-146 is up-regulated and acts as an oncogenic molecule ^[24]. Another significant finding reveals that IRAK1 is transcriptionally upregulated by the chromatin-binding DEK protein, promoting cell survival ^[25]. In an effort to heighten the sensitivity of chemotherapy-resistant cells to chemotherapy, inhibiting IRAK1 pharmacologically can consider as a potentially effective cytostatic method ^[26].

2.10. Melanoma

Within melanoma cells, the expression of chemokines and cytokines associated with cancer cell survival, division, and the promotion of angiogenesis strongly correlates with the activation of IRAK1/IRAK4 signaling ^[27]. Melanoma and its stem cells could respond to the aurora kinase inhibitor CCT137690 because of its effect on a significant decrease in the expression of IRAK1 ^[28].

2.11. Activated B-cell-like diffuse large B-cell lymphoma

In activated B-cell-like diffuse large B-cell lymphoma (ABC DLBCL) with MyD88 mutation, IRAK1 functions as a scaffold protein, facilitating tumor cell proliferation and apoptosis ^[29].

2.12. Stem cell leukemia/lymphoma syndrome

IRAK1 regulates the activity of interferon-gamma (IFN- γ), which facilitates the accumulation of myeloid-derived suppressor cells. These cells inhibit the T-cell response to leukemic cells, contributing to the progression of stem cell leukemia/lymphoma syndrome (SCLL) ^[30].

2.13. Acute myeloid leukemia

IRAK1 is implicated as an oncotarget in acute myeloid leukemia (AML). Targeting IRAK1 has shown promising results in reducing AML progenitors in vitro and decreasing the leukemia burden in xenograft model ^[31]. Moreover, IRAK1 has been identified as a viable target to overcome adaptive resistance in the FLT3-mutant subtype ^[32].

2.14. T-cell acute lymphoblastic leukemia

IRAK1 plays a critical role in T-cell acute lymphoblastic leukemia (T-ALL) cell proliferation and survival through

the stabilization of the antiapoptotic protein MCL1^[33]. Additionally, the DNA methylation of miR-204 has been shown to promote cell proliferation and enhance apoptosis through IRAK1^[34].

2.15. Mixed lineage leukemias

In mixed lineage leukemias (MLL), the inhibition of IRAK1/4 has been shown to delay leukemia progression and improve survival in murine models by stabilizing the normal MLL protein^[35].

2.16. Waldenström macroglobulinemia

Waldenström macroglobulinemia (WM) typically manifests with the presence of a MYD88 mutation. In WM cells, inhibiting the kinase activity of IRAK1/4 leads to apoptosis in WM cells^[37].

3. Application of irak1 inhibitor in tumor therapy

3.1. IRAK1/4 inhibitor

The IRAK1/4 inhibitor shows potential in weakening the stability of the antiapoptotic protein MCL1, demonstrating promising potency in combination treatment for T-ALL with ABT-737 or vincristine^[36]. In the context of anaplastic thyroid cancer (ATC), inhibition of IRAK1 exhibits anti-proliferation and anti-tumor effects its cell lines^[37]. Moreover, combining IRAK-1/4 Inhibitor with ABT-737 proves more effective in restoring white blood cell count in peripheral blood and reducing mortality in a T-ALL mouse model^[38]. Additionally, this inhibitor sensitizes the curative effect of methotrexate chemotherapy in breast cancer cell lines^[39]. In TNBC, the IRAK1/4 inhibitor induces massive apoptosis to reverse paclitaxel resistance^[16]. To address MDS and eliminate MDS-initiating clones, an IRAK1/4 inhibitor is employed to impair MDS cells while preserving normal CD34 positive cells^[40]. Furthermore, the IRAK1/4 inhibitor decreases the expression of inflammatory cytokines and prevents tumor growth in colorectal cancer. Notably, it also inhibits EMT, effectively slowing down colitis-induced tumorigenesis^[12].

3.2. NCGC1481

NCGC1481 demonstrates a novel strategy to overcome

adaptive resistance via inhibiting IRAK1 and its associated signaling^[34]. This approach holds great promise in enhancing treatment outcomes and addressing the challenge of adaptive resistance in AML.

3.3. JH-X-119-01

JH-X-119-01 has been published as a highly potent and selective covalent inhibitor of IRAK1. In the MYD88-mutated B-cell lymphomas, JH-X-119-01 acts as a potent antiproliferative effector, offering a potential therapeutic approach^[41]. Moreover, JH-X-119-01 shows favorable outcomes in LPS-induced septic mice. It not only improves the survival of septic mice but also protects macrophages with reduced toxicity when compared to non-selective IRAK1/4 inhibitors^[42].

3.4. Pacritinib

Recent evidence has shown that pacritinib also acts as a specific inhibitor of IRAK1. Building on this, pacritinib exerts a dual effect on the immune system and tumors by restraining IRAK1. It attenuates leukemogenesis through the suppression of CD4+/CD8+ T-cells and myeloid-derived suppressor cells. Furthermore, pacritinib demonstrates potential as an anti-pan cancer inhibitor by effectively inhibiting tumor proliferation via impacting the PD-1/PD-L1 axis and mediating immunosuppression^[33,43].

3.5. HS-243

HS-243, a takinib analog, is used to suppress IRAK1 in human rheumatoid arthritis, it exhibits a notable responsiveness to cytokine/chemokine signaling in fibroblast-like synoviocytes^[44].

3.6. Takinib

Takinib was developed as a selective inhibitor of TAK1, but because of the similar ATP-binding pocket, takinib could also be used as the inhibitor of IRAK1^[45,46].

3.7. JNJ-1013

Recognizing the significance of IRAK1's scaffolding function, which is crucial for tumor cell survival and distinct from its kinase activity, an IRAK1 degrader Degradar-3 (JNJ-1013) specifically aims to disrupt this function. JNJ-1013 displays valid anti-proliferative

properties in ABC DLBCL cells possessing MyD88 mutation^[30].

4. Conclusion

Amid its functions, IRAK1's involvement in cancer

emerges especially. This association emphasizes the potential of IRAK1 as a valuable target for therapeutic intervention, with selective IRAK1 inhibitors garnering attention. In the broader context, our comprehensive review unveils IRAK1's multifaceted contributions to tumorigenesis, tumor immunity, and progression.

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Diagnosis and Treatment of Appendicitis Combined with Delayed Egerter Blood Infection

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Abstract:

Objective: To summarize the effective diagnosis and treatment methods for appendicitis complicated with delayed Escherichia coli blood infection.

Methods: A retrospective analysis of the medical course of one patient with appendicitis complicated with delayed E. coli blood infection was conducted.

Results: The main clinical symptom of appendicitis complicated with delayed E. coli blood infection is high fever. Due to the long culture time of delayed E. coli, early empirical antimicrobial therapy is extremely important. Cefoperazone-sulbactam is one of the effective drugs for treating appendicitis complicated with delayed E. coli blood infection.

Keywords:

Slow Egerterella
Blood infection
Appendicitis

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1. Data analysis

The patient, male, 52 years old, visited the hospital emergency department at around 10:06 AM on October 30, 2022, due to “fever for one day.” The patient developed a fever without any obvious cause about one day prior, with the highest temperature reaching 41°C. He experienced chills, shivering, headache, and dizziness, but had no nausea, vomiting, sore throat, coughing, sputum production, abdominal pain, diarrhea, frequent urination, urgency, or dysuria. After self-administering medication,

his symptoms did not improve. The specific medications taken are unknown. Following an investigation by the fever clinic, he was admitted to the department’s intensive care unit. After symptomatic treatment for fever reduction, he broke out in a heavy sweat. The hospital administered cefmetazole for infection control and fluid replacement. Currently, his blood pressure is lower than baseline. For further diagnosis and treatment, he was admitted to the department with “undetermined fever.” Throughout the course of the illness, the patient has been

in good spirits, able to eat, and has normal bowel and bladder function. Past medical history includes over 10 years of hypertension, regularly taking Lopressor and Irbesartan for antihypertensive treatment, which has controlled his blood pressure. One year ago, he underwent coronary stenting after a myocardial infarction and now takes aspirin, clopidogrel, and rosuvastatin regularly. On admission, physical examination revealed: temperature 39°C, pulse rate 88 beats per minute, respiratory rate 20 breaths per minute, blood pressure 137/63 mmHg. He was wheeled into the ward, conscious and cooperative during the examination. His lips were not cyanotic, and there were no rashes, jaundice, or petechiae on the skin or mucous membranes. Physical examination of the heart and nervous system showed no abnormalities, and auscultation of the lungs revealed normal breath sounds coarse, wet rales heard at the right lung base. Abdomen soft, mild tenderness below the xiphoid process, no rebound tenderness or muscle rigidity, liver and spleen not palpable, shifting dullness (-), normal bowel sounds, no water-hammer sound, positive percussion pain in both renal areas. Ancillary tests: Complete blood count: White blood cells: $4.70 \times 10^9/L$; Neutrophil ratio: 77.20%; Red blood cells: $4.17 \times 10^9/L$; Hemoglobin: 131.00 g/L; Platelets: $120 \times 10^9/L$; Urine routine: Ketones 1+. Electrolytes and kidney function showed no significant abnormalities.

2. Medical treatment process

After admission to the emergency internal medicine department, active treatment was provided with intravenous administration of cefoperazone and tazobactam sodium for anti-infection, oral administration of ibuprofen suspension, and intramuscular injection of paracetamol for fever reduction and other symptomatic supportive treatments. On the day of admission, the patient developed a high fever with a peak temperature reaching 41°C. An enhanced abdominal CT scan indicated peri-appendiceal exudation. The general surgeon was consulted, and the initial diagnosis was appendicitis with exudation. Due to the presence of peri-appendiceal exudation, surgical resection was not suitable. It was recommended to complete relevant examinations to determine the cause of the fever, provide

symptomatic supportive anti-inflammatory treatment, and closely monitor the patient's condition changes. Continued symptomatic supportive treatments such as anti-infection were provided. On the second day of admission, follow-up tests included routine blood tests, liver function, kidney function, electrolytes, C-reactive protein, procalcitonin, 11 respiratory virus tests, blood culture, coagulation profile, D-dimer, myocardial enzymes, infectious disease screening, peripheral blood morphology analysis, and bedside electrocardiogram. On the second day of admission, outpatient blood culture results showed: aerobic bottle initial report: Gram-negative bacilli; anaerobic bacteria initial report: Gram-positive bacilli. The current diagnosis is "fever of unknown origin, bacteremia, appendicitis with exudation, hypertension, coronary artery atherosclerotic heart disease, post-coronary stent surgery, hypokalemia, multiple cysts in both kidneys." Further relevant auxiliary examinations were actively completed, and the results of the enhanced abdominal CT scan are currently available. No specific infection site was indicated, but blood culture reported the presence of bacteria. The specific results will be reported later. Currently, the antibiotics used are cefoperazone and sulbactam, which can cover infections of abdominal organs. Although the patient has been feverish since admission, there has been no recurrence of chills, indicating effective anti-infection treatment. Treatment will continue as is for now, with close monitoring of the patient's abdominal condition. If necessary, follow-up abdominal CT scans or other relevant examinations may be required. On the third day of hospitalization, C-reactive protein: 119 mg/L, Procalcitonin: 2.330 ng/mL; Complete blood count: White blood cells: $4.70 \times 10^9/L$, Neutrophil ratio: 77.20%, Red blood cells: $4.17 \times 10^9/L$, Hemoglobin: 131.00 g/L, Platelets: $120 \times 10^9/L$; Urinalysis: Ketones 1+. No significant abnormalities were found in electrolytes or renal function. Based on the patient's medical history, physical examination, and auxiliary tests, the following considerations are made:

- (1) Blood cultures indicate Gram positive bacilli and Gram negative bacilli. Temporary administration of cefoperazone and sulbactam for anti-infection treatment. The peak temperature and related inflammatory indicators have both decreased, suggesting effective anti-infection treatment.

There is currently no evidence of urinary tract infection, so continue current anti-infection treatment and schedule a follow-up abdominal CT scan.

- (2) The patient has diarrhea without significant abdominal pain. Please consult the gastroenterology department for assistance in diagnosing and adjusting medication. Oral administration of *Bifidobacterium trilactis* enteric-coated capsules is recommended.

On the fifth day of hospitalization, physical examination of the heart, lungs, and abdomen showed no abnormalities. Rechecked C-reactive protein: 7.25 mg/L, procalcitonin: 0.387 ng/mL; blood culture for five days showed no growth of bacteria or anaerobes. The patient had not been feverish in the past three days, and routine blood tests, white blood cell count, and neutrophil ratio were significantly lower than before. It is considered that the anti-infection treatment has been effective, and further consolidation therapy is recommended. During the five-day hospital stay, the patient's vital signs remained stable, with no fever, abdominal pain, diarrhea, or significant discomfort. After communicating with the patient and their family, they requested discharge to continue treatment at a local hospital. It was informed that anti-infection treatment may still lead to perforation, abscess formation, peritonitis, or septic shock. The patient and their family expressed understanding but insisted on discharge. A higher-level doctor was consulted to approve the discharge. On November 10th, the blood culture returned a slow-growing *Escherichia coli*.

3. Discussion

Cheratococcus elegans is an obligate anaerobic gram-positive bacillus that grows slowly and forms visible colonies within five days. It was first isolated from human feces by scientist Ernst Egerth in 1935 and initially classified as an anaerobic bacillus. After sequencing in 1999, it was subdivided into the Ernst Egerth genus [1]. This bacterium is mainly found in the digestive tract and is a rare pathogen of appendicitis, liver abscess and renal abscess. Slow-growing bacteria can enter the blood with primary diseases and form bacteremia [2]. At present, there are few reports on the blood infection

caused by slow Egerteria both at home and abroad. This study summarizes the effective diagnosis and treatment of appendicitis combined with slow Egerteria blood infection based on the diagnosis and treatment process of one patient with appendicitis combined with slow Egerteria blood infection.

Infections caused by slow Egerterella include blood infection, myelitis, liver abscess, kidney abscess, etc., and are also related to appendicitis in adults and children. Blood infection is rarely reported, and if not treated effectively in time, it will endanger the life safety of patients [3,4]. According to the latest literature at home and abroad, when slow Egerterella causes blood infection, the average time of positive blood culture is about one week [5]. The time of blood culture positivity in this study was similar to that of the patients, mainly because of the slow growth of the bacteria. Therefore, empirical antibiotic therapy is particularly important. Summarizing the clinical characteristics and antibiotics used for delayed *Escherichia coli* bloodstream infection can provide reference for empirical clinical treatment.

A clinical study of a case of slow Egerterella bloodstream infection abroad found that the main symptoms of patients at admission were fever, nausea and vomiting, and abdominal pain and diarrhea [6]. Most of the clinical symptoms of patients in this study were consistent. Although the number of cases observed in this study was limited, it cannot be ruled out that gastrointestinal diseases are a high-risk factor for delayed *E. coli* bacteremia. The reason may be that delayed *E. coli* can colonize the normal gastrointestinal mucosa, and when the gastrointestinal mucosa is damaged or the body's immune function declines, this bacterium can invade the bloodstream, leading to bacteremia. In a clinical study of cases in Canada, it was found that almost all patients with delayed *E. coli* bacteremia had underlying gastrointestinal diseases, with adult appendicitis accounting for the highest proportion at 32.8% [7,8]. Because of the few clinical reports on this bacterium, there is no unified drug guide for the selection of antibiotics. Many domestic and foreign literature reports have proved that slow Egerter bacteria are resistant to penicillin, but highly sensitive to amoxicillin, metronidazole and vancomycin [9,10].

4. Conclusion

In short, the main clinical symptoms of appendicitis combined with delayed Egerter blood infection are high fever and mild right lower abdominal pain, which often leads to missed diagnosis by clinicians. Blood culture and 16sRNA gene sequence analysis can be used to identify

delayed Egerter^[11,12]. However, the cultivation time is long, so it is necessary to apply empirical antibiotics in advance. This study proved that cefoperazone-sulbactam sodium was one of the effective antibiotics for the treatment of appendicitis combined with delayed Egerter blood infection.

Disclosure statement

The authors declare no conflict of interest.

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Advancements in Molecular Detection Technology of Senecavirus A: A Comprehensive Review

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Abstract:

In recent years, the *Seneca Valley virus* (SVV) has impeded the sustainable development of the swine industry, posing a major challenge to disease prevention and control in swine populations. The emergence of *Seneca Valley virus* (SVV) presents twofold challenges for swine production systems: it not only significantly interferes with routine farm management protocols, but also substantially complicates clinical differentiation due to its pathognomonic similarity to foot-and-mouth disease (FMD) and swine vesicular disease (SVD). To effectively control the spread of the virus, developing a more convenient and user-friendly rapid detection scheme has become the key focus of disease diagnosis innovation. This paper collected reports on the innovation and application of molecular detection technology of the *Seneca virus*, and sorted out these methods, to provide some scientific basis for the prevention and control of the SVV epidemic in the future, reduce economic losses, and prevent further spread of the virus.

Keywords:

Seneca virus A
Molecular detection
Rapid detection
RPA

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1. Introduction

Seneca Valley virus (SVV), also known as *Seneca Virus A* (SVA), is classified as the sole species within the genus *Senecavirus* (family *Picornaviridae*)^[1]. The clinical manifestations of SVV infection in swine populations closely resemble those induced by vesicular diseases, particularly *Foot-and-mouth disease virus* (FMDV) and

Swine vesicular disease virus (SVDV), as evidenced by comparative histopathological analyses. SVV can cause vesicular lesions on the mouth, nose, and hoof crown of adult pigs, with occasional symptoms such as fever and diarrhea, and increase the mortality of newborn piglets. This makes clinical diagnosis difficult. Also, there is currently no commercially available SVV vaccine. This

has caused a lot of economic losses to the pig breeding industry.

Early diagnosis through validated assays represents a pivotal strategy to control epidemic transmission of SVV in swine populations. The timeliness and accuracy of detection are key determinants for interrupting viral spread, especially within intensive production systems where rapid pathogen transmission occurs via direct contact or fomites. Molecular diagnosis has quickly become a popular pathogen detection method because of its fast detection speed and high sensitivity. Recent advancements in diagnostic technologies have substantially enhanced assay performance, with notable improvements in processing efficiency and analytical sensitivity across multiple detection platforms. In this paper, the molecular detection methods of SVV reported in recent years are sorted out, which provides more choices for the detection methods of this pathogen and also provides a reference for the development of rapid detection technology.

2. Introduction of SVV

Seneca Valley virus (SVV) was incidentally isolated in 2002 from the PER.C6 (transformed fetal retinoblast) cell line [2]. In 2015, Brazil first reported an outbreak of SVV in pigs [3]. Subsequently, the United States [4], Thailand [5], Vietnam [6], Colombia [7], and other countries reported that SVV broke out in their country.

The susceptible animals of *Seneca virus* are pigs, and pigs of all ages are susceptible. Viruses can spread through direct and indirect contact with viral pollutants or aerosols. The pathogenicity and fatality rate of the virus are related to the age, breed, and geographical factors of pigs, and generally occur in spring and autumn [8]. Current epidemiological studies have demonstrated a significant association between SVV infection and elevated mortality rates in neonatal piglets during perinatal stages. The mortality rate of adult pigs is extremely low, usually subclinical infection or recessive infection. The mortality rate of piglets is higher than that of adult pigs, and the incidence rate of sows is as high as 70–90% [9].

3. SVV detection methods

3.1. Pathogenic detection

Virus isolation is the most accurate method to identify and diagnose SVV. It has been found that cells that can be used to isolate the *Seneca virus* include PER.C6 [10], NCI-H1299 [11], HEK293T [12], ST [13], PK-15 [14], and so on. While virus isolation-based detection protocols for SVV demonstrate high diagnostic specificity, their technical complexity, requiring specialized biosafety containment facilities (BSL-2+), and prolonged turnaround time (> 48 hours post-sample collection) render these methods suboptimal for field applications requiring expedited diagnostics during outbreak investigations. The clinical similarity between SVV and FMDV infections in swine poses significant diagnostic challenges. Given that FMDV is a zoonotic pathogen, virus isolation protocols for differential diagnosis necessitate stringent biosafety containment measures (BSL-3), particularly during epizootic investigations where misidentification could amplify public health risks.

3.2. Antibody detection

Antibody detection methods are suitable for handling a large number of samples in epidemiological surveillance or mass diagnostic programs [15]. Serodiagnostic approaches currently implemented for SVV surveillance in swine populations encompass indirect enzyme-linked immunosorbent assay (iELISA) [16], competitive ELISA (cELISA), indirect fluorescent antibody (IFA) testing, and virus neutralization test (VNT) [17,18]. Compared with other Antibody detection assays, ELISA is famous for its high sensitivity, specificity, convenience, rapid, and cost-effectiveness. SVV ELISAs have been developed to detect IgG antibodies against non-structural proteins such as 2C, 3C, 3D, L, and 3AB proteins and Virus-like particles (VLPs) [19,20]. However, serological detection needs a period after virus infection to produce a reliable antibody reaction, so it cannot meet the requirements of rapid detection in the early stage of the epidemic.

3.3. Molecular biological detection

Nucleic acid-based detection methodologies in molecular diagnostics primarily involve polymerase chain reaction (PCR) and its advanced derivative, real-time quantitative reverse transcription PCR (qRT-PCR)

^[21]. Currently, these techniques serve as the primary standard for diagnosing animal vesicular diseases due to their rapidity, sensitivity, and strong specificity in pathogen identification. Conventional PCR relies on agarose gel electrophoresis for result analysis. While cost-effective, this method involves biohazard risks from nucleic acid dyes and requires both thermal cyclers and horizontal electrophoresis units, limiting its application in settings with unstable power supply. Moreover, PCR detection requires not only a precise thermal cycler but also a horizontal electrophoresis instrument, which is very inconvenient when there are not enough electricity resources. qRT-PCR detection methods have high sensitivity and can detect rare targets, which is a very mature detection method. However, this method requires professional laboratory equipment and operators. Meanwhile, to ensure accurate temperature control, it is necessary to supply power to the fluorescence quantitative PCR instrument continuously. A multiplex real-time RT-PCR assay for detecting and distinguishing FMDV from SVV was also recently developed and evaluated ^[22]. The method can identify FMDV and SVV at the same time, aiming at improving the efficiency of disease detection.

3.4. Development of molecular detection technology

3.4.1. Molecular detection method based on polymerase chain reaction technology

Insulated isothermal PCR (iiPCR), a fluorescent probe-mediated nucleic acid amplification system under constant temperature conditions ^[23]. iiPCR technique achieves nucleic acid amplification through sequential thermal cycling across distinct temperature phases (denaturation, annealing, and elongation) within a microfluidic capillary, facilitated by a portable thermal control system. This approach employs an integrated nucleic acid processing system capable of executing automated PCR amplification and result interpretation within approximately one to one and a half hours. Nucleic acid amplification can be completed in 30–40 minutes. Two molecular assays targeting conserved SVV genomic regions were established for viral RNA detection: a reverse transcription PCR (RT-PCR) assay specific to the 5'UTR and a reverse transcription insulated isothermal PCR (RT-iiPCR) method focusing on the 3D gene, with

inter-assay consistency reaching 98.4% ^[24].

Reverse transcription droplet digital PCR (RT-ddPCR) is considered to be an accurate and sensitive technique, showing good sensitivity and specificity in SVV detection. Beyond diagnostic applications, RT-ddPCR facilitates absolute SVV RNA quantification independent of calibration curve construction ^[25]. However, this method requires high personnel operation, and it still can't get rid of expensive precision instrument detection, which can't meet the requirements of on-site rapid detection ^[26].

3.4.2. Molecular detection method based on constant temperature amplification technique

Constant temperature amplification technology is a kind of molecular biological detection method at constant temperature. This methodology demonstrates operational simplicity, minimal instrumentation requirements, and rapid processing timelines when contrasted with standard PCR protocols. At present, this technology is mainly divided into LAMP ^[27], RCA ^[28], RAA ^[29], and RPA. Through the engineering of sequence-specific primers and enzyme systems, the exponential amplification of target DNA or RNA can be realized at constant temperature.

Loop-mediated isothermal amplification (LAMP) is an efficient DNA amplification method, which can rapidly amplify the target DNA sequence at constant temperature. LAMP technology uses multiple primers and DNA polymerase to realize continuous amplification of target DNA. LAMP technology shows good sensitivity and specificity in SVV detection, and its operation is relatively simple, so it is a potential rapid detection method.

Recombinant enzyme polymerase amplification (RPA) is a new isothermal amplification technology, that can rapidly amplify the target nucleic acid sequence at low temperature (37–42 °C) ^[30]. At present, RPA technology can be divided into three categories, including basic RPA, fluorescent RPA, and lateral flow RPA ^[31]. The fundamental RPA system comprises four core components: recombinase, ssDNA-binding protein, DNA polymerase, and amplification-optimized buffer formulation. After adding templates and primers, it can react quickly at room temperature, and the results can be judged within 30 minutes by gel electrophoresis.

The principle of fluorescent RPA is similar to that of fluorescent quantitative PCR. During the amplification reaction, this RPA can cut the recognition sites of special fluorescent probes through the nucleic acid exonuclease in the reagent and release fluorescent signals, which can be combined with a fluorometer for real-time quantitative detection. In response to the lack of professional detection equipment in some areas, some companies have developed portable fluorescence meters that can even be powered by solar energy. These portable fluorescence meters are small in size and light in weight, and nucleic acid amplification can be observed in real-time on the spot through RPA fluorescence meters ^[32].

4. Application of isothermal amplification technology in SVV detection

Recently, isothermal amplification technology has been widely used in the rapid detection of SVV ^[33]. The researchers designed primers and probes for isothermal amplification of SVV-conserved regions, which showed good sensitivity and specificity in detection. Some researchers combined RPA technology with the CRISPR/Cas12a system to develop an accurate and sensitive diagnosis and detection platform for SVV. This methodology demonstrated an analytical sensitivity threshold of 10 copies per reaction ^[34]. This method integrates RPA reaction and CRISPR/Cas system in a centrifuge tube, which reduces the risk of sample pollution and has great practical application potential in an environment with limited resources.

5. Summary

At present, most molecular detection technologies need harsh laboratory environments and professional detection personnel. Infectious diseases are more likely to spread in areas with difficult conditions or poor sanitation.

Therefore, developing more convenient, sensitive, and fast on-site detection methods is the direction of future research. By sorting out the main molecular detection methods at present, RPA has shown its unique advantages in the field of rapid on-site detection because of its characteristics of rapidity, simplicity, and convenience, and has been gradually paid attention to and applied to the detection of zoonotic pathogens. The reaction temperature of RPA is close to human body temperature and its reaction time is short (5–20 min), which makes it more suitable for on-site rapid detection. In recent years, scholars have been trying to combine RPA with LFD, CRISPR/ Cas system, and other diagnostic techniques to develop more sensitive and convenient molecular diagnostic methods. It has been reported that a nucleic acid detection method without RNA is described, which greatly improves the detection speed ^[35]. Another multienzyme isothermal amplification technique used by some scholars is called multienzyme isothermal rapid amplification (Mira), which uses a recombinant enzyme named *Streptomyces azure* recA (SC-recA) to improve the reaction stability and anti-interference ability ^[36]. Researchers have engineered a regenerable dual-channel fiber-optic immunosensing platform (DOFIS) for enhanced diagnostic applications. The detection can be completed in 10 min with low cost and simple operation ^[37]. All the above rapid detection methods can provide some reference for the development of SVV rapid detection.

In addition, using freeze-drying technology, lateral chromatography test strips, and other technical means, developing portable detection reagents or consumables that are easy to carry and use can better meet the needs of grassroots veterinarians for on-site detection. Future research should further improve the detection sensitivity and specificity, and develop portable detection equipment to provide more powerful support for the prevention and control of SVV. In the future, we will continue to pay attention to and explore the research progress in this field, and make greater contributions to the rapid detection of SVV and the prevention and control of diseases.

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