# **ORIGINAL RESEARCH**



# Exploring the efficacy of interferon nebulization combined with immunoglobulin in the treatment of adenovirus pneumonia in children

Qi Zhang<sup>1,</sup>\*, Fengqin Xu<sup>1</sup>, Fuzhe Chen<sup>1</sup>

<sup>1</sup>Pediatric Respiratory Medicine, Anhui Provincial Children's Hospital, 230051 Hefei, Anhui, China

\*Correspondence zq\_dr26@163.com

(Qi Zhang)

#### Abstract

Background: This study explores the efficacy of interferon nebulization combined with immunoglobulin in treating adenovirus pneumonia in children. Methods: Based on existing case records, a retrospective analysis was conducted on the clinical data of 100 pediatric patients with adenovirus pneumonia treated in our hospital from August 2020 to August 2023. According to the recorded different treatment methods, this study included 50 cases in the observation group (receiving interferon nebulization combined with immunoglobulin treatment) and 50 cases in the control group (receiving interferon nebulization treatment). Comparing the effects of the two treatment methods on the children's efficacy. Results: The total effective rate in the observation group was significantly higher than that in the control group, with a lower inefficacy rate ( $\chi^2$  = 5.263, p = 0.022 < 0.05). After treatment, the clinical indicators in the observation group, including the disappearance times of cough, fever, sputum production, and lung rales, were shorter than those in the control group (t = 16.159, p < 0.001; t = 23.804, p < 0.001; t = 17.247, p < 0.001; t = 28.159, p < 0.001). Before treatment, there was no significant difference in the levels of inflammatory factors (White Blood Cell (WBC), C-Reactive Protein (CRP)) between the observation and the control groups (t > t0.05); seven days after treatment, the levels of WBC and CRP in the observation group were lower than the control group (t = 12.082, p < 0.001; t = 8.828, p < 0.001). The incidence of complications in the observation group was lower than in the control group  $(\chi^2 = 4.000, p = 0.046 < 0.05)$ . Conclusions: Interferon nebulization combined with immunoglobulin demonstrates significant clinical efficacy in children with adenovirus pneumonia, rapidly alleviating clinical symptoms, reducing inflammatory response, improving immune function, and ensuring high safety, worth of promoting in clinical practice.

#### Keywords

Interferon; Immunoglobulin; Children's adenovirus pneumonia; Efficacy; Inflammatory factors

### 1. Introduction

Adenovirus pneumonia is a respiratory infection that primarily impacts infants and young children, posing as one of the most critical forms of pneumonia in the pediatric population [1]. From a clinical perspective, adenoviruses are responsible for around 4% to 10% of pneumonia cases. Common symptoms associated with adenovirus pneumonia comprise prolonged high fever, cough, wheezing, shortness of breath, and respiratory distress [2]. Due to the low immunity in children, the disease can easily progress to severe cases, potentially causing damage to the digestive, nervous, circulatory, and respiratory system, and even becoming life-threatening. This severity has made adenovirus pneumonia a growing focus of clinical attention [3]. Current pharmaceutical treatments lack standardization, often involving antiviral, anti-inflammatory, and symptomatic approaches, but they have not achieved ideal clinical outcomes. Ribavirin, cidofovir and ganciclovir are frequently utilized antiviral medications for managing adenovirus pneumonia; however, their efficacy in clinical settings has been suboptimal [4]. Studies have indicated decreased immunoglobulin levels in pneumonia patients [5]. Immunoglobulin, a passive immune product that includes antibodies targeting diverse microorganisms, is commonly utilized in clinical settings to address immune deficiencies like immunoglobulin deficiency, thus enhancing effectiveness to a certain degree [6]. In recent years, interferon has emerged as an effective drug in the clinical treatment of viral pneumonia. Interferon, with its broad-spectrum antiviral properties, stimulates host cells to generate defense mechanisms upon viral invasion, helping bolster cellular resistance to viral infections and exhibiting efficacy against a wide range of diseases [7]. However, the efficacy of interferon alone in treating adenovirus pneumonia is limited, necessitating more effective treatment options. From a clinical perspective, it is common to combine interferon with other drugs in order to enhance treatment effectiveness. However, there is a scarcity of research on the use of interferon in conjunction with immunoglobulin for the treatment of pediatric adenovirus pneumonia C-reactive protein (CRP) is an acute-phase protein that typically increases during infection or inflammation. Increased levels of white blood cells (WBC), especially neutrophils, may suggest the presence of an infection. These markers play a crucial role in aiding doctors in the identification of adenovirus pneumonia and evaluating its seriousness. Thus, the research focuses on assessing the effectiveness of combining immunoglobulin with interferon nebulization in the treatment of adenovirus pneumonia in children and its influence on inflammatory markers (WBC, CRP) in the young patients. The goal is to provide a reference for promoting recovery and improving prognosis in pediatric patients, and to offer a basis for the rational clinical use of these drugs.

#### 2. Materials and methods

#### 2.1 General information

The clinical data of 100 children with adenovirus pneumonia who were treated in our hospital were retrospectively reviewed from existing case records. The study population was divided into two groups based on the treatment methods recorded: an observation group with 50 cases and a control group with 50 cases.

Inclusion Criteria: (1) Met the diagnostic criteria for pediatric adenovirus pneumonia [8], and tested positive for adenovirus nucleic acid in sputum or throat swab samples, with chest X-ray or Computerized tomography (CT) scan showing patchy shadows; (2) Exhibited symptoms such as cough, fever, wheezing, and difficulty breathing at the time of enrollment; (3) Aged between 0–6 years; (4) First onset of the disease, with no use of immunosuppressants or antiviral treatments within the 3 months prior to enrollment; (5) Had a complete medical history; (6) Met the indications for nebulized inhalation therapy (no airway malformations).

Exclusion Criteria: (1) Allergic reactions to the drugs used in this study; (2) Concurrent other infectious diseases (*e.g.*, bacterial infection, congenital syphilis); (3) Concurrent coagulation disorders, liver and kidney dysfunction, severe malnutrition, central nervous system dysfunction, congenital and hereditary lung diseases; (4) Other potential immunodeficiency diseases; (5) Poor treatment compliance or withdrawal from the study midway.

#### 2.2 Methods

As a retrospective study, the intervention methods were documented in existing case records.

(1) Patient selection

Based on previous studies, it was hypothesized that the

complication rate in the observation group could be reduced by 30%. Assuming a test level of 0.05 and a test power of 0.8, each group was expected to need 43 patients. Considering a 15% dropout rate, it was estimated that 50 patients were needed in each group, totaling 100 patients for the study.

(2) Treatment plan

Upon admission, both groups underwent blood tests, chest CT scans, X-rays, and clinical data analysis. Treatment strategies were implemented to address symptoms such as sticky sputum, hypoxia, and oliguria. These included actions such as suctioning and nebulization to clear the airways, ensuring electrolyte balance, and utilizing mechanical ventilation as needed. Fundamental care practices included maintaining a humidity level of 60% and a temperature of 26 °C, promoting proper air circulation, regularly repositioning the patient, utilizing back patting techniques, and offering easily digestible food [9, 10].

Control Group: Based on this, the control group received nebulized inhalation therapy with recombinant human interferon for injection (rhIFN-a2b) (Anhui Anke Biotechnology Co. Ltd, Hefei, Anhui, China, S20000013) at a dose of 200,000 to 400,000 IU/kg, twice daily. This was added to terbutaline sulfate nebulizer solution (AstraZeneca, Sydney, NSW, Australia, JX20180163) and ipratropium bromide solution (Boehringer Ingelheim Pharma GmbH&CO.KG, Ingelheim am Rhein, RP, Germany, H20150159). The three medications were administered through oxygen-powered atomization inhalation. Nebulization treatments were scheduled either in the morning or in the evening, with timing tailored to suit the patient's condition and tolerance level. Each inhalation session typically spanned 15-20 minutes until all the medication had been effectively nebulized, utilizing a specialized compressed air nebulizer (PARY BOY Nebulizer, PARI GmbH, Starnberg, BY, Germany) to guarantee equipment cleanliness and optimal functionality. During nebulization, patients should remain calm and avoid vigorous activities.

Observation Group: In addition to the treatment provided to the control group, the observation group received intravenous gamma globulin (Sichuan Yuanda Shuyang Pharmaceutical Co. Ltd. 2.5 g/bottle, Chengdu, Sichuan, China, S10980026) at a dose of 1 g/(kg·d) continuously for 2 days. The infusion started at 1.0 mL/min initially, and if no adverse effects were observed within 15 minutes, the rate could be slowly raised, ensuring it did not exceed 3.0 mL/min. The duration of administration typically ranged from 2 to 4 hours, varying based on both the infusion rate and the patient's individual tolerance level. Healthcare professionals vigilantly monitored the patient's reaction to the medication, promptly managing any unfavorable responses. Both groups were treated according to their actual conditions for 5–7 days.

Specific instructions for medical personnel:

1. Monitoring: Regularly monitor the patient's vital signs, such as heart rate, blood pressure, respiratory rate, and oxygen saturation, to assess the effectiveness of the treatment.

2. Adverse Reaction Management: Educate medical personnel to recognize possible adverse reactions caused by interferon and immunoglobulin, such as allergic reactions, fever, and headache, and to handle them promptly.

3. Patient Education: Explain the treatment plan, possible side effects, and their management measures to the patient's

family to improve treatment compliance and safety.

These plans should be adjusted according to the specific clinical condition of the patient and the doctor's guidance to ensure the effectiveness and safety of the treatment.

#### (3) Data collection and analysis

After the children are admitted to the hospital, basic information such as age, gender, duration of illness, weight, admission time, and previous treatment plans (if any, record the proportion of these children) are collected. Clinical manifestations of the children are observed, including fever, runny nose, cough, shortness of breath, cyanosis around the lips, choking while feeding, drooling, inspiratory chest retractions, pulmonary rales, and wheezing. Chest X-ray findings are documented. Before treatment and on the seventh day posttreatment, 2 mL of peripheral venous blood is obtained from fasting children in the morning to assess inflammatory factor levels. The clinical manifestations and overall status of the children are evaluated and documented after 7 days of therapy to evaluate effectiveness, specifically focusing on the time taken for clinical indicators to improve in the children. Adverse reactions during hospitalization are recorded, including fever, chills, tachycardia, rash, injection site infection, induration and bleeding.

The collected data are analyzed using SPSS 21.0 statistical analysis software (IBM, Armonk, NY, USA) and GraphPad Prism 8.0.2 software (GraphPad Software Inc., San Diego, CA, USA). Normally distributed measurement data are expressed as mean  $\pm$  standard deviation (SD), and inter-group comparisons are performed using the independent sample *t*-test; intragroup comparisons are performed using the paired sample *t*-test. For non-normally distributed data or data with unequal variances, the Mann-Whitney U test is used and expressed as median (M) and interquartile range (M (P25, P75)). Count data are expressed as numbers and percentages (%), and inter-group comparisons are performed using the chi-square test or Fisher's exact test; *p* < 0.05 indicates statistical significance.

#### 2.3 Observation indicators

As a retrospective study, the outcome indicators have been recorded in existing case records.

(1) Clinical Efficacy: Based on the assessment standards for effectiveness outlined in the relevant literature, the enhancement of children's symptoms is assessed holistically. Evaluation of the effectiveness after a week of treatment yielded the following results: Cured: X-ray examinations showed complete absorption of inflammatory lesions, disappearance of rales and cough, and normalization of body temperature. Effective: X-ray examinations showed that most of the inflammatory lesions were absorbed, rales and cough were alleviated, and low-grade fever or normalization of body temperature was observed. Ineffective: No relief or worsening of signs and symptoms [11]. Total effective rate = (cured + effective)/total cases  $\times$  100%. (2) Clinical Indicators: Observation of the disappearance times of symptoms such as cough, fever, sputum production, and pulmonary rales. (3) Inflammatory Marker Levels: These included WBC and CRP. In the morning before any treatment, 2 mL of peripheral venous blood is drawn from the children on an empty stomach. Similarly, blood samples

are also collected on the seventh day following the treatment. The collected blood samples are then centrifuged at 4000 r/min for 10 minutes using a centrifuge radius of 6 cm to separate the serum. The serum CRP levels in each group are measured using a double-antibody sandwich enzyme-linked immunosorbent assay, with kits purchased from Shanghai Hengyuan Co., Ltd. (Shanghai, China, HB2272-Hu) following the kit instructions strictly. WBC is measured using an automated analyzer. (4) Adverse Reactions: The occurrence of diarrhea, rash, mild vomiting, and exacerbation of asthma during hospitalization is recorded.

#### 3. Results

#### 3.1 General information

In the observation group, there were 28 males and 22 females, aged  $1.25 \pm 0.26 (0.5-4.1)$  years, and the course of disease was  $6.08 \pm 1.15 (4.0-8.2)$  days. In the control group, there were 25 males and 25 females, aged  $1.28 \pm 0.31 (0.5-4.2)$  years, and the course of disease was  $5.95 \pm 0.86 (4.1-7.7)$  days. The data of the two groups were comparable (p > 0.05).

#### 3.2 Comparison of treatment efficacy

The total effective rate in the observation group was significantly higher than that in the control group and the inefficacy rate was lower than that of the control group ( $\chi^2 = 5.263$ , p = 0.022 < 0.05), suggesting that combining interferon with nebulization yielded superior effectiveness when compared to using interferon alone alongside nebulization (Table 1).

#### 3.3 Comparison of clinical indicators

Following the intervention, it was observed that the clinical parameters in the treatment group (including the duration of cough, fever, sputum production, and lung rales) were significantly reduced compared to the control group (t = 16.159, p < 0.001; t = 23.804, p < 0.001; t = 17.247, p < 0.001; t = 28.159, p < 0.001), (Table 2).

#### 3.4 Inflammatory marker levels

Before treatment, the inflammatory factor levels (WBC, CRP) in the observation group showed no significant difference (t = 0.279, p = 0.781; t = 0.138, p = 0.891); After 7 days of treatment, the levels of WBC and CRP in the observation group were lower than those in the control group (t = 12.082, p < 0.001; t = 8.828, p < 0.001), signifying a notable amelioration in inflammation in the observation group post-treatment (Table 3).

#### 3.5 Adverse reactions

The incidence of adverse reactions (diarrhea, erythra, mild vomiting, exacerbation of asthma) in the observation group was lower than that in the control group ( $\chi^2 = 4.000$ , p = 0.046 < 0.05) (Table 4).

<b>IABLE 1.</b> Comparison of patient efficacy (n (%)).							
Group	n	Cured	Effective	Ineffective	Total effective rate		
Observation group	50	30 (60.00)	15 (30.00)	5 (10.00)	45 (90.00)		
Control group	50	24 (48.00)	12 (24.00)	14 (28.00)	36 (72.00)		
$\chi^2$					5.263		
р					0.022		

TABLE 2. Comparison of clinical indicators ( $ar{x} \pm s$ , d).							
Group	n	Cough	Time of fever	Time of sputum	Time to lung rales		
	11	disappearance time	disappearance	disappearance	disappearance		
Observation group	50	$4.10\pm0.52$	$1.60\pm0.25$	$5.10\pm0.28$	$4.45\pm0.24$		
Control group	50	$6.35\pm0.83$	$3.20\pm0.40$	$6.50\pm0.50$	$6.50\pm0.45$		
t	-	16.159	23.804	17.247	28.159		
р	-	< 0.001	< 0.001	< 0.001	< 0.001		

**TABLE 3.** Comparison of inflammatory factors levels  $(\bar{x} \pm s)$ .

Group	n	WBC (×10 <sup>9</sup> /L)		CRP (mg/L)		
		Before treatment	After 7 d of treatment	Before treatment	After 7 d of treatment	
Observation group	50	$16.78\pm3.50$	$6.58\pm0.57$	$29.11\pm4.54$	$5.27 \pm 1.25$	
Control group	50	$16.98\pm3.37$	$8.35\pm0.86$	$28.97 \pm 5.02$	$8.70\pm2.45$	
t	-	0.279	12.082	0.138	8.828	
p	-	0.781	< 0.001	0.891	< 0.001	

WBC: white blood cells; CRP: C-reactive protein.

TABLE 4. C	omparison o	of the compl	lications (n	(%)).
------------	-------------	--------------	--------------	-------

Group	n	Diarrhea	Erythra	Mild vomiting	Exacerbation of asthma	Total
Observation group	50	1 (2.00)	0	0	1 (2.00)	2 (4.00)
Control group	50	2 (4.00)	1 (2.00)	2 (4.00)	3 (6.00)	8 (16.00)
$\chi^2$	-					4.000
р	-					0.046

## 4. Discussion

In the early stages of adenovirus pneumonia in children, patients commonly present with fever [12]. As the disease progresses, the increase in body temperature can become significant. Respiratory symptoms, such as coughing are also prevalent. Research conducted in clinical settings has indicated that certain children may encounter symptoms such as nausea, vomiting, and diarrhea [13]. If not treated promptly, the condition can worsen, significantly increasing the risk of mortality [14]. In clinical practice, non-invasive treatment methods are often used, such as the administration of medications like ribavirin and recombinant human interferon  $\alpha$ 2b. It is crucial to explore the mechanisms of action of these drugs and evaluate their clinical outcomes in order to improve treatment effectiveness and patient outcomes [15].

Currently, clinical treatment primarily focuses on conservative management, supplemented by antibacterial therapy, antispasmodics, bronchodilators, and antipyretics; however, the results are often unsatisfactory [16]. Interferon  $\alpha$ 2b, a small protein that occurs naturally in the human body, is

renowned for its ability to combat both DNA and RNA viruses due to its antiviral properties. It is extensively utilized in the treatment of viral infectious diseases [17]. The results of this study indicate that the total effective rate of the observation group was significantly higher than that of the control group, suggesting that the combination of interferon inhalation and immunoglobulin is more effective in treating pediatric adenovirus pneumonia than interferon nebulization alone. The reason for this improved efficacy may be due to the broad distribution of interferon  $\alpha$ 2b in the human body, where rhIFN- $\alpha$ 2b plays a significant role in antiviral therapy by possessing broad-spectrum antimicrobial properties [18, 19]. The primary mechanism of interferon  $\alpha$ -2b's antiviral action involves blocking viral replication and proliferation. After entering the body, rhIFN- $\alpha$ 2b stimulates cells to generate antiviral proteins. This action results in the breakdown of viral mRNA and the blockage of its transcription, translation, and replication procedures. As a result, a wide-ranging antiviral impact is achieved and treatment effectiveness is improved [20, 21]. Moreover, interferon has the potential to boost the phagocytic capabilities of macrophages, thereby inhibiting the entry of viruses into healthy cells. By utilizing nebulization, the medication can be swiftly administered to the patient's mucosal tissues, facilitating rapid absorption and efficiently managing the spread of the virus [22]. Clinically, immunoglobulin can be used to prevent infections from viral diseases like viral hepatitis and measles. When combined with antibiotics, it shows good efficacy in severe bacterial and viral infections [23]. Administering immunoglobulin to children as a form of passive immunotherapy for adenovirus pneumonia results in the rapid introduction of a high concentration of antibodies, effectively elevating the patient from a state of little to no immunity to a state of immune protection [24]. This interaction between antibodies and antigens neutralizes toxins within the body, kills viruses and bacteria, enhances immune function, and regulates immune cell levels, thus achieving therapeutic effects [25]. The synergistic effect of combining immunoglobulin and interferon leads to a decrease in lung parenchymal involvement, enhances the secretion of immune factors by the thymus, promptly alleviates clinical symptoms, and enhances the overall effectiveness of treatment [26, 27]. The clinical efficacy of using interferon  $\alpha$ 2b alone has certain limitations, and most children do not achieve the desired therapeutic effect, leaving their immune system weak. Therefore, the combined use of both is more effective than using interferon aerosol alone. In the study by Liangkang Lin, a 10-monthold infant with severe adenovirus pneumonia complicated by plastic bronchitis (PB) was treated with intravenous ribavirin combined with aerosolized recombinant human interferon  $\alpha$ 1b (INF $\alpha$ 1b), which ultimately led to an improvement in his condition. No side effects were observed during the treatment, and the long-term prognosis was favorable. This report also demonstrated that the combination of INF $\alpha$ 1b with other drugs appears to alleviate adenovirus pneumonia, consistent with the results of this study.

Following the treatment, it was observed that the duration of cough, fever, sputum production, and lung rales in the observation group was shorter in comparison to the control group. This indicates that the use of interferon and immunoglobulin in combination may lead to a swift alleviation of clinical symptoms in children. It is speculated that recombinant human interferon combined with immunoglobulin improves clinical symptoms by modulating immunity and reducing inflammation, thereby accelerating recovery, reducing hospitalization time, and enhancing clinical efficacy. Interferon  $\alpha$ 2b occurs naturally in the human body. The recombination of interferon  $\alpha$ 2b *in vitro* to produce recombinant human interferon  $\alpha$ 2b is frequently utilized for antiviral therapy [28]. Upon entering the body, it induces cells to generate antiviral proteins continuously, inhibiting the gene expression process of viral mRNA [29]. Moreover, the use of recombinant human interferon  $\alpha$ 2b is intended to modulate immune response, leading to improved macrophage and lymphocyte activities in children, consequently contributing to better disease prognosis [30]. Immunoglobulin inhibits the formation of antigen-antibody complexes to some extent, reducing inflammatory responses. Inhibiting alveolar exudation can enhance clinical symptoms in children [31, 32]. The combination of the two may improve clinical symptoms of adenoviral pneumonia through synergistic inhibition of inflammation and enhancement of

immunity, thereby exerting therapeutic effects. Consequently, the combined use shortens the time required to improve clinical symptoms in children. In the research conducted by Cai Sha, a total of 75 children who were 14 years old or younger and diagnosed with severe adenovirus pneumonia (AVP) were enrolled. They were categorized into three groups (A, B and C) according to the sequence of their visits, with 25 children in each group. Group A received only symptomatic supportive treatment. In addition to symptomatic supportive treatment, Group B received intravenous immunoglobulin (IVIG) treatment at a dose of 1 g/(kg·d) for 2 consecutive days before progressing to severe AVP. Group C received the same IVIG treatment after progressing to severe AVP. The efficacy and related laboratory indicators were compared among the three groups after treatment. The results showed that Group B had the shortest fever duration and hospital stay after treatment. The findings indicate that IVIG treatment before progression to severe AVP is more effective in treating children with severe adenovirus pneumonia, directly demonstrating the efficacy of IVIG treatment for severe adenovirus pneumonia in children.

After 7 days of treatment, the levels of WBC and CRP in the observation group were significantly lower than those in the control group. This suggests that interferon aerosol combined with immunoglobulin can markedly reduce inflammation in children. This effect may be due to the enhanced antiviral activity from the combination therapy, which improves clinical symptoms and boosting immune function in children. Immunoglobulin, a key immune component produced by lymphocytes, can block cell Fc receptors and inhibit cytokine production to some extent, thereby reducing the release of pro-inflammatory factors in the bronchi and preventing the formation of antigen-antibody complexes [33]. It works to counteract inflammatory agents within the body, thereby boosting the immune system of the child. Immunoglobulin serves as a shield not only against bacterial infections (such as Staphylococcus aureus, Corynebacterium diphtheriae, Streptococcus) but also demonstrates effectiveness in combating viral infections like adenovirus, echovirus, and respiratory syncytial virus [34]. The product consists of a variety of antibodies targeting human tumor necrosis factor, interleukin-1, and interleukin-6. These antibodies work by directly inhibiting the activity of these cytokines, leading to anti-inflammatory outcomes [35]. Additionally, immunoglobulin reduces alveolar exudates, prevents mucus obstruction in the respiratory tract, thereby decreasing severe complications and alleviating symptoms in children [36, 37]. Recombinant human interferon functions by attaching to interferon receptors located on the surface of target cells. This action triggers the generation of various antiviral proteins that hinder viral replication, synthesis, and transcription. Consequently, this process helps to dampen the inflammatory response [38]. Therefore, the combined use of interferon and immunoglobulin can effectively improve microcirculation, decrease inflammation, and regulate immune function. The observation group experienced fewer complications than the control group, indicating that recombinant human interferon  $\alpha 2b$  aerosol inhalation combined with immunoglobulin is safe, with a low incidence of adverse reactions and high tolerability.

This study is constrained by a limited sample size and a lack

of thorough investigation into patient baseline characteristics, such as pre-existing medical conditions. The single-center design and younger age of the study population may also limit the generalizability of the findings. Additionally, there is a lack of research on factors influencing the recurrence rate. Supplementing this data will enhance understanding of the impact of these therapies on disease recurrence. Moreover, there is still a need for more in-depth investigation into the risk factors associated with complications. It is essential to conduct additional analysis in order to enhance the effectiveness of treatment and overall clinical care. Future studies should involve larger, more diverse samples, multi-center designs, and detailed analysis of complication risk factors and recurrence rates to improve the accuracy and comprehensiveness of the findings.

# 5. Conclusions

In summary, the combination of immunoglobulin and interferon aerosol therapy demonstrates significant clinical efficacy in treating children with adenoviral pneumonia. It quickly relieves clinical symptoms (shortening the disappearance time of cough, fever, sputum, and lung rales), decreases levels of inflammatory response (reducing WBC count and CRP levels), enhances immune function, and helps them recover quickly. The treatment demonstrates a favorable safety profile, rendering it appropriate for clinical application.

#### AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

#### AUTHOR CONTRIBUTIONS

QZ—designed the study and carried them out; prepared the manuscript for publication and reviewed the draft of the manuscript. QZ, FQX and FZC—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

# ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Anhui Provincial Children's Hospital Approval no. 2023029). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

#### ACKNOWLEDGMENT

Not applicable.

#### FUNDING

This research received no external funding.

#### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

#### REFERENCES

- [1] Tian J, Wang X, Li Q, Zhang L, Ai J, Feng G, *et al.* Clinical epidemiology of adenovirus pneumonia among Chinese hospitalized children. Archives of Microbiology. 2024; 206: 135.
- [2] Li M, Han XH, Liu LY, Yao HS, Yi LL. Epidemiological characteristics, clinical characteristics, and prognostic factors of children with atopy hospitalised with adenovirus pneumonia. BMC Infectious Diseases. 2021; 21: 1051.
- [3] Jiang J, Sun L, Huang M. Abnormal changes in IL-13 and IL-17A serum levels in children with adenovirus pneumonia and their diagnostic value. Iranian Journal of Immunology. 2024; 21: 81–88.
- [4] Lin L, Tang M, Li D, Fei H, Zhang H. Combined intravenous ribavirin and recombinant human interferon α1b aerosol inhalation for adenovirus pneumonia with plastic bronchitis in children: a case report and review of literature. Frontiers in Pediatrics. 2024; 12: 1295133.
- [5] Wang N, Fang Y, Dong H, Wang L, Hou M, Wang W, *et al.* Clinical features and prediction of risk factors for severe adenovirus pneumonia in children. Translational Pediatrics. 2024; 13: 63–71.
- [6] Almontasheri A, Al-Husayni F, Alsuraihi AK, Binyahib H, Albanna AS. The clinical course of COVID-19 pneumonia in a 19-year-old man on intravenous immunoglobulin replacement therapy for X-linked agammaglobulinemia. American Journal of Case Reports. 2021; 22: e929447.
- [7] Harada N, Sonoda M, Ishimura M, Eguchi K, Kinoshita K, Matsuoka W, *et al.* Pretransplant ribavirin and interferon-α therapy for rhinovirus interstitial pneumonia in a RAG1-deficient infant. Journal of Infection and Chemotherapy. 2024; 30: 362–365.
- [8] Subspecialty Group of Respiratory, the Society of Pediatrics, Chinese Medical Association; Editorial Board, Chinese Journal of Pediatrics; China Medicine Education Association Committee on Pediatrics. Guidelines for the management of community-acquired pneumonia in children (2024 revision). Chinese Journal of Pediatrics. 2024; 62: 920–930. (In Chinese)
- [9] Shen YY, Feng ZQ, Wang ZP, Wang XQ, Luo C, Liu QZ. Efficacy of azithromycin combined with intravenous immunoglobulin in the treatment of refractory mycoplasma pneumoniae pneumonia in children: a meta-analysis. BMC Pediatrics. 2024; 24: 678.
- <sup>[10]</sup> Li ZZ, Xie LL, Wang H, Wang SG, Wu JG. Clinical observation of reduning combined with recombinant human interferon  $\alpha$ -2b in the treatment of children with viral pneumonia. Evidence-Based Complementary and Alternative Medicine. 2022; 2022: 1739561.
- [11] Lin ZL, Xu X, Yang JJ, Lu LQ, Huang H, Hua XZ, *et al.* Efficacy of budesonide/formoterol inhalation powder in treating viral pneumonia in children. World Journal of Clinical Cases. 2024; 12: 4469–4475.
- [12] Yu X, Ma Y, Gao Y, You H. Epidemiology of adenovirus pneumonia and risk factors for bronchiolitis obliterans in children during an outbreak in Jilin, China. Frontiers in Pediatrics. 2021; 9: 722885.
- [13] Rajbanshi A, Giri P, Laha S, Poddar S. Epidemiology, clinical presentation, and respiratory sequelae of severe adenoviral pneumonia in children admitted in a tertiary care pediatric intensive care unit from Eastern India: a single-center observational study. Journal of Pediatric Critical Care. 2022; 9: 131–138.
- [14] Cai JY, Yan CY, Wang XQ, Luo ZX, Luo J, Li QB, *et al.* Clinical characteristics and risk factors for bronchoscopic airway mucus hypersecretion in childhood pneumonia infected by different pathogens. Chinese Journal of Pediatrics. 2023; 61: 719–725. (In Chinese)
- [15] Jain H, Singh G, Bhuta K, Thapa SS, Sah BP. Successful treatment of severe adenovirus pneumonia with cidofovir in a immunocompetent patient. Chest. 2022; 162: A315.
- <sup>[16]</sup> Cai S, Zhu CH, Chen FG, Liu F, Gao ML, Xiong Y. Establishment of a risk model for severe adenovirus pneumonia and prospective study of the timing of intravenous immunoglobulin therapy in children. Chinese Journal of Contemporary Pediatrics. 2023; 25: 619–625. (In Chinese)
- <sup>[17]</sup> Zeng QL, Chen RY, Lv XY, Huang S, Li WZ, Pan YJ, et al. Functional

cure induced by tenofovir alafenamide plus peginterferon-alpha-2b in young children with chronic hepatitis B: a case series study. BMC Infectious Diseases. 2024; 24: 830.

- [18] Chen L, Wu Y, Sun Y, Qiao S, Xiao B, Wang J, *et al.* Combined therapy of local recombinant human interferon α1b injection and acupuncture on verruca vulgaris: a retrospective study. Archives of Dermatological Research. 2023; 315: 2365–2373.
- <sup>[19]</sup> Luo J, Yang M, Zeng L, Pan X, Liu D, Diao S, *et al.* Safety and effectiveness of inhaling different dosage recombinant human interferon  $\alpha$ 1b for bronchiolitis in children: a systematic review and meta-analysis. Evidence-Based Complementary and Alternative Medicine. 2022; 2022: 2229735.
- [20] Yin P, Meng J, Chen J, Gao J, Wang D, Liu S, *et al*. Antiviral drugs arbidol and interferon alpha-1b contribute to reducing the severity of COVID-19 patients: a retrospective cohort study. Virology Journal. 2021; 18: 142.
- [21] Yang L, Zhang G, Huang L, Ren X, Su Y, Wang C, *et al.* The effect of recombinant human interferon α1b treatment of infants hospitalized with lower respiratory tract infection on subsequent wheezing. Jornal de Pediatria. 2021; 97: 617–622.
- [22] Roquilly A, Francois B, Huet O, Launey Y, Lasocki S, Weiss E, et al.; Atlanrea study group and the Société Française d'Anesthésie Réanimation (SFAR) Research Network. Interferon gamma-1b for the prevention of hospital-acquired pneumonia in critically ill patients: a phase 2, placebo-controlled randomized clinical trial. Intensive Care Medicine. 2023; 49: 530–544.
- [23] Ramachandram DS, Kow CS, Hasan SS, Thiruchelvam K. Effect of intravenous immunoglobulin on mortality in hospitalized patients with COVID-19: a systematic review and meta-analysis of randomized controlled trials. Health Science Reports. 2024; 7: e2239.
- [24] Li Y, Chen B. Gamma globulin combined with acyclovir for children with infectious mononucleosis and their effect on immune function. American Journal of Translational Research. 2023; 15: 4399–4407.
- <sup>[25]</sup> Hu T, Liu CH, Lei M, Zeng Q, Li L, Tang H, et al. Metabolic regulation of the immune system in health and diseases: mechanisms and interventions. Signal Transduction and Targeted Therapy. 2024; 9: 268.
- <sup>[26]</sup> Abdolahi N, Kaheh E, Golsha R, Khodabakhshi B, Norouzi A, Khandashpoor M, *et al.* Letter to the editor: efficacy of different methods of combination regimen administrations including dexamethasone, intravenous immunoglobulin, and interferon-beta to treat critically ill COVID-19 patients: a structured summary of a study protocol for a randomized controlled trial. Trials. 2020; 21: 549.
- [27] Cai S, Zhu CH, Chen FG, Liu F, Gao ML, Xiong Y. Establishment of a risk model for severe adenovirus pneumonia and prospective study of the timing of intravenous immunoglobulin therapy in children. Chinese Journal of Contemporary Pediatrics. 2023; 25: 619–625. (In Chinese)
- [28] Inga P, Pavel T, Tatiana D, Svetlana S, Timur S, Irina A, et al. Interferon alpha-2b treatment for exophytic nasal papillomas and human papillomavirus infection. Brazilian Journal of Otorhinolaryngology.

2024; 90: 101449.

- [29] Ferri DM, Nassar C, Manion KP, Kim M, Baglaenko Y, Muñoz-Grajales C, *et al.* Elevated levels of interferon-α act directly on B cells to breach multiple tolerance mechanisms promoting autoantibody production. Arthritis & Rheumatology. 2023; 75: 1542–1555.
- [30] Sun L, Bi J, Zhen W, Wang M, Song H. Effects of ganciclovir combined with recombinant human interferon-α on clinical efficacy and immune function in children with infectious mononucleosis. Pakistan Journal of Medical Sciences. 2024; 40: 1473–1478.
- [31] Ma X, Gao W, An J. Clinical effect of reduning combined with gamma globulin treatment on symptom improvement serum levels of IL-6, 25-(OH)D and LDH in children with severe mycoplasma pneumonia. Pakistan Journal of Medical Sciences. 2022; 38: 826–832.
- [32] Baek DW, Song GY, Lee HS, Do YR, Lee JH, Yhim HY, et al. Clinical efficacy of prophylactic intravenous immunoglobulin for elderly DLBCL patients with hypogammaglobulinemia in the COVID-19 pandemic era. Frontiers in Oncology. 2024; 14: 1380492.
- [33] Wang XX, Han HW, Jiao FY, Zhang WH. Timing of vaccination in children after intravenous immunoglobulin therapy for Kawasaki disease. Asian Journal of Pediatric Research. 2024; 14: 57–64.
- [34] Pontali E, Volpi S, Antonucci G, Castellaneta M, Buzzi D, Tricerri F, et al. Safety and efficacy of early high-dose IV anakinra in severe COVID-19 lung disease. Journal of Allergy and Clinical Immunology. 2020; 146: 213–215.
- [35] Xu N, Xu J, Li H, Qian L, Qiao L. Analysis of curative effects of human gamma globulin on bacterial pneumonia in pediatric patients. Pakistan Journal of Pharmaceutical Sciences. 2019; 32: 2385–2390.
- [36] Atosuo J, Karhuvaara O, Suominen E, Virtanen J, Vilén L, Nuutila J. The role of gamma globulin, complement component 1q, factor B, properdin, body temperature, C-reactive protein and serum amyloid alpha to the activity and the function of the human complement system and its pathways. Journal of Immunological Methods. 2024; 531: 113709.
- [37] Léo JGP, Siqueira CB, Motta JOCD, Vasconcellos IF, Araujo YR, Glehn FV, *et al.* The use of intravenous immunoglobulin as a rescue therapy for refractory parainfectious leprosy-related neuritis: a case series. Anais Brasileiros de Dermatologia. 2024; 99: 736–739.
- [38] Won J, Jo A, Gil CH, Kim S, Shin H, Jik Kim H. Inhaled delivery of recombinant interferon-lambda restores allergic inflammation after development of asthma by controlling Th2- and Th17-cell-mediated immune responses. International Immunopharmacology. 2022; 112: 109180.

**How to cite this article:** Qi Zhang, Fengqin Xu, Fuzhe Chen. Exploring the efficacy of interferon nebulization combined with immunoglobulin in the treatment of adenovirus pneumonia in children. Signa Vitae. 2025; 21(3): 53-59. doi: 10.22514/sv.2025.036.