Clinical effect of Jingfang Granule combined with oseltamivir phosphate granule in the treatment of influenza A in children

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Introduction. To observe the clinical efficacy of Jingfang Granule combined with oseltamivir phosphate granule in the treatment of influenza A in children.

Methods. A total of 110 children with influenza A diagnosed in the outpatient and emergency department of Tianjin First Central Hospital from October 2022 to April 2023 were selected as the study objects. They were randomly divided into control group and observation group, 55 cases in each group. The control group was treated with oseltamivir phosphate granules alone, and the observation group was treated with Jingfeng granules on the basis of the control group. Both groups were treated continuously for 5 days. Clinical efficacy, fever, cough, nasal congestion, sore throat and other symptoms disappear time, serum CRP, white blood cell levels, adverse reactions and virus negative time of the two groups were compared and analyzed.

Results. The effective rate of treatment in observation group was significantly higher than that in control group, the difference was statistically significant (P < 0.05). The disappearance time of fever, nasal congestion, cough and sore throat in observation group was earlier than that in control group, the difference was statistically significant (P < 0.05). Before treatment, there was no significant difference in serum CRP and white blood cell levels between 2 groups (P > 0.05). After treatment, serum CRP and white blood cell levels in 2 groups were lower than before treatment, and observation group was lower than control group, with statistical significance (P < 0.05). The incidence of adverse reactions in observation group was lower than that in treatment group, but the difference was not statistically significant (P > 0.05). The virus turning negative time in observation group was shorter than that in control group, and the difference was statistically significant (P < 0.05).

Conclusion. Jingfang Granule combined with oseltamivir phosphate granule has significant clinical effect in the treatment of influenza A in children, which can effectively alleviate clinical symptoms, inhibit the release of inflammatory factors, shorten the time of virus negative transition and reduce adverse reactions during treatment, and is recommended for clinical use. Keywords. Influenza A; Children; Oseltamivir phosphate; Jingfang granules; Clinical effect; Adverse reactions; Time for virus to turn negative

INTRODUCTION

Influenza is an acute respiratory infectious disease caused by the influenza virus that circulates every winter [1]. Seasonal influenza is mainly caused by influenza type A, B, C, and D viruses. Among them, influenza A virus is the most variable and has the largest variation range. Through antigenic drift and transfer, a local outbreak occurs every 1-2 years, and a worldwide pandemic occurs every 10-20 years [2]. China is a temperate region, the peak time of influenza is from November to March of the

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following year, and the duration of local outbreaks is about 6-8 weeks [3]. The body function of children is not yet mature, and the immune response of the body may be delayed. This may contribute to higher levels of viral replication and make them more vulnerable to influenza viruses due to age-dependent differences. Young children not only become infected with influenza themselves, but can also transmit the virus to family members and cause widespread transmission in schools, kindergartens and the community [4]. Compared with other respiratory infectious diseases, children with influenza have more school absences, and parents have more absences from work due to family care, which brings heavy economic burden to society and families [5]. Common symptoms of the disease include high fever of 40 ry infectious diseases, children with influenza have more school abRespiratory symptoms such as nasal congestion, runny nose, sore throat, cough, etc., and complications such as ear infection or pneumonia, nervous system damage, myositis and rhabdomyolysis syndrome may even be life-threatening [6-7]. Therefore, if the above symptoms occur in children, they should seek medical attention in time to avoid further aggravation of the condition and delay the best time for treatment. At present, the treatment of influenza A is mainly antiviral therapy, of which the most commonly used clinical oseltamivir phosphate granules, which is a neuraminidase inhibitor. Neuraminidase is mainly distributed on the surface of influenza A and B viruses, and neuraminidase inhibitors competitively bind to them, which prevents the sialic acid residues of the formed influenza virus particles from splitting, resulting in the inability of newly formed viruses to be released from host cells [8]. However, there are also some patients with influenza A after taking this drug symptoms improve slowly, repeated high fever does not return, the clinical effect is not satisfactory. Jingfang granule has the effect of reducing inflammation and improving immunity, can inhibit virus activity, and is effective in anti-influenza and anti-inflammatory aspects. This drug is widely used in the prevention and treatment of influenza A and acute upper respiratory tract infection [9]. It can alleviate the symptoms of influenza, shorten the course of treatment, reduce drug resistance, and make up for the shortcomings of oseltamivir treatment. However, the clinical data of randomized controlled studies on its treatment of influenza A are lacking. Based on this, this article analyzed the treatment process and results of 110 children with influenza A in the outpatient department of our hospital, and discussed the clinical effect of oseltamivir phosphate combined with Jingfeng granules in the treatment of influenza A in children, as reported below.

1. DATA AND METHODS

1.1 General Information

A total of 110 children diagnosed with influenza A in the outpatient and emergency department of Tianjin First Central Hospital from October 2022 to April 2023 were selected as the study objects, and were divided into observation group and control group according to random number table method, with 55 cases in each group. Control group: 28 males and 27 females; Age ranged from 1 to 13 years old, mean

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(6.87m October 2022 to April 2023 were selected as the3d, mean (1.2121m 1 to 13 years old, mean (6.87m October 2022 to April 2023 were selected as the study objyears old; The duration of disease was 0.2-3d, with a mean of (1.1616 of (1.16e mean (6.87m October 2022 to April 2023 were selected as the study objects, and were divided into observation group and control grouComparison of gender (Chi-square test) and disease course of remaining age (independent sample T test) between the two groups

Inclusion criteria: (1) Children who met the diagnostic criteria for influenza A in the Expert Consensus on the Diagnosis and Treatment of Influenza in Children, that is, children with fever, headache, cough, chills and other symptoms, and throat swabs tested positive for influenza A virus antigen [11]. (2) Clinical data were complete and there were no drug contraindications; (3) family members were informed of the study, voluntarily accepted clinical treatment, and signed informed consent; (4) children with good cooperation; (5) The study met the requirements of the hospital ethics committee and was approved by it.

Exclusion criteria : (1) children with disease course of more than 72 hours; (2) children with severe bacterial infection; (3) children with underlying diseases; (4) children with congenital diseases; (5) children with lower respiratory tract infection; (6) children with drug allergy; (7) Children who had used antiviral and immune agents before enrollment; (8) Children with lung shadow.

1.2 Treatment Methods

The control group was treated with oseltamivir phosphate granules (Manufacturer: Yichang Dongyangguang Changjiang Pharmaceutical Co., LTD.; Approval number: Sinopyma Approval number H20080763, specification: 15 mg), oral, body weight ion: 15 30mg each time; Body weight 15-23 kg, 45mg each time; Patients with body weight ght 40kg were given medication twice a day for 5 days. Observation group on the basis of control group, combined with Jingfang granules (manufacturer: Shandong New Times Pharmaceutical; Approval number: Z37020357, specification: 15g), 1~3 years old, 3-5G each time; 4~6 years old, 5-10g each time; \geq each time; e; 5-15g each time, 3 times a day, with warm water, continuous medication for 5 days.

1.3 Evaluation of therapeutic effect

Efficacy evaluation: Clinical efficacy of the two groups after treatment, the evaluation criteria are: Obvious effect: After 3 days of treatment, the body temperature of the children has returned to normal, and the flu-related symptoms, such as nasal congestion, runny nose, etc., have disappeared; Effective: After 3 days of treatment, the body temperature of the children returned to normal, and the flu-related symptoms such as runny nose and nasal congestion were improved; Ineffective: After 3d treatment, the child's body temperature did not change, and other symptoms did not improve, or even aggravated. Total response rate = (apparent + effective)/total cases *100%.

1.3.2 Comparing the time when symptoms of fever, cough, nasal congestion and sore throat disappeared between the two groups (independent sample T-test)

1.3.3 Comparison of serum CRP and white blood cell levels before and after treatment between the two groups (paired sample T test and independent sample T test)

1.3.4 Comparing the occurrence of adverse reactions such as abdominal pain, diarrhea, nausea and vomiting, dizziness and lethargy after treatment between the two groups (Chi-square test)

1.3.5 Comparison of the time of virus turning negative after treatment between the two groups (independent sample T-test)

1.4 Statistical Analysis

SPSS20.0 software was used for statistical analysis of the data. $(x\pm s)$ was used to represent the measurement data, and T-test was performed between groups

 χ w test and % were used to represent the statistical data, and P < 0.05 indicated that the difference was statistically significant.

2 RESULTS

2.1 Comparison of clinical efficacy The effective rate of the observation group was 87.27%, which was significantly higher than 96.36% of the control group, and the difference was statistically significant (P < 0.05). See Table 1.

roups	umber of cases	onspicuous effect	ffective	neffective	otal valid
ontrol group	5	5 (45.45%)	7 (30.90%).	(3.64%).	3 (96.36%).
bservation group	5	6 (65.45%).	2 (40.00%).	(14.55%)	7 (85.45%).

Table 1 Comparison of treatment effect between the two groups [example	e (%)]
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 $\chi^2 = 6.225 P = 0.044$

Note: Compared with the control group, P<0.05

2.2 Comparison of the disappearance time of clinical symptoms between the two groups The disappearance time of fever, nasal congestion, cough and sore throat in the observation group was earlier than that in the control group, with statistical significance (P < 0.05). (Independent sample T-test), as shown in Table 2.

Table	2 Comparison	of symptom reso	lution time	between the two	o groups (xab, d)	

roups	umber of cases	eat regression time	asal congestion and runny nose relief time	ore throat relief time	ough relief time
ontrol group	5	.25 + / - 0.57	.44 + / - 0.66	.58 + / - 0.68	.89 + / - 1.01
bservation Group	5	.70 + / - 0.63	.90 + / - 0.90	.78 + / - 0.72	.68 + / - 0.75

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value	.955	.576	1.098	3.127
value	.000	.000	.000	.000

Note: Compared with control group, P<0.05

2.3 Comparison of serum CRP and white blood cell levels between the two groups before and after treatment There was no significant difference in serum CRP and white blood cell levels between the two groups before treatment (P > 0.05). After treatment, serum CRP and white blood cell levels in 2 groups were lower than before treatment, and the differences were statistically significant compared with the control group (P<0.05). (Paired sample T test, independent sample T test) See Table 3.

Table 3 Comparison of serum CRP and white blood cell levels between the two groups before and after treatment

			CRP		White
			CKP	blood cells	
roups					
		re-treatment	fter treatment	efore treatment	fter treatment
ontrol (n=55)	group	3.61 + / - 3.65	.86 + / - 2.02	.69 + / - 3.90	4.91 + / - 1.38
bservation (n=55)	group	.94 + / - 4.50	.08 + / - 2.69	6.85 + / - 2.06	5.25 + / - 2.17
value		.743	1.08	.012	.088
value		0.05	0.05	0.05	0.05

2.4 Comparison of adverse reactions between the two groups The incidence of adverse reactions in the observation group was lower than that in the treatment group, with no statistical significance (P > 0.05). (Chi-square test) see Table 4.

Table 4 Comparison	of adverse reaction	s between the two	groups [example (%)]

vomiting	roups	umber of cases	bdominal pain	iarrhea	ausea and	izziness	rowsiness	otal	
voiniting					vomiting	_			

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ontrol	5	(3.64%).				(1.82%).	
group			(1.82%).	(5.45%)	(1.82%).		(14.55%)
bservation	5	(1.82%).			(0.00%)	(1.82%).	(5.45%)
group			(0.00%)	(1.82%).			

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2.5 Comparison of virus negative transition time between the two groups after treatment The virus negative transition time in the observation group was shorter than that in the control group, and the difference was statistically significant (P < 0.05). (Independent sample T-test) is shown in Table 5.

	Table 5 Virus negative transition tin	ne (xab,d) in th	ne two groups [–]	
	Gro	Nu		Tim
ups	mber of cases		e to turn negative	
	Con	55		5.9
trol group			6 + / - 0.85	
	Obs	55		5.2
ervation Group			1 + / - 0.61	
	t			9.9
value			13	
	p-v			0.0
alue			00	

Note: Compared with the control group, P < 0.05

3 DISCUSSION

Influenza is one of the most common types of respiratory infectious diseases, and it is susceptible to all genders and ages, and children are the group with a high incidence [10]. Many studies have shown that children play a leading role in influenza pandemic [11]. Influenza is one of the most common respiratory diseases and is spread by sneezing or coughing droplets in the air and by contact with an infected person. [12] During the 2019-2020 non-influenza outbreaks, influenza cases were found to be dominated by type A and type B. Among them, the prevalence of influenza A is much higher than that of influenza B, which may indicate that influenza A has a stronger ability to cause local pandemics [13]. The disease causes fever, cough, nasal congestion, nasal discharge, sore throat, myalgia, headache and other symptoms [14]. In severely ill children, symptoms can rapidly progress to respiratory failure, heart failure, septic shock. acute kidney failure, influenza-virus infection-associated encephalopathy/encephalitis (IAE), and even death [15]. At present, oseltamivir phosphate is the most commonly used clinical anti-influenza virus drug, which is an inhibitor of enzyme activity targeting the surface glycoprotein neuraminidase of

influenza A virus. By preventing viral neuraminidase-mediated sialic acid lysis of cell surface receptors and HA particles of budding virus, thus further preventing virus release from cell surface and further spread [16-17], oseltamivir phosphate is considered as the first-line drug for clinical treatment of pediatric influenza [18]. As children are in the growth and development stage, the functional development of various organs is not complete, the development of various enzyme systems in the body is immature, and the drug metabolism rate is slow, so the simple application of western medicine is not safe. Therefore, the exploration of the application of traditional Chinese medicine in the treatment of influenza has become a hot spot in clinical research. Traditional Chinese medicine therapy has the advantages of multi-targeting, including combating influenza virus [19], enhancing immune response, reducing drug resistance and reducing adverse outcomes caused by drug reaction [20].

With the development of Chinese medicine, the technology of traditional Chinese medicine continues to mature, and has been widely used in clinical aspects, and has accumulated a lot of experience in the treatment of influenza. Jingfangxidu powder was recorded in Zhang Shiche's Recipe for Health Preservation in the Ming Dynasty. It is applicable to "the initial stage of plague" and is often used in the treatment of epidemic and infectious diseases, such as acute viral upper respiratory tract infection, dengue fever, influenza A (H1N1), chickenpox and mumps [21]. The prescription contains 11 kinds of Chinese medicinal materials, and the prescription includes ten Chinese herbs, such as Schizonepeta, parsnips, Qianghua, Duhuo, bupleurum, Qianhu, Chuanxiong, Fructus aurantii, Poria, platycodon, and licorice, etc., and it is widely used in clinical treatment of influenza A, acute bronchitis and bronchitis [9]. Jingfang granules is a proprietary Chinese medicine preparation of Jingfang Septuxidou powder, which has the same efficacy as the original formula and is convenient to use and carry. Targeting influenza virus, network pharmacology and molecular docking methods were used to find that Jingping granules may act on cyclooxygenase 2 (PTGS2), Serine protease 1 (Serine protease 1, Serine protease 1, kercetin, luteolin and kaempferol via quercetin, kaempferol and other components. PRSS1 and adrenergic receptoreptoADRB2) serve as the therapeutic effect on influenza, and the mechanism of the action may be related to intervening in cell death, inhibiting the expression of influenza virus and regulating immune response [22]. A variety of compounds were identified from Jingfang granules by LMS, in which coumarins and flavonoid/flavonoid glycosides were the main compounds. Studies have shown that flavonoids/flavonoid glycosides mainly have anti-inflammatory [23], antioxidant [24], anti-tumor [24], antiviral [25] and other pharmacological effects. The coumarin compound acanthopicrin B1 acts on chemokine signaling pathways and cytokine - cytokine receptor interactions. Acanthopsin B1 fights influenza virus infection by inhibiting the POLR2A gene responsible for viral polymerase expression [26]. A thiazolyl coumarin hybrid synthesized by Osman et al. showed antiviral effects against H3N2 and H1N1

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influenza strains on a MDCK cell-based basis. This anti-influenza activity may be due to inhibition of the viral envelope protein neuraminidase [27]. Jingphang granules can

act on nuclear factor Kg(NF-KN), IL-1, IL-6, TNF-NF-L-1IFN-FN-L-1, IL-6, TNF-n

nuclear factor r factor ral envelope protein neuraminidase [27]. Jin promoting cytokine release, affecting the release of influenza virus RNP and the expression of viral protein [22].

The results showed that the total effective rate of observation group was 96.36%, which was higher than that of control group 85.45% (P < 0.05). The remission time of fever, cough, sore throat, nasal congestion and runny nose in the observation group were shorter than those in the control group (P < 0.05), suggesting that it may inhibit the occurrence of respiratory symptoms after influenza virus infection. The results also showed that CRP and WBC levels in serum of children with influenza A could be significantly reduced in the observation group. CRP is a common pro-inflammatory factor in clinic and belongs to acute phase reaction protein. It is synthesized by liver cells mediated by interleukin-6, and is closely related to the degree of body injury. In a healthy state, the content of CRP in the body is relatively low. If the body is infected by bacteria and viruses, the serum CRP concentration will increase significantly, which is a classic marker to evaluate the inflammatory response of the body. Studies have shown that CRP can be used as a potential indicator to assess the severity of influenza A in children [28]. In conclusion, Jingfang granules have the clinical effect of inhibiting inflammatory response in children with influenza A and reducing the risk of serious complications. In addition, there was no significant difference in adverse reactions between the two groups after treatment, suggesting that Jingfang granules did not increase the incidence of adverse reactions. The study also showed that the influenza virus turning negative time in the observation group was significantly shorter than that in the control group after treatment (P < 0.05), suggesting that Jingfang granules had a significant anti-influenza virus effect.

In summary, Jingping granule combined with oseltamivir phosphate granule has definite clinical efficacy in the treatment of influenza A, which can quickly control the disease, reduce the inflammatory response, shorten the course of the disease and reduce the time of virus turning negative. High safety, and reduce the incidence of adverse reactions, can reduce the risk of serious complications, with clinical application and promotion value.

The clinical effect of Jingfang Granule combined with oseltamivir phosphate granule in the treatment of influenza A in children was studied and analyzed. At present, there are few studies on Jingping granules in the treatment of influenza at home and abroad. This study explored this aspect and provided a certain theoretical basis for clinical rational treatment, hoping to help improve the clinical symptoms and family burden of children with influenza. There are still some shortcomings in this study. For example, the study subjects are all children in Tianjin area, and the majority of them are urban children. There is a certain regional error, and the influence of Jingfang Granule on liver and kidney function and immune function is not further evaluated. More prospective clinical observation and research are needed to explore the related problems of Jingfang granules in the treatment of influenza A.

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