Therapeutic Effect of Combined Pediatric Chiqiao Qingre Granules and Oseltamivir Phosphate Granules in Treating Influenza A

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To observe the therapeutic effect of pediatric Chiqiao Qingre granules in conjunction with oseltamivir phosphate granules in treating influenza A. A total of 300 pediatric patients diagnosed with influenza A, admitted to Nanjing Pukou District Traditional Chinese Medicine Hospital from February 2022 to February 2023, were randomly allocated into two groups; the control group and the observation group (150 cases in each group). Routine treatments, including anti-infection measures, cough relief, and correction of acid-base balance, were administered to both groups. Alongside these treatments, the control group received phosphoric oseltamivir granules, while the observation group received a combination of Chiqiao Qingre granules and oseltamivir phosphate granules for the duration of 7 consecutive days. Clinical efficacy, relief duration of nasal congestion, cough, fever, and pharyngeal congestion, as well as the concentrations of C-reactive protein and serum amyloid A, were investigated and compared between the two groups in this study. Moreover, adverse reactions that occurred during the treatment period were closely monitored and recorded. Following treatment, the observation group exhibited a substantially higher total effective rate of 96.67 % in comparison to the control group's rate of 79.67 %, thus indicating a statistically significant difference ($p<0.05$). The observation group exhibited remarkably shorter durations of nasal congestion, cough, fever, and pharyngeal congestion relief as opposed to the control group ($p<0.05$). Following the treatment, decreased levels of both C-reactive protein and serum amyloid A were observed in both groups, with the observation group exhibiting significantly lower levels compared to the control group ($p<0.05$). There were no notable distinctions observed in the incidence of adverse reactions between the two groups ($p>0.05$). The simultaneous administration of pediatric Chiqiao Qingre granules and oseltamivir phosphate granules showcased remarkable therapeutic efficacy and an excellent safety profile in treating influenza A.

Key words: Pediatric Chiqiao Qingre granules, oseltamivir phosphate granules, influenza A, clinical efficacy

The respiratory disease influenza A, more widely recognized as the flu, is attributed to the presence of the influenza A virus[1]. Millions of individuals, including children and adolescents, are annually infected with the influenza A virus, as indicated by estimates from the World health organization[2-4]. Due to their less-developed immune systems, children and adolescents are particularly vulnerable to infection with influenza A, placing them at a heightened risk[2-4]. Respiratory symptoms including cough, sore throat, and fever are common manifestations of influenza A, accompanied by additional discomforts such as general malaise, headache, and muscle aches[5,6]. Effective management of influenza A encompasses the utilization of antiviral drugs alongside symptomatic treatment, providing relief from symptoms and reducing the risk of complications[7-9]. Nevertheless, a specific cure for influenza A is currently unavailable, and certain antiviral drugs used for treatment may have limitations and pose risks of side effects[10,11]. Therefore, the pursuit of alternative treatment methods is imperative. Chiqiao Qingre Granules (CQG) is a well-known

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traditional Chinese medicine formulation comprised of different herbs, and it has gained considerable recognition for its effectiveness in treating colds and related respiratory infections[12,13]. CQG is reputed for its heat-clearing, detoxifying, anti-inflammatory, and immune-enhancing properties, rendering it effect in alleviating symptoms such as fever and sore throat. Oseltamivir Phosphate Granules (OPG) is an antiviral drug commonly utilized in treating symptoms and complications related to influenza A virus infection[14]. OPG works by inhibiting viral replication and transmission, which can shorten the duration of the illness and reduce the severity of symptoms[15,16]. Although both CQG and OPG have shown certain efficacy when used separately, there is currently a knowledge gap regarding their combined use for influenza A, with limited comprehensive research available. Hence, this study seeks to examine the clinical effectiveness, safety, and feasibility of combining CQG and OPG in the treatment of influenza A among children. In total, 300 pediatric patients with influenza A, who sought treatment at Nanjing Pukou District Traditional Chinese Medicine Hospital from February 2022 to February 2023, were chosen for participation in this study. Randomization resulted in an equal distribution of 150 patients in each of the two groups. The control group consisted of 81 males and 69 females, with an age range of 1 y to 12 y and an average age of (6.8±0.5) y. The duration of illness spanned from 4 h to 48 h, with an average duration of (21.9±3.8) h. With an age range of 1 y to 12 y, the observation group comprised of 78 males and 72 females, and had a mean age of (6.5±0.7) y. The average duration of illness was (22.7±3.7) h, ranging from 3 h to 48 h. Between the two groups, no noteworthy distinctions in gender, age, and duration of illness were found ($p>0.05$), indicating their comparability. The Medical Ethics Committee of our hospital granted approval for this study. Patients were enrolled in this study based on the inclusion criteria, which encompassed the confirmation of influenza A through positive symptoms and detection of the influenza A virus antigen. In addition, patients with illness duration of ≤2 d were considered eligible. Complete medical records for the cases were available, and informed consent from the families was obtained. Exclusion criteria for this study encompassed patients with congenital diseases, pulmonary shadows, mental or consciousness disorders, as well as colds resulting from non-influenza viral infections. Both groups were subjected to routine treatments, encompassing anti-infection measures, antitussive therapies, and correction of acid-base balance. However, the control group received additional treatment with OPG (produced by Yichang Changjiang Pharmaceutical Co., Ltd., Approval Number: NMPA H20080763) at dose levels adjusted according to body weight; 30 mg per administration for those weighing less than 15 kg, 45 mg per administration for those weighing between 15-23 kg, 60 mg per administration for those weighing between 23-40 kg, and 75 mg per administration for those weighing over 40 kg. The medication was administered twice daily for 7 d. CQG for pediatric use (Approval Number: NMPA Z20123090), manufactured by Jiangsu Jichuan Pharmaceutical Co., Ltd., were administered to the observation group alongside the medication employed in the control group. CQG were administered at the following dosages; for children aged 1 y-3 y, 2-3 g per administration; for children aged 4 y-6 y, 3-4 g per administration; for children aged 7 y-9 y, 4-5 g per administration; and for children aged 10 y and above, 6 g per administration. The medication was administered three times daily for a total of 7 d. The clinical effectiveness of the treatment was assessed by comparing the outcomes between the two groups. The assessment criteria were defined as follows; significant efficacy, which referred to the disappearance of symptoms and normalization of body temperature within 48 h of treatment; initial efficacy, indicating significant symptom improvement and near-normal body temperature within 48 h of treatment; and no efficacy, signifying no improvement in symptoms and no change in body temperature within 48 h of treatment[17]. The total effective rate was calculated by combining the significant efficacy rate and initial efficacy rate. A comparison was made between the two groups to evaluate the duration of symptom resolution for nasal congestion, cough, fever, and pharyngeal congestion. The degree of inflammation was determined by measuring the concentrations of Serum Amyloid A (SAA) and C-Reactive Protein (CRP) in the serum, both pre and post-treatment. These markers served as the primary indicators for monitoring. A comparative analysis was conducted to examine the presence of

adverse reactions, including diarrhea, nausea/vomiting, abdominal pain, and drowsiness, during the treatment period between the two groups. Statistical Package for the Social Sciences (SPSS) 25.0 will be employed to perform the statistical analysis in this research. Continuous variables will be presented as mean and standard deviation, and their analysis will be conducted using t-tests. Categorical variables, on the other hand, will be expressed as frequencies and percentages (n %) and assessed using Chi-square (χ^2) tests. A significance level of $p<0.05$ will be employed to determine statistical significance. According to the findings depicted in Table 1, the observation group achieved a substantially higher overall effective rate of 96.67 % in comparison to the control group's rate of 79.67 % ($p<0.05$). The observation group exhibited a remarkably shorter duration of resolution for nasal congestion, cough, fever, and pharyngeal congestion compared to the control group, with the differences being significant ($p<0.05$) (Table 2). The serum CRP and SAA levels did not substantially differ ($p>0.05$) between the two groups prior to treatment. However, after treatment, both groups experienced a decrease in serum CRP and SAA levels compared to pre-treatment levels, with the observation group demonstrating lower levels than the control group. These differences were determined to be statistically remarkable ($p<0.05$) (Table 3). With an incidence of 13.33 %, the observation group displayed a slightly higher rate of adverse reactions compared to the control group's rate of 12.00 %. However, no remarkable difference was observed between the two groups ($p>0.05$) (Table 4). In children, influenza A is a widespread flu variant that plays a crucial role in influencing their overall well-being. Oseltamivir phosphate is a commonly employed pharmacological intervention for influenza A. Administered orally during the initial phases of influenza A, it has demonstrated remarkable efficacy in alleviating symptoms, shortening the duration of illness, and mitigating the likelihood of complications. However, even after several days of medication, certain children may still encounter ongoing flu symptoms, resulting in less satisfactory treatment outcomes[18,19]. Researchers have successfully improved the treatment of influenza A in children by integrating CQG with OPG, yielding exceptional outcomes. Modern medicine recognizes several effects of CQG, such as immune regulation, digestion promotion, fever reduction, anti-inflammatory properties, perspiration induction, spasm relief, bacteria inhibition, and pain relief. Generally, the medication is well-tolerated by children, leading to minimal side effects and few significant adverse reactions[20,21]. This study seeks to determine the effectiveness and safety of CQG in conjunction with OPG in managing influenza A in children. The study results revealed a marked difference ($p<0.05$) in the total effective rate between the observation group, which achieved a rate of 96.67 %, and the control group, which achieved a rate of 79.67 %. In addition, the observation group had a shorter recovery time from nasal congestion, cough, fever, and throat congestion compared to the control group, with statistically remarkable differences ($p<0.05$). Following the treatment, a reduction in serum levels of both CRP and SAA was observed in both groups, with notably lower levels observed in the observation group compared to the control group. Both SAA and CRP serve as prevalent pro-inflammatory factors commonly employed in clinical practice, and their levels are closely linked to the degree of tissue damage. They have a direct effect on activating inflammatory cells and vascular endothelium. SAA and CRP are induced by Interleukin-6 (IL-6) to be produced by liver cells. During the acute phase of tissue damage, they are synthesized by the liver. SAA and CRP are regarded as sensitive markers of inflammation as their serum concentrations rapidly increase in response to inflammatory stimulation[22,23]. These results suggest that CQG may have immune regulation and anti-inflammatory effects. Regarding safety, the incidence of adverse reactions in the observation group was slightly elevated at 13.33 % compared to the control group's rate of 12.00 %, but the statistical analysis did not reveal a significant difference ($p>0.05$). The safety of CQG in treating respiratory tract infections in children has been well-established in previous studies[24,25]. Consistent with the findings, the current study supports the view that combining CQG with OPG does not induce a higher occurrence of adverse reactions. In conclusion, CQG in conjunction with OPG in treating influenza A has shown significant clinical efficacy. The observation group exhibited a notable difference, surpassing the control group, in terms of the total effective

rate. Additionally, the observation group outperformed the control group in both symptom relief time and serum inflammatory marker levels. Furthermore, the combined treatment regimen exhibited a good safety profile, with no notable discrepancy found in the incidence of adverse reactions between the two groups. Despite the valuable findings of this study, it is essential to acknowledge its inherent limitations. The small sample size constitutes a significant limitation of this study, potentially impacting the stability and generalizability of the results. Additionally, the relatively short duration of the study restricted the assessment of long-term outcomes and potential complications. In conclusion, the utilization of CQG and OPG in combination has demonstrated positive effectiveness and safety in managing influenza A in children. However, in order to strengthen the clinical relevance of this combined treatment, future research should focus on conducting larger-scale, multicenter studies with long-term follow-up to provide further validation and foster continuous improvement.

TABLE 1: CURATIVE EFFECT

Group (n=150)	Marked improvement	Improvement	Ineffectiveness	Overall effective rate
Observation	118 (78.67)	27 (18.00)	5 (3.33)	145 (96.67)
Control	97 (64.67)	22 (14.67)	31 (20.67)	119 (79.33)
χ^2		21.338		
p		0.000		

TABLE 2: TIME FOR SYMPTOM RESOLUTION

Group (n=150)	Time for nasal congestion to disappear	Cough disappearance time	Fever extinction time	Throat congestion resolution time
Observation	3.04±0.90	2.88±1.29	2.94±1.11	3.04±0.83
Control	4.40±1.14	4.82±1.32	3.68±1.33	4.96±1.29
t	14.596	13.001	8.102	15.056
p	0.000	0.000	0.000	0.000

TABLE 3: SERUM CRP AND SAA

Group (n=150)	CRP		SAA	
	Before	After	Before	After
Observation	19.02±4.00	5.10±1.47*	36.76±3.23	5.08±0.78*
Control	19.96±3.59	8.24±1.71*	38.00±3.67	15.98±1.29*
t	1.641	18.88	0.832	85.361
p	0.102	0.000	0.423	0.000

Note: (*) indicates noteworthy difference after treatment compared with before treatment

TABLE 4: ADVERSE REACTIONS (n %)

Group (n=150)	Diarrhea	Nausea and vomiting	Celialgia	Drowsiness	Overall incidence
Observation	5 (3.33)	5 (3.33)	6 (4.00)	4 (2.67)	20 (13.33)
Control	4 (2.67)	3 (2.00)	5 (3.33)	6 (4.00)	18 (12.00)
χ^2	0.121	38.00±3.67	38.00±3.67	38.00±3.67	38.00±3.67
p	0.728	38.00±3.67	38.00±3.67	38.00±3.67	38.00±3.67

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Conflict of interests:

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