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Original Article

Potency of Lianhua Qingwen granule combined with paramivir sodium chloride injection in treating influenza and level changes of serum inflammatory factors

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Abstract: Objective: To evaluate the therapeutic efficacy and serum inflammatory factors changes of influenza patients received Lianhua Qingwen granule combined with peramivir sodium chloride injection. Methods: The clinical data of 100 influenza patients enrolled in our infirmary from January 2018 to January 2020 were retrospectively analyzed. Among them, 50 patients received eramivir sodium chloride injection (the control group) and 50 patients received Lianhua Qingwen granule plus (the experimental group). The clinical efficacy and serum inflammatory factor, including C-reactive protein (CRP), interleukin (IL)-6, and procalcitonin (PCT) were recorded and compared. Results: The overall effective rate of the experimental group was significantly higher than that of the control group (96.0% vs. 80%, P=0.014). There was difference in the antipyretic time, sore throat relief time, cough relief time and general ache relief time between the two groups (all $P < 0.05$). Before treatment, there was no difference in IL-6, CRP, and PCT levels between the two groups (all $P > 0.05$). After treatment, the IL-6, CRP, and PCT levels were decreased in the two groups, and lower in the experimental group compared with the control group (all P=0.014). The ADRs rate in the experimental group was significantly lower than that of the control group (6.0% vs. 24%, χ^2=6.353, P=0.012). Conclusion: Lianhua Qingwen granule combined with peramivir sodium chloride injection shows a remarkable potency in influenza patients. It can reduce the treatment span and improve the inflammatory factors, which is worthy of clinical promotion and application.

Keywords: Lianhua Qingwen granule, peramivir sodium chloride injection, influenza, serum inflammatory factors

Introduction

Influenza, a seasonal epidemic caused by the influenza virus, is a branchy chronic respiratory infectious disease with high incidence, rapid propagation, and it rappidily causes spread and epidemic [1]. Influenza is prone to children and the elderly who is with low immune function. If it was not treated and controlled in time, it would cause acute sinusitis, otitis media, myocarditis, nephritis, and so on. Influenza virus hosts are widely distributed with patients and recessive infected persons as the main sources of infection. The primary transmission routes include droplet transmission and contact transmission [2, 3]. Except for the usual clinical symptoms such as high fever, fatigue, headache, body ache, etc., it also has characteristic clinical manifestations including nasal congestion, rhinorrhea, dry cough, discomfort behind sternum, facial flushing, conjunctival congestion, etc. [4]. In this study, we adopted Lianhua Qingwen granule combined with paramivir sodium chloride injection on influenza patients.

Data and methods

General data

The clinical data of 100 sufferers with influenza treated in our medical center from January 2018 to January 2020 were analyzed retrospectively. Among them, 50 patients received eramivir sodium chloride injection (the control group) and 50 patients received Lianhua Qingwen granule plus (the experimental group). In the control group, there were 21 males and 29 females, with a mean age of (45.2±5.7) years and an average course of disease of (23.5±3.2) hours. In the experimental group, there were 24 males and 26 females, with a

mean age of (45.4±5.6) years and an average course of (24.3±3.8) hours. There was no remarkable difference in general data of the two groups, which was comparable ($P > 0.05$).

Inclusion criteria

① Meet the criteria for influenza; ② With fever, cough, sore throat, fatigue, and other symptoms; ③ Duration of onset within 48 hours; ④ With certain cognitive and communication skills; ⑤ Approved by the hospital ethics committee, and the written informed consent was provided by the participants.

Exclusion criteria

① Complicated with lower respiratory tract infection; ② With severe heart, kidney, liver and other organs of severe dysfunction; ③ With malignant tumors; ④ With drug allergy.

Method

All patients received conventional examination after admission to hospital. Nasopharyngeal secretions examination and rapid influenza antigen detection were performed by professional stuffs. All patients were given cough-relieving, phlegm-reducing drugs, and atomization, and cooperated with physical cooling according to their conditions. Patients in the control group received peramivir sodium chloride injection (Guangzhou Nanxin Pharmaceutical Co., Ltd., Bibliography of National Drugs: H20130029, specification: 100 ml/bottle). The specific usage: qd, 10 mg/kg each time, intravenous drip. In addition to peramivir sodium chloride injection, the experimental group received Lianhua Qingwen granule (Beijing Yiling Pharmaceutical Co., Ltd., Bibliography of National Drugs as supplementary: Z20100040, specification: 6 g*10 bags) plus, 6 g each time, tid. All patients were continuously treated for 5 days.

Observation indexes and evaluation criteria

The overall effective, antipyretic time, sore throat relief time, cough relief time and general ache relief time between the two groups were compared. The adverse drug reactions (ADRs) rate of the two groups was compared. Enzyme-linked immunosorbent assay (ELISA) was applied to detect the levels of serum inflammatory factors, interleukin (IL)-6 and procalcitonin (PCT). And automatic biochemical analyzer was used to measure the content of serum C-reactive protein (CRP).

Evaluation criteria: The patients were assessed according to symptoms, signs, temperature, and syndrome scores. Syndrome scores mainly included cough, sore throat, fever, generalized pain, nasal congestion and other symptoms, with scores of 0, 1, 2 and 3 respectively according to severity. The higher the score, the more severe the symptoms. Cured: After 48 hours of treatment, the body temperature returns to normal, the symptoms and signs disappear entirely, and the condition had not been repeated. Remarkably effective: After 48 hours of treatment, the body temperature returned to normal, and the syndrome scores decreased by more than 2/3. Effective: After 72 hours of treatment, the body temperature returned to normal, but there was a relapse; the syndrome scores decreased by 1/3-2/3; Ineffective: After 72 hours of treatment, the syndrome scores decreased by less than 1/3, and the condition had not been improved or deteriorated. Overall effective rate (%) = (cured + remarkable effective + effective)/total × 100%.

Statistical methods

In this research, SPSS20.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was selected as the data processing software, and GraphPad Prism 7 (Graphpad Software, San Diego, USA) was used to draw the figure. χ^2 test was adopted for counting data and [n (%)] was used, while *t*-test was adopted for measuring data and ($\bar{x} \pm s$) was used. When $P < 0.05$, the difference was statistically remarkable.

Results

Comparison of the overall efficacy the two groups

The overall effective rate of the experimental group was significant higher than that of the control group (96.0% vs. 80%, χ^2=6.061, t=0.014). See **Table 1** for details.

Comparison of the symptoms relief time of the two groups

There was difference in the antipyretic time, sore throat relief time, cough relief time and general ache relief time between the two

Table 1. Comparison of the overall efficacy of the two groups [n (%)]

	Cases	Cured	Remarkably effective	Effective	Ineffective	Overall effective rate
control group	50	30	12	6	2	48 (96.0%)
experimental group	50	21	9	10	10	40 (80%)
χ^2						6.061
P						0.014

Table 2. Comparison of the symptoms relief time of the two groups ($\overline{x} \pm s$)

Groups	Cases	Antipyretic time	Sore throat disappearance time	Cough disappearance time	General ache disappearance time
control group	50	35±6	67±5	64±4	38±6
experimental group	50	23±5	47±4	46±3	26±3
T		10.8643	22.0863	25.4558	12.6491
P		< 0.001	< 0.001	< 0.001	< 0.001

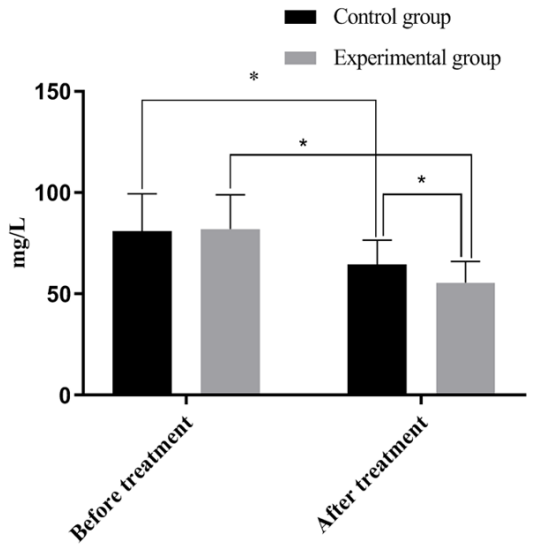

Figure 1. Comparison of levels of IL-6 of the two groups. Note: The abscissa indicated the level of IL-6 in mg/L before and after treatment. The levels of IL-6 in the control group were (68±26) mg/L and (56±17) mg/L before and after treatment, respectively. The levels of IL-6 in the experimental group were (70±24) mg/L and (48±15) mg/L before and after treatment, respectively. *It indicated that there was a remarkable difference in IL-6 level between sufferers among the experimental group before and after treatment (t=3.1868, *P=0.0019). It indicated that there was a remarkable difference in IL-6 level between sufferers among the experimental group before and after treatment (t=5.4966, *P < 0.05). It indicated that there was a remarkable difference in IL-6 level between sufferers in two groups after treatment (t=2.4951, *P=0.0143).

groups (t=10.86, 22.09, 25.46, 12.65, respectively and all P < 0.05). See **Table 2** for details.

Comparison of levels of IL-6 of the two groups

Before treatment, there was no difference in IL-6 level between the two groups (t=0.400, P=0.690). After treatment, the IL-6 level was decreased in the two groups (t=3.187 and 5.500, all P < 0.05), and lower in the experimental group compared with the control group (t=2.500, P=0.014). See **Figure 1** for details.

Comparison of CRP levels of the two groups

Before treatment, there was no difference in CRP level between the two groups (t=0.200, P=0.842). After treatment, the CRP level was decreased in the two groups (t=7.856 and 12.99, all P < 0.001), and lower in the experimental group compared with the control group (t=5.580, P < 0.001). See **Figure 2** for details.

Comparison of PCT levels of the two groups

Before treatment, there was no difference in PCT level between the two groups (t=0.056, P=0.955). After treatment, the CRP level was decreased in the two groups (t=16.43 and 20.33, all P < 0.001), and lower in the experimental group compared with the control group (t=9.5900, P < 0.001). See **Figure 3** for details.

Comparison of ARDs rate of the two groups

In the control group, 12 patients encountered adverse events (12/50), with 2 cases of nausea, 1 case of vomiting, 3 cases of diarrhea, 4 cases of abdominal pain, and 2 cases of dizziness. In the experimental group, 3 patients

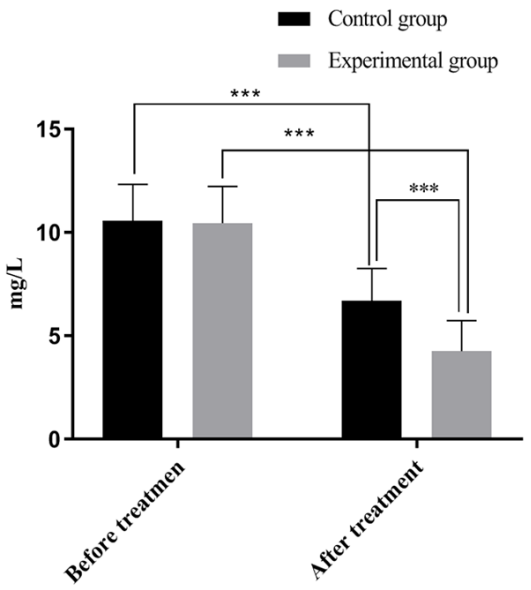

Figure 2. Comparison of CRP levels of the two groups. Note: The abscissa indicated CRP level before and after treatment, and the ordinate indicated CRP level in mg/L; The CRP levels of sufferers among the injected patients before and after treatment were (9.3±2.5) mg/L and (5.6±2.2) mg/L, respectively. The levels of CRP among the injected patients before and after treatment were (9.2±2.5) mg/L and (3.2±2.1) mg/L, respectively. It indicated that there was a remarkable difference in CRP level of the injected patients before and after treatment (t=7.8564, ***P < 0.001); It indicated that there was a remarkable difference in CRP level of the medicated cases before and after treatment (t=12.9944, ***P < 0.001); It indicated that there was a remarkable difference in CRP level between the two groups after treatment (t=5.5799, ***P < 0.001).

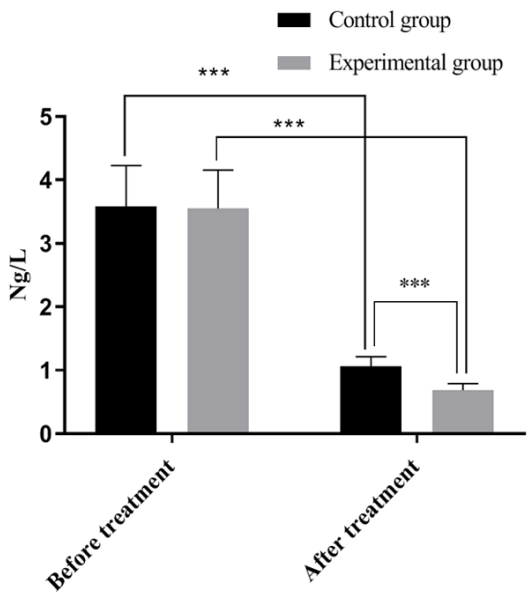

Figure 3. Comparison of PCT levels of the two groups. Note: The abscissa indicated the PCT level before and after treatment, and the ordinate indicated the PCT level in ng/L; PCT levels before and after treatment among the injected patients were (3.13±0.91) ng/L and (0.96±0.21) ng/L, respectively; PCT levels before and after treatment among the experimental group were (3.12±0.86) ng/L and (0.61±0.15) ng/L, respectively; It indicated that there was a remarkable difference in PCT level of the patients without taking medicine before and after treatment (t=16.4300, ***P < 0.001); It indicated that there was a remarkable difference in PCT level of the experimental group before and after treatment (t=20.3307, ***P < 0.001); It indicated that there was a remarkable difference in PCT level between the experimental group and the control group after treatment (t=9.5899, ***P < 0.001).

encountered adverse events (3/50), with 1 case of nausea, 1 case of vomiting, and 1 case of abdominal pain. The ADRs rate in the experimental group was significantly lower than that of the control group (6.0% vs. 24%, χ^2=6.353, P=0.012). See **Table 3** for details.

Discussion

Influenza is a highly contagious disease; it can be spread through air droplets, people-to-people contact, etc. Due to the fast transmission speed, it is easy to diffuse and spread widely [5]. To prevent influenza's serious spread on a large scale, we should pay more attention to and actively deal with it [6]. Influenza is a self-limited disease, but some people develop pneumonia or other complications, which would cause serious health effects and even death. Because of the rapid development, patients may die of brachy chronic respiratory distress syndrome or multiple organ failure [7]. In Traditional Chinese Medicine (TCM), influenza is a category of diseases such as epidemic colds, anemofrigid syndrome, epidemic disease, and infectious damp heat. The etiology of influenza in TCM is mainly exogenous pathogenic qi, which is grumpy, strong in pathogenic qi, and unable to be resisted by healthy qi, so pathogenic qi invades the muscle surface and enters from the nose and mouth, resulting in various symptoms [8, 9].

Previous studies have noted the importance of peramivir, which can effectively inhibit the activity of neuraminidase and then inhibit the bond breakage between viral hemagglutinin and sialic acid of infected cells. Peramivir thus prevents the release of the virus and improve

Table 3. Comparison of incidence of adverse reactions (ADRs) of the two groups

Group	n	incidence of ADRs	non-occurrence rate
control group	50	24% (12/50)	76% (38/50)
experimental group	50	6% (3/50)	94% (47/50)
X^2		6.3529	
P		0.012	

the clinical symptoms [10, 11]. TCM is widely used in the clinic and has obvious advantages in curative effect. Lianhua Qingwen granule, a kind of TCM, consists of forsythia suspensa, honeysuckle, isatis root, houttuynia cordata, gypsum, ephedra, basket fern rhizome, rhodiola rosea, patchouli, bitter almond, rhubarb, menthol, and licorice. Modified and refined based on classic famous prescriptions such as Yinqiao powder and Maxing Shigan decoction, It is hypothesized that Lianhua Qingwen granule could clear away plague and detoxification and dispersing lung heat [12-14]. Forsythia suspensa and honeysuckle, as the chief drugs in the prescription, could light and get transparent, clear away heat and toxic materials, and dissipate stagnation and reduce swelling. Matched with menthol, isatis root, houttuynia cordata, and basket fern rhizome to dispel wind and heat, it has the effect of cooling blood, reducing swelling, and eliminating phlegm and detoxification. Accompanied with Gypsum and rhubarb, it can clear away heat and purge fire, detoxify, relieve cough and asthma, ephedra can clear away lung heat, relieve cough and asthma. Besides, when used together, gypsum and ephedra can prevent ephedra from spreading too much heat, which can obviously enhance the efficacy of dispersing lung heat. Furthermore, rhodiola rosea and bitter almond can clear away heat and phlegm, relieve cough and asthma, and breathe smoothly; patchouli could clear away turbidity and relieve summer heat; Licorice can clear away heat and toxic materials, relieve cough and asthma, and harmonize various drugs [15-17]. This medicine embodies the characteristics of traditional Chinese medicine, which gives consideration to both health and qi and has both exterior and interior solutions.

In this research, the overall effective rate of the experimental group was significant greater than the control group ($P < 0.05$). The symbols relief time in the experiment group were remarkably shorter than the control group ($P < 0.05$). It shows that Lianhua Qingwen granule combined with paramivir sodium chloride injection has an obvious effect on influenza. A recent study by Mitchell [19] has obtained the similar results that Lianhua Qingwen granule can effectively improve the symptoms of fever, cough, sore throat and so on. The serum levels of IL-6, CRP and PCT in the two groups were not remarkably different at baseline ($P > 0.05$). After treatment, the levels of IL-6, CRP and PCT in the experimental group were remarkably lower than the control group ($P < 0.05$), indicating that Lianhua Qingwen granule can effectively reduce the levels of inflammatory factors as CRP and PCT and regulate IL-6 immunity and promote the recovery of immune function. Detailed examination of Lianhua Qingwen granule by David S [20] showed that Lianhua Qingwen granule combined with paramivir sodium chloride injection can regulate immune function, reduce immune damage and inhibit immune imbalance. During the treatment period, the incidence of ADRs in the control group was 24%. The incidence of ADRs in the experimental group was 6%, which was remarkably lower than that in the control group ($P < 0.05$). However, due to the selection bias rooted in retrospective study, confounding factors may result in overestimation of the benefits in this study. Besides, the sample size in the present study was small, future prospective trials with larger sample size are needed.

To sum up, Lianhua Qingwen granule combined with peramivir sodium chloride injection shows a remarkable potency in influenza patients. It can reduce the treatment span and improve the inflammatory factors, which is worth further clinical application.

Disclosure of conflict of interest

None.

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