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Original Article

Effects of levofloxacin hydrochloride and ciprofloxacin on pelvic inflammation and risk factors related to their effects

Huiling Zou*, Wenqian Zhang*, Mingshan Wang, Zhe Li

*Bin Zhou People's Hospital, Binzhou 256600, Shandong Province, China. *Equal contributors and co-first authors.*

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Abstract: Objective: This study aimed to analyze the clinical effect of levofloxacin hydrochloride and ciprofloxacin on pelvic inflammation. Method: One hundred twenty patients with pelvic inflammation were randomly divided into the experimental group (n = 60) and the control group (n = 60). Patients in the experimental group were treated with intravenous infusion of 200 mg levofloxacin hydrochloride twice a day for two weeks, whereas patients in the control group were treated with intravenous infusion of 400 mg ciprofloxacin twice a day for two weeks. Clinical effect after treatment and expression of serum TNF-α and hs-CRP before treatment and 14 days after treatment were measured. Patients were divided into two groups based on the curative effect. The ROC curve was plotted according to multi-factors logistic retrospective analysis to observe the predictive value of each risk factor for the curative effect. Results: Expression of TNF-α and hs-CRP in the serum of patients after treatment was significantly lower than that before treatment ($P < 0.05$). The changes of TNF-α and hs-CRP in the experimental group were significantly higher than those in control group ($P < 0.05$). There was no statistical difference in the incidences of adverse reactions between the two groups ($P > 0.05$). The curative effect of the control group was worse than that of the experimental group ($P < 0.05$). Analysis from single factors showed that there were differences in the course of disease, TNF-α and hs-CRP between the two groups after 14 days of treatment ($P < 0.05$). Multi-factor logistic retrospective analysis showed that the course of disease, TNF-α 14 days after treatment and hs-CRP 14 days after treatment were independent risk factors affecting the curative effect. Conclusion: The expression of TNF-α, hs-CRP and the course of disease after treatment are independent risk factors affecting the curative effects of patients with pelvic inflammation. Levofloxacin hydrochloride can improve the curative effect of patients, which is suitable for clinical promotion.

Keywords: Levofloxacin hydrochloride, ciprofloxacin, pelvic inflammation, curative effect

Introduction

Pelvic inflammation, characterized by high recurrence, long course of disease and repeated attacks, is a common gynecological disease. At present, pelvic inflammation is mainly subjected to drug treatment. Levofloxacin hydrochloride is twice as effective as ofloxacin in terms of antibacterial and bactericidal effects [1]. Ciprofloxacin, as the third generation quinolone antibiotic with the same antimicrobial spectrum as norfloxacin, and is the most effective antibacterial quinolones drug [2]. However, there are few studies to explore the differences between Levofloxacin hydrochloride and ciprofloxacin [3].

TNF-α is an inflammatory factor secreted by NK cells and T lymphocytes, which can regulate the immune response. In the case of inflammation, tumors and other diseases, TNF-α induces the release of CRP and IL-6 to promote the inflammatory response [4]. CRP is one of the most common clinical indicators to indicate inflammation, the expression of which is significantly increased when the body experiences infections, inflammation and tissue damage. While hs-CRP is a more sensitive and accurate detection index [5]. Studies show that the expression of TNF-α and hs-CRP [6-8] in patients with pelvic inflammation increased significantly. However, whether these two indicators can be used as indicators of curative effects after treatment has not been studied.

Therefore, the study explored the effect of levofloxacin hydrochloride and ciprofloxacin on

Table 1. Evaluation of curative effect

Curative effect classification	Evaluation criteria
Healed	Gynecological examination uterus adnexa, pelvic cavity, etc. Normal, no lumbosacral or lower abdominal pain, blood routine indicators returned to normal
Excellence	Pelvic hydronephrosis or mass was significantly reduced by 2/3 or disappeared, uterine appendages were normal or hypertrophic, lumbosacral or lower abdominal pain was alleviated, and blood routine indexes were significantly improved or normal
Effective	Pelvic hydronephrosis or mass was significantly reduced by one third, lumbosacral or lower abdominal pain was alleviated, and blood routine was improved
Of no avail	None of these standards have been met, or even worse

patients with pelvic inflammation and risk factors related to the curative effects.

Methods and materials

Clinical data of patients

In this study, 120 patients with pelvic inflammation who were admitted to our hospital form December 2016 to October 2017 were randomly divided into the experimental group (n = 60) and the control group (n = 60). The experimental group included patients aged 23 to 55 years old, average age was 37.57 + 7.25 years old. The control group included patients aged 22 to 60 years old and their average age was 38.10 + 8.41 years old. The study was approved by the medical ethics committee of the hospital. All patients and their family members were informed of the purpose of the study and signed the informed consent.

Patient eligibility

The inclusion criteria were patients who were diagnosed with pelvic inflammation in Obstetrics and Gynecology [7], patients who were diagnosed with pelvic inflammation through laparoscope or ultrasound guidance, patients with a normal menstrual cycle (28-35 days), and patients who were married or having sexual intercourse.

The exclusion criteria were patients who were pregnant, breast-feeding, patients with other malignant tumors, or other inflammatory diseases, patients with serious conditions that need surgery, patients with contraindications to test drugs, patients with the presence of significant renal impairment (creatinine clearance of < 50 ml/min), or require hemodialysis (either conventional hemodialysis or continuous renal replacement therapy), and patients who experienced cerebrovascular diseases in the past three months.

Drugs and kits

Levofloxacin hydrochloride sodium chloride injection (Shandong Qidu Pharmaceutical Co., Ltd., China, SFDA approval No. H20060437, 0.3 g in 100 mL normal saline), Ciprofloxacin Lactate and Sodium Chloride Injection (Chongqing Saint Pharmaceutical Group Co., Ltd., China, SFDA approval No. H20034158, 0.2 g in 100 mL of normal saline). TNF-α and hs-CRP ELISA kit (Wuhan Moshake Biotechnology Co., Ltd., 69-98069, 69-98807).

Treatment

Patients were treated with levofloxacin hydrochloride and ciprofloxacin lactate in the two groups. In the control group, patients were treated with 400 mg ciprofloxacin intravenously twice a day for a week, with a total of two courses [9]. In the experimental group patients were treated with 200 mg levofloxacin hydrochloride intravenously twice a day for a week, with a total of two courses [10].

Detection of TNF-α and hs-CRP

The expression of TNF-α and hs-CRP in the serum of patients before treatment and 14 days after treatment were tested by Elisa. The Elisa assay protocol were operated in strict accordance with the manufacturer's kit instructions. Three groups of repetitive wells were set up and the experiment was repeated three times.

Outcome measures

Primary observation indices were as follows: the curative effect of the two groups 14 days after treatment was observed (**Table 1**). The

Table 2. Comparison of clinical data of patients

Factor	Control group (n = 60)	Experimental group (n = 60)	t/χ^2 value	*P* value
Age	38.10 ± 8.41	37.57 ± 7.25	0.370	0.712
BMI (kg/m^2)	22.65 ± 1.52	22.84 ± 1.35	0.724	0.470
Anamnesis				
Diabetes mellitus	15 (25.00)	10 (16.67)	1.263	0.261
Hyperlipemia	8 (13.33)	6 (10.00)	0.324	0.570
Smoking history			1.154	0.283
Yes	6 (10.00)	10 (16.67)		
No	54 (90.00)	50 (83.33)		
History of alcoholism			0.536	0.464
Yes	3 (5.00)	5 (8.33)		
No	57 (95.00)	55 (91.67)		
Course of disease (month)	6.42 ± 1.52	6.55 ± 1.49	0.473	0.637
Disease type			0.642	0.886
Endometritis	25 (41.67)	21 (35.00)		
Salpingitis	13 (21.67)	15 (25.00)		
Ovarian abscess	12 (20.00)	14 (23.33)		
Pelveoperitonitis	10 (16.66)	10 (16.67)		
History of induced abortion			1.768	0.184
Yes	16 (26.67)	10 (16.67)		
No	44 (73.33)	50 (83.33)		
Childbearing history			0.901	0.343
Yes	53 (88.33)	56 (93.33)		
No	7 (11.67)	4 (6.67)		

expression of TNF-α and hs-CRP in serum of the two groups before treatment and 14 days after treatment was observed.

Secondary observation indices were as follows: adverse reactions such as rash, abdominal pain, nausea and vomiting, and anorexia were compared in the course of treatment.

Patients were divided into two groups based on the curative effect. Among them, recure and excellence were the group with good curative effects while effective and of no avail were the group with poor curative effect. Clinical data of patients were collected to identify the risk factors. The ROC curve was plotted according to multi-factors logistic retrospective analysis to observe the predictive value of each risk factor for curative effects.

Statistical analysis

In this study, SPSS 20.0 software was used to analyze the collected data. The distribution of data was analyzed by KS. The count data were expressed as percentages (%) and were analyzed using the chi-square test. Fisher exact test was used when the number of cases was less than 5 and the result of the number of trials minus the number of cases was less than 5. Grade data was analyzed with non-parametric test, denoted by Z. Measurement data is expressed by Mean ± Standard deviation (SD ± means). All data were normally distributed, the groups were compared using t test. Paired t test was used for an intra-group before-after comparison. Independent t-test was used for inter-group comparison. Data without a normal distribution was analyzed by the rank sum test. Binary logistic regression was used to identify risk factors. The area under the ROC curve (AUC) was drawn to determine the optimal threshold of the regression model. $P < 0.05$ indicated significant differences.

Results

Comparison of baseline clinical data of patients

According to the clinical data of patients, there were no statistical differences in age, BMI, past medical history, smoking history, history of alcoholism, course of disease, disease type, history of induced abortion and childbearing history ($P > 0.05$) between the control group and the experimental group (**Table 2**).

Expression of TNF-α and hs-CRP in serum of patients before and after treatment

The expression of TNF-α and hs-CRP in the serum of the two groups before and after treatment was examined. There was no significant difference in the expression of the two indicators before treatment ($P > 0.05$). After treat-

Table 3. Comparison of serum TNF-α and hs-CRP expression before and after treatment

Group	TNF-α (μg/mL)					hs-CRP (mg/L)		
	Pretherapy	Treatment for 14 days	t	p	D-value	Pretherapy	Treatment for 14 days	D-value
Control group (n = 60)	2.60 ± 0.34	1.24 ± 0.32*			1.34 ± 0.49	13.56 ± 3.20	7.69 ± 2.34*	5.79 ± 3.84
Experimental group (n = 60)	2.62 ± 0.35	0.78 ± 0.22*			1.81 ± 0.47	13.46 ± 3.06	4.33 ± 1.30*	9.01 ± 3.51
t value	0.317	9.176			5.362	0.175	9.723	4.794
P value	0.751	< 0.001			< 0.001	0.861	< 0.001	< 0.001

Note: *indicates there is a significant different between the comparison after treatment and before treatment ($P < 0.05$).

Table 4. Comparison of adverse reactions in patients

Group	Erythra	Abdominal pain	N and V	Anorexia	Total incidence
Control group (n = 60)	1 (1.67)	1 (1.67)	1 (1.67)	3 (5.00)	6 (10.00)
Experimental group (n = 60)	0 (0.00)	1 (1.67)	1 (1.67)	1 (1.67)	3 (5.00)
χ^2 value	0	0	0	1.905	1.905
P value	> 0.999	> 0.999	> 0.999	0.619	0.168

Table 5. Clinical efficacy of patients

Group	Cured	Excellence	Effective	Of no avail	Z value	*P* value
Control group (n = 60)	27 (45.00)	14 (23.33)	13 (21.67)	6 (10.00)	-2.017	0.044
Experimental group (n = 60)	34 (56.67)	19 (31.67)	6 (10.00)	1 (6.66)		

ment the expression of TNF-α and hs-CRP in serum was significantly lower than before treatment ($P < 0.05$). The expression of TNF-α and hs-CRP in the serum of patients in the experimental group was significantly lower than that of the control group after treatment. By comparing the difference of TNF-α and hs-CRP between the two groups during treatment, changes in the experimental group were significantly higher than those in the control group ($P < 0.05$) (**Table 3**).

Adverse reactions during treatment

By comparing adverse reactions between the two groups, there was no statistical difference in adverse reactions such as erythra, abdominal pain and anorexia ($P > 0.05$). There was no difference in the total incidence of adverse reactions between the two groups ($P > 0.05$) (**Table 4**). Patients with mild symptoms were not given targeted treatment, but still recovered, which had no effect on daily life and post-treatment.

Clinical efficacy of patients

By comparing the clinical efficacy of patients after treatment, the control group was worse than that of the experimental group. There was a significant difference between the two groups ($P < 0.05$) (**Table 5**).

Risk factors of clinical efficacy

According to the curative effect of patients, patients were divided into 94 cases in the group with good curative effect and 26 cases in the group with poor curative effect. According to the data of patients there were no significant differences in age, BMI, past medical history, smoking history, history of alcoholism, disease type, history of induced abortion and childbearing history ($P > 0.05$). Significant differences were observed in the course of disease, therapeutic regimen, TNF-α and hs-CRP 14 days after treatment ($P < 0.05$) (**Table 6**).

Multi-factor logistic analysis

We assigned values to the indicators with differences (**Table 7**). Results indicated that the course of disease, TNF-α and hs-CRP after 14 days of treatment were independent risk factors affecting the efficacy of patients (**Table 8**).

ROC curve analysis

The ROC curve was plotted according to the different indicators of multifactor Logistic analy-

Table 6. Single factor analysis

Factor	Poor curative effect group (n = 26)	Good curative effect group (n = 94)	t/χ^2 value	*P* value
Age	37.95 ± 7.68	38.59 ± 8.15		
BMI (kg/m^2)	22.54 ± 1.45	22.94 ± 1.60		
Anamnesis				
Diabetes mellitus	6 (23.08)	19 (20.21)	0.101	0.750
Hyperlipemia	2 (7.69)	12 (12.77)	0.509	0.476
Smoking history			0.093	0.761
Yes	3 (11.54)	13 (13.83)		
No	23 (88.46)	81 (86.17)		
History of alcoholism			1.266	0.260
Yes	3 (11.54)	5 (62.50)		
No	23 (88.46)	89 (94.68)		
Course of disease (month)	8.31 ± 0.96	6.18 ± 1.24		
Disease type			0.261	0.967
Endometritis	11 (42.31)	35 (58.33)		
Salpingitis	6 (23.00)	22 (36.67)		
Ovarian abscess	5 (19.23)	21 (35.00)		
Pelveoperitonitis	4 (15.38)	16 (26.67)		
History of induced abortion			0.540	0.462
Yes	7 (26.92)	19 (20.21)		
No	19 (73.08)	75 (79.79)		
Childbearing history			1.541	0.214
Yes	22 (84.62)	87 (92.55)		
No	4 (15.38)	7 (7.45)		
Post-treatment TNF-α (μg/mL)	1.42 ± 0.27	0.90 ± 0.31	7.771	< 0.001
Post-treatment hs-CRP (mg/L)	8.34 ± 2.53	5.37 ± 2.13	6.036	< 0.001
Therapeutic regimen				
Levofloxacin	7 (26.92)	53 (45.38)		
Ciprofloxacin	19 (73.08)	41 (43.62)	7.070	0.008

sis, among which AUC of the course of disease was 0.916, 95% CI: 0.867~0.964, AUC of TNF-α, 0.897, 95% CI: 0.842~0.951 and AUC of hs-CRP, 0.813, 95% CI: 0.724~0.902 (T**able 9** and **Figure 1**).

Discussion

Pelvic inflammation, a common disease of the female reproductive system, is easily transformed into chronic pelvic inflammation due to infection of the reproductive system and lack of effective treatment. Patients with severe symptoms are prone to infertility caused by adhesion of endosalpinx, which affects the daily lives and health of patients [11, 12]. The main cause of pelvic inflammation is a defect in the immune system of patients, leading toinvasiveinfection.Theclinical manifestations of pelvic inflammation are increased leucorrhea and abdominal distension [13]. Pelvic inflammation is mainly treated with tinidazole and antibiotics but with poor curative effects. Therefore, a new choice of therapeutic drugs that really matters.

In this study, patients with pelvic inflammation were treated with levofloxacin hydrochloride and ciprofloxacin. As the third-generation quinolone drug, levofloxacin exerts its antibacterial effect by inhibiting bacterial DNA gyrase, and shows better effects and less adverse reactions than that of ofloxacin [14]. Ciprofloxacin also shows excellent effects on respiratory infections, gonadal infections, urinary infections, as well as other inflammatory diseases [15]. In this study, levofloxacin hydrochloride and ciprofloxacin were used to treat the patients. According to curative effect of patients in two groups, the clinical efficacy of the experimental group was better than that of the control group, indicating that levofloxacin hydrochloride played an important role in treating pelvic inflammation. A study by Judlin et al. [16] showed patients suffering from pelvic inflammation without complications were treated with metronidazole and levofloxacin for 2 weeks, 67.5% of patients recovered after treatment while 56.67% patients recovered by using levofloxacin alone accounting for 56.67%. With the same curative effect, the effect of combined drugs was improved, but the cost of combined drugs was higher, which causes a burden on patients. There was no difference in the adverse reactions by using levofloxacin and ciprofloxacin in pelvic inflammation. The efficacy

Table 7. Assignment tables

Index	Assignment
Curative effect	Good curative effect group = 1, Poor curative effect group = 0
Course of disease	Because the data is a continuous variable, use the raw data to analyze
Posttreatment TNF-α	Because the data is a continuous variable, use the raw data to analyze
Post-treatment hs-CRP	Because the data is a continuous variable, use the raw data to analyze
Therapeutic regimen	Levofloxacin = 1, Ciprofloxacin = 0

Table 8. Multi-factor Logistic analysis

Factor	β	S.E,	Wals	Sig.	Exp (B)	EXP (β) 95% CI	
						Superior limit	Lower limit
Course of disease	-1.387	0.479	8.377	0.004	0.250	0.098	0.639
Posttreatment TNF-α	-4.069	1.475	7.606	0.006	0.017	0.001	0.308
Post-treatment hs-CRP	-0.401	0.157	6.513	0.011	0.670	0.492	0.911
therapeutic regimen	-0.579	0.954	0.368	0.544	0.560	0.086	3.638

Table 9. ROC curve data

Factor	AUC	95% CI	Specificity	Sensitivity	Youden index	Cut-off
Course of disease	0.916	0.867~0.964	77.66%	96.15%	73.81%	7.075
Posttreatment TNF-α	0.897	0.842~0.951	72.60%	96.15%	72.75%	1.056
Post-treatment hs-CRP	0.813	0.724~0.902	81.91%	69.23%	51.16%	6.616

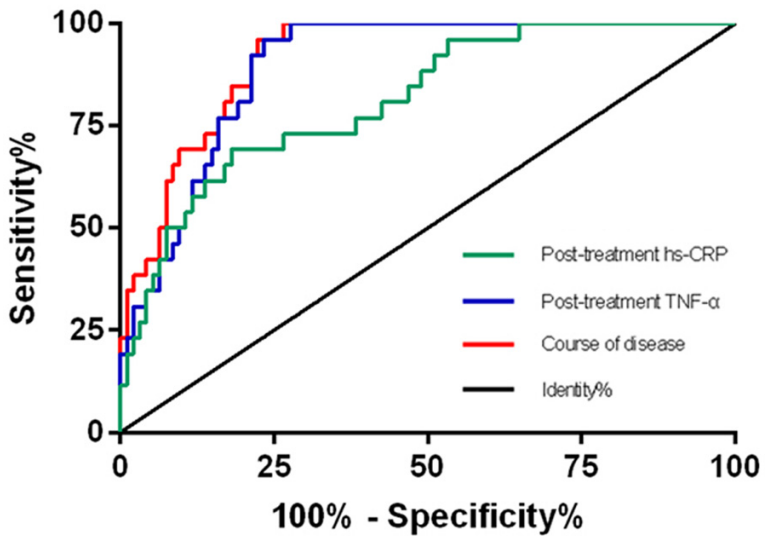

Figure 1. ROC curve: Course of disease, the AUC of TNFα and hs-CRP after treatment.

of levofloxacin is better than ciprofloxacin. Therefore, levofloxacin maybe a better choice for treating pelvic inflammation.

At present, there are few clinical observations on the clinical efficacy of pelvic inflammatory disease which needs to be observed through a variety of tests. As a multi-functional cytokine, TNF-α activates a large number of secretions through monocytes and macrophages, which can reduce the synthesis by the degradation of proteoglycan and collagen [17, 18]. CRP, one of the most sensitive indicators of non-specific inflammatory responses in the human body, is a protein synthesized by hepatocytes mediated by IL-6 inflammatory factors. When tissues are damaged, hypoxia and ischemia occur. CRP in the blood will increase dramatically when trauma and acute inflammation occurs. The expression of CRP in patients was tested by hs-CRP than through more sensitive standard [19, 20]. Based on the expression of TNF-α and hs-CRP in the serum of patients before and after treatment, the expression of TNF-α and hs-CRP in the two groups were significantly decreased after treatment, especially the experimental group, and was significantly

lower than that of the control group. So, the expression of the two indicators can be used to judge the conditions of patients after treatment. Moreover, patients were divided into groups according to clinical efficacy. The difference of clinical data between the group with poor curative effect and group with good curative effect was analyzed by single factors. The results showed that the expression of TNF-α and hs-CRP in the serum of patients with good curative effect was significantly lower than those with poor curative effect. While the course of disease in patients with poor curative effect was longer than that in patients with good curative effect. Analyzed by multi-factor logistic analysis, TNF-α after treatment, hs-CRP after treatment and course of disease were independent risk factors affecting the efficacy of patients. Based on the ROC curve, TNF-α and hs-CRP after treatment, course of the disease, are of great significance in observing the clinical efficacy of patients.

In this study, the clinical efficacy and safety of levofloxacin hydrochloride and ciprofloxacin in the treatment of pelvic inflammation were compared. Levofloxacin hydrochloride was better than ciprofloxacin in the treatment of pelvic inflammation. Multi-factor analysis showed that the expression of TNF-α, hs-CRP and course of disease after treatment were independent risk factors affecting the efficacy of patients. However, there are some limitations in this study. The expression of TNF-α and hs-CRP in the serum between patients with pelvic inflammation and healthy people was not compared. Moreover, the curative effect of the two drugs in this study is far from ideal. Therefore, a healthy group will be added to compare the difference of expression of TNF-α and hs-CRP in the serum of patients with pelvic inflammation and healthy people. We also need to find other drugs to increase the cure rates of patients.

In conclusion, the expression of TNF-α, hs-CRP and course of disease after treatment are independent risk factors affecting the clinical efficacy of patients with pelvic inflammation. Levofloxacin hydrochloride can improve the clinical effect of treatments, which is suitable for clinical promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Mingshan Wang, Bin Zhou People's Hospital, No. 515 Huanghe 7th Road, Bincheng District, Binzhou 256600, Shandong Province, China. Tel: +86-18554300911; E-mail: msawa11@163.com

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