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Original Article

Clinical study of minocycline hydrochloride combined with implant surface mechanical debridement in the treatment of dental peri-implantitis

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Abstract: Background: This clinical study aimed to analyze the curative effect of minocycline hydrochloride combined with implant surface mechanical debridement in the treatment of dental peri-implantitis. Methods: Eighty-six patients with peri-implantitis admitted in our hospital were randomly and evenly divided into the study group and control group. The patients in the control group were treated with mechanical debridement combined with iodine glycerin, while those in the study group were treated with mechanical debridement combined with minocycline hydrochloride. The therapeutic efficacy, probing pocket depth (PPD), modified plaque index (mPLI), and modified sulcus bleeding index (mSBI) were compared between the two groups. Results: One month after treatment, the total effective rate of the study group was higher than that of the control group, and the difference was statistically significant (P<0.05). Before treatment, there was no significant difference in the PPD, mPLI, mSBI, and the expression of IL-6 and TNF-α in the gingival crevicular fluid (GCF) between the two groups. However, after treatment, the PPD, mPLI, and mSBI and the expression of IL-6 and TNF-α in the GCF of the two groups were greatly decreased (P<0.05), with those of the study group being lower than those of the control group. This difference was also statistically significant (P<0.05). Conclusion: Mechanical debridement combined with minocycline hydrochloride exhibits a good curative effect on peri-implantitis. It can effectively improve dental plaque, hemorrhaging, and inflammatory factors in the GCF. Moreover, it has fewer adverse reactions and higher safety and thus is worth promoting in clinical practice.

Keywords: Minocycline hydrochloride, mechanical debridement, peri-implantitis, treatment

Introduction

Oral implantology is a subject technology which has been developed since the twentieth century and it can better treat prosthodontics [1]. However, with the gradual promotion of implant restoration treatment, various implant complications have begun to appear, including peri-implantitis [2]. Peri-implantitis is a disease caused by the accumulation of dental plaque around the implant due to poor oral hygiene, which leads to inflammation of the surrounding soft tissue and may even involve the bone beds, thus inducing bone resorption diseases [3, 4]. Moreover, peri-implantitis has a high prevalence rate. If it is not treated in time, the implant will loosen or even fall out, which will greatly impact the quality of life of the patients [5].

Studies [6] have shown that microbial infection is one of the important causative factors of peri-implantitis. Therefore, the treatment should focus on controlling infection and pathogenic bacteria in the peri-implant probing pocket [7]. In addition, previous studies [8] have shown that instruments or ultrasound devices can effectively improve the patients' clinical symptoms during the treatment of peri-implantitis. Since mechanical debridement alone is difficult to completely remove the infection around the implant, it is suggested to combine it with antibiotics, particularly minocycline hydrochloride, which has broad-spectrum activity against bacteria such as *Escherichia coli* and *Staphylococcus*. Compared with the traditional broad-spectrum antibiotics, minocycline hydrochloride has a high concentration and long acting time [9]. Previous studies [10] have shown that

minocycline hydrochloride can inhibit the pathogenic bacteria in periodontal tissues, which can effectively prevent the occurrence of periodontitis.

Although both treatments are common, there are relatively few studies on mechanical debridement combined with minocycline hydrochloride in the treatment of peri-implantitis. Therefore, in order to provide a better approach for peri-implantitis treatment, we compared the curative effect of mechanical debridement on the implant surface combined with minocycline hydrochloride and iodine glycerin.

Materials and methods

General information

Eighty-six patients with peri-implantitis admitted to our hospital were included in this study, including 47 males and 39 females. The average age was (27.13±5.86) years. The patients were randomly and evenly divided into the study and control groups. The patients of the control group were treated with mechanical debridement combined with iodine glycerin, while those of the study group were treated with mechanical debridement combined with minocycline hydrochloride. Inclusion criteria: patients meeting the diagnostic criteria for peri-implantitis [11], and those with implanted dental restorations. Exclusion criteria: patients allergic to minocycline hydrochloride; patients with other immune or bleeding disorders; patients who had taken antibiotics or immunosuppressants within the past 3 months; patients who received other periodontal treatments, and patients with cognitive and communication impairments. This study has been approved by the Ethics Committee of Hainan Stomatological Hospital. All patients and families involved in the experiment have signed the informed consent.

Experimental equipment and drugs

The carbon fiber ultrasonic scaler required for mechanical debridement was purchased from Swiss Electro Medical Systems. Iodine glycerin was purchased from Dongfanghong Branch, Harbin Renhuang Pharmaceutical Co., Ltd., with registration number GYZZ H20073628. The minocycline hydrochloride was purchased from Sunstar INC Japan, with registration number H20100244. The periodontal probe was purchased from Shenzhen Yuyilingtai Technology Co., Ltd. IL-6 and TNF-α ELISA kits were purchased from Shanghai Good ELISA kit producers.

Treatment methods

An ultrasonic scaler was first used to scale the gingiva in both groups of patients. Stimulations like the dental plaque and periodontal calculus were removed. To rinse and disinfect the lesions, 3% hydrogen peroxide and 0.9% physiological saline were used. Subsequently, 0.5 ml of iodine glycerin was slowly injected into the bottom of the periodontal pocket in the control group until it overflowed. Minocycline hydrochloride (0.5 ml) was injected into the periodontal pocket of the study group, and the injection was stopped when the cataplasm overflowed. All patients refrained from gargling or eating for 2 hours. The treatment was performed once a week for a total of 4 weeks.

Indicator detection method

(1) Probing method of probing pocket depth (PPD): The long axis of the implant was parallel to the probe, and the probe tip was attached to the tooth surface. When the probe was placed into the pocket bottom, the probe depth, which ranges from the pocket bottom to the gingival margin, was recorded.

(2) Test method of modified plaque index (mPLI) was as follows: Dental plaque was not found on the implant surface by the gentle scraping of the probe tip. Dental plaque was found on the implant surface by the gentle scraping of the probe tip. Dental plaque was macroscopic. A large amount of mild scale could be seen.

(3) mSBI: No bleeding was found on the probe. There was punctate hemorrhaging. There was linear hemorrhaging in the gingival sulcus. There was severe or spontaneous hemorrhaging.

(4) ELISA was used to test the expression of inflammatory factors IL-6 and TNF-α in the GCF of the patients. It was conducted based on the instructions.

Outcome measures

(1) The efficacy of treatment in the two groups 1 month after treatment was compared, which was classified into recovery, marked improve-

Table 1. General data table of two groups of patients

Factor	Study group n=43	Control group n=43	X^2/t	P
Gender			0.047	0.829
Male	24 (55.81)	23 (53.49)		
Female	19 (44.19)	20 (46.51)		
Age			0.046	0.830
≥27	23 (53.49)	22 (51.16)		
<27	20 (46.51)	21 (48.84)		
BMI (kg/m^2)			0.049	0.825
≤22	16 (37.21)	17 (58.82)		
>22	27 (62.79)	26 (41.18)		
Implanting time (year)	2.41±0.45	2.42±0.46		
Whether drink alcohol			0.050	0.822
Yes	15 (34.88)	16 (37.21)		
No	28 (65.12)	27 (62.79)		
Coagulation				
PT (s)	14.71±1.23	14.68±1.25	0.006	0.995
APTT (s)	33.67±2.06	33.72±2.08	0.112	0.911
TT (s)	16.27±1.09	16.26±1.10	0.043	0.966
FIB (g/L)	2.93±0.21	3.01±0.23	1.684	0.100

ment, improvement, and ineffective. Recovery: The clinical symptoms and signs disappeared completely, the bleeding of the roots and gingival sulcus disappeared, and the depth of the periodontal pocket was less than 2 mm. Marked improvement: The clinical symptoms and signs basically disappeared, the periodontal pocket depth was greater than 2 mm but less than 3 mm, and the bleeding of the root and gingival sulcus disappeared. Improvement: All clinical symptoms and signs were reduced. Ineffective: The clinical symptoms, signs, and various indicators were not improved. Total effective rate = (number of patients with recovery outcome + number of patients with marked improvement outcome)/total number of patients × 100%. (2) Detection and comparison of PPD before and after treatment between the two groups. (3) mPLI before and after treatment was detected and compared among all patients. (4) mSBI before and after treatment was detected and compared among all patients. (5) The expression of inflammatory factors IL-6 and TNF-α in the GCF before and after treatment was detected and compared among all patients. (6) The adverse reactions of patients in both groups were recorded and compared during the treatment. Adverse reactions included nausea and vomiting, loss of appetite, dizziness, and headache.

Statistical methods

In this study, the statistical software SPSS 20.0 (Shanghai YuchuangNetwork Technology) was used for analyzing and processing the data. The enumeration data were indicated by the percentage and number of cases [n (%)]. The comparison between groups was carried out by *Chi*-square test; the measurement data was indicated expressed as "Means ± SD". The comparison within groups was performed by t test was; $P<0.05$ was considered statistically significant.

Results

General data comparison

There were no marked differences in gender, age, body mass index (BMI), and implant time between the two groups ($P>0.05$), which were comparable (**Table 1**).

Comparison of curative effects among all patients

In the study group, the number of patients having recovered, being markedly improved, improved, and ineffective outcomes was 25, 15, 2, and 1, respectively; while that in the control group was 20, 11, 8, and 4, respectively. The

Table 2. Clinical curative effect evaluation of two groups of patients [n, (%)]

Efficacy	Study group n=43	Control group n=43	X^2	P
Recovery	25 (58.14)	20 (46.51)	0.031	0.861
Marked Improvement	15 (34.88)	11 (25.58)	0.882	0.348
Improvement	2 (4.65)	8 (18.60)	4.074	0.044
Ineffective	1 (2.32)	4 (9.30)	1.911	0.167
Total effective rate	40 (93.02)	31 (72.09)	6.541	0.011

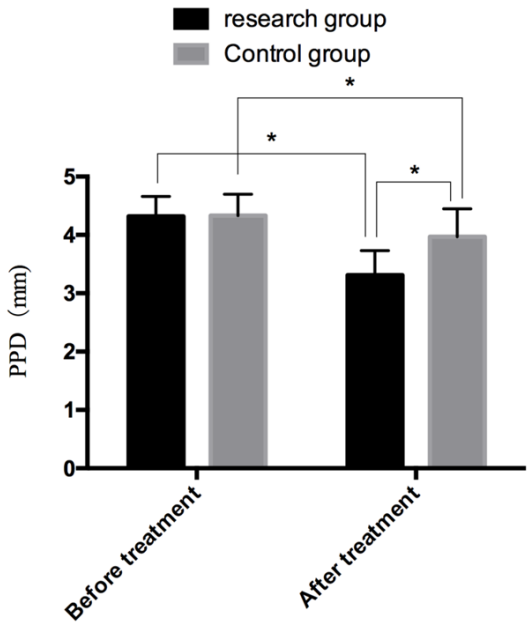

Figure 1. Comparison of PPD between the study group and control group before and after treatment. Before treatment, no marked difference occurred in the PPD between the two groups of patients (P>0.05). The PPD in the two groups after treatment was lower than that before treatment, but the PPD of the study group was lower than that of the control group. The difference was significant (P<0.05). Note: *indicates P<0.05.

total efficacy rate of the study group was 93.02%, which was notably higher compared with that of the control group (72.09%) (P<0.05) (**Table 2**).

Comparison of PPD before and after treatment between the two groups of patients

The PPD of the study group before and after treatment was (4.32±0.34) mm and (3.31±0.42) mm, respectively; while those of the control group was (4.33±0.37) mm and (3.97±0.48) mm. The PPD in the two groups after treatment was lower than that before treatment, with the PPD of the study group being significantly lower than that of the control group (P<0.05) (**Figure 1**).

Comparison of mPLI before and after treatment between the two groups of patients

The mPLI of the study group before and after treatment were (1.81±0.38) and (1.27±0.36), respectively; while those of the control group were (1.84±0.37) and (1.26±0.37), respectively. In addition, the mPLI before treatment was not significantly different between the two groups (P>0.05); however, after treatment, it was lower and the difference was significant (P<0.05) (**Figure 2**).

Comparison of mSBI before and after treatment between the two groups of patients

The mSBI of the study group before and after treatment was (1.93±0.25) and (0.79±0.27), respectively; while those of the control group were (1.94±0.23) and (1.23±0.34), respectively. After treatment, the mSBI of the two groups was lower, of which the mSBI of the study group was lower than that of the control group. This difference was significant (P<0.05) (**Figure 3**).

Comparison of inflammatory factors IL-6 and TNF-α expression in the GCF before and after treatment between the two groups

Before treatment, the expression of IL-6 and TNF-α of the study group was (22.78±0.31) and (46.31±4.87), respectively. The expression of IL-6 and TNF-α of the study group after treatment were (12.26±0.22) and (30.64±3.41), respectively. Before treatment, the expression of IL-6 and TNF-α in the control group was (23.02±0.29) and (45.87±4.54), respectively. After treatment, the expression of IL-6 and TNF-α in the control group was (17.81±0.26) and (37.78±3.38), respectively. The expression of IL-6 and TNF-α after treatment in the two groups was lower than those before treatment.

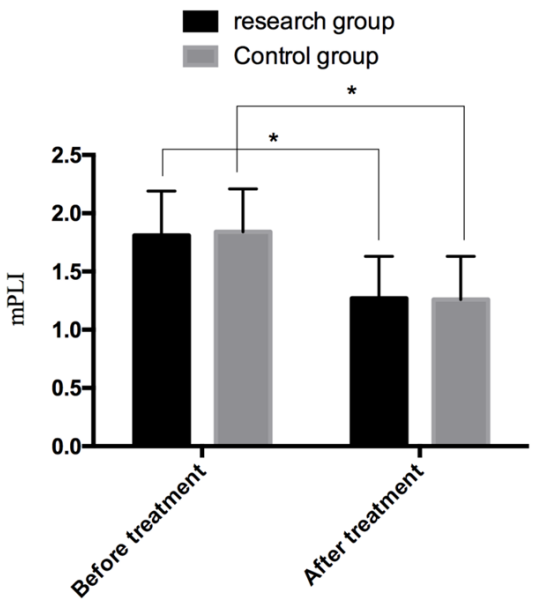

Figure 2. Comparison of mPLI between the two groups before and after treatment. There was no marked difference in the mPLI before treatment between the two groups of patients (P>0.05). After treatment, the mPLI in the two groups was lower than that before treatment, and the difference was significant (P<0.05). There was no dramatic difference in mPLI between the two groups after treatment (P<0.05). Note: *indicates P<0.05.

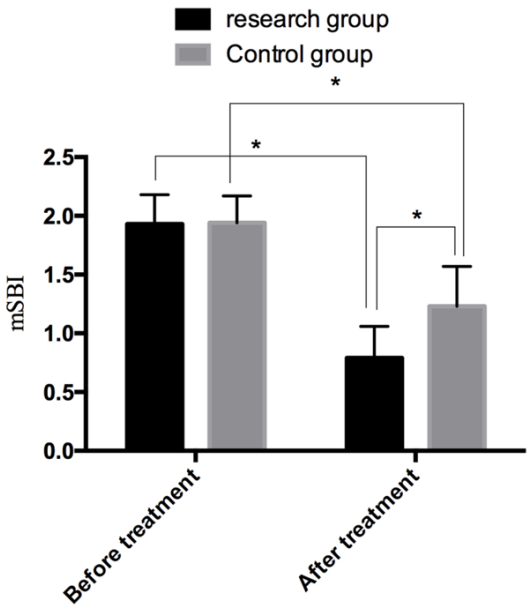

Figure 3. Comparison of mSBI between the two groups before and after treatment. There was no marked difference in the mSBI before treatment between the two groups of patients (P>0.05). The mSBI of the two groups after treatment was lower than that before treatment, but the mSBI of the study group was lower than that of the control group. The difference was statistically significant (P<0.05). Note: *indicates P<0.05.

However, the expression of IL-6 and TNF-α of the study group was lower (P<0.05) (**Figures 4** and **5**).

Adverse reactions between the two groups

After treatment, there were 1, 1, and 0 cases of nausea and vomiting, loss of appetite, and dizziness, respectively in the study group; while those in the control group were 3, 4, and 3, respectively. The incidence rate of adverse events of the study group was 4.64%, which was lower than that of the control group (23.25%) (P<0.05) (**Table 3**).

Discussion

Peri-implantitis is a disease that has the same nature as periodontitis and is an infectious disease induced by bacterial microorganisms [12]. However, as there is no periodontal membrane around the implant and only a small amount of blood vessels exist between the bone tissue and the surrounding tissue, and it possesses weak defense ability. Once infection occurs, the inflammation around the implant develops rapidly, and the bone absorption speed is faster than in periodontitis [13, 14]. At present, the main treatment method for peri-implantitis is to control the infection and remove the dental plaque. The common treatment methods include mechanical debridement and drug treatment [15]. Mechanical debridement therapy has proven to be a safe and effective treatment method, with improved efficacy when combined with drug therapy, as demonstrated by previous studies [16]. However, which drug should be combined with mechanical debridement for treating the peri-implantitis needs further investigation.

In the present study, the curative effects of mechanical debridement combined with minocycline hydrochloride and combined with iodine glycerin were investigated in the treatment of peri-implantitis. For the mechanical debridement, an ultrasonic scaler made of carbon fiber was used to scale the implant; which is the basic treatment for removing dental plaque and calculus. It is said that the carbon fiber ultrasonic scaler can significantly improve the

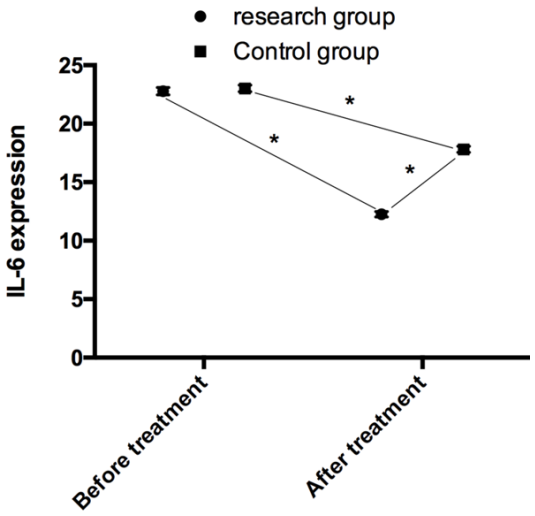

Figure 4. Comparison of IL-6 between the two groups before and after treatment. Before treatment, there was no marked difference in the expression of IL-6 between the two groups ($P>0.05$). After treatment, the expression of IL-6 in the two groups was lower than that before treatment. However, the expression of IL-6 in the study group was lower than that in the control group, and the difference was significant ($P<0.05$). Note: *indicates $P<0.05$.

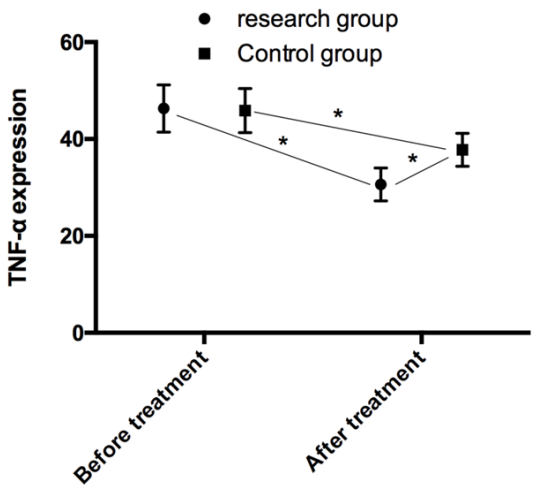

Figure 5. Comparison of TNF-α expression in the GCF before and after treatment in two groups of patients. Before therapy, no marked difference occurred in the expression of TNF-α between the two groups ($P>0.05$). The expression of TNF-α in the two groups after treatment was lower than that before treatment. However, the expression of TNF-α in the study group was lower than that in the control group, and the difference was statistically significant ($P<0.05$). Note: *indicates $P<0.05$.

efficiency of mechanical debridement [17], which is the reason why we chose the carbon fiber ultrasonic scaler. In terms of drugs, we used minocycline hydrochloride ointment, which can effectively release antibiotics from the carrier and help antibiotics play a role directly in the lesion site. The release of microparticles in the soluble oiliness of the ointment is slow and continuous, which can effectively maintain the drug concentration in the periodontal pocket [18, 19]. Iodine glycerin is one of the common medicines for periodontal disease [20], which was chosen as a control drug.

First, the efficacy was compared between the two groups of patients. The results indicated that the total efficacy rate of the study group was higher than that of the control group. To better compare the curative effects in the two groups of patients, their mPLI, PPD, and mSBI indices were also compared. mPLI can reflect the control status of dental plaque [21]. PPD and mSBI can also accurately reflect the patients' oral status [22]. Our results indicated that after treatment, the mPLI, PPD, and mSBI indices of the two groups were lower, suggesting that mechanical debridement combined with minocycline hydrochloride and iodine glycerin can cure peri-implantitis in patients. However, the PPD and mSBI of the study group were lower than those of the control group, suggesting that in peri-implantitis treatment, the efficacy of mechanical debridement combined with minocycline hydrochloride is better than that with iodine glycerin. As one of the strong antibacterial agents among tetracyclines, minocycline hydrochloride has high lipid solubility, making it easier to penetrate into the tissues and body fluids, and conferring it a better antibacterial role [23]. The main mechanism of antibacterial activity is to organize the peptide chain extension and inhibit bacterial protein synthesis by binding to the A-position of the 30S subunit of the bacterial ribosome [24]. Previous studies [25] have shown that the minocycline hydrochloride decreases the local bacterial content in patients with periodontitis. At the same time, it is believed that as a liquid preparation, iodine glycerin is easily lost during treatment, which may be one of the reasons why its efficacy is not as good as that of minocycline hydrochloride [26]. Our conclusions can be explained through the abovementioned study. Next, the inflammatory factors and adverse reactions in the GCF of the two groups were further compared. The results indicated

Table 3. Comparison of adverse reaction rates between the two groups of patients [n, (%)]

Adverse reactions	Research group n=43	Control group n=43	X^2	P
Nausea and vomiting	1 (2.32)	3 (6.98)	1.049	0.306
Loss of appetite	1 (2.32)	4 (9.30)	1.911	0.167
Dizziness	0	3 (6.98)	3.108	0.078
Adverse reaction rate	2 (4.64)	10 (23.25)	6.198	0.013

that there was no marked difference in the expression of IL-6 and TNF-α before treatment in the two groups of patients. The expression of IL-6 and TNF-α after treatment was lower than those before treatment, but the expression of IL-6 and TNF-α in the study group was lower than those of the control group. The incidence of adverse reactions of the study group was lower than that of the control group. This suggests that as compared with iodine glycerin, minocycline hydrochloride can better improve the PPD and mSBI indices, lower the expression of inflammatory factors in the GCF, control the local inflammation of patients, and effectively reduce the adverse reactions during the treatment process. Previous studies [27] have shown that adjuvant therapy of minocycline hydrochloride ointment at the local sites of periodontitis can reduce the expression of TNF-α and IL-17 and other inflammatory factors in the serum of patients. For the differences in adverse reactions, it is suspected that as an ointment with good water solubility, minocycline hydrochloride can maintain better therapeutic effect at a lower dose, while as a liquid preparation, iodine glycerin is easily diluted during treatment. It is necessary to supplement the dose repeatedly, which may induce more adverse reactions.

In summary, mechanical debridement combined with minocycline hydrochloride has a good curative effect on peri-implantitis. It can effectively improve dental plaque, hemorrhaging, and inflammatory factors in the GCF. Moreover, it has fewer adverse reactions and higher safety and is worth promoting in the clinical practice. However, this study also has certain shortcomings. For example, other drugs for treating peri-implantitis were not compared with minocycline hydrochloride, which makes it impossible to confirm that mechanical debridement combined with minocycline hydrochloride is the best treatment for peri-implantitis. To obtain more accurate conclusions, this comparison will be further improved in a follow-up study.

Disclosure of conflict of interest

None.

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