Research Paper

Comparative Study on the Effect of Sipayi Gingival Solution and Tinidazole Tablets for Treating Chronic Periodontitis and its Impact on Periodontal Index

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To analyze the effect of Sipayi gingival solution and tinidazole tablets in the treatment of chronic periodontitis and to conduct a comparative study on their impact on periodontal index. Data of 84 individuals having chronic periodontitis admitted to Shaoxing Stomatological Hospital from January 2020 to January 2023 were selected and were randomly divided into two groups, observation and control group, each with 42 individuals (n=42). On the basis of basic treatment, the control group was treated with tinidazole, and the observation group was treated with Sipayi gingival solution. After treatment, clinical efficacy, periodontitis index levels, changes in inflammatory factors and drug safety were compared between the two groups. After taking the medication, efficacy of the medication in the observation group was higher than that in the control group ($p<0.05$). After treatment, periodontitis indicators in both groups were lower than before treatment, and the observation group was even lower ($p<0.05$). Levels of inflammatory factors in both groups were reduced after treatment, and the observation group was lower. Similarly, the incidence of adverse reactions in the observation group was lower than the control group ($p<0.05$). Sipay gingival fixing liquid medication regimen for chronic periodontitis can effectively control local periodontal infection, with good clinical efficacy and low incidence of adverse reactions and it is suitable for clinical promotion and application.

Key words: Sipayi gingival solution, tinidazole, chronic periodontitis, antibiotics

Chronic Periodontitis (CP) is a chronic infectious oral disease with clinical symptoms such as red and swollen gums, periodontal abscess, and loose teeth[1]. Periodontitis not only invades the periodontal soft tissue and causes inflammatory damage, but it also develops complications such as retrograde pulpitis, root furcation lesions, secondary occlusal trauma, further damaging the periodontium and tooth body, as a result of inflammation[2]. Clinical treatment helps to eliminate pathogenic lesions and inflammation and it also contributes to enhance the morphology and function of dental tissue. Additionally, it also reduces periodontal inflammation. Tinidazole can block the transcription and synthesis of bacterial Deoxyribonucleic Acid (DNA), thereby killing the bacteria[3]. However, because the drug does not completely eliminate inflammation and is prone to recurrence after drug withdrawal, it cannot completely eliminate periodontal complications and easily lead to re-infection. In patients with chronic periodontitis, bacterial infection is one of the main causes of disease progression. Using tinidazole to treat chronic periodontitis can effectively remove bacteria, reduce inflammation, and promote healing. This is also the core reason for choosing tinidazole in this study.

Xipayi gingival liquid is a new Chinese patent medicine preparation that has appeared in the recent years. It is composed of gall seeds and they have the effects of reducing swelling, analgesic, hemostasis and anti-inflammation[4]. It can effectively reduce the level of inflammatory factors in the gingival crevicular fluid, reduce oxidative stress reaction, and shorten the period of tooth decay. Weekly probing depth[5]. CP brings a lot of inconvenience to patients' lives, and the current medication is relatively confusing. This study uses the representative antibiotic drug tinidazole and the new Chinese patent medicine

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preparation, Sipayi gingival solution. This has certain implications for standardizing clinical medication guiding significance.

MATERIALS AND METHODS

General information:

84 patients with CP who were admitted to Shaoxing Stomatological Hospital from January 2020 to January 2023 were selected. All the individuals were randomly divided into 2 groups namely, observation group and control group, each containing 42 patients (n=42). The difference in general data was not significant ($p>0.05$). This study was approved by the ethics committee of our hospital.

Inclusion criteria:

Patients who met the diagnostic criteria for CP; patients who had not undergone periodontal treatment recently; patients who had 16 teeth or above, patients who were eligible for periodontal evaluation and patients who have signed the consent form were included in the study.

Exclusion criteria:

Patients who are allergic to the drugs used for the treatment in this study; patients who were treated with antibiotics within 2 mo and patients having medical complication such as presence of severe hepatobiliary diseases were excluded from the study.

Treatment method:

Patients in both the groups were primarily given basic treatment including scaling, subgingival scaling, root planning and blending. 3 % Hydrogen peroxide (H_2O_2) was used for irrigating the roots of the periodontal pockets.

The patients in the control group were given 0.5 g of tinidazole tablets (Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., with national drug approval number: 20123324 and batch number: B210801H81) with product specifications: 0.5×20 tablets, orally twice a day consecutively for 3 d. Additionally, all the patients were suggested not to eat or drink anything within 1 h after drug administration to ensure better results of drug efficacy.

Similarly, the observation group was given 5 ml of Sipagi gingival fluid (Xinqikang Pharmaceutical Co., Ltd., with national drug approval number: Z65020012 and batch number: 210308) with product specification: 30 ml/bottle) and the patients were advised to rinse for 3 min, twice a day consecutively for 8 d.

Further the patients were also suggested not to eat, drink, rinse or brush their teeth within 1 h after receiving medication in order to avoid reduction of drug efficacy. Patients of both the groups received basic treatment for 3 mo.

Observation indicators:

Observation indicators such as clinical efficacy, periodontitis indicators, changes in inflammatory factor levels, changes in oxidative stress indicators and occurrence of adverse effects during the treatment period were comparatively observed between both the groups and were evaluated. Periodontitis indicators majorly included periodontal Probing Depth (PD), Bleeding on Probing (BOP), gingival Plaque Index (PLI) and Sulcus Bleeding Index (SBI).

Clinical efficacy: The clinical efficacy was evaluated according to the guidelines for diagnosis and treatment of oral diseases[6]. Patients of both the groups were compared and the drug efficacy was assessed using different grades, such as significantly effective, effective and invalid.

After treatment, if there was no gingival redness or swelling, and if periodontal pain disappears and the PD is <2 mm, then it was considered to be significantly effective. Similarly, after receiving the treatment if the root-gingival sulcus bleeding is significantly reduced, periodontal pain is relieved and PD is 2~3 mm, then it was considered as effective. Similarly if no improvement was observed among the patients of both the groups or if even worsened condition of clinical symptoms and various other indices was observed then it was considered to be invalid.

Total effective rate=significantly effective+effective/total number of cases (n)×100 %

Periodontitis indices: The patients of both the groups were assessed for changes the periodontitis levels after treatment. There are 4 periodontitis indicators, namely PD, BOP, PLI and SBI. PD is the periodontal pocket depth and is generally defined as the distance between the gingival margin and

the periodontal pocket bottom. Among them, PD and BOP refer to the percentage of bleeding area in the total tooth area while PLI is the area covered by dental plaque on the tooth surface, which is further divided into 3 levels. Level 0 means there is no plaque on the tooth surface, and level 3 means there is a significant amount of periodontal bacteria. Higher the score, more severe is the plaque; SBI reflects gum bleeding, which is divided into 5 levels, with level 0 indicating healthy gums and level 5 indicates spontaneous bleeding. Higher the score, more severe is the gum bleeding. The above index values are positively correlated with periodontitis symptoms.

Inflammatory factors: The levels of inflammatory factors were assessed. Gingival crevicular fluid was collected from patients in both groups to detect the changes in inflammatory factors between the two groups. Using Enzyme-Linked Immunosorbent Assay (ELISA) the levels of factors like high sensitivity-C-Reactive Protein (hs-CRP), Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and IL-8 were detected and analyzed.

Drug safety: The adverse drug reactions such as itchy skin, dizziness, vomiting and hypotension that occur during medication were recorded and evaluated between the two groups. The incidence rate of adverse effects were recorded.

Statistical analysis:

Statistical Package for Social Sciences (SPSS) version 20.0 software was used for analyzing the data using t-test or Chi-square (χ^2) test. $p<0.05$ was considered as a statistically significant difference.

RESULTS AND DISCUSSION

After treatment, drug efficacy between the two groups was compared. The total effective rates of the observation group and the control group were comparatively assessed and it was found to be 95.24 % and 78.57 % respectively (Table 1).

Subsequently, after treatment, periodontitis index levels were compared. Periodontitis indicators of the two groups of patients were lower before treatment. But it was observed that the observation group depicted even low values when compared with the control group (Table 2).

Levels of inflammatory indices were comparatively analyzed between the two groups. After treatment, the levels of inflammatory factors in both groups were lower than before treatment, and the observation group was even lower (Table 3).

Similarly, the adverse reactions between the two groups were evaluated. 2 patients had adverse drug reactions from the observation group while the control group denoted 9 patients who had adverse reactions during the medication period (Table 4). It was observed that no patients had itchy skin and vomiting. It can be observed that control group showed more adverse reactions compared with the observation group.

TABLE 1: COMPARISON OF DRUG EFFICACY BETWEEN THE TWO GROUPS, n %

Group	n	Effective	Efficient	Invalid	Total effective rate
Control group	42	28 (66.67)	5 (11.90)	9 (21.43)	33 (78.57)*
Observation group	42	36 (85.71)	4 (9.52)	2 (4.77)	40 (95.24)*
χ^2		0.569	0.100	3.960	3.610
p		0.450	0.751	0.046	0.047

Note: *p<0.05

TABLE 2: COMPARISON OF PD, BOP, PLI AND SBI INDICATORS BETWEEN THE TWO GROUPS (x̄±s)

Group	n	PD (mm)		BOP (%)		PLI		SBI	
		Before medication	After medication	Before medication	After medication	Before medication	After medication	Before medication	After medication
Control group	42	5.42±0.75	3.35±0.48*	86.45±1.20	55.64±1.15*	2.64±0.40	1.95±0.49*	3.34±0.22	1.98±0.12*
Observation group	42	5.53±0.71	2.27±0.44*	85.28±1.28	36.12±1.82*	2.62±0.38	1.06±0.32*	3.21±0.24	1.36±0.15*
t		0.690	10.748	4.321	59.694	0.234	10.129	2.587	20.917
p		0.926	0.000	0.956	0.000	0.671	0.000	0.195	0.000

Note: *p<0.05

TABLE 3: COMPARISON OF LEVEL OF INFLAMMATORY MARKERS BETWEEN THE TWO GROUPS

Group	n	hs-CRP (μmol/l)		TNF-α (μg/l)		IL-6 (μg/l)		IL-8 (μg/l)	
		Before medication	After medication	Before medication	After medication	Before medication	After medication	Before medication	After medication
Control group	42	21.69±4.21	14.72±3.48*	9.25±3.29	2.95±0.29*	12.12±1.50	7.40±1.55*	5.41±1.55*	4.53±1.65*
Observation group	42	22.15±4.52	10.95±2.45*	6.04±3.31	1.61±0.30*	11.05±1.50	3.62±1.30*	5.92±1.50	2.25±0.37*
t		0.482	5.740	4.457	20.812	3.268	12.109	1.532	8.738
p		0.000	0.001	0.049	0.000	0.8434	0.002	0.887	0.003

Note: *p<0.05

TABLE 4: COMPARISON OF ADVERSE REACTIONS BETWEEN THE TWO GROUPS, n %

Group	n	Itchy skin	Dizziness	Vomiting	Hypotension	Incidence of adverse reactions
Observation group	42	0	1 (2.38)	0	1 (2.38)	2 (4.76)
Control group	42	2 (4.76)	3 (7.14)	2 (4.76)	2 (4.76)	9 (21.4)
χ^2		1.955	0.955	1.955	0.322	7.960
p		0.1620	0.328	0.1620	0.5741	0.026

Pathogenesis of CP disease has been studied. CP is an anaerobic oral disease caused by plaque microorganisms. Sometimes it is also infected by aerobic bacteria. It is caused by plaque bacteria attacking the periodontal period to form dental plaque and calculus[7]. During weekly infection, the early symptoms are not obvious or mild. As the inflammatory reaction worsens, the periodontal microorganisms and the toxins produce inflammatory factors which are released by the plaque host cells penetrate into the gingival crevicular fluid deep in the periodontal pocket and cause an inflammatory chain reaction[8]. Further damage to dental tissue may lead to alveolar bone resorption[9], resulting in loosening or loss of teeth, and might also cause other adverse consequences. In severe cases, it may also cause systemic diseases.

Clinical manifestations include gum bleeding or swelling, periodontal pocket formation and periodontal abscess. Clinically, supragingival scaling and subgingival scaling are mainly performed, as well as root planning and other therapies to remove the plaque, calculus and other pathogenic irritants. Additionally, anti-infective treatment is also given to eliminate the inflammation and promote periodontal tissue regeneration[10]. However, when periodontal infection occurs, it is difficult to completely remove the plaque at the bottom of the periodontal pocket and the root furcation area. Such conditions might also increase the risk of adverse reactions, resulting in the recurrence of the infection[11].

Further, impact of the two drugs on clinical efficacy and symptoms was also studied. Tinidazole tablets are a new generation nitroimidazole derivatives that have high antibacterial activity against anaerobic bacteria. Tinidazole tablets are mainly used for oral infections caused by sensitive anaerobic bacteria. They can effectively inhibit the DNA synthesis, transcription of anaerobic bacteria and make them inactive for reproduction leading to death, and helps to effectively inhibit the development of inflammation. Clinical studies have shown that the nitro group in tinidazole tablets can reduce cytotoxicity; it can be excreted through the liver, causing less damage to human organs with high bioavailability[12]. Therefore, tinidazole is often used clinically to treat periodontal infections. However, clinical studies have shown that long-term use of tinidazole can cause the rapid growth of non-sensitive microorganisms in the oral cavity, leading to changes in periodontal indices. However, long-term use might also lead to drug resistance. Further, in some patients, it can cause nausea, headaches, dizziness and rashes and some other adverse reactions after administration; the effect of single application is not ideal[13].

Xipayi gingival liquid is a traditional Chinese medicine preparation, which contains gallotannins,

gallic acid and resins, etc. It has strong sore-absorbing, hemostatic and sperm-fixing effects. It is effective in treating sores, aphtha, toothache and other diseases. Clinical studies have shown that gallic acid can activate multinucleated macrophages, reduce free radical levels, resist dental plaque, protect gum tissue and improve the body's non-specific immune system function[14]. At the same time, Sipayi gum liquid has good analgesic, antibacterial and endotoxin degradation effects. It can control the development of the disease in the early stage of inflammation and reduce the damage to gum tissue. The drug effect lasts for a long time and can effectively inhibit the inflammatory response[15]. In this study, the total effective rate in the observation group was significantly higher than that in the control group ($p<0.05$), indicating that the efficacy of Sipayi gum liquid in the treatment of CP is accurate and stable, which is consistent with the research results of Jing[16].

Effects of two drugs on periodontal clinical indices were studied. During CP, local tissue inflammatory infiltration is severe and a large amount of free radicals are produced that not only destroys the periodontal tissue environment, but also causes gum bleeding, abscesses, and formation of periodontal pockets as the inflammation continues to worsen. Therefore, deeper the periodontal pockets, more likely are the teeth to be damaged and more severe is the peripheral inflammation[17]. Normal periodontal probing will not cause bleeding, but when there is local inflammation in the oral cavity, bleeding will occur easily during probing. Sipayi gingival liquid can reduce the levels of superoxide anions, hydrogen peroxide and other free radicals around the gums, degrade endotoxins, increase the permeability of periodontal capillaries, thereby improving the inflammatory response of tissues around the teeth and rejuvenating damaged gums. Once the tissue is repaired[18] then the periodontal indicators are effectively reduced.

In this study, after treatment with Sipayi gingival fixing solution, the periodontal indicators PD, BOP, PLI and SBI of the observation group significantly improved and were significantly better than those in the control group ($p<0.05$), suggesting that Sipayi gingival fixing solution. It has a good therapeutic effect, which is consistent with the research results of Ying *et al*.[19].

Effects of two drugs on the levels of inflammatory factors IL-6, IL-8, TNF-α and CRP was studied. During the periodontal infection, gingival crevicular fluid can be detected in subgingival plaque and serum, and the amount of gingival crevicular fluid exudation is closely related to the degree of periodontal infection. Gingival crevicular fluid contains a variety of inflammatory factors. Clinically, the degree of periodontal infection can be predicted by detecting the levels of inflammatory factors in gingival crevicular fluid. High levels of IL-6 are closely associated with the progression and tissue destruction of periodontitis[20]. IL-8 is a peptide cytokine that can promote the release of proteases, damage endothelial cells, block microcirculatory blood flow, cause tissue necrosis, cause damage to organ function and aggravate inflammatory reactions. Hs-CRP is a protein substance produced in the blood when the human body is infected by microorganisms. When bacteria invades the body, the CRP value will rise sharply which is an important indicator of inflammation in the body. Patients with CP are accompanied by systemic inflammatory reactions, so CRP can be used as a basis for judging the efficacy of antibiotics. TNF-α comes from a variety of cells and is a cytokine which is related to inflammation. After infection, high levels of TNF-α and other inflammatory factors can be detected in the gingival sulcus. Increase in TNF-α concentration indicates that the inflammatory reaction is aggravated.

Sipayi gingival solution can inhibit the expression and release of inflammatory factors, effectively reduce capillary permeability in response to oxidative stress, promote the necrosis and shedding of inflammatory tissue, thereby reducing the exudation and edema of periodontal tissue[21]. In this study, the levels of inflammatory factors IL-6, IL-8, TNF-α and CRP in the observation group were lower than those in the control group ($p<0.05$). The treatment effect was definite and consistent with the study of Zhang *et al*.[21].

Analysis of the incidence of adverse reactions was summarized. In this study, the incidence rate of adverse reactions in the observation group was 4.76 %, which was <21.4 % of the control group ($p<0.05$). It has been shown that the application of Sipayi gum solution to treat periodontal inflammation has a low incidence of adverse reactions, and the ingredients of this mouthwash

do not contain any irritating substances, it will not have adverse effects on the oral mucosa and its safety is guaranteed[19]; so the clinical treatment is safe and reliable.

The mechanisms of drug-drug interactions were not studied in this study. The interaction mechanism between the drugs itself is relatively complex and future research should be divided into different drug combinations to explore the drug effects of different drug combinations. Only in this way the advantages of combination therapy can be explained well.

In short, the application of Sipayi gingival liquid to treat periodontitis can effectively improve the condition of periodontal tissue of the patients, reduce local periodontal infection, control the development of inflammation and can help to promote tissue repair. This effect is significant and is suitable for clinical application.

Conflict of interests:

The authors declared no conflict of interests.

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