Diferentes formas de dosificación farmacéutica de tinidazol para pacientes con periodontitis

Different Tinidazole Pharmaceutical Dosage Forms for Patients with Periodontitis

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Resumen
El tinidazol pertenece a la clase de antibióticos de nitroimidazol y tiene un amplio espectro antibacteriano. Puede ejercer una actividad antibacteriana superior contra muchas bacterias anaerobias. Ha sido relativamente común en el tratamiento de pacientes con periodontitis, y el efecto es bueno. Este artículo es para observar el efecto de diferentes formas de dosificación de drogas de tinidazol en pacientes con periodontitis. Métodos Noventa pacientes con periodontitis se inscribieron en el estudio. Se dividieron en el grupo de estudio para el tratamiento del parche oral de tinidazol y el grupo de referencia para el tratamiento de tabletas orales de tinidazol. Comparado. Los resultados mostraron que la eficacia global del tratamiento y la incidencia de reacciones adversas se compararon entre los dos grupos. Los resultados mostraron que el grupo de estudio fue significativamente mayor y menor que el grupo de referencia, P <0.05, estadísticamente significativo. Para pacientes con periodontitis, los resultados de diferentes tratamientos no son los mismos, y el resultado Los ts del programa de tratamiento con parche oral de tinidazol son más significativos: el parche oral de tinidazol se puede administrar en un modo de administración local para elevar la concentración local del fármaco mientras se mantiene un efecto del fármaco a largo plazo sin causar serios problemas de reacción adversa.

Palabras clave: forma de dosificación del fármaco tinidazol; eficacia de la periodontitis; efecto clínico; tasa de depuración bacteriana

Abstract
Tinidazole belongs to the class of nitroimidazole antibiotics and has a broad antibacterial spectrum. It can exert superior antibacterial activity against many anaerobic bacteria. It has been relatively common in the treatment of patients with periodontitis, and the effect is good. This article is to observe the effect of different tinidazole drug dosage forms in patients with periodontitis. Methods Ninety patients with periodontitis were enrolled in the study. They were divided into the study group for the treatment of tinidazole oral patch and the reference group for the treatment of tinidazole oral tablets. Compared. The results showed that the overall treatment efficiency and the incidence of adverse reactions were compared between the two groups. The results showed that the study group was significantly higher and lower than the reference group, P < 0.05, statistically significant. For patients with periodontitis, the results of different treatments are not the same, and the results of the tinidazole oral patch treatment program are more significant. The tinidazole oral patch can be administered in a local administration mode to make the local drug concentration high while maintaining a long-term drug effect without causing serious adverse reaction problems.

Key words: Tinidazole drug dosage form; Periodontitis efficacy; Clinical effect; Bacterial clearance rate

1. Introduction

Periodontitis is mainly chronic inflammation of periodontal support tissue caused by local factors. The age of onset is more common after 35 years of age. If phlegm is not treated in time, inflammation can progress to periodontitis by spreading the gums deep into the periodontal ligament, alveolar bone and cementum[1]. Because it has no obvious symptoms in the early stage, it is easy to be neglected, and it is already serious when the symptoms are present, and even the teeth cannot be retained. Therefore, it is necessary to strengthen the mission to enable patients to see early and timely treatment[2-3].

Early symptoms are not obvious, patients often only have secondary gingival hemorrhage or bad breath, similar to sputum inflammation. At the time of examination, the swelling of the gingival margin, licking nipple
and attached sputum, the softness of the sputum, the dark red or the dark red color, the bleeding is easy to detect. With the further spread of inflammation, the following symptoms occur: (1) periodontal pocket formation: due to the expansion of inflammation, the periodontal ligament is destroyed, the alveolar bone is gradually absorbed, the gums are separated from the root, and the gingival sulcus is deepened to form a periodontal pocket. The depth of the periodontal pocket can be measured with a probe[4–5]. (2) periodontal pus: the periodontal pocket wall ulcers and inflammatory granulation tissue formation, purulent secretions in the bag, so gently press the gums, visible pus. And often have bad breath. (3) loose teeth: due to the destruction of periodontal tissue, especially when the alveolar bone is aggravated, the supporting tooth strength is insufficient, and the teeth are loose and displaced[6]. At this time, the patient often feels occlusal weakness, dull pain, bleeding gums and bad breath.

When the body's resistance is reduced and the periodontal bag is leaky, the periodontal abscess can form, which is a common concomitant symptom of deep periodontal pockets[7-8]. At this time, the gums are oval-shaped, red and swollen, and the surface is bright; the tooth looseness increases, and there is pain; the patient is accompanied by local severe pain[9-10]. At the same time, patients may have elevated body temperature, general malaise, submandibular lymphadenopathy, tenderness and other symptoms. This study compared the effects of different tinidazole pharmaceutical dosage forms (2 types) in the treatment of patients with periodontitis. The report is as follows.

2. Materials and methods

2.1 General Information

The study subjects were 90 patients who were diagnosed with periodontitis, and the time was selected from September to September 2017. The patients were divided into 45 study groups and reference groups. There were no patients with severe organic diseases, patients with coagulopathy, mental disorders, or drug allergy. In the study group, male and female patients were 25 and 20, respectively, with an average age of (45.8 ± 0.2) years; in the reference group, male and female patients were 23 and 22, respectively, with an average age of (48.2 ± 9.6) year old. Observing and comparing the data of the two groups of patients, comparable, P>0.05, no statistical significance.

2.2 Method

Different treatment modes were given to the two groups of patients, that is, the study group was treated with tinidazole oral patch, and the reference group was treated with tinidazole orally. The treatment mode of the study group patients was: taking tinidazole oral patch (specification 5 mg per tablet) for treatment, mainly on the buccal medial gingival surface and lesions, and twice daily treatment. The patient's treatment mode in the reference group was: instructing the patient to take tinidazole oral tablets (0.5 g per tablet), each time using a tablet, and treating it 3 times a day.

2.3 Observation indicators

The overall treatment effectiveness of the two groups of patients was compared, including three criteria: markedly effective, effective, and ineffective. Among them, the effective evaluation standard is that after treatment, the plaque bacterial clearance rate is 60% or more; the effective standard is that after treatment, the plaque bacterial clearance rate is in the range of 20%–59%; The ineffective criterion is that the patient's plaque bacterial clearance rate after treatment is 9% or less. At the same time, the incidence of adverse reactions in the two groups was compared, including allergies, dizziness, and gastrointestinal discomfort.

2.4 Statistical methods

Using SPSS 21.0 statistical software, the measurement data were expressed by mean ± standard deviation (Mean ± SD), and the count data were expressed by (n, %), respectively, using t, χ² test for comparison between groups. When P < 0.05, it was of statistical value.

3. Results

3.1 Comparison of the overall treatment effectiveness of the two groups of patients

As shown in Table 1, the total effective rate of the study group patients was higher than that of the reference group, P < 0.05, statistically significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>Significant effect</th>
<th>Effective</th>
<th>Invalid</th>
<th>Total efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>30</td>
<td>13</td>
<td>2</td>
<td>43 (95.56)</td>
</tr>
<tr>
<td>Reference group</td>
<td>15</td>
<td>20</td>
<td>10</td>
<td>35 (77.78)</td>
</tr>
</tbody>
</table>
3.2 Comparison of various treatment indicators
The therapeutic effect indicators of the study group patients were better than the control group, the difference was significant, \( P < 0.05 \), see Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>Gingival bleeding index</th>
<th>Periodontal pocket probing depth (mm)</th>
<th>Plaque index</th>
<th>Gingival attachment level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference group</td>
<td>1.80±0.36</td>
<td>3.45±1.13</td>
<td>1.63±0.37</td>
<td>3.41±0.27</td>
</tr>
<tr>
<td>Research group</td>
<td>0.66±1.32</td>
<td>2.77±0.42</td>
<td>0.82±0.32</td>
<td>2.61±0.32</td>
</tr>
<tr>
<td>( X^2 )</td>
<td>5.5268</td>
<td>3.7416</td>
<td>10.9834</td>
<td>12.6743</td>
</tr>
<tr>
<td>( P )</td>
<td>0.0000</td>
<td>0.0003</td>
<td>0.0000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

3.3 Comparison of inflammatory factor levels between the two groups
There were no significant differences in inflammatory markers between TNF-\( \alpha \), IL-6 and CRP before treatment (\( P > 0.05 \)). The level of inflammatory markers in the observation group was significantly lower than that in the control group (\( P < 0.05 \)). See Table 3.

<table>
<thead>
<tr>
<th>Group</th>
<th>TNF-( \alpha )(( \mu )g/L)</th>
<th>IL-6(( pg/\mu L ))</th>
<th>CRP(mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>Before treatment</td>
<td>6.95±1.58</td>
<td>11.28±3.02</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>2.36±0.28</td>
<td>5.02±1.14</td>
</tr>
<tr>
<td>Reference group</td>
<td>Before treatment</td>
<td>6.79±1.72</td>
<td>11.32±3.05</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>4.11±0.98</td>
<td>7.52±2.36</td>
</tr>
</tbody>
</table>

3.4 Comparison of the incidence of adverse reactions between the two groups of patients
As shown in Table 4, by comparing the adverse reaction rates of the two groups, the results showed that the study group was lower than the reference group, \( P < 0.05 \), statistically significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>Gastrointestinal reaction</th>
<th>Dizziness</th>
<th>Allergy</th>
<th>Adverse reaction rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2 (4.44)</td>
</tr>
<tr>
<td>Reference group</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>8 (17.78)</td>
</tr>
<tr>
<td>( X^2 )</td>
<td></td>
<td></td>
<td></td>
<td>6.70</td>
</tr>
<tr>
<td>( P )</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussion

4.1 Pathological analysis of periodontitis
4.1.1 Periodontitis concept
Periodontitis is a relatively common disease, and the important factors are plaque, calculus, traumatic occlusion, poor prosthesis, etc[11]. Clinical manifestations include toothache and bleeding gums, loose teeth, periodontal empyema, etc. Severe, it will lead to tooth loss, posing a serious threat to the health of the patient's teeth, while posing damage to other important organs. Therefore, it is necessary to carry out timely and effective treatment for periodontitis diseases[12-14].

4.1.2 Causes of periodontitis
4.1.2.1 Plaque
Microorganisms adhering to the surface of the teeth cannot be removed by mouthwash, water rinse, or the like.
4.1.2.2 Calculus
Dental calculus refers to mineralized plaque deposited on the tooth surface. According to its deposition site and nature, it is divided into two types: iliac calculus and subgingival calculus[15-17].
(1) Supra gingival calculus
Located on the tooth surface above the gingival margin, it can be seen directly by the naked eye. There is more deposition in the neck of the teeth, especially in the opposite part of the opening of the large parotid duct. The buccal side of the maxillary molar and the lingual side of the mandibular anterior teeth are deposited more.
The main source of inorganic salts in the calculus is the mineral salts such as calcium and phosphorus in saliva [18-21].

2) Underarm calculus
Located on the root surface below the gingival margin, in the sac pocket or in the periodontal pocket, the naked eye can not be directly viewed, and probes must be probed to know the deposition site and deposition amount. The main source of inorganic salts in the gingicular calculus is the gingival crevicular fluid. The damage of tartar to periodontal tissue is mainly a good environment for plaque adhesion and bacterial growth.

4.1.2.3 Traumatic occlusion
In the case of occlusion, if the occlusal force is too large or the direction is abnormal, the occlusion that causes the damage of the periodontal tissue beyond the periodontal tissue can be absorbed, which is called traumatic occlusion. Traumatic occlusion includes early contact during occlusion, occlusion interference, and night molars [22].

4.1.2.4 Other
Including food impaction, poor prosthesis, mouth breathing and other factors also promote inflammation of periodontal tissue.

4.1.3 Treatment of periodontitis
4.1.3.1 Topical treatment
(1) For local stimuli
It can be used for scaling or subgingival scaling, adjusting the bite if necessary, eliminating food impaction and correcting bad restorations.

(2) Periodontal pocket treatment
When the periodontal pocket overflows, it can be washed with 1% to 3% hydrogen peroxide solution. The bag contains 10% iodine or spiramycin, metronidazole and other membranes. After removing local factors, the shallow periodontal pocket can be cauterized with iodine phenol; deeper periodontal pockets require periodontal surgery to eliminate periodontitis. When the periodontal pocket is deep to the apex and the teeth are loose, consider removing it [23].

(3) Loose teeth fixed
If the tooth is still loose, it can be used as a temporary or permanent periodontal splint to fix the loose teeth.

4 treatment of periodontal abscess
When the abscess has been confined, the drainage can be cut open. Periodontal pockets should also be rinsed, applied to the drug or iodine glycerin.

4.1.3.2 Systemic treatment
Enhance the body's resistance and actively treat systemic diseases associated with periodontitis. In the case of periodontal abscess, patients with severe systemic reactions should take oral antibiotics. In short, the treatment of periodontitis includes a series of comprehensive treatments. In order to consolidate the efficacy and prevent recurrence, oral hygiene education should be conducted and reviewed regularly.

4.2 Pharmacological analysis of tinidazole
Tinidazole is a white or light yellow crystal or a crystalline powder; the taste is slightly bitter. This product is dissolved in acetone or chloroform and slightly soluble in water or ethanol. Melting point This product has a melting point of 125~129 °C. The absorption coefficient is taken from the product, accurately weighed, dissolved in water and diluted to prepare a solution containing about 12 μg per 1 ml. The absorbance is measured by spectrophotometry at a wavelength of 317 nm. The absorption coefficient (E1%1 cm) is 352~378.

This product is 2-methyl-1-[2-(ethylsulfonyl)ethyl]-5-nitro-1H imidazole. Calculated according to the dry product, containing (C8H13N3O4S not less than 98.5% (for oral use) or 99.0% (for injection). %, metronidazole tablets were 43.5%, the difference was significant (P <0.01), tinidazole The total effective rate of the tablets was 79.3%, and the metronidazole tablets were 43.6%. The difference was significant (P<0.01). The results showed that tinidazole could quickly eliminate the inflammation caused by oral anaerobic bacteria and alleviate the symptoms [24-25].

4.2.1 Pharmacological action
This product has high activity against protozoa and anaerobic bacteria. It has antibacterial activity against Bacteroides, Bacillus, Clostridium, Peptococcus, Streptococcus pneumoniae, Vescococcus, and Gardnerella, and the concentration of 2~4mg/L can inhibit most of the anaerobic activity. Oxygen bacteria; microaerobic bacteria, Helicobacter pylori sensitive to it; the MIC of vaginal trichomoniasis is similar to metronidazole, and its metabolites are more active against tinidazole than tinidazole. The mechanism of action of this product has not been fully elucidated, and the nitroreductase of anaerobic bacteria plays an important role in the energy metabolism of sensitive strains. The nitro group of this product is reduced to a cytotoxicity, which acts on the DNA metabolism process of bacteria and causes the bacteria to die. Drug-resistant bacteria often lack
4.2.2 Kinetics
The product was completely absorbed after oral administration. The peak time (Tmax) of the healthy female single dose after oral administration of 2g was 2 hours, and the peak plasma concentration (Cmax) was 51 mg/L. The excretion of tinidazole was slow, and the plasma concentrations at 24 hours, 48 hours, and 72 hours after oral administration of 2 g were 19.0 mg/L, 4.2 mg/L, and 1.3 mg/L, respectively. Oral administration of 1g per day, blood concentration can be maintained above 8mg / L. Tinidazole is widely distributed in the body, and has a high concentration in the reproductive organs, intestinal tract, abdominal muscles, and milk. The concentration in the liver and fat is low, and the concentration in bile and saliva is similar to the blood concentration in the same period. The penetration of the blood-cerebrospinal fluid barrier is higher than that of metronidazole. The concentration of cerebrospinal fluid in the meninges without inflammation is 80% of the blood concentration in the same period, which is related to the higher fat solubility of tinidazole. Tinidazole can pass through the blood placental barrier and can reach high concentrations in the fetus and placenta. The protein binding rate was 12%. Metabolism in the liver, about 16% after a single dose of 0.25g orally, is excreted from the urine in its original form. The blood elimination half-life (t1/2β) was 11.6 to 13.3 hours with an average of 12.6 hours.

4.2.3 Indications
(1) For various anaerobic infections, such as sepsis, osteomyelitis, abdominal infection, pelvic infection, pulmonary bronchial infection, sinusitis, skin cellulitis, periodontal infection and postoperative wound infection. (2) Preoperative prophylaxis for colorectal surgery, obstetrics and gynecology surgery and oral surgery. (3) For the treatment of intestinal and extra-arterial amebiasis, vaginal trichomoniasis, giardiasis, venom vaginitis. 4 can also be used as an alternative to metronidazole for the treatment of antral sinusitis and peptic ulcer caused by Helicobacter pylori.

4.2.4 Usage and dosage oral
1 Anaerobic infection: 1g once a day, the first dose is doubled, the general course of treatment is 5 to 6 days, or according to the condition. 2 Prevention of anaerobic infection after surgery: 2g twice a day before surgery. 3 Protozoal infection: (1) vaginal trichomoniasis, giardiasis: a single dose of 2g tons of clothing, children by weight 50mg / kg tons of service, interval 3 to 5 days can be repeated once. (2) Intestinal amebiasis: 0.5g once a day, 2 times a day, 5 to 10 days of treatment; or 2g once a day, 2 to 3 days for treatment; 50mg/kg for children by weight, Dayton The course of treatment is 3 days. (3) parenteral amebiasis: once 2g, once a day, the course of treatment is 3 to 5 days.

4.2.5 Adverse reactions
Adverse reactions are rare and mild, mainly nausea, vomiting, upper abdominal pain, loss of appetite and oral metal taste. There may be headache, dizziness, itchy skin, rash, constipation and general malaise. In addition, there may be neutropenia, disulfiram-like reactions and black urine. High doses can also cause seizures and peripheral neuropathy.

4.2.6 Taboo
Those who are allergic to this product or azoles and those with active central nervous system diseases and blood diseases are prohibited.

4.2.7 Precautions
(1) Carcinogenic, mutagenic effect: animal test or in vitro measurement found that this product has carcinogenic, mutagenic effects, but there is still no data in the human body. (2) If the central nervous system adverse reactions occur during the treatment, the drug should be stopped in time. (3) This product can interfere with the test results of alanine aminotransferase, lactate dehydrogenase, triglyceride, hexokinase, etc., and its measured value is reduced to zero. (4) Do not drink alcoholic beverages during medication, because it can cause acetaldehyde accumulation in the body, interfere with the oxidation process of alcohol, lead to disulfiram-like reaction, patients may have abdominal cramps, nausea, vomiting, headache, facial flushing and so on. (5) Liver function decline, the metabolism of this product slows down, drugs and their metabolites are easy to accumulate in the body, should be reduced, and blood concentration monitoring. (6) This product can be continuously removed from the gastric juice. Some people who place the stomach tube for suction and decompression can cause the blood concentration to drop. During hemodialysis, this product and metabolites are quickly removed, so there is no need to reduce the amount of this product. (7) Candida infected patients with this product, its
symptoms will be aggravated, need to give antifungal treatment at the same time. (8) This product has little
effect on the amoeba encapsulation. It is advisable to add a cysticidal drug. (9) When treating vaginal
trichomoniass, it is necessary to treat their sexual partners at the same time, uncertain. This product can quickly
enter the fetal circulation through the placenta. Animal experiments have found that intrauterine
administration is toxic to the fetus and is not toxic by oral administration. The effect of this product on the fetus
is not sufficient and closely controlled observation, so it should be banned within 3 months of pregnancy.
Pregnant women who have more than 3 months are only allowed to use this product when they have a clear
indication. The concentration of this product in milk is similar to the concentration in blood. Animal tests have
shown that this product is carcinogenic to young rats, so lactating women should avoid using it. If medication is
necessary, breastfeeding should be suspended and breastfeeding should be given after 3 days of withdrawal. Due
to liver dysfunction in the elderly, the pharmacokinetics of the product is changed when the product is applied,
and the blood drug concentration needs to be monitored.

4.2.8 Interaction

(1) This product can inhibit the metabolism of warfarin and other oral anticoagulants, strengthen their role,
and cause prolonged prothrombin time. (2) When combined with phenytoin, phenobarbital and other drugs that
induce liver microsomal enzymes, it can speed up the metabolism of this product, reduce the blood drug
concentration, and slow down the excretion of phenytoin. (3) combined with cimetidine and other drugs that
inhibit liver microsomal enzyme activity, can slow down the metabolism and excretion of this product in the
liver, prolong the blood elimination half-life of this product (t1/2 ), should be based on blood drugs The results
of concentration determination adjust the dose. (4) This product interferes with the metabolism of disulfiram.
When the two are combined, the patient may have psychiatric symptoms after drinking alcohol. Therefore, it is
not suitable to use this product for disulfiram within 2 weeks. (5) This product can interfere with serum. The
results of the measurement of aminotransferase and lactate dehydrogenase can decrease the level of cholesterol
and triacylglycerol. (6) When combined with oxytetracycline, oxytetracycline can interfere with the removal of
vaginal trichomoniass.

4.3 Experimental analysis

Tinidazole belongs to the class of nitroimidazole antibiotics and has a broad antibacterial spectrum. It can
exert superior antibacterial activity against many anaerobic bacteria. It has been relatively common in the
treatment of patients with periodontitis, and the effect is good. However, the oral treatment with tinidazole,
although it can get a certain effect, but the role of drugs in the body, is also an important factor leading to
adverse reactions, so safety needs to be improved. The tinidazole oral patch can be administered in a localized
mode, so that the local drug concentration is high, while maintaining a long-term drug effect, and does not cause
serious adverse reaction problems, and has been widely used in the treatment of patients with periodontitis. The
practice has achieved remarkable results. The results of this study showed that by comparing the overall
treatment effectiveness and incidence of adverse reactions between the two groups, the results showed that the
study group was significantly higher and lower than the reference group, P <0.05.

5. Conclusion

In summary, for patients with periodontitis, the effect of the tinidazole oral patch treatment program is
more significant, and the adverse reaction problem can be significantly reduced, and the safety and reliability
are high. Therefore, this mode can be widely applied.

References

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