Clinical efficacy of semiconductor laser combined with compound betamethasone and valacyclovir in the treatment of trigeminal herpes zoster

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Abstract

Purpose: This study aims to investigate the clinical efficacy of semiconductor laser combined with compound betamethasone and valacyclovir in the treatment of trigeminal herpes zoster. Method: Sixty trigeminal herpes zoster patients admitted in the Oral Mucosal Clinic of Qingdao Municipal Hospital from January 2017 to March 2019 were divided randomly into two groups with 30 patients in each group. The control group was treated with compound betamethasone and valacyclovir, and the treatment group was given semiconductor laser treatment on the basis of the control group. The efficacy of the two approaches were evaluated separately. Results: In the treatment group, 19, 9, and 2 cases were cured, effective, and ineffective, respectively. The effectivity rate was 93.3%. In the control group 14, 8, and 8 cases were cured, effective, and ineffectively, respectively. The effectivity rate was 73.3%. The difference between the two groups was statistically significant ($P < 0.05$). Two months into the study, postherpetic neuralgia (PHN) developed in 1 (3.3%) and 8 (26.7%) cases for the treatment and control groups, respectively. The difference was statistically significant ($P < 0.05$). Conclusion: The semiconductor laser combined with compound betamethasone and valacyclovir could effectively improve clinical efficacy, reduce the incidence of PHN, and improve the cure rate of patients in the treatment of herpes zoster.

Keywords

Semiconductor laser, compound betamethasone, valacyclovir;, clinical efficacy,Post-herpetic neuralgia.

1. Introduction

Trigeminal herpes zoster is an acute viral infection caused by the varicella–zoster virus (VZV), which is a herpes-like lesion on the skin and mucous membranes along the trigeminal nerve [1]. The VZV moves through the sensory nerve endings of the human skin and mucous membranes, toward the center along the nerve fibers of the posterior root of the spinal cord, and then lurks in the neurons of the posterior root of the spinal cord for a long time. When the host has low body resistance, the virus can grow and reproduce into herpes zoster, thereby causing nerve inflammation and pain [2]. Older patients experience intense neuralgia. The disease commonly occur in adults during spring and autumn. The incidence rate increases significantly with age, especially after the age of 50. The course of the disease generally takes 2 to 3 weeks and 3 to 4 weeks for the elderly. Postherpetic neuralgia (PHN) is a common complication of herpes zoster. Rowbotham et al. [3] first identified PHN as the recurrent pain that patients experience 1 month after herpes zoster. The incidence rate of herpes zoster in middle-aged and elderly people was 19.2% [4]. The incidence of PHN reached 56.6% and exceeded

75% for over 60 year old patients [5]. PHN often develops into refractory neuralgia after several months and seriously impacts the quality of life of patients. The main methods for clinically treating herpes zoster are the use of antivirals, analgesics, nutritional neuropharmacological treatment, physical therapy, corticosteroid therapy, or a combination of any of two treatments. However, the treatment effect is unsatisfactory. This study was designed to investigate the clinical efficacy of semiconductor laser combined with betamethasone and valacyclovir in the treatment of trigeminal herpes zoster.

2. Materials and methods

2.1 general information

This study was approved and implemented by the Medical Ethics Committee of Qingdao Municipal Hospital(Batch number: 2019 Linyizi No. 020). The patients and their families signed the informed consent forms. Sixty herpes zoster patients aged 60 to 75 years old that were admitted in the Department of Oral Mucosal Diseases in our hospital from January to February 2019 and received no formal treatment were included in this research. All participants were diagnosed with trigeminal nerve belts. Herpes zoster, including herpes on the left and right sides of the face with oral mucosa, were diagnosed in in 32 and 28 cases, respectively. The heart, liver, lung, and kidney functions of patients were normal, and no history of drug allergy, mental and neurological diseases, diabetes, high blood pressure, and blood disease were found. All patients were divided randomly into two groups (control and study groups) with 30 participants in each group. The control group consisted of 12 males and 18 females with an average age of (69.9 ± 5.7) years and an average body weight of (66.7 ± 8.7) kg. The study group comprised 11 males and 19 females with an average age of (68.5±6.8) years old and an average weight of (64.4 ± 9.1) kg. No significant difference existed in the general data between the two groups ($P > 0.05$), thereby indicating that both groups were comparable.

2.2 Method

DThe control group received oral valacyclovir capsules (0.3 g) twice daily for 7–10 days, compound betamethasone suspension (1 mL) (Debaosong, Guoyao Zhu J20140160), and lidocaine hydrochloric acid (20 g/L volume fraction). The injection (Shandong Hualu Pharmaceutical Co., Ltd., Guoyao Zhunzi H37022147) was mixed in a 1:1 ratio and slowly injected into the mucosa of the lesion base, and the injection volume was 0.2 mL/cm$^{2.}$ The treatment group was given the semiconductor laser treatment based on the treatment of the control group. The Italian SMI D5 semiconductor laser therapeutic apparatus (LA5D01 001.1) was utilized to output a laser wavelength of 810 nm with an output power of 1 W and continuous illumination; the spot diameter was 30–50 mm. Each lesion was irradiated for 5 minutes once a day and treated 9 times. Both groups underwent follow-up sessions for 2 months after the treatment.

2.3 Evaluation of efficacy

The clinical effect was observed after 10 days, and the treatment was considered cured, effective, or invalid. (1) Cured: herpes scarring, shedding, skin or mucosal lesions gradually healed and turned into normal skin or mucous membrane; the pain was relieved or completely disappeared; and painless touching or stimulation of the original pain area. (2) Effective: herpes gradually dried up, crusting was observed, skin or mucosal lesions recovered better than or equal to 40%, no fresh herpes appeared, pain was significantly reduced, touching or stimulating pain areas could cause pain. (3) Invalid: skin or mucosal lesions demonstrated less than 40% recovery, herpes change was not evident or fresh herpes appeared, pain relief was unclear. Total efficiency = cure rate + significant efficiency. The visual analog scale was also utilized to assess the degree of pain in the patient. Specifically, a 10 cm horizontal line was drawn on a piece of paper with one end of the horizontal line marked as 0 (no pain) and the other end as 10 (severe pain). The middle part showed different degrees of pain. The patient marks the horizontal line accordingly to indicate his/her degree of pain. Mild, moderate, and severe pain is less than or equal to 3, 4–7, and 8–10 points, respectively. The incidence of PHN was observed at the time point of 2 months after the study began (January to February 2019).

2.4 Statistical methods

The analysis was performed with SPSS 22.0 software. The adoption rate of count data (%) was used. The comparison between groups was performed via the χ^2 test, and the measurement data were utilized for the t test. $\alpha < 0.05$ was statistically significant.

2.5 Results

In the treatment group, 19, 9, and 2 patients exhibited cured, effective, and ineffective treatments; the effectivity rate was 93.3%. In the control group, 14, 8, and 8 patients demonstrated cured, effective, and ineffective effects; the effectivity rate was 73.3%. The difference between the two groups was statistically significant ($P < 0.05$) (Table 4). At the 2-month follow-up check up, postoperative neuralgia occurred in 1 (3.3%) and 8 (26.7%) cases from the treatment and control groups, respectively. The difference was statistically significant ($P < 0.05$). Blistering time, disappearance time of erosion, and time of pain relief were statistically significant ($P < 0.05$). The VAS score of the treatment group was significantly lower than that of the control group after 10 days, and the difference was statistically significant ($P < 0.05$).

Table1 General Statistics

Group	Male	Female	average age (Year)	Average weight (kg)
Therapy group	12	18	69.9±5.7	66.7±8.7
Control group	11	19	68.5±6.8	64.4±9.1

Table2 Comparison of clinical symptoms in 2 groups of patients (x±s, d)

Group	Anti-blister time	Erosion disappears time	Pain relief time	Number of cases
Therapy group	2.9±0.7	5.6±1.0	2.9±0.5	30
Control group	3.4±0.8	8.4±0.8	6.0±0.7	30

Table3 Comparison of VAS scores after treatment for 10 days in both groups

Group	Before treatment	After 10 days of treatment	Number of cases
Therapy group	5.06±0.82	1.01±0.21	30
Control group	5.19±0.46	2.47±0.43	30

Table4 Comparison of treatment effects between groups of patients after 10 days [n%]

Group	Cure	Effective	Invalid	Efficient
Therapy group	19 (63.3%)	9 (30%)	2 (6.7%)	28 (93.3%)
Control group	14 (46.6%)	8 (26.7%)	8 (26.7%)	22 (73.3%)

Table5 Comparison of the number of PHN cases in two groups after 2 months of treatment

Group	PHN occurs	No PHN occurred	Total
Therapy group	1 (3.3%)	29 (96.7%)	30
Control group	8 (26.7%)	22 (73.30%	30

3. Typical clinical cases

3.1 Clinical data

A female 71-year-old patient came to the Oral Mucosal Clinic of our hospital on February 18, 2019 complaining of “paroxysmal pain for 3 days in the upper right ankle and suffering of mild fever.” Three days before the patient’s visit, she experienced a paroxysmal acupuncture-like pain with mild

fever after overworking, and the type of food she ate aggravated the pain. At the onset, no treatment was given and no medication was taken. The patient was physically healthy and had no history of drug allergy.

Physical examination: no abnormalities were found in the system check. In the second and third branches of the right cheek of the patient, the right upper palate mucosa, right cheek and right margin, right flank and right lower lip, and the right lower lip were visible. protruded from the surface of the mucosa with the size of a band, exhibited in a band-like distribution, and covered with yellow–white aponeurosis. The aponeurosis could be removed with minimal force. Palpation pain was evident, and the VAS pain score was 6 points. No clear abnormalities were found on the left side of the corresponding mucosa.

Laboratory examination: white blood cell ($11.6 \times 10^{9/}$L) and neutrophil (7.90×10^{9}/L) counts slightly increased. The serum for anti-VZV IgM antibody tested positive. Human immunodeficiency virus antibody was absent. No tumors were found. No abnormalities were observed in the markers. Urine routine, liver function, renal function, and coagulation routine were normal.

Diagnosis: trigeminal herpes zoster (Maxillary nerve,Mandibular nerve)

3.2 Treatment

First visit and on the 4th day after the first visit, a 1:1 ratio of compound betamethasone suspension (1 mL) (Debaosong, Guoji Zhunji J20140160) and lidocaine hydrochloride (20g/L volume fraction) injection (Shandong Hualu Pharmaceutical Co., Ltd., Guoyao Zhunzi H37022147) was prepared. After mixing the solution, it was slowly injected into the mucosa of the lesion base, and the injection volume was 0.2 mL/cm2. Valacyclovir capsule doses of 0.3 g each were given orally twice a day for 10 days. The semiconductor laser was irradiated, and the Italian SMI D5 semiconductor laser therapeutic apparatus (LA5D01 001.1) was used to output a laser wavelength of 810 nm with an output power of 1 W, continuous illumination, and spot diameter of 30–50 mm. Each lesion was irradiated for 5 minutes every day for 9 treatments.

After 4 days of treatment, the range of the erosion surface was reduced, pain was gradually reduced, pain duration was shortened, frequency was reduced, and the VAS score was 3 points. After 7 days, the erosion area was significantly reduced, and the VAS score was 2 points. After 9 days, the erosion basically healed, the pain completely disappeared, and the VAS score was 0. No PHN occurred during the follow-up observation for 2 months, and no recurrence was noted

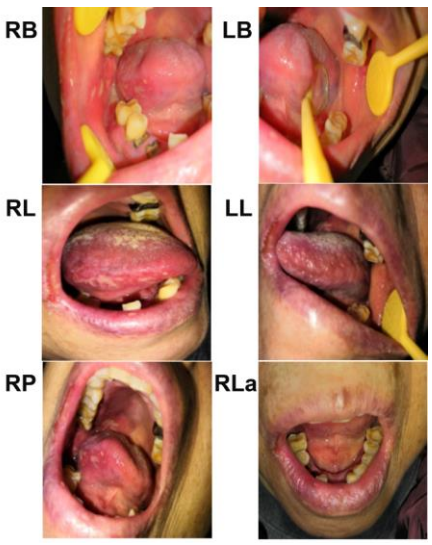

Fig. 1 Initial diagnosis 2019-2-18 (same clinical examination)

RB: Many areas of the right cheek and the posterior molar area are smashed and covered with a yellow pseudomembrane, which can be wiped off. LB: No evident abnormality is found in the left buccal mucosa. RL: The lateral margin of the right tongue is enlarged and covered with a yellow

pseudomembrane. LL: No clear abnormality occurs in the lateral margin of the left tongue. RP: The upper right ankle is smashed and covered with a yellow pseudomembrane. RLa: The right corner is smashed and covered with a yellow fake film. LP\LRa: No evident abnormality is observed in the upper left and left corners.

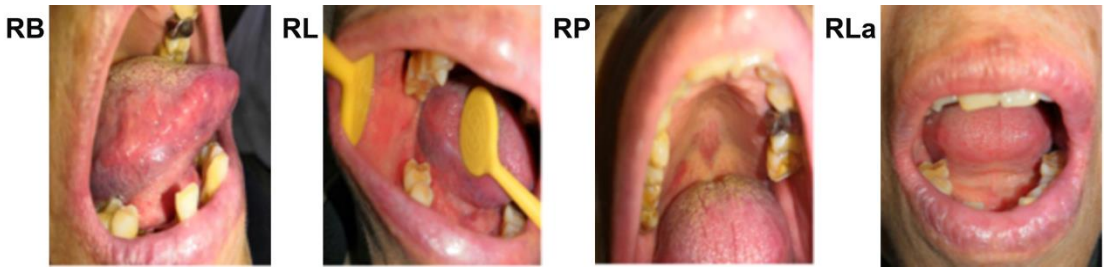

Fig. 2 Review after 9 days of treatment. After 9 days, the RB, RL, RP, and RLa erosions basically healed, and the VAS score was 0 points.

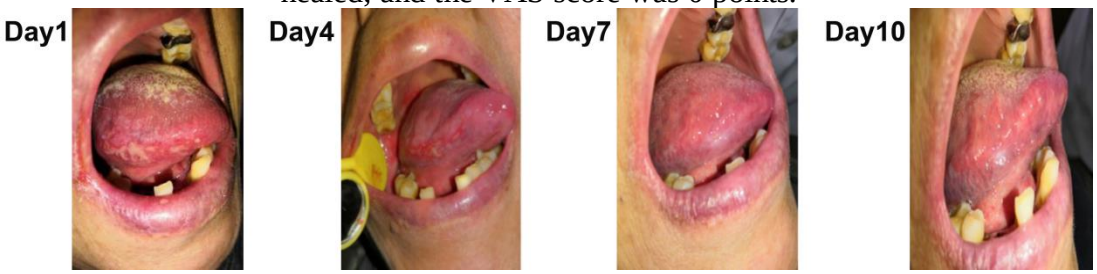

Fig. 3 Changes in the lingual lesion on the right side. The lesion at RL gradually decreased on the first day, the fourth day, the seventh day, and the ninth day.

Table 1 Three Scheme comparing

Numble	Scheme 1	Scheme 2	Scheme 3
1	456	456	123
2	789	213	644
3	213	654	649

4. Discussion

Trigeminal herpes zoster is caused by the VZV. After chickenpox is cured, the virus lurks in the Trident Festival. When the body's resistance is low, the latent virus is reactivated and proliferates in the trigeminal ganglion along the sensory nerve and replicates along the skin of the ipsilateral peripheral nerve innervation, thereby clinically manifesting as unilateral trigeminal herpes zoster [6]. Patients with herpes zoster often experience severe pain mainly due to sensory ganglion neurons from the herpes zoster infection. The pain of acute herpes zoster is evidently reduced at approximately 20 days [7]. In this study, the pain sensation disappears on the 9th day and demonstrates the clear curative effect of the treatment on rapid pain relief.

As people age, their immunity gradually declines, and the incidence of herpes zoster increases. Herpes zoster in China and Taiwan occurs at a rate of (3.4–5.8)/1000 person-years and (4.89–5.67)/1000 person-years [8,9,10,11], and the incidence of herpes zoster in North America and Western Europe each year are essentially similar [12,13,14].

Herpes zoster incidence in Taiwan is reportedly higher in women than in men [15], and such finding is consistent with reports from Mainland China [16]. In this case report, the patient was an elderly female, which was consistent with the gender incidence of herpes zoster in China.

Trigeminal herpes zoster can occur in the scalp of the head and skin on the face and lips of the oral mucosa, buccal, tongue, and sputum. Initially, it appears as a blister. After its rupture, the patient will experience erosion and severe pain. Trigeminal PHN is a common complication of herpes zoster. PHN is related to the age of onset, and the incidence of PHN in elderly people over 60 years old reaches up to 50% to 75% [17]. Approximately 30% to 50% of patients experience PHN for more

than 1 year, and some studies report that PHN can last up to 10 years [18]. These pain symptoms seriously affect the quality of life of patients.

Trigeminal herpes zoster therapy mainly entails drug treatment. Common drugs include antiviral and glucocorticoid drugs alone or a combination of both. Antiviral drugs inhibit viral growth and reproduction but do not alleviate the acute phase pain in patients [19-20]. When administered, glucocorticoids can inhibit the inflammatory reaction in patients, thereby reducing pain and tissue edema and also accelerating the rapid healing of the patient's skin area that alleviates the acute pain of the patient. N. Chen et al. [21] reported that the use of systemic glucocorticoids or antiviral drugs alone during acute herpes zoster [22] did not reduce PHN incidence. The biological effect of a semiconductor laser involves enhancing the phagocytic ability of macrophages and the immune function of the body [23], improving local blood circulation, promoting local blood flow, advancing inflammation absorption and pain-induced substance metabolism, and activating the endorphin system. A semiconductor laser relieves pain; accelerates the metabolism and maturation of tissue repair cells; and promotes the production, deposition, and cross-linking of collagen fibers, thus rendering it beneficial for the growth and functional recovery of nerve cells. Yu-Tsung Chen et al. [24] indicated that the early application of low-level laser could reduce PHN occurrence. In this patient, pain was relieved rapidly after treatment with a semiconductor laser combined with glucocorticoids and antiviral drugs. Moreover, the PHN symptoms have yet to appear. Therefore, the application of semiconductor laser combined with glucocorticoids and antiviral drugs can rapidly reduce pain and promote healing. This outcome shows that the semiconductor laser combined with glucocorticoid and antiviral drugs has good clinical application value and is worthy of promotion.

The prevention of herpes zoster in the elderly is often achieved by administering the herpes zoster vaccine, and the R adjuvant zoster subunit vaccine (HZ/su) is more effective than the existing live attenuated vaccine (ZVL) [25]. Research indicates that the immunogenicity induced by HZ/su is still higher than the prevaccination level in adults ≥ 60 years old for at least 9 years after the initial vaccination [26]. Therefore, injecting the HZ/su vaccine in the elderly can effectively prevent the occurrence of herpes zoster among them.

In summary, the combined treatment of low-level laser and antiviral drugs and hormones in elderly trigeminal herpes zoster can rapidly reduce pain, promote the healing of erosion caused by herpes zoster, and effectively prevent PHN occurrence. Hence, the proposed combined treatment is a satisfactory clinical treatment approach.

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• All data generated or analyzed during this study are included in this published article.

SNW\XL\SLLmake a significant contribution to conception and design, data acquisition, and data analysis and interpretation;

HR,YYS,YQW, GRLSubstantial revisions to the important content of drafting manuscripts or manuscripts;

SLL approval of the publication of the final version.

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