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Clinical and histological evaluation of the efficacy of antimicrobial photodynamic therapy used in addition to antibiotic therapy in pericoronitis treatment

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ABSTRACT

Background: Although antimicrobial efficacy of photodynamic therapy has been studied several times, there is no study investigating its efficacy on pericoronitis. This study aimed to determine whether antimicrobial photodynamic therapy combined with antibiotic therapy is clinically and histologically superior to antibiotic therapy alone in pericoronitis treatment.

Methods: Patients (n = 40) with pericoronitis were divided into two groups (20 patients for each) to receive either antibiotic + indocyanine green + 810 nm wavelength diode laser (antimicrobial photodynamic therapy group) or antibiotic alone. Initial biopsy samples were obtained from the affected tissue of the patients at their first presentation to the clinic before any intervention. The second biopsy samples were obtained on the 3rd day of treatment in both groups from the tissue part not biopsied before; tooth extraction was then performed. All tissue samples were histologically examined to assess inflammatory cell response. Patients' pain (using Visual Analogue Scale) and lymphadenopathy (presence or absence) were clinically evaluated in the first 3 days and on the 7th day of treatment.

Results: In the antimicrobial photodynamic therapy group, 100% improvement was achieved regarding pain and lymphadenopathy at the end of the 7th day. Comparison of the inflammatory cell scores of the 2nd biopsy samples between the antibiotic alone and antimicrobial photodynamic therapy groups revealed a significant difference in favor of antimicrobial photodynamic therapy group.

Conclusions: Antimicrobial photodynamic therapy combined with antibiotic therapy for pericoronitis treatment was found to be more successful as compared with the antibiotic therapy alone regarding clinical and histological outcomes.

1. Introduction

Photodynamic therapy is a therapeutic method with a wide range of usage from cancer treatment to root canal treatment and with an increasing popularity owing to its antibacterial effect [1–3]. Photodynamic therapy leads to cell death due to the combination of its two components, photosensitizer and strong light source. Photodynamic therapy includes the following mechanism of action: photosensitizer absorbs the energy of the same wavelength from the light source, transmits this energy to the substrate, and destroys the microorganisms by irreversibly oxidizing the cellular components through formation of short-lived reactive molecules [4–6].

Pericoronitis is a clinical condition that is caused by Gram-negative anaerobic bacteria (motile rods) and that may require clinical support depending on the symptoms [7,8]. It has been demonstrated that the microflora in the pouches in the presence of periodontal disease is similar to the microflora in pericoronitis [9]. The basic principle in treating pericoronitis is the elimination of causative agent by disinfecting the area [10]. The treatment of pericoronitis may require antibiotic therapy in addition to the procedures preserving regional hygiene such as operculectomy, debridement, and irrigation [10].

Efficacy of indocyanine green, which is used for Gram-negative and Gram-positive bacteria as a photosensitizing agent in photodynamic therapy, has been proven with many studies [11–13]. To our knowledge, there is no study on antimicrobial photodynamic therapy in pericoronitis treatment; however, there are studies reporting successful

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outcomes of antimicrobial photodynamic therapy in periodontitis treatment [14,15]. On the other hand, it has been suggested that antimicrobial photodynamic therapy has no effect in periodontitis treatment in smokers and patients with Type 2 diabetes mellitus [16]. Accordingly, the present study aimed to determine whether antimicrobial photodynamic therapy in combination with antibiotic therapy is clinically and histologically superior to antibiotic therapy alone in the treatment of pericoronitis.

2. Materials and methods

Among patients admitted to the Faculty of Dentistry of Yuzuncu Yil University, those who had pericoronitis in the distal aspect of the mandibular third molars and pericoronitis-related lymphadenopathy, had indication for extraction of the third molars due to recurrent infections (at least two times) occurred at certain intervals, had tooth in the vertical position, and had operculum covering 1/2–2/3 of the outer surface of the tooth were included in the study. Patients who had a systemic disease, smokers, pregnant women or women having suspicion of pregnancy, lactating women, patients who received bisphosphonate at any time, patients who received antibiotic or anti-inflammatory drugs within the last month, and patients who had any disease that is likely to influence submandibular lymph node such as sinusitis, upper respiratory tract infection, aphthous lesions, and herpes infection were excluded. The study was approved by the Ethics Committee of Yuzuncu Yil University (reference number: YYU-22.01.2015/12) and written informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki.

The patients were randomly allocated to two groups (antibiotic group and antibiotic + antimicrobial photodynamic therapy group) by the coin-toss method, each containing 20 patients. At presentation, before any intervention, a small triangular specimen (1st biopsy sample) was obtained from the distolingual part of the soft tissue covering the distal aspect of the third molar for histological examination in all patients. All patients were prescribed amoxicillin (Largopen®, 1 g tablets; Bilim Pharmaceuticals, Tekirdag, Turkey) to be taken every 12 h via oral route, paracetamol (Parol®, 500 mg tablets; Atabay Pharmaceuticals, Istanbul, Turkey) to be taken every 8 h via oral route, and chlorhexidine gluconate 4% mouthwash (Klorhex® 200 mL; Drogsan Pharmaceuticals, Ankara, Turkey) to be applied 3 times a day for 7 days. Considering the day of patients' presentation to the clinic as Day 1, inflamed tissues were removed and the problematic tooth was extracted on Day 3 under local anesthesia (4% articaine hydrochloride + 1:100,000 epinephrine, 1 ampoule [Maxicaine Fort; Vem Pharmaceuticals, Istanbul, Turkey]). In the meantime, the distobuccal aspect of the soft inflamed tissue covering the tooth was taken as the second specimen (2nd biopsy sample). The patients were monitored in the first 3 days and on Day 7 for lymphadenopathy (present = painful on palpation, absent = painless on palpation) and to obtain their Visual Analog Scale scores. This protocol was considered standard and performed without any application of laser to 20 patients comprising the control group (antibiotic alone group).

In the antibiotic + antimicrobial photodynamic therapy group, after obtaining the first soft tissue specimen, indocyanine green (Perio green, Elexxion AG, Radolfzell, Germany) prepared according to manufacturer's instructions in a concentration with 0.1 mg/mL was administered via fine-needle syringe as the photosensitizer beneath the operculum of the 3rd molar as well as inside the distal, buccal and lingual pockets at tooth midpoints. Thereafter, laser beam was applied for 40 s to each relevant area in the continuous mode using an 810 nm diode laser (Cheese Diode Laser, Wuhan Gigaa Optronics Technology Co. Ltd., China) with a 200 μm polymethyl methacrylate optical fiber tip and with a power of 0.3 W and sweeping technique was used. Pulse frequency was 10,000 Hz, energy density was 600 J/cm^2 for each area, and power density was 15 W/cm^2. The same procedure was repeated for all patients on the next day.

The 1st and 2nd biopsy samples were transferred for histological examination in 10% neutral buffered formalin. After fixing the tissues for 24 h, they were monitored in an automated vacuum tissue processor (Leica ASP® 300; Leica microsystems, Germany) and then embedded into paraffin blocks. Sections of 4 μm in thickness were obtained from the paraffin blocks using a rotary microtome device (Leica RM® 2135; Leica microsystems, Germany). These sections, which were placed onto the slides, were stained with hematoxylin and eosin.

Histopathological examination of the obtained preparations were performed using a light microscope (Olympus BX53F; Olympus, Tokyo, Japan). Histological examination of the tissue samples was performed using the inflammatory grading scale defined by Kaufman et al. [17] and inflammatory response was scored as follows: 0 = minimal cells, 1 = chronic mild macrophages, 2 = mixed-neutrophils/macrophages, 3 = predominantly neutrophils/diffuse. Finally, their images were obtained using the Olympus E-330 camera.

In the present study, the surgeon performing the tooth extraction and the pathologist scoring the inflammatory response were blind to the study groups and procedures.

2.1. Statistical analysis

Data analysis was performed using the IBM SPSS Statistics for Windows, version 20.0. (IBM Corp., Armonk, NY, USA). Mann Whitney-*U* test was used for statistical analysis. The sample size was calculated with a power of at least 0.80 and a type 1 error of 0.05 for each variable. The level of statistical significance (p value) was considered as 5%.

3. Results

The study included 40 patients (mean age, 22.97 years ± 3.4), of whom 21 were female and 19 were male. None of the patients developed any complication during either treatment or healing period.

No significant difference was determined between the antibiotic alone and antibiotic + antimicrobial photodynamic therapy groups in terms of the mean Visual Analog Scale scores on the 1st day ($p = 0.713$). On the 2nd day, the mean Visual Analog Scale score decreased in the antibiotic group but remained unchanged in the antibiotic + antimicrobial photodynamic therapy group. On the 3rd day, a decrease by 49.4% was observed in the mean Visual Analog Scale score in the antibiotic + antimicrobial photodynamic therapy group (Fig. 1). While the mean Visual Analog Scale scores on the 2nd and 3rd days did not significantly differ between the two groups ($p = 0.398$ and $p = 0.859$, respectively), the mean score on the 7th day was significantly higher in the antibiotic group ($p = 0.042$).

The mean inflammatory cell scores of the study groups are presented in Table 1. Accordingly, the mean inflammatory cell score was

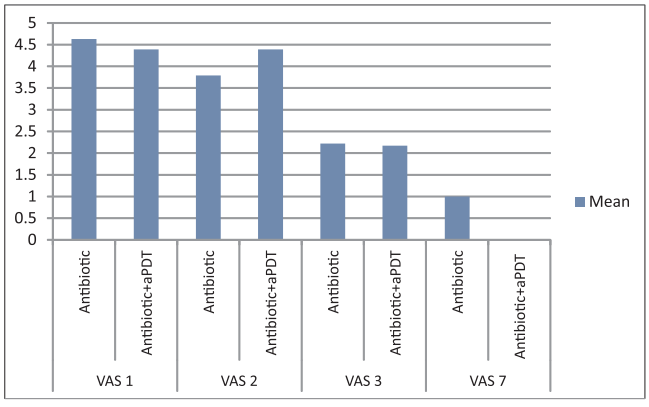

Fig. 1. Mean Visual Analog Scale scores of the study groups on the 1st, 2nd, 3rd, and 7th days.