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# ADJUNCTIVE ANTIBIOTIC THERAPY IN CASES OF PERIODONTITIS AND PERI-IMPLANTITIS

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## ABSTRACT

**INTRODUCTION:** Periodontitis and peri-implantitis are plaque-induced diseases, which are associated with certain bacteria. The conventional treatment aims primarily at tooth or implant surface debridement. In certain cases, surgical therapy is necessary. To improve the outcome of the treatment, systemic or topical antibiotics could be considered.

**AIM:** The aim of this review is to investigate the effect of the adjunctive systemically or topically delivered antibiotics on the outcome of the periodontitis and peri-implantitis treatment.

**MATERIALS AND METHODS:** Articles related to the topic were searched in the PubMed database. Articles published from 2000 to 2019, only in English language, were included in the review. The search was conducted with a variety of keywords in different combinations being used. These were: “periodontitis”, “peri-implantitis”, “antibiotic”, “local”, “metronidazole”, “amoxicillin”, “azithromycin”, “tetracycline”.

**RESULTS:** Forty-seven articles were included in the review. The selected articles described the adjunctive systemic and/or local delivery of metronidazole, azithromycin, the combination of metronidazole and amoxicillin and some representatives of the tetracycline group, such as doxycycline and minocycline in cases of periodontitis and peri-implantitis.

**CONCLUSION:** The adjunctive systemic and topical antibiotic therapy could benefit the outcome of periodontitis and peri-implantitis treatment.

**Keywords:** *antibiotic, peri-implantitis, periodontitis, treatment*

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## INTRODUCTION

Periodontitis and peri-implantitis are plaque-induced diseases, which are associated with certain bacteria. The conventional treatment aims primarily at tooth or implant surface debridement. In certain cases, surgical therapy is necessary. To improve the outcome of the treatment, systemic or topical antibiotics could be considered.

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## MATERIALS AND METHODS

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### Metronidazole

Systemic metronidazole, in addition to the non-surgical therapy of peri-implantitis, is an effective treatment in terms of radiographic parameters and probing depth (PD) (1). According to a study, bacterial genes encoding for tetracycline resistance are typical for healthy sulci around implants and for cases of peri-implantitis. To a lesser extent, resistance to beta-lactams is observed. The authors did not detect any resistance to metronidazole and support its use (2).

Lan et al. (3) introduced personalized poly-ε-caprolactone/alginate rings loaded with metronidazole, whose purpose was to ensure controlled release of the agent. The authors concluded that this system has the potential to reduce the bacterial biofilm development and thereby could be used for peri-implantitis prevention.

Tang et al. (4) compared 25% metronidazole gel and ultrasonic scaling with carbon fiber tip and concluded that both treatment modalities are reliable for peri-implantitis therapy.

The local application of metronidazole could lead to a destabilization of the supragingival biofilm (5). The combination of topically delivered metronidazole and zinc hyaluronate has a comparable effect to that of amoxicillin on the oral pathogens (6). The topical delivery of 5% metronidazole along with the debridement could also have a positive effect on the periodontitis therapy (7).

Systemic administration of metronidazole combined with full-mouth disinfection is an efficient

strategy in cases where *P. gingivalis* and *T. forsythia* are detected (8).

### Amoxicillin + Metronidazole

The systemic administration of metronidazole and amoxicillin together is used in periodontitis (9,10,11,12,13) and in peri-implantitis treatment (14).

In vitro evaluation of the antibiotic resistance of the bacterial pathogens, typical for the submucosal microbiota in peri-implantitis patients demonstrated that these bacteria are frequently resistant to doxycycline, clindamycin, metronidazole and amoxicillin. The authors also found that the bacteria are only infrequently resistant to both metronidazole and amoxicillin (15).

The combination of metronidazole and amoxicillin, in addition to scaling and root planing (SRP), has led to improvement of the results of the periodontal treatment of patients with type 2 diabetes mellitus (16). El-Makaky and Shalaby (17) also studied the effect of periodontal therapy on the clinical parameters and metabolic response in patient with uncontrolled type 2 diabetes suffering from periodontitis and concluded that the non-surgical therapy of periodontal disease combined with metronidazole and amoxicillin resulted in better metabolic outcome and improved clinical parameters in regard to the periodontitis. The authors observed bleeding on probing (BOP), pocket depth, plaque, clinical attachment level (CAL), and glycated hemoglobin. Other authors also came to a similar conclusion: the adjunctive amoxicillin and metronidazole administration increased the positive effects of the periodontal therapy, considering clinical parameters, such as PD, CAL and BOP (18).

McGowan et al. (19) recommended a 7-day course of metronidazole and amoxicillin. A study supported the regimen of 500 mg metronidazole and 500 mg amoxicillin, three times a day for 7 days in combination with SRP. The authors compared a 3-day and a 7-day course and reported better results with the longer antibiotic course, considering improved clinical parameters, decreased detection of some periopathogens and oxidative stress (20).

As an alternative of the combination of metronidazole and amoxicillin, Araujo et al. (21) proposed clarithromycin, although the authors suggested that this antibiotic was not superior to the aforementioned

combination. Both antibiotic therapies led to reduced bacterial count of *A. actinomycetemcomitans* and *P. gingivalis*. The duration of both treatments was 7 days with the dose of metronidazole and amoxicillin being 400 mg three times a day and 500 mg three times a day, respectively. The dosage of clarithromycin was 500 mg twice a day.

The systemic use of amoxicillin and metronidazole in addition to surgical protocol for peri-implantitis treatment including also surgical access debridement and decontamination of implant surface resulted in a positive effect, which was maintained for 12 months (14).

During a peri-implantitis treatment, Stein et al. (22) administered amoxicillin and metronidazole for a period of 7 days to the patients with severe periodontitis. Other authors did not observe any improvement of the results considering the clinical and microbiological parameters, adding metronidazole and amoxicillin to the non-surgical peri-implantitis treatment (23).

### **Tetracyclines**

Local antimicrobial agents may improve the outcomes of periodontal surgical treatment and may reduce the peri-implantitis manifestations (24). Treatment of peri-implantitis by topical application of tetracyclines led to improvement of the microbiological and clinical parameters (25).

Locally delivered tetracyclines are available in different forms, such as ointment (26), fibers (25, 27, 28), and nanoparticles (29). Topical application of tetracycline is associated with significant positive effect on the clinical parameters, such as PD, sulcular bleeding index, and CAL (30). According to a study, the use of systemic and local antibiotics could decrease the inflammation at the surgical site after implant placement (31). Minocycline hydrochloride ointment and erythromycin eye ointment were applied locally at the implant surgery site. The effect on the healing was assessed and certain parameters were measured. The authors concluded that the effect of both ointments was comparable in regard to the early stage of the healing process (31). Local minocycline demonstrated considerable anti-inflammatory effects (29). The combination of tetracycline fibers and SRP is a reliable treatment, resulting in an improvement of the periodontal health (32). Tetracy-

cline fibers combined with SRP are superior to SRP alone considering the clinical parameters, such as pocket depth and CAL (27).

Topical application of minocycline in combination with surgical treatment of peri-implantitis improves the outcome of the therapy regarding the clinical and radiological results (33). Radiographic and clinical parameters are also improved using nonsurgical treatment of peri-implantitis combined with irrigation with chlorhexidine and local application of minocycline hydrochloride (34).

Topical application of controlled-release doxycycline was included in an anti-infective non-surgical peri-implantitis treatment protocol, which demonstrated improvement of peri-implant health, considering the clinical parameters (35). A new gel was proposed, which included metronidazole and doxycycline in its formulation. The gel was efficient in vitro against planktonic species and against bacterial biofilm. The effect continued 13 days. The authors concluded that its use in cases of peri-implantitis could be discussed (36). Nano-doxycycline gel in addition to SRP also demonstrated anti-inflammatory effect (37).

According to a study, systemic doxycycline treatment did not influence *A. actinomycetemcomitans* infection associated with peri-implantitis. The authors also concluded that periodontitis of the remaining teeth could contribute to the development of peri-implantitis (38). Residues of a minocycline hydrochloride agent could be found on the implant surface. Because it was hydrophobic it could not be removed well using water.

Residual local agents on the implant surface in cases of peri-implantitis might compromise the reosseointegration and lead to bacterial colonization (39). In a study in dogs, it was reported that the application of topical tetracycline hydrochloride solution was an effective method for decontamination of implant surfaces, which were infected (40).

### **Azithromycin**

Systemic delivery of azithromycin in combination with mechanical debridement could contribute to the management of peri-implant mucositis in the therapy of peri-implantitis (41). Some authors concluded that the systemic administration of azithromycin in addition to the surgical peri-implantitis

treatment was not superior to the surgical therapy alone (42). According to Tada et al. (43) the reduction of the bacterial number, caused by the systemic azithromycin, was followed by new increase thereafter. Gomi et al. (44) concluded that the increase of the periodontal bacteria was observed 6 months after the therapy, which included combination of azithromycin and full-mouth SRP. According to O'Rourke (45), systemically delivered azithromycin could contribute to the positive effect of the non-surgical periodontal treatment, especially when the pocket depth was  $\geq 6$  mm. Yashima et al. (46) reported comparable results from full-mouth SRP, with and without systemic administration of azithromycin, considering the clinical parameters. Renatus et al. (47) supported the opinion about the positive effect of the systemic delivery of azithromycin during periodontitis treatment.

## RESULTS

Forty-seven articles were included in the review. The selected articles described the adjunctive systemic and/or local delivery of metronidazole, azithromycin, the combination of metronidazole and amoxicillin, and some representatives of the tetracycline group, such as doxycycline and minocycline in cases of periodontitis and peri-implantitis.

## DISCUSSION

The majority of the studies supported the topical application of tetracyclines in adjunct to the periodontitis and peri-implantitis treatment (24,25,27,29,30,32-35,37). One study reported debatable results because of the difficulty of removing completely one of the minocycline hydrochloride agents of the implant surface (39).

Many authors observed positive effect of the systemic administration of the metronidazole and amoxicillin combination in adjunct to the periodontal treatment in terms of the outcomes of the therapy (16-18,20).

Topical metronidazole was found efficient in cases of periodontitis and peri-implantitis (4-7).

The reports about the effect of systemically administered azithromycin on the peri-implantitis and periodontitis treatment are debatable. According to some of the authors the adjunctive systemic delivery of azithromycin benefits the periodontitis (45)

and peri-implantitis treatment (41), while according to others, the results of the treatment with and without azithromycin administration were comparable (42,46).

## CONCLUSION

The adjunctive systemic and topical antibiotic therapy could benefit the outcome of periodontitis and peri-implantitis treatment.

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