

# A Clinical Study of Combined Systemic Co-Amoxiclav and Metronidazole as Adjuncts to Periodontal Surgery in the Treatment of Advanced Periodontal Disease

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**Abstract** Mechanical surgical treatments of periodontal pockets are usually effective in arresting the progression of the disease. The aim of present investigation was to determine if the simultaneous administration of systemic amoxicillin, clavulanic acid and metronidazole as adjunct to periodontal pocket surgery. Fifty patients with advanced chronic periodontal lesions took part in this study of which 36 completed the study. Only at the first surgical visit, the patients in test group received co-amoxiclav 625mg tablets tid for one week plus metronidazole 250mg tablets for one week. The control group received amoxicillin 500 mg capsules tid for one week. Before the first surgical visit, and 6 weeks after the last surgical visit, probing pocket depth, clinical attachment level and bleeding on probing were measured by a single examiner. The difference between the probing pocket depth reductions of the 2 groups was not statistically significant ( $p=0.59$ ). The difference between the attachment gains of the 2 groups was not statistically significant ( $p=0.58$ ). The difference between BOP reductions of the 2 groups was not significant ( $p=0.75$ ). It was concluded from this study that the addition of clavulanic acid and metronidazole, provided no additional improvement beyond that could be achieved by periodontal surgical debridement plus amoxicillin.

**Keywords** Co-amoxiclav, Amoxicillin, Periodontal Surgery, Metronidazole

## 1. Introduction

Despite considerable advancement in the understanding of periodontal pathogenesis and etiology, the treatment of periodontal disease is still primarily based on non-specific methods i. e. mechanical techniques. In other words, treatment strategies have had little progress, imposing an imbalance between etiology and treatment rarely seen in any other disciplines of medical and dental sciences. Mechanical treatment affects a wide spectrum of bacteria. Among several hundreds of microorganisms comprising the human dental plaque, only a few have shown correlation with the disease progression. Putative periodontal pathogens have been identified based on their pathogenicity in animal models and their virulence factors. Among these bacteria *Porphyromonas gingivalis* (P.g)[1], and *Actinobacillus actinomycetemcomitans* (A.a)[2], have particularly attracted much attention. Longitudinal studies have demonstrated an increased risk of periodontal destruction at sites colonized by

these two bacteria[1]. If it is accepted that periodontal disease is caused by only a limited number of bacteria, then a non-specific elimination of plaque bacteria is not the sole treatment. Instead, specific elimination of periodontal pathogens seems a more credible approach[2].

Infection refers to the presence and proliferation of microorganisms inside or on body tissues. Plaque-associated periodontal diseases are considered infectious diseases, although bacterial invasion into tissues rarely takes place. Evidence of bacterial penetration into severely diseased periodontal tissues such as periodontal abscesses and acute necrotizing ulcerative gingivitis (ANUG) has been reported, however, the actual invasion of tissues by periodontal bacteria has not been unequivocally accepted yet[3].

Decision as to whether antibiotics should be used in periodontal therapy was initially based on empirical data and performed primarily using systemic penicillins. Penicillins act via inhibition of cell wall synthesis. They have a narrow spectrum of activity and are bacteriocidal. Among penicillins, amoxicillin has been widely used in periodontal therapy because of its considerable concentration in the gingival fluid and its effectiveness against several periodontopathic bacteria. Molecular structure of penicillins include a beta lactam ring which is amenable to enzymatic

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cleavage by some bacteria. Clavulanic acid has been successfully added to amoxicillin to prevent beta lactamase activity of bacteria[4-5]. Among several attempts of investigators to test effectiveness of antibiotics in periodontal therapy[6-7], amoxicillin plus clavulanic acid has been reported to be effective in the non-surgical treatment of refractory periodontitis patients[8]. Several other clinical testings have been reported in the literature with some variable results[9-13]. To date, there has been no report on the efficacy of amoxicillin plus clavulanic acid (designated now as co-amoxiclave) as adjunct to surgical treatment of periodontitis. The aim of this study was to compare the efficacy of systemic administration of co-amoxiclave plus metronidazole as compared to amoxicillin alone as adjuncts to periodontal surgery in the treatment of aggressive periodontitis patients.

## 2. Material & Methods

This study was a controlled randomized clinical trial which was conducted in 2010 at the Periodontology Department of Mashhad Dental School and Jahad-Daneshgahi Dental Clinic. Fifty patients requiring full-mouth periodontal surgery referring to the above mentioned clinics were consecutively assigned for the study. Prior to the study, informed consent forms were taken from the patients. Inclusion criteria were as follow: 1) The patients had completed the initial phase of periodontal treatment including supra-and subgingival scaling and root planning as well as oral hygiene instruction. 2) Having at least one periodontal pocket of  $\geq 5$ mm in each quadrant with bleeding on probing. The exclusion criteria were a history of antibiotic treatment during the past 6 months as well as systemic conditions known to interfere with the outcome of periodontal treatment. The patients were randomly allocated to one of the two test and control treatment groups. The test group received quadrant periodontal flap surgery as required. In addition, following the first surgical session, the subjects of this group received systemic oral antibiotic regime consisting of co-amoxiclave 625mg tid plus metronidazole 250mg tid for one week. If further surgical sessions were needed for the test group patients, this was supplemented with systemic amoxicillin 500 mg tid for one week.

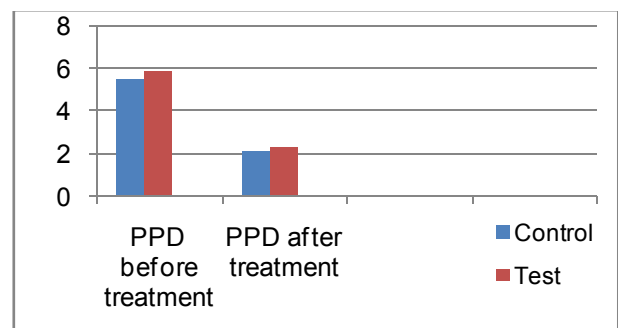
The control group received the same surgical protocol as the test group, but it was supplemented with systemic amoxicillin 500 mg tid for one week at all surgical sessions.

Clinical measurements included of periodontal pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP) using a Williams periodontal probe (Hufriday, USA) by an operator unaware of the assigned treatments. Clinical measurements were recorded at baseline and 6 weeks following the last surgical visit.

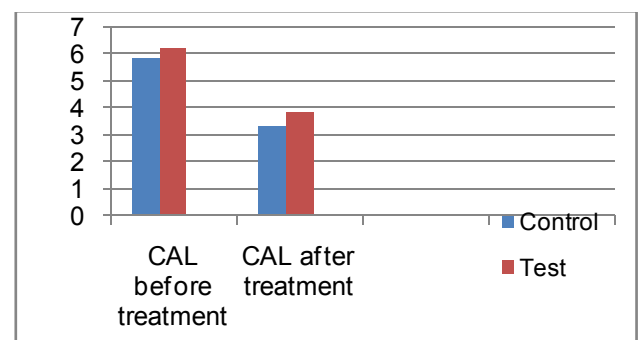
Statistical analysis was performed using a statistical package (SPSS version 11.5). The improvement in the PPD, CAL and BOP percentage were compared across the 2 groups using the 2-sample t test.

## 3. Results

Of the 50 patients presenting for treatments, 36 completed the study course. The mean age of the patients were  $38.83 \pm 4.99$  and  $35.78 \pm 6.66$  for the test and control groups respectively ( $P=0.13$ ). The proportions of females across the 2 groups were 77.8% and 72.2% for the test and control groups respectively with no significant difference among them. About changes in the PPD among the subjects of the 2 groups before and 6 weeks after treatment, a considerable reduction took place in the PPD at both groups. The mean probing pocket depth of the study sites decreased from  $5.52 \pm 0.66$ mm to  $2.16 \pm 0.73$ mm and from  $5.95 \pm 1.06$  to  $2.37 \pm 0.69$  in the control and test groups respectively. However, the difference between the probing pocket depth reductions of the 2 groups was not statistically significant ( $p=0.59$ )(Graph 1). The mean probing attachment level of the study sites, before and 6 weeks after treatment, decreased from  $5.89 \pm 1.12$ mm to  $3.34 \pm 1.38$ mm and from  $6.24 \pm 1.32$  to  $3.90 \pm 1.25$  in the control and test groups respectively. The difference between the attachment gains of the 2 groups was not statistically significant ( $p=0.58$ )(Graph 2). Finally, about the percentage of study sites with BOP among the 2 groups before and 6 weeks after the treatments, the percentage of study sites with BOP decreased from 100% to 19.9% and from 100% to 24.1% in the control and test groups respectively and the reduction in the BOP% were not different significantly among the groups ( $P=0.75$ ).



**Graph 1.** The mean of PPD in the control and test groups, before and after treatment



**Graph 2.** The mean of CAL in the control and test groups, before and after treatment

## 4. Discussion

This study is the only report on the effect of adjunctive systemic co-amoxiclav plus metronidazole in surgical periodontal treatment. The effect of co-amoxiclav plus metronidazole or amoxicillin plus metronidazole in the non-surgical periodontal treatment have been investigated by van Winkelhoff et al (1989), van Winkelhoff et al (1992) and Pavicic et al (1994) and Sugano N (2012) and Mombelli A(2012)[14-19]. It seemed, therefore, quite necessary to investigate the effect of these antibiotic in the surgical periodontal therapy.

Our study demonstrated that PPD, CAL and BOP reduced considerably as a result of both treatment regimens, however, there was no significant difference between the 2 groups in this respect. The reason might be that surgical pocket elimination through removal of epithelium and granulation tissue from the soft tissue lining of pocket wall together with bone recontouring is probably adequately sufficient in controlling periodontal destruction. Although we did not perform any microbiological testing on our samples, this could have provided a greater insight into the role of antibiotics plus surgical treatment on periodontopathic bacteria. Nevertheless, our clinical outcomes indicating that no added benefit was obtained as a result of more complex antibiotic therapy is quite interesting and warrants future clinical and microbiological investigations.

van Winkelhoff et al reported that a combination of amoxicillin and metronidazole and non-surgical mechanical treatment was effective in eradicating A.a. in most patients[14-19]. One explanation of no difference between test and control groups in our study could be that A.a. which is thought to penetrate in to the soft tissue wall of pocket is more readily eradicated through surgical elimination of this soft tissue wall. Therefore the lack of difference between two groups which both included pocket surgery is conceivable.

Only patients with remaining pockets  $\geq 5$ mm following the initial phase of treatment were entered into study. One could argue that if the study populations have consisted of patients who did not responded favourably to non-surgical and surgical mechanical treatment, a different outcome could be observed with some added effect due to adjunctive combined antibiotic treatment. Such patients, categorized as refractory periodontitis could be the subjects of another future clinical investigation.

This was a relatively short-term follow-up study. It could be argued that if the patients were followed for more extended periods of time than 6 weeks, then a different result could have been obtained. Although clinical improvement following periodontal treatment might continue for prolonged periods such as 6-month to one year,

The major improvement is expected to occur with in the first 4 week following the treatment. Nevertheless, more extended follow-up studies with similar design as our study could be valuable and is recommended.

## 5. Conclusions

This study demonstrated that there was no benefit in adjunctive co-amoxiclav and metronidazole over amoxicillin alone when used as adjuncts to periodontal surgery. Therefore viewing greater risk and cost, the use of these antibiotics seems unjustifiable for patients requiring routine periodontal treatments. Further investigations using more stringent patient criteria, more extended follow-up and supplemented with microbiologic monitoring is warranted.

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