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### The clinical, microbiological and systemic characteristics of periodontitis and their changes after periodontal therapy

Bizzarro, S.

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## CHAPTER 9

### **Summary and conclusions**



The aim of this PhD research was to study the clinical, microbiological and systemic characteristics of periodontitis and their change after treatment.

In the first part of this thesis (chapters 2 and 3) the association between periodontitis and a prothrombotic state was investigated. The latter is a condition involved in the development of cardiovascular diseases. In chapter 2, a case-control study is reported in which the association between the amount of periodontal bone loss and markers of prothrombotic state was investigated. The results showed that increased periodontal bone loss was strongly associated with increased plasma levels of plasminogen activator inhibitor-1 activity, in a dose-dependent manner.

In chapter 3 it was investigated whether the host immune response to two established periodontal pathogens was associated with a prothrombotic state. The results of this study showed that in periodontitis patients, serum levels of anti-*Aggregatibacter actinomycetemcomitans* IgG's correlated positively with plasma levels of von Willebrand factor (another marker of prothrombotic state). The results from the research reported in the two above-described chapters add further evidence to the association between periodontitis and cardiovascular diseases.

In the second part of this thesis, an intervention trial is described, in patients with periodontitis, in order to study the clinical, microbiological and systemic effects of periodontal therapy.

Basic periodontal therapy, which includes scaling and root planning and oral hygiene measures, is the basis of a successful therapy of periodontitis. Adjunctive therapies could enhance the clinical and microbiological effects of the basic periodontal therapy. In chapter 4, the clinical and microbiological effects of adjunctive use of a local disinfectant (sodium hypochlorite [NaOCl]) with or without the use of systemic antibiotics (amoxicillin and metronidazole) were investigated. The results revealed that the adjunctive use of local disinfection with NaOCl did not contribute to a better periodontal clinical outcome. The adjunctive use of systemic antibiotics in the basic treatment of periodontitis resulted in a mild additional reduction of periodontal inflammation and residual deep pockets. Both adjunctive therapies did not show any additional reduction on prevalence and proportion of 7 well-established bacteria associated with periodontitis. Considering, on one hand, the modest clinical improvements in relation to the risk of adverse events and, on the other hand, the

possible increased risk of bacterial resistance, these results support the view that the systematic use of antibiotics in the treatment of periodontitis is, in general, not justified.

The same research protocol and study population, described in chapter 4, was used, in chapter 5, to investigate the systemic effects of periodontal treatment in patients with periodontitis. To this aim, the changes in markers of metabolic syndrome, were explored before and after periodontal therapy. Metabolic syndrome is a conditions associated to a higher risk for cardiovascular diseases, The results showed that the treatment of periodontitis could contribute to a decrease of systolic hypertension and decrease of levels of triglycerides, and therefore contribute to an improvement of the profile of the metabolic syndrome. The adjunctive therapies (systemic antibiotics and local disinfection) did not contribute to a further improvement of the systemic markers of metabolic syndrome. However, next to the decrease of periodontal inflammation, we cannot exclude that changes in patient's lifestyle (e.g smoking habit, physical activity, diet) would have contributed to the improvement of their metabolic status.

In chapters 6 and 7 it has been investigated more in depth the microbiological characteristics of periodontitis and the effects on the subgingival microbiome of the periodontal therapy, with or without the use of antibiotics.

In chapter 6 the microbiological results of two traditional targeted techniques (culturing and polymerase chain reaction) are compared with an open-ended next generation DNA-sequencing technique (454-pyrosequencing). The results showed that 454-pyrosequencing provided a much larger amount of information in comparison to the two traditional techniques. Above all, it was noted that patients sharing the same disease phenotype and life style conditions (smoking) had different taxonomic composition of the subgingival microbiome.

In the study reported in Chapter 7, using the 454-pyrosequencing, the effect of systemic antibiotics, as adjunct to basic periodontal therapy, on the subgingival microbiome was investigated. The results showed that administration of systemic antibiotics during basic periodontal therapy led initially to a larger shift in the composition of the subgingival microbiome in comparison to basic periodontal therapy alone. However, this effect was already no longer significant after 6 months. Furthermore, it was found that the characteristics of the microbiome before treatment and not the use of antibiotics, were potentially predictive for the treatment outcome.

In conclusion, it can be assessed that the increased levels of markers of prothrombotic state, in patients with periodontitis, corroborate the relation between periodontitis and cardiovascular diseases. Basic periodontal therapy alone remains the first choice for the treatment of periodontitis. The adjunctive use of local disinfection with NaOCl to basic periodontal therapy does not contribute to an improvement in the clinical and microbiological parameters of periodontitis. The adjunctive use of antibiotics could be used to improve the clinical outcome of basic periodontal therapy, but with caution, considering the possibility of incidence of systemic adverse events and the increase of bacterial resistance. Open-ended DNA sequencing techniques provide a large amount of microbiological information and this can be useful to improve our understanding in the dynamics of the subgingival microbiome.