

Periodontal disease in pregnant women: possible connections with gestational adverse effects. Recent evidence and news on prevention

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L Periodontal disease (or periodontitis) can severely alter the tissues supporting the teeth. The infectious factors that can produce it have been known for some time. It sets in at the onset as gingivitis, and then evolves towards a broader and more structured clinical picture. If the bacterial component is the primary etiological factor, however, other genetic or environmental components must be taken into account that can contribute to the development of the disease.

Although it locally affects the gum, ligament and alveolar bone, periodontitis can have a negative impact on the general health of the subject: it is the concept of an "infectious focus" within the oral cavity capable of altering, even strongly, the systemic physiological balance.

In the last thirty years, a large number of clinical studies have demonstrated evidence of an association between periodontal disease and other systemic diseases, including cardiovascular diseases, diabetes, pre-term births or birth of underweight children, chronic pulmonary diseases. More recently, periodontitis has been indicated as a hypothetical factor favoring intestinal pathologies, including neoplastic ones, and Alzheimer's disease. In the literature, therefore, the term "Periodontal Medicine" has made its way to describe those various pathologies that, starting from periodontal, can affect overall health.

In this short contribution, we want to focus on the relationships between periodontal disease and adverse outcomes in pregnancy, following the evidence emerging from recent international literature and hypothesizing prevention or therapy protocols, the prerogative of the figures of the Dentist and the Dental Hygienist.

Pioneering research on this subject dates back to the second mid-90s¹⁻³: these are observational studies, in a fair number of pregnant women but with methodological limitations, but able to describe this association. In the years that followed, other more in-depth clinical research was able to demonstrate the causal link between periodontitis and gestational diseases such as preterm births or births of underweight children, pre-eclampsia (hypertension, proteinuria, edema), abortions, neonatal mortality. This evidence led in 2013 to the publication of a joint workshop between the European Federation of Periodontology and the American Academy of Periodontology⁴ in which the "biological plausibility" between periodontitis and gestational disorders was demonstrated. Further research has highlighted both the direct action of periopathogenic bacteria on the fetal-placental unit and the indirect action of inflammatory mediators⁵, as well as the relationship between the severity of the level of periodontitis and the severity of gestational consequences⁶.

Other studies of those years have tried to highlight the role of early periodontal treatment, surgical or non-surgical, in pregnant women in order to avoid adverse consequences in pregnancy. Unfortunately, randomized controlled trials seem to highlight limited beneficial and preventive effects on these unpleasant disorders^{7,8}: it should be considered that the existence of periodontitis can often be documented well before the gestational period with the consequent very early presence of bacteria that will contaminate the fetal placental unit. Intra-oral antibacterial treatments to avoid bacterioemia may therefore prove insufficient to prevent a condition that has already set in. Hence the need to advise the woman preparing for pregnancy to include timely prophylactic periodontal procedures.

implemented with the most effective times and methods.

In the last three years, further clinical research has strengthened the relationship between periodontitis and adverse outcomes in distress. Zhi-Wei Guan et al.⁹ have shown that intrauterine infections caused by bacteria of periodontal origin occur by blood transmission and above all by interaction with other bacterial colonies typical of the placenta. Tang et al.¹⁰ exclude a genetic predisposition for these diseases, emphasizing instead how periopathogenic bacteria are able to alter systemic immune regulation. These bacteria can also induce an abnormal systemic inflammatory response in the liver, which can itself trigger pre-term births or miscarriages to the point of increasing neonatal mortality.

Al Sharief et al.¹¹, investigating the results of periodontal therapy and prevention, state that the bacteria present in the tissues affected by periodontitis reach the fetal placental barrier very quickly. This situation justifies the poor results that can be obtained with periodontal therapy, which normally requires several operational steps, before and during pregnancy. However, the risk for women is higher if, together with periodontitis, other factors such as advanced age, obesity, smoking, gestational diabetes and low socio-economic level are associated.

Up-to-date epidemiological data emerge from the research of Bobetsis et al.¹² according to which periodontal disease determines no less than 5% of pre-term births, 6% of births of underweight children and 10% of cases of pre-eclampsia. Even the simple gingivitis of the pregnant woman, which is far from rare, is able to promote pre-term births. According to the authors, there is a clear statistical correlation between "bleeding gums and the birth of underweight babies" and between "periodontitis and amniotic and placental infections". The research therefore shows the usefulness in pregnant women and in those who decide for an upcoming pregnancy to have a scrupulous control of the supra- and subgingival plaque.

The prophylactic and therapeutic approach of the Dentist and Dental Hygienist towards pregnant women has been known and practiced for a long time¹³. It arises from the consideration of the changes in the oral cavity typical of the pregnant woman. High levels of estrogen in the circulation modify the trophism of the oral mucous membranes. In particular, gingival tissue responds to local irritants in different ways by inducing easy edema, thickening of tissue and bleeding (gingivitis and pregnancy epulids). For these reasons, the need to improve the level of oral hygiene is evident. Cofactors that affect the inflammatory receptivity of the tissues, in this particular period, are the qualitative / quantitative alterations of salivation, nausea and hyperemesis gravidarum, the need for small and

frequent meals (grazing) due to stomacho-uterine compression.

Dental prevention protocols in pregnant women are also standardized and provided for in international guidelines. In their exhaustive volume of the 2003¹⁴, Madau and Strohmenger masterfully outline the strategies of oral prevention both in the phases before pregnancy and in the course of it. The authors outline the following procedural steps:

- instilling motivation in the pregnant woman at a time of particular receptivity of the same;
- increase women's education by using ad hoc structures, including childbirth preparation courses;
- implement an outpatient dental protocol that includes periodic visits, saliva tests, control of bacterial mother-fetus transmission, professional hygiene adapted to the woman's condition, non-surgical periodontal therapy, collaboration between dentists, obstetrician-gynecological figures and the general practitioner.

In these procedures, we believe that specific bioadhesive gels made with a mix of substances can find clinical utility that make them suitable for use in female subjects of childbearing age. These include a toothpaste gel (Hobagel 365) that contains cetylpyridinium chloride with a strong antiseptic action on all gram+ bacteria and almost all gram- bacteria in the biofilm. It is associated with a mix of essential oils including commifora myrrh, eucalyptus, thyme vulgaris and, above all, tea tree and manuka which have a prominent bactericidal and bacteriostatic action due to the presence of specific monoterpenes and sesquiterpenes. There is no tri-closan, replaced by stabilizing substances (O-cimen-5 and P-anisic acid). Three fluorides (Na monofluorophosphate, Na fluoride and potassium chloride) are also present in the gel. These are concentrated at 1200 ppm. and perform a continuous mineralizing action as they are retained on the enamel by an effective adhesive system. In addition, specific restructuring components on the gum tissues have been included such as hyaluronic acid, Na hyaluronate, provitamin B5, vitamin E, bisabolol. Finally, specific hydrated silicas confer low abrasiveness of the gel towards the dental tissues (declared RDA 30).

Gels for local application on soft tissues can also be effective. One of these (Hobagel Plus) has been designed to obtain a temporary persistence on fabrics thanks to an innovative adhesive system that makes use of the mixed salt of Na/Ca of the methyl-vinyl-ether copolymer, polyvinylpyrrolidone and Na carboxymethyl cellulose. This also contains active substances (cetylpyridinium chloride, mix of essential oils, hyaluronic acid and its oligomers, allantoin, bisabolol, vitamin E ace-



Fig. 1



Fig. 2



Fig. 3

to which are added enhancing active ingredients such as hydrogen peroxide (antioxidant). In the gel, the effectiveness of essential oils comes from their rich content in monoterpenes, sesquiterpenes and triketones: they are widely present in tea tree oil but above all in manuka oil which is considered at least twenty times higher: hence the anti-inflammatory and antibacterial action.

One of the peculiar aspects of compromised periodontal tissues is represented by the presence of hyaluronic acid in the gel, which is also used with different molecular weights expressed in K-Daltons. The combination of high molecular weight hyaluronic acid with a moisturizing and cell differentiation/stabilization function and low molecular weight oligomers of the same that guarantee deep cell absorption and migration justify the effective regenerative capacity after topical application of the gel. It therefore occurs more quickly than other gels that contain hyaluronic acid, but not oligomers of the same.

Of great importance in obtaining the results described is the peculiar mucus-adhesive characteristic of the gel obtained by inserting natural rubbers and resins into the tested product. Polymeric excipients of this type are able to enhance adhesion to the mucosa and obtain a controlled release of active ingredients.

The photos of the article are by Dr. Alberto Pispero.

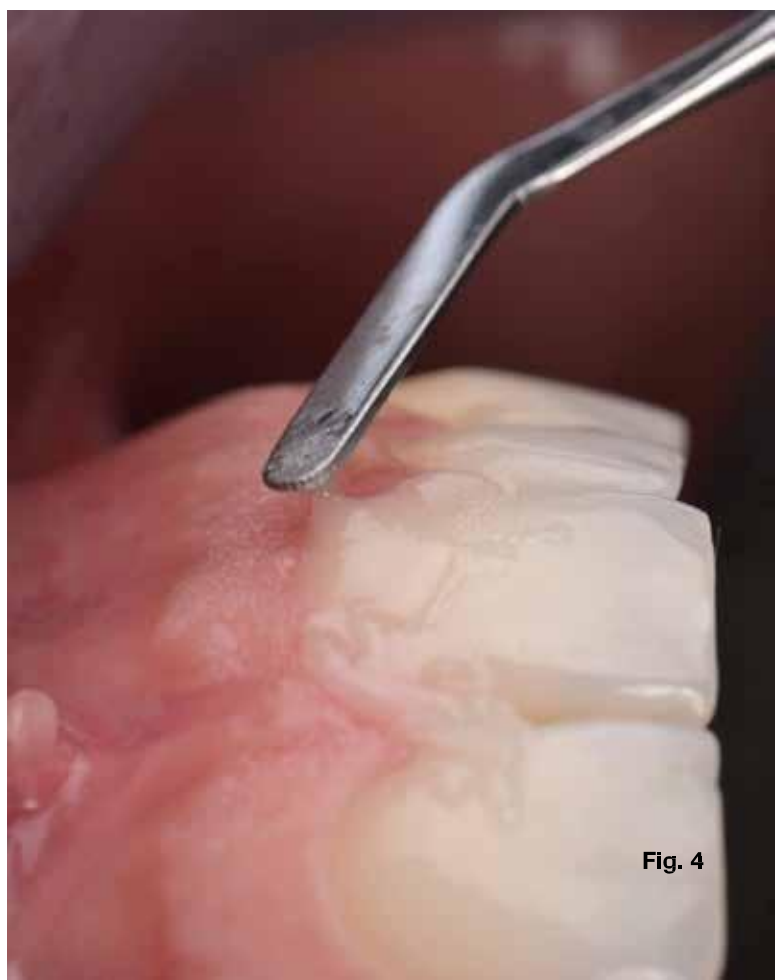


Fig. 4

Fig. 1 - Initial situation.
Figs. 2.3 - Product applications.
Fig. 4 - Viscosity of the product.



Fig. 5

Fig. 5 - After closing and reopening the mouth, you can see how the product is distributed inside it.

Bibliography

1. Offenbacher S., Kats V., Fertik G., Collins J., Boyd D., Maynor G. Periodontal infection as a possible risk factor for preterm low birth weight. *J. Period.* 1996;67:1103-13.
2. Dasanayake A.P. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. *Ann Period.* 1998; 3: 206-12.
3. Davenport E.S., Williams C.E., Sterne J.A., Murad S., Sivapathasundram V., Curtis M.A. Maternal periodontal disease and preterm low birthweight: case-control study. *J. Dent. Res.* 2002; 81:313-8.
4. Ide M., Papapanou P.N. Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes – systematic review. *J. Period.* 2013;84:181-94.
5. Madianos P.N., Bobetsis Y.A., Offenbacher S. Adverse pregnancy outcomes (APOs) and periodontal disease: pathogenic mechanisms. *J. Clin. Period.* 2013; 40: 170-80.
6. Michalowicz B.S., Gustafsson A., Thumbigere-Math V., Buhlin K. The effects of periodontal treatment on pregnancy outcomes. *J. Period.* 2013;84:195-208.
7. Iheozor-Ejiofor Z., Middleton P., Esposito M., Glenny A.M. Treating periodontal disease for preventive adverse birth outcomes in pregnant women. *Cochrane Database Syst. Rev.* 2017; 6: CD005297.
8. Bobetsis Y.A., Graziani F., Gursoy M., Madianos P.N. Periodontal disease and adverse pregnancy outcomes. *Periodontol 2000* 2020;83:154-74.
9. Zhi-Wei Guan et al. Pathways and Mechanisms of periodontitis contributing to adverse pregnancy outcomes. *Sichuan Da Xue Xue Bao Yi Xue Ban.* 2023; 54: 39-48.
10. Tang L. et al. Association between periodontitis and adverse pregnancy outcomes: two-sample mendelian randomization study. *Int. Dent. J.* 2024; 74:1397-1404.
11. Al Sharief M., Alabdurubalnabi E. Periodontal pathogens and adverse pregnancy outcomes: a narrative review. *Life (Basel)* 2023; 13: 1559-65.
12. Bobetsis Y.A., Ide M., Gursoy M., Madianos P.N. Periodontal diseases and adverse pregnancy outcomes. Present and future. *Periodontol 2000.* 2023: doi 10.1111/prd12486.
13. Montagna F., Ferro R. Dental treatment during pregnancy, in the first years of life and in the disabled. *I quaderni della professione (Promoass Ed.)* 1999: 5-10.
14. Madau M., Strohmer L. Prevention and promotion of oral health in children. *Quintessenza Ed.* 2003: 246-264.