Preeclampsia and maternal periodontal disease

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Abstract

Preeclampsia is one of the adverse outcomes of pregnancy. The Gram-negative anaerobes harbored in gingival pockets of pregnant women suggest that maternal periodontal disease might be a risk factor. However, the epidemiological studies are oscillating between positive and no association of preeclampsia with chronic marginal periodontitis. The periodontal treatment during pregnancy aiming to suppress the outcome of pathogenic mechanisms developed by periopathogens is thought to be beneficial for the general status of preeclamptic women. Nevertheless, at present, it is not clear to what extent the maternal periodontal disease might be a risk factor of preeclampsia or only an epiphenomenon of the systemic inflammatory response.
Keywords: *pregnancy, maternal periodontal disease, preeclampsia*

Rezumat

Preeclampsia este una dintre complicațiile sarcinii. Anaerobii Gram-negativi din pungile parodontale ale gravidelor sugerează că boala parodontală maternă ar putea fi un factor de risc. Totuși, studiile epidemiologice au avut rezultate diverse, de la găsirea unor corelații pozitive între preeclampsie și parodontita marginală cronică până la lipsa unei relații cauzale. Tratamentul parodontal în cursul sarcinii, care urmărește îndepărtarea consecințelor exercitării mecanismelor patogene asupra parodonțiului marginal de către periopatogeni, este considerat a fi benefic pentru sănătatea generală a gravidelor cu preeclampsie. Cu toate acestea, în prezent nu este clar în ce măsură boala parodontală maternă poate fi un factor de risc pentru preeclampsie sau este numai un epifenomen al răspunsului inflamator sistemic.
Cuvinte-cheie: *sarcină, boală parodontală maternă, preeclampsie*

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Introduction

The medical and dental literature of the last 20 years highlighted a putative association between adverse pregnancy outcomes and maternal chronic marginal periodontitis[1-7]. No doubt that due to its worldwide morbidity and risk of mortality, affecting 5-10% of all pregnancies, with a lower rate in western countries and in United States, preeclampsia is one of the most debated issues of maternal and perinatal pathology[8]. Since usually a long-standing inflammatory process is suspected to be a potential risk factor of adverse pregnancy outcomes, it is thought that preeclampsia could be also induced by the progressive gingival inflammation in pregnant women[8-13].

Preeclampsia – definition and etiology

According to ISSHP (International Society for the Study of Hypertension in Pregnancy) guidelines[14,15], preeclampsia is defined as a multisystem disorder characterized by high blood pressure (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) measured on two different occasions at least 4 hours apart after 20 weeks of gestation, peripheral edema, and proteinuria (≥300 mg/24 h). In more advanced cases, there may occur liver dysfunctions and coagulation modifications[7,8,14-16].

The multifactorial etiology of preeclampsia includes various risk factors such as placental insufficiency induced by local hypoxia and acute atherosis, pregestational hypertension and obesity, gestational weight gain, genetic susceptibility, advanced maternal age, race, nulliparity, personal history of preeclampsia, diabetes mellitus, dyslipidemia, renal disorders, urinary tract infections, immune responses such as anti-phospholipid antibody syndrome, and enhanced systemic inflammation[7,8,16,17].

Though currently it is established that a prolonged inflammation of fetal-placental unit and a high blood level of systemic inflammatory markers may result in adverse pregnancy outcomes, actually the etiology of preeclampsia still remains unclear[8,18].

Maternal periodontal disease and preeclampsia

In pregnancy, the interaction of sex steroid hormones with inflammatory mediators progressively deteriorates the initial gingival condition triggered by dental plaque. Moreover, the prolonged daily release of sex steroid hormones throughout pregnancy (estradiol 20 mg, estriol 80 mg, progesterone 300 mg) results in higher prevalence and severity of maternal gingival inflammation when compared with postpartum women[19]. However, despite

the exacerbation of gingival inflammation, the plaque scores during pregnancy remained unchanged following parturition[19].

The clinical inspection in pregnant women suggests a positive association between maternal inflammatory gingival status and preeclampsia. It was observed an overall increase of gingival probing depth, bleeding on probing, and the gingival crevicular fluid as compared with controls. However, there was not observed any attachment loss[19]. The meta-analysis of case-control studies is consistent with these findings[18], which were also described in postpartum women[10].

The pathogenic relationship between periodontal disease and preeclampsia

Basically, the pathogenic mechanisms involved in preeclampsia are placental ischemia and by blood steered circulating inflammatory mediators[16]. As well known, the inflammatory process is a common feature of cardiovascular disease, adverse pregnancy outcomes and periodontal disease[20-23]. Relying on a meta-analysis study, maternal periodontal disease and urinary tract infections might be important risk factors for preeclampsia. However, no significant associations were found between the presence of antibodies to some typical microorganisms involved and this adverse outcome of pregnancy[24].

Neither the anti-inflammatory periodontal treatment proved a significant lowering of preeclampsia incidence[7]. Moreover, since the risk of preeclampsia was not found in all population studies, it seems that maternal periodontal disease might not have a causal effect[7].

When evaluating the association between maternal periodontal infections and the risk of preeclampsia, it is mandatory to avoid the fluctuation of "periodontitis case definition", because the analysis outcome might be detoured[5]. Accordingly, unlike the usual periodontitis definition that supports a significant cause-effect association, the use of continuous variables such as probing depth describes a non-significant one[5,7,18,24]. The disparate conclusions found in literature are also influenced by the chosen criteria in case definition, study design, sample size and statistical analysis[7]. It also seems that during assessment of pregnant women, the maternal periodontal disease must be rather considered an independent risk factor for preeclampsia[8].

Additionally, during the last decade, the maternal periodontal disease is also considered a putative risk factor of preeclampsia, relying on pathogenic mechanisms secondary induced by chronic systemic inflammation[8]. Periopathogens and their by-products may enter the maternal blood circulation and settle afterwards into the fetal-placental unit, inducing an oxidative stress, which is in charge with preeclampsia occurrence[16]. Additionally, it was found that two main components of red complex microorganisms, well-known for their virulence trait and the ability of releasing pro-inflammatory cytokines, *Porphyromonas gingivalis* and *Tannerella forsythensis*, were more prevalent in a preeclamptic study group than in controls[25].

The exacerbation of gingival inflammatory response in pregnant women is substantiated by increased expression of inflammatory markers. It was observed that the adverse pregnancy outcomes are mainly associated with increased level of blood pro-inflammatory cytokines[20], C-reactive protein[16,22,26], and Pentraxin 3 (PTX3)[27]. Numerous studies related about the elevated serum levels of CRP (C-reactive protein) found in both preeclampsia and maternal chronic periodontal disease[7,28,29].

Of special interest is the functional perturbation of VEGF, resulting in endothelial dysfunction[30]. In preeclampsia, there is also discussed the possible role of TNF-α, NO, endothelin-1, and thromboxane A2[16]. It was observed that one of the main periopathogens, *Porphyromonas gingivalis*, obviously increased in gingival tissue the expression of endothelin-1, which at its turn elevated the local IL-1β, IL-6 and TNF-α[31].

Epidemiological studies worldwide

In case-control and cross-sectional studies, the maternal periodontal disease was significantly associated with preeclampsia[5,11,12,18].

A clinical and microbiological Colombian survey found maternal chronic periodontitis in 63.8% of preeclamptic women versus 36.6% of controls, and highlighted the increased prevalence of *red complex* periopathogens in case of preeclamptic adverse outcome of pregnancy[25].

Evaluating the anaerobic microflora of subgingival biofilms and placental samples, an Egyptian study found that the number of anaerobes in both locations was increased in preeclamptic women. A significant higher level of serum TNF-α was also triggered in affected individuals than in controls. Accordingly, it was highlighted a statistic relationship between chronic periodontal infection and preeclampsia[32].

An Indian study on pregnant women affected by periodontal disease, namely 100 preeclamptic and 100 non-preeclamptic, revealed that moderate to severe periodontal infection increased the risk and rate of preterm delivery in preeclamptic women[33].

Though clinical attachment level, gingival recession, and bleeding on probing were significantly increased in a group of 105 Iranian preeclamptic women, the same periodontal examination of 105 non-preeclamptic pregnant women proved that there were no differences in the pocket depth[34].

According to a cross-sectional postpartum study in Northern Tanzania describing a significant association of maternal periodontal disease with preeclampsia, it must be considered the chronic marginal periodontitis as an independent risk factor in triggering this adverse pregnancy outcome[35].

A meta-analysis of literature until 2013, based on the evaluation of epidemiologic relationship between oral infections and preeclampsia, suggested that maternal chronic periodontal disease raised the risk of this adverse outcome in pregnancy[36].

Although recognizing the periodontal disease as putative risk factor for preeclampsia, another meta-analysis

underlined that important differences were found in definition and diagnosis of maternal periodontitis. Moreover, the quality of studies methodology was sometimes doubtful[37].

A comparative survey in Thailand found after delivery insignificant variations in clinical parameters of maternal periodontal disease between preeclamptic and normotensive women. No linear increase in risk of preeclampsia could be linked to the degree of periodontal disease progress. However, despite the different diagnostic criteria of periodontal inflammation, the magnitude and direction of associations between maternal periodontal disease and preeclampsia were mainly alike[8].

Though the majority of papers support the possible association of preeclampsia and maternal periodontal disease, another Iranian study observing at delivery plaque index, gingival bleeding index and attachment loss could not find statistically significant differences between preeclamptic pregnant women and controls[13].

Similarly, a blinded case-control study after delivery on 115 preeclamptic women and 230 normotensive controls investigating plaque index, gingival index, periodontal probing depth, clinical attachment loss and gingival recession did not confirm this pathogenic hypothesis[38].

Incidentally, about one third of papers analyzed in a review study did not describe an association between preeclampsia and maternal disease[11]. Nevertheless, the overview of literature confirms that a generalized inflammatory response of pregnant women substantiates the role of inflammation as pathogenic mechanism in triggering preeclampsia[11]. Since no paper reported that the periodontal treatment during pregnancy could reduce the preeclamptic rate, presently it seems still doubtful if the maternal periodontal disease might be considered a causal factor. Moreover, it is also forwarded the hypothesis that periodontal disease in pregnancy could be rather an epiphenomenon of the systemic enhanced response[11]. Further research is required in this field.

Periodontal therapy and preeclampsia

Unlike preeclampsia, which despite the possibility to be treated it is more difficult to be precluded, clinical experience demonstrated that periodontal disease in pregnant women may be efficiently prevented and treated[8].

Despite the conflicting data concerning the efficacy of periodontal therapy, there is a general agreement that the oral hygiene during pregnancy may be improved since the pregnant women can safely reduce the bacterial biofilms by managing gingival cleaning. Commonly, the periodontal therapy in pregnancy is conducted to eliminate or reduce the risk of maternal periodontal disease[7,39].

The basic periodontal therapy is non-surgical and proved to be safe. However, according to literature, it is still doubtful if the routine non-surgical periodontal therapy may significantly reduce the incidence of preeclampsia since the published results are contradictory[7].

Usually, in pregnant women the conventional scaling and root planning associated with daily rinsing by using 0.12% chlorhexidine resulted in the improvement of periodontal status, including reducing of probing depth and bleeding on probing, comparable with controls (non-pregnant women)[7].

During the first trimester of pregnancy, it is recommended basic preventive therapy following home-care instruction. The second trimester is dedicated to routine dental care in order to control the ongoing maternal periodontal disease and prevent the potential risky issues which could appear during late pregnancy. Any major surgical management of gingival should be rescheduled after delivery. However, due to potentially increased inflammation, a periodontal maintenance visit is recommended until mid-third trimester, with caution to avoid a prolonged chair time[39].

At present, according to guidelines of California Dental Association, preeclampsia is not considered a contraindication for the dental care of pregnant women[39,40].

Conclusions

An increased number of publications suggest that maternal chronic periodontal disease, due to its characteristics of polymicrobial infection, can be considered a potential risk factor of preeclampsia. The periodontal treatment during pregnancy aiming to suppress the outcome of pathogenic mechanisms developed by periopathogens is thought to be beneficial for the general status of preeclamptic women. However, at present, it is not yet clear to what extent the maternal periodontal disease might be a risk factor or it is an epiphenomenon of the systemic inflammatory response. ■

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