

GENGIGEL[®]
Hyaluronic Acid



ORAL HEALTH & PREGNANCY

FACT FILE

HOW CAN PREGNANCY AFFECT ORAL HEALTH?

During the course of a normal pregnancy, several deep and dynamic physiological changes occur in both the mother and the developing baby. Some of the endocrine and immune changes induced by pregnancy increase the susceptibility of the mother to various infections, including those of the oral cavity (Silva de Araujo Figueiredo, 2017; Loe, 1963; Silness, 1964; Barak, 2003; Leal, 2004; Minozzi, 2008; Armitage, 2013).

Researches have shown that **pregnant women are exposed to a higher risk of gingival alterations**. The increased susceptibility to infections in the oral cavity can occur due to pH decrease and, consequently, the salivary buffer capacity during pregnancy, which, along with



the change of dietary and oral hygiene habits, contributes to bacterial growth and increases the risk of caries (Laine, 2002; Martínez-Pabón, 2014).

Among the changes most frequently cited in the literature are pyogenic granuloma, gingivitis, and the periodontal disease, also known as periodontitis (Gürsoy, 2008; Russel, 2008; Silk, 2008).

WHICH ARE THE RISKS FOR THE WOMAN AND HER CHILD?

Several studies have investigated the occurrence of periodontal disease during pregnancy, yielding a wide variation in prevalences (11% to 100%; Ifesanya, 2010; Piscocya, 2012). Pregnant women with periodontal disease have been reported to be at increased risk of adverse pregnancy outcomes (Pihlstrom, 2005), including preeclampsia (Kunnen, 2007; Siqueira, 2008), preterm delivery (Jarjoura, 2005; Offenbacher, 2006), and low birth weight (LBW; Marin, 2005; Martins Mo-



ltern, 2005). This association has been confirmed even by recent meta-analyses on the matter (Daalderop, 2017), that confirmed a strong evidence exists for a link between periodontal disease and adverse pregnancy outcomes, with substantial proportions of preeclampsia, preterm birth, and LBW cases being estimated to be attributable to periodontal disease. The authors conclude that, given the high global prevalence of periodontal disease and the ad-

verse pregnancy outcomes associated with it, it is pivotal that preventive and therapeutic strategies be developed to prevent adverse pregnancy outcomes via improving oral health. Although randomized trials and systematic reviews of antibiotics and dental procedures during pregnancy generally demonstrate a positive impact on periodontal disease, the evidence for improvement of pregnancy outcomes is conflicting (Offenbacher, 2009). There is thus a need to evaluate novel strategies of preventive and therapeutic approaches.



HOW DOES THIS LINK OCCUR?

The mechanism linking periodontitis and pregnancy adverse outcomes has still not been established with precision; yet, aberrant inflammatory and immunological responses are certainly involved (Ren, 2017). The periodontal disease is caused by gram-negative microaerophilic and anaerobic bacteria that colonize the subgingival area and produce significant amounts of proinflammatory mediators, mainly IL-1 β , IL-6, PGE2, and TNF- α (Pihlstrom, 2005). Periodontitis may therefore act as a distant reservoir of both microbes and inflammatory mediators that may influence pregnancy and contribute to induction of pregnancy adverse outcome, the most frequent being preterm birth. Periodontal microorganisms can act as pathogens not only in the oral cavity but also in other body areas. This

is due to the following characteristics of bacteria: (Zi, 2014) the ability to rapidly colonize, (Goldenberg, 2008) the ability to elude the host's defense mechanisms, and (Beck, 2010) the ability to produce substances that directly contribute to the destruction of tissue. Periodontal pathogens/ byproducts may reach the placenta and enter the amniotic fluid and fetal circulation, serving to activate inflammatory signaling pathways. Further, clinical attachment loss, as the main periodontal measure, is associated with plasma levels of IL-1 β and TNF- α in pregnant women (Mesa, 2016; Cetin, 2012), which may promote labor activation through placental and chorion-amnion production of PGE2 (Cetin, 2012). Clinical studies support the association between increased levels of circulating proinflammatory me-

diators and PTB (Lyon, 2010; Malaeb, 2009) and have implicated IL-1 β and IL-6 as major players in the onset of PTB (Tanaka, 1998; Jun, 2000). Summarizing, the two mechanisms that might explain the link are: first, periodontal pathogens/byproducts can disseminate toward the placental and fetal tissues, inducing immune/inflammatory reactions within the placental tissues of the pregnant woman; the consequent release of proinflammatory mediators in the amniotic fluid may increase and further contribute to preterm birth. Second, systemic inflammatory changes induced by periodontitis can exacerbate local inflammatory responses within the fetoplacental unit and again increase the risk for preterm birth.

WHY RESORTING TO NON-DRUG TREATMENTS?

As the link between the disease and adverse pregnancy outcomes is not fully understood, such is the mechanism of action of periodontal treatment in preventing them (Iheozor-Ejiofor, 2017). The general aims of treatment of periodontal disease are to resolve the inflammation by bringing the amount of plaque and calculus down to minimal levels; and to prevent or limit the tissue destruction to preserve dentition, maintain appearance and minimise discomfort (Pilot, 1980; Sheiham, 2002; Wennström, 1990). Periodontal treatment must be followed by good oral hygiene in order for the inflammation to remain under control; resolution of this inflammation/ infection may be an important outcome for preventing preterm



birth. Thus, instructing and motivating individuals to clean their teeth properly is an important component of periodontal treatment. Dental care providers may be concerned that commonly used drugs such as anaesthetics, antibiotics and analgesics may harm the foetus. There may also be concern that bacteraemia caused by some dental procedures may lead to uterine infections, spontaneous abortions or preterm labour (Michalowicz, 2009). **Experts have sometimes recommended that dental treatment be avoided early in pregnancy during organogenesis and also late in pregnancy to avoid supine hypotension** (Michalowicz, 2008).

WHY HIGH MOLECULAR WEIGHT HYALURONIC ACID?

Hyaluronic acid (HA), or hyaluronan, is a naturally occurring non-sulphated, linear polymer composed of repeating units of glucuronic acid and N-acetylglucosamine (Chen, 1999; Kavasi, 2017). **HA levels are particularly high in the extracellular matrix of tissues undergoing rapid turnover, where regeneration and repair are occurring, such as the oral mucosa** (Valachová, 2016). HA has many different functions, including maintenance of tissue homeostasis and cell surface protection, but is also involved in many physiological processes, such as cell attachment, migration and proliferation, embryogenesis, wound healing, and regulation of immune response and inflammation (Kavasi, 2017). High molecular weight hyaluronic acid (HMWHA) is deposited in normal tissues and interacts with other components of the ECM to control the structural organization of ECM and signalling. In general, endogenous HMWHA possesses



enhanced anti-angiogenic, anti-inflammatory and immunosuppressive properties (Kavasi, 2017). High molecular weight hyaluronic acid (HMWHA) is a linear molecule with a highly complex secondary and tertiary structure in aqueous solution; its amphophilic nature allows this molecule to trap large quantities of water and, at the same time, to bond to hydrophobic molecules such as the lipidic substances of cell membranes (Scott, 1998). This property is relevant in controlling hydration and contributes to retardation of viral and bacterial passage through the hyaluronan-rich pericellular zone, as well as during periods of change when HA levels are elevated, during inflammatory processes (Chen, 1999). **Clinical studies have shown that HA accelerates the healing of various types of wounds, including burns, epithelial surgical wounds, and chronic wounds** (Shaharudin, 2016).

Why Gengigel®?

The devices belonging to the Gengigel® family achieve their expected performance due to the action of its principal component, high molecular weight hyaluronic acid, (HMWHA), which makes Gengigel® strongly bioadhesive, an effect that may be enhanced by using a calibrated mixture of some ancillary glycopolymers. In this way Gengigel® adheres to the oral mucosa for long enough to promote the activation of the physiological tissue repair process, improving the healing response and reducing healing time. Further, by maintaining the balance of extracellular fluids, again because of the presence of high molecular weight hyaluronic acid, it promotes resorption of oedema in inflammatory states, rapidly reducing the associated pain. Last but not least, it protects the oral mucosa from harmful agents, preserving the micro-environment of the mucosal surface,



and regularizing the growth of bacterial flora.

Clinical evidence concerning Gengigel® includes clinical data from prospective, comparative studies, which can thus be considered to be of high quality. Furthermore, several studies had a split-mouth design, which facilitated their interpretation by minimizing the effects of inter-patient variability. The studies covered different Gengigel® indications, including management of clinical signs associated with periodontal disease or gingival inflammation following surgical periodontal therapy. In all cases, the patients were treated with the gel formulation, either in a single application given at the time of surgery, or with multiple applications following the initial periodontal surgery/treatment. Depending on the study, the follow-up period varied between 7 days and 6 months, providing sound clinical data on the effectiveness of long-term treatment with Gengigel®.

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