Periodontal disease is ranked among the 10 most prevalent chronic diseases worldwide, and is considered a major public health problem. Its etiology has been associated with local and general conditions that could interfere in the host immune response. Obesity, like periodontal disease, has emerged as a prevalent chronic disease in high-, low- and medium-income countries, recognized as risk factor for cardiovascular disease and cancer. A relationship between periodontal health and obesity may exist, but the mechanism that would explain this association remains unclear. Life-course epidemiology could be a useful instrument to investigate a casual association between early exposures and later outcomes, being appropriate for understanding the establishment of chronic conditions. This approach comprehends different theories, considering the time, the duration and the intensity of early exposition, and its impact on the development of chronic diseases in later life. Thus, the aim of this study is to hypothesize the different life-course epidemiology theories to explain the possible association between periodontal health and nutritional status in adulthood.

Introduction

Periodontal disease is mainly a chronic inflammatory condition induced by dental biofilm accumulation on tooth surfaces (1). It is a highly prevalent condition worldwide and represents a major public health problem for developed and developing countries (2). It figures among the 10 most prevalent chronic diseases (2). There are different clinical manifestations of periodontal conditions, such as gingivitis, an acute inflammation of gingival soft tissue caused by bacteria accumulation along the gingival margin; and periodontitis, a more advanced inflammatory form of periodontal disease, in which breakdown of the supporting tissues of the teeth occurs (3). Periodontitis is clinically characterized by periodontal pockets resulting from an attachment loss, which progressively can lead to loosening and ultimately loss of the teeth. Tooth loss is a worldwide public health problem caused mainly by dental caries and periodontal disease, the last especially in later adulthood, with impacts on quality of life (4). Periodontal destruction may be caused by local factors, such as dental biofilm, and systemic factors, like diabetes, HIV infection or other diseases that may depress the host immune response (3).

Evidence suggests that obesity associated with periodontal disease seems to exist, as several studies have observed this association in different life-course stages, since childhood to adulthood (5-8). Focusing on the biological aspects, a low-grade inflammation caused by excessive adipose tissue might be responsible for important alterations in the oral conditions. It has also been suggested that there is a high production of pro-inflammatory cytokines, such as interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-6, by the adipocytes and macrophages of the white adipose tissue (9). These cytokines play a significant role in the development and progression of periodontal disease because the release of inflammatory cytokines is closely linked to a higher susceptibility to bacterial infection, caused by an alteration in the host immune response (10,11).

In order to identify the role of early exposures in the development of chronic diseases in later life, life-course epidemiology provides different tools that may help understanding the possible mechanisms involved in this relationship. Life-course epidemiology has been defined as the study of long-term effects of physical and social exposures that influence the development of chronic diseases across life course of individuals (12). It aims to establish potential causal links between exposures and outcomes, considering the duration and timing of the exposure (13).

Although many studies have explored the association between obesity and periodontal disease, the literature is scarce on prospective studies focused on this theme. The aim of this paper is to discuss on the relationship between obesity and periodontal disease according to four different life-course epidemiology theories: a) critical period (programming model); b) critical period with modifier...
effect model; c) accumulation of risk model; d) chain-of-risk model (13,14).

**Life-Course Epidemiology Approach**

**Critical Period Model**

This model emphasizes that an exposure occurred in a specific period of life affecting some body structure or system and causing irreversible or permanent damage or disease later in life (12,15).

If one considers that this model explains the association between obesity and periodontal disease, subjects who presented obesity or overweight at a certain time period, e.g. childhood, will present higher prevalence of periodontal disease and more severe clinical attachment loss, resulting in worse periodontal condition compared with those that were eutrophic in early life. According to this theory, obesity in early life would permanently affect periodontal tissues, and he weight of the subject in adulthood is not relevant for the development of periodontal disease.

**Critical Period with Modifier Effect Model**

This model considers that the exposure at a certain age could interact with events that happened during different life periods, enhancing or decreasing the likelihood of developing a chronic condition (12,13). Therefore, this model assumes the possibility of risk change or "mobility" across the classes during life-course.

Taking this model into account, subjects would present a compatible periodontal situation respecting the trajectory of weight status during life course. The hypothesis of this study is that different outcomes are expected according to the different obesity/overweight trajectories during life: a) Subjects who were obese/overweight in early life and gained weight in adulthood would present the most severe clinical attachment loss and consequently the worst periodontal condition, since the early deleterious effects of obesity on periodontal health would be aggravated by the later weight gain, exacerbating the deficiency in host immune response already caused by early obesity event; b) individuals that were obese/overweight in early life and lost weight in adulthood would present the second worst periodontal condition, since even with the effects of obesity exposure in early life, with enduring damages to the periodontal tissue and the host defense mechanism, the decrease of inflammatory cytokine levels in later life would increase the intensity of host response in front of a potential pathogen infection; c) subjects who were eutrophic in childhood and adolescence, but gained weight in adulthood would have better periodontal conditions than always obese subjects and obese earlier in life, but worse than the never obese individuals, because that exposure to inflammatory cytokines in later life would be less harmful than in early life, as this later exposure would not modify permanently the biological properties of periodontal tissues; d) always eutrophic subjects would present the best periodontal condition among the established trajectories.

**Accumulation of Risk Model**

The third model suggests that injuries are accumulated incrementally through the life-course. It considers that the number, duration and severity of exposures have a cumulative effect on the chronic disease development (12).

In this way, the disease load will be related to the amount of time that the subject was exposed to the risk condition. Therefore, periodontal disease development in adulthood would be directly proportional to the number of obesity episodes during life, independent from the life period when obesity/overweight occurred. In sum, subjects who were obese for a longer period of time would have a higher risk of periodontal diseases. Therefore, subjects with more episodes (longer periods of time) of obesity would be the ones with the most severe clinical attachment loss reflecting the worst periodontal status.

**Chain-of-Risk Model**

The fourth life-course model is a modified version of the accumulation of risk model and basically considers that one adverse or beneficial exposure conducts to other benefic/adverse event as a chain of events, impacting in health conditions. This model takes into consideration a complex interaction between exposures, such as individual social resources and extrinsic factors, e.g. social environment (13).

Considering the possible association between nutritional status and periodontal disease, obese subjects are expected to present low self-esteem, influencing directly in the oral and general health self-care, with neglected attitudes, like poor oral hygiene and poor dietary habits. Associated with these factors, obese individuals present altered metabolic and inflammatory profiles, like increased levels of C-reactive protein and pro-inflammatory cytokines, which would exert a major role in the periodontal disease development and progression.

**Final Considerations**

Based on the above, the hypothesis of this study is that life-course epidemiology has an important role in understanding the possible association of nutritional status and periodontal disease in later life. Accordingly, prospective studies are required to verify the sequence of events in the life course that may affect the development of chronic oral conditions. Such investigations could provide basis for the most appropriated time to start preventive strategies in order to reduce disease occurrence and severity, saving public resources and improving the quality of life.
Resumo

As doenças periodontais apresentam-se entre as dez doenças crônicas mais prevalentes mundialmente, sendo consideradas um relevante problema de saúde pública. Sua etiologia tem sido associada com fatores locais e com fatores sistêmicos que poderiam influenciar na resposta imune do hospedeiro. A obesidade, de forma semelhante à doença periodontal, emergediu como uma doença crônica altamente prevalente, tanto em países de alta renda, como em países de média e de baixa renda, sendo considerada um conhecido fator de risco às doenças cardiovasculares e ao câncer. Há uma possível relação entre as doenças periodontais e a obesidade, mas os mecanismos envolvidos nesta associação permanecem desconhecidos. A epidemiologia do ciclo vital pode ser considerada um eficiente instrumento para investigar associações causais entre exposições precoces e desfechos tardios, sendo apropriada para a compreensão do desenvolvimento de doenças crônicas. Esta abordagem abrange diferentes teorias, considerando o tempo, a duração e a intensidade da exposição, e o seu impacto no desenvolvimento de doenças crônicas em fases tardias da vida. Assim, o objetivo deste estudo é fazer hipóteses sobre as diferentes teorias da epidemiologia do ciclo vital para explicar a possível associação entre a saúde periodontal e o estado nutricional na vida adulta.

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