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Arteriosclerosis and Periodontitis: Correlation Expressed in the Amount of Fibrinogen in Blood

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Abstract**—**Periodontitis as an oral pathology caused by specific bacterial flora functions as a focal infection for the onset and aggravation of arteriosclerosis. These two distant pathologies, since they affect organs at a distance from each other, communicate with each other with correlation at the level of markers of inflammation in the blood. Fluctuations in the level of fibrinogen in the blood, depending on the active or passive phase of the existing periodontitis, affect the promotion of arteriosclerosis. The study is of the brief communication article type with the aim to analyze the effect of non-surgical periodontal treatment on fluctuations in the level of fibrinogen in the blood. The reduction of fibrinogen's level in blood after non-surgical periodontal treatment of periodontitis in the patient's oral cavity, is a common consequence supported by literature sources. Also, the influence of a high amount of fibrinogen in blood on the occurrence of arteriosclerosis at the same patient, is also another important data that again rely on many sources of literature. Thromboembolism and arteriosclerosis, as risk factors expressed in clinical data, have temporary bacteremia in the blood, which can occur significantly and often between phases of non-surgical periodontal treatment of periodontitis, treatments performed with treatment phases and protocols of predetermined treatment. Arterial thromboembolism has a significant factor, such as high levels of fibrinogen in the blood, which are significantly reduced during the period of non-surgical periodontal treatment.

Keywords**—**Fibrinogen, refractory periodontitis, atherosclerosis, non-surgical, periodontal treatment.

I. Introduction

DESPITE appearing in different areas of the body, periodontitis and arteriosclerosis are two pathologies that are often found to be associated with each other. At first glance, it may seem like an unlikely connection. However, both diseases share a common basis as inflammatory conditions. The inflammatory nature of periodontitis is more pronounced and is characterized by clinical signs that are visible in the oral cavity. In contrast, the inflammatory nature of arteriosclerosis is less obvious and may be more clinically hidden. In this case, greater emphasis is given to the amount of plasma lipoproteins (LDL/ VLDL) [1]-[3]. The connecting point of these pathologies is the inflammatory response at abnormal levels, expressed abnormally in the presence of the monocyte/macrophage hyperinflammatory phenotype. Chronic periodontitis is a concomitant disease that can fluctuate between active and phasic phases. Patients with this disease do not fully recover and must learn how to maintain the disease in a passive phase. As a result, patients with chronic periodontitis often present as individuals with a highly pronounced inflammatory response. Interestingly, these patients also tend to exhibit abnormal monocyte phenotype and hyperinflammatory macrophages. These hyperinflammatory phenotypes of monocytes and macrophages produce pro-inflammatory mediators such as Il-1 TNF-alfa and PGE2 [1]-[10]. Aggressive periodontitis and refractory periodontitis are two types of periodontitis that are distinguished from other types based on their level of association with arteriosclerosis. These two types of periodontitis are known for being particularly difficult to manage and treat, and are often associated with a higher risk of developing arteriosclerosis. The risk is identified by the risk factors associated with them risk factors are evaluated to determine their effect on the occurrence, induction, or slowing of the pathology through cross-sectional or longitudinal studies. These studies are conducted on relatively average patient samples that are selected based on specific inclusion criteria. By analyzing these studies, we can better understand the risk factors associated with these pathologies and develop prevention and treatment strategies. In this way, we analyze the effects of risk factors that need the time element to express the accumulative action of the act, as the latter cannot be immediate. Both periodontitis and arteriosclerosis have a prolonged time span until the onset of clinical signs of pathology diagnosis. But there are also risk factors that not only act locally on the oral cavity but also have an immediate systemic effect on vasoconstriction or vasodilation in blood vessels, as a systemic action that can be observed with the acute effect of action, such as smoking, diabetes, hypertension, dyslipidemia. We evaluate these elements with cross-sectional study, and they emerge as elements that promote both arteriosclerosis and the appearance of periodontitis. Thus, the clinical picture of pathology is affected because the existing systemic vices or diseases in the body affect the appearance of aggressive periodontitis and arteriosclerosis, one by one, but with the appearance of these pathologies, they interact with each other to further aggravate the clinical signs of each pathology, both existing and superimposed on the patient's pathological clinical picture [11]-[19]. Periodontal pathologies contribute to the onset of arteriosclerosis by supplying normal and uninterrupted vascular endothelium with gram-negative bacterial lipoproteins and proinflammatory cytokines [19]-[23]. This article follows the study of the same group of authors, already published in 2020 based on the number of subsequent references [16].

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II. Main Text

The study is a concerted as brief communication about the data published at articles about the interconnection of arteriosclerosis and periodontitis. The classification of periodontal diseases varies in relation to denominations but also to subdivisions of periodontal diseases. This type of variation has been significantly expressed in terms chronic periodontitis and aggressive periodontitis. It is these pathologies that have been part of the studies despite the same pathogenic causes of the oral flora the clinical signs of pathologies are significantly distinguishable. On the other hand, improper treatment of these pathologies can lead to the development of refractory periodontitis as a more severe form of the two previous pathologies. This can occur as a result of non-compliance with the treatment protocol for aggressive periodontitis and chronic periodontitis by the dentist [11]-[19]. The purpose of this study is to analyze published data to identify any reports of changes in the level of fibrinogen in the blood, based on the depth of the probe or the difference in assessment using selected periodontal indices, before and after non-surgical periodontal treatment for patients with aggressive periodontitis, chronic periodontitis, and refractory periodontitis [3], [19]-[23]. Non-surgical periodontal therapy involves a treatment protocol that includes treatment phases spaced 7 days apart. This is intended to allow for physiological atrophy of the gingival tissue after treatment, without the need for systemic antibiotics. This treatment protocol is based on the idea that the removal of plaque and tartar also removes the living oral flora that is fixed on tooth surfaces, which can be a source of temporary bacteremia. This can potentially lead to the development or aggravation of arteriosclerosis, which in turn can lead to thrombosis [1]-[3].

III. Discussions

The vulnerability of patients to chronic, aggressive, and refractory periodontitis tends to increase after the age of 40 years, with reports showing that 62% of cases occur in patients over the age of 40 years, and 39% occur in those under-40 years. These data are consistent with the idea that a slow-progressing inflammatory disease such as periodontitis tends to manifest during stages of declining immunity and systemic pathologies that are often associated with pre-geriatric and geriatric ages, during which systemic pathologies are identified and treated. Operative dentistry provides additional evidence that supports the fact that carious lesions in the oral cavity have a higher incidence up to the age of 40. The highest percentage of caries occurs in younger age groups and declines significantly at around age of 40. This decline coincides with an increase in the incidence of periodontal pathologies, which further increase in percentage with the age of the individual. In addition to periodontal pathologies, other systemic pathologies are identified and treated in the geriatric age [5], [24]-[29]. If we divide patients by gender, it can be seen that males are affected by about 65% of cases of aggressive periodontitis, chronic periodontitis, and refractory periodontitis, compared to females who have a vulnerability of 35% to these oral pathologies. Among men, there is a prevalence of about 33% for chronic periodontitis compared to 24% for refractory periodontitis, while among women, the combination is 15% for refractory periodontitis and 11% for aggressive periodontitis. These data provide more information on the occurrence of oral pathologies based on gender. It provides evidence that sexual hormonal fluctuations in women can induce periodic changes in existing periodontitis in the oral cavity, transitioning from the passive phase to the active phase due to the periodic decline in hormone levels [25]-[30]. In the clinical picture of chronic, aggressive, and refractory periodontitis, a significant reduction in the tissue mass of the interdental papilla is observed, which is due to the pathologies' effects on individual patient oral hygiene. The interdental papilla may appear pink, but the inner surface may have visible ulcers that can bleed spontaneously and form wall pockets deeper than 3 mm. The PMA evaluation index (papilla, marginal, attached gingiva) and probing evaluations performed on the patient samples indicate that up to 50% of patients have an inactive phase for all three types of periodontitis, and a totally active phase according to both indices is observed in 20% of patients. Thus, in cross-sectional values, the active presentation of periodontal disease in ad-hock samples of patients reaches up to 20%. This value is supported by the literature. The transition from the passive phase to the active phase of the disease is observed in approximately 30% of the study population [3], [7], [11], [25]-[30]. Fibrinogen is a coagulation factor with a normal blood concentration of 1.5-4 g/L. It plays a key role in primary and secondary hemostasis [6]. If we consider the values of fibrinogen before and after non-surgical periodontal treatment, it can be observed that about 40% of healthy patients who are in the passive stages of periodontal disease experience a reduction in fibrinogen values in the range of 10-30 mg/dL. Only 10% of these patients belong to the range of 0-10 mg/dL. For patients in the active phase of the disease, about 30% of patients show a reduction in fibrinogen values in the range of 10-30 mg/dL and 20% of them in the range of 0-10 mg/dL [11], [15], [16]. This is a good clinical data on the importance of routine maintenance and control for periodontitis, as it is expressed in large values of fibrinogen reduction in blood circulation. As well, there should also be an intermediate phase between the treatment and maintenance therapy phases. This phase can serve as a period of stabilization during which patients are recommended to adopt lifestyle changes to reduce other risk factors for arteriosclerosis, such as alcohol consumption and cholesterol levels, etc. Regardless of age, reduction of fibrinogen with an interval of 10-20 mg/dL only for chronic periodontitis is achieved in about 20% of patients. This is the interval with the highest percentage results for fibrinogen reduction, divided into 50% for those under 40 years of age and 50% for those over 40 years. So, it is understood that the age effect no longer has an impact on the ability to reduce overproduction rash or reduce fibrinogen in the blood [3], [13], [23], [27]-[29]. Divided by gender, this value is again 50% female and 50% male in 20% of patients with fibrinogen reduction in the range 10-20 mg/dL. These data also support the fact that gender does not affect the occurrence of arteriosclerosis or the transition of periodontitis from the active phase to the passive phase, or vice versa [2],

[23]-[29].

Noires et al. in 2022 [31] published an article about apical periodontitis and cardiovascular diseases in adults. The article was of the review type, highlighting the potential relationship between the existence of oral diseases and cardiac diseases, but questioning the existence of sufficient data in the published literature regarding this relationship between pathologies. The studies included in this publication were divided depending on their type as case-report, cohort, or cross-sectional, and depending on the type of study, the relationship between the two pathologies was analyzed. Cross-sectional studies showed a strong connection between the two pathologies, leaving as a conclusion the need for longitudinal studies on this type of connection. Jimenez et al. published the article regarding the risk of cardiovascular diseases versus infection with *Porphyromonas gingivalis* species causing apical periodontitis [32]. In this article, it is emphasized that these pathologies are related as a result of the appearance of temporary bacteremia in the blood and the impact on the reactive protein. The study is cross-sectional with a control group in patients, *in vivo*. Not only clinical parameters but also cardiovascular risk factors were recorded. Serum concentrations of antibodies against *P. gingivalis* were evaluated. This study supports the correlation between the existence of the oral pathology of apical periodontitis with the causes of *P. gingivalis* and the risk of cardiovascular pathologies [32]. Jakovjevic et al. published the article regarding the review type study on the relationship between the pathology of apical periodontitis and cardiovascular diseases [33]. It is emphasized that the studies in this field are shallow and not conclusive regarding these pathologies. The number of patients included after the detailed observation of the selected articles showed that other studies, especially of the longitudinal type, are needed to really understand the relationship between apical periodontitis and cardiovascular pathologies. Under these conditions in this published study, a weak association between apical periodontitis and cardiovascular disorders was observed [33].

Chauhan et al. published an article about the relationship between apical periodontitis and cardiovascular diseases by non-invasive evaluation between epithelial function and subclinical arteriosclerosis [34]. This study emphasizes that the articles published so far, regarding this connection of pathologies are few and very controversial in the results presented, the markers used are very expensive, making them very difficult to apply clinically. The control was performed between the vasodilatation of the blood vessels influenced by the blood flow and the measurement of the thickness of the carotid intima-media. In this study, it was observed that patients with apical periodontitis had impaired cardiac parameters compared to the control group. This study supports the potential link between the two pathologies [34]. Gomes et al. published an article about the relationship between apical periodontitis and cardiovascular disease in a longitudinal study [35]. Studies of "*in vivo*" type that include the assessments of patients not only for endodontic pathologies but also for periodontal pathologies, point out that it is the same type of pathogenic bacteria but positioned in different areas of the tooth. An exciting relationship between the pathologies was observed, but the study shows that it is also related to the patient's age. As a conclusion, it is emphasized that prospective studies are needed for further analysis of pathologies [35].

Garrido et al. published the article regarding systemic inflammatory burden and cardiovascular risk in young adults with apical endodontic lesions. Correlation would be assessed with the level of C-reactive protein [36]. Cross-sectional study performed *in vivo,* in individuals with a diagnosis defined as non-symptomatic apical periodontitis aged between 18 and 40 years. This study showed high values of C-reactive protein, IL-6 and metalloproteinase 8 and soluble selectin E in patients with apical periodontitis. This study confirmed the relationship between cardiovascular risk and oral pathology [36]. Bergand et al. published an article regarding the variation of markers of endothelial dysfunction in adults with chronic apical periodontitis before and after endodontic treatment [37]. The study was of the "*in vivo*" type with values recorded from the patients included in the study. This study supports the relationship between apical periodontitis and cardiovascular disease and tends to further confirm it by recording improved clinical outcomes after endodontic treatment compared to outcomes before endodontic treatment of apical periodontitis [37]. Evaluation of patients was performed after 2 months of endodontic treatment and after 12 months of endodontic treatment. Endodontic pathology significantly increases markers of inflammation in the blood, for example IL-1, E-selectin, etc. and these markers are reduced after endodontic treatment. The study shows the relationship between apical periodontitis and the risk of cardiovascular disease, which is also supported in cases where endodontic treatment significantly improves this relationship [37]. These articles once again bring to attention the important role of temporary bacteremia caused by various dental interventions, against the manifestation of the possibility of aggravation of existing arteriosclerosis in patients, but also of the possibility of causing or manifesting it as a pathology that does not have pre-existing in the dental patient.

IV. Conclusions

Close coordination and cooperation between the dentist and the patient are necessary to maintain passive periodontitis and prevent its transition to active stages through non-surgical periodontal treatment. This joint effort can reduce the potential for oral bacteria to enter the bloodstream and prevent the appearance of proinflammatory monocytes, which can cause a marked increase in the level of fibrinogen in the blood, leading to arteriosclerosis or worsening of existing pathology.

Declarations

Ethics Approval and Consent to Participate

Not Applicable.

Consent for Publication

Not Applicable.

Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author.

Competing Interests

The authors declare that they have no competing interests.

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Author Contributions

IR collected the scientific data and wrote the manuscript. SH and NA revised and edited the manuscript. Literature research was conducted by IR and NA. SH and VO collected the scientific data. All authors read and approved the final manuscript. This article follows the study of the same group of authors, already published in 2020 based on the number of subsequent references [16]. All authors ensure that all data and materials, as well as software application or personal code, support their published claims and conform to field standards.

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