

An Association Between Periodontal Disease and Ischemic Stroke with Specific Dental Therapy: An Integrated Review

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Abstract: Numerous researches have mentioned the interaction between periodontal disease (PD) and ischemic stroke. However, whether treatment of PD reduces ischemic stroke remains controversial. In this study, we review how periodontitis is a risk factor for stroke among the identified inflammatory mechanisms and how different types of specific periodontal treatments reduce the hazard of ischemic stroke. Based on the concept of inflammatory mechanisms between two diseases, whether all types of dental treatment can be effective to interrupt ischemic stroke development or instead lead to an irritating effect. The possibility of preventing recurrent stroke by treating PD is present in the discussion.

Keywords: Periodontal Disease; Ischemic Stroke; Inflammation; Dental Therapy

1. Introduction

This article aims to review the relationship between periodontal disease (PD) and ischemic stroke and examine the impact of specific dental therapy, both prophylactic and periodontal, on the occurrence of stroke. Stroke has become one of the top-ranked diseases leading cause of death worldwide. Around 20% of strokes are haemorrhagic, whereas the other 80% cause localized cerebral ischemia^[1]. PD is a common, complex, and chronic inflammatory illness affecting a large population. Signs and symptoms of PD encompass gum infection, bleeding problems, and resorption to the unstable attachment between the tooth and its surrounding alveolar bone. These two diseases link through inflammatory mechanisms, with dental plaque and oxidative stress playing an important role. However, there is still insufficient evidence that dental treatment provides adequate protection against subsequent ischemic stroke. Clarifying and exploring different dental or combination treatments to reduce the incidence and recurrence of ischemic stroke is essential.

2. Periodontal disease is a factor in raising stroke incidence

Last decade, it has been widely adopted the correlation between ischemic stroke and PD in the field of medicine^[2]. A combination of two prospective studies indicated PD was associated with a nearly 3-fold increased risk of stroke^[3]. In recent meta-analysis, it investigated the interaction between PD and the incidence of various strokes separately. PD showed an association with a 1.6-fold increased risk of stroke with focal cerebral ischaemia^[2]. Ischemic stroke refers to situations in which an obstruction prevents perfusion in the blood vessel in the regional brain, with four categories. The occurrence rate of cardioembolic, atherothrombotic and lacunar stroke especially had a strong connection with PD^[4].

Dental plaques as a type of bacterial biofilm having attachments to the teeth induce inflammatory mechanism. Periodontal tissue inflammation not only leads to the destruction of periodontium and alveolar bone but also causes dysfunction of the endothelium of the arterial wall by body circulation. The dominating pathogens in the periodontal pockets are *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, which exist in atherosclerotic plaques as well^[5]. In addition, elevated serum antibody titers to *Prevotella intermedia* and *Fusobacterium nucleatum* are related to people with

atherothrombotic stroke^[6] and lead to adverse consequences after stroke. It is crucial to minimize the number of pathogens and control the accumulation of dental plaque in the oral environment.

3. Role of inflammation between two diseases

Several studies concluded that diabetes mellitus, cardiovascular, cerebrovascular diseases and some systemic diseases linked to PD by chronic inflammation. Pathogenic bacteria and metabolites in periodontal pockets enter the bloodstream temporarily or repeatedly, causing or exacerbating systemic inflammation, and increasing atherosclerotic plaque. *Porphyromonas gingivalis* induce platelet aggregation and adheres to endothelial cells^[5]. Oxidative stress has great dominance in the development of dysfunctional endothelium and atherosclerosis (Fig 1.). It also reduces total serum antioxidant concentrations and salivary antioxidant capacity^[7].

In periodontal injuries, stimulated by periodontal pathogens, neutrophils and other phagocytes along with other periodontal cells enhance the production of reactive oxygen species (ROS). Altered redox signalling due to increased bioavailability of ROS stimulate the form of atherosclerosis, hypertension and even the progression of related diseases. Oxidative stress due to its induction of inflammation further enhance the production of ROS^[8].

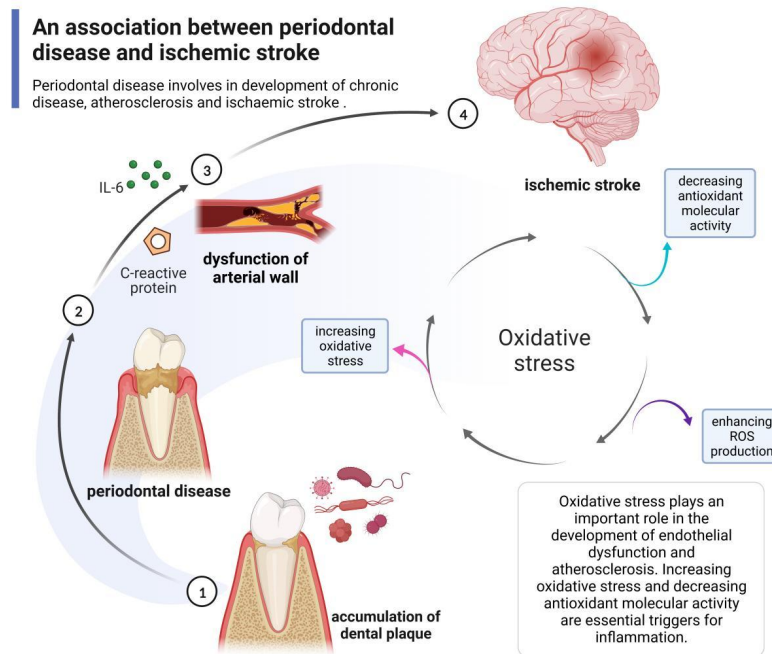


Figure 1. Inflammation between periodontal disease and ischemic stroke^[7] [Created with BioRender.com]

4. Specific dental therapy comparison

Based on the pathogenesis, periodontal therapy is available for reducing ischemic stroke events and controlling the spread of inflammation. The previous studies showed that there was an opposite impact on the risk of ischemic stroke from treatment options for different levels. The association between stroke and periodontitis is clear, but the relationship with gingivitis is controversial^[3].

For preventive treatment such as dental scaling, a retrospective cohort study conducted by Lin et al. concluded that gingivitis (Hazard ratio (HR) = 0.76; 95%CI = 0.66–0.86) and periodontitis groups (HR = 0.79; 95%CI = 0.66–0.92) show a significant reduction of the risk of stroke^[9]. In the other cohort study conducted by Lee et al., people with PD receiving dental prophylaxis had the lowest stroke incidence rate (0.14%/year)^[10]. These studies revealed the effectiveness of the

prophylactic treatment is expectable. Assuming the possible reasons, one is preventive treatment lowers the amount of dental plaque and avoids the over-accumulation of biofilm; another is patients who receive dental prophylaxis are often in gingivitis or mild periodontitis.

Intensive treatment is the main surgery to cure the periodontal disease, alleviate the periodontal inflammation and minimize the stimulus of infection. Both gingivitis (HR = 0.73; 95% CI = 0.56–0.95) and periodontitis groups (HR= 0.77; 95% CI = 0.66–0.89) with intensive treatment had a considerably lower risk of stroke^[9]. The incidence of stroke (0.39%/year) in patients receiving intensive treatment or tooth extraction was higher than in receiving dental prophylaxis^[10]. It seemed that these two studies showed the contrary. The previous one emphasized the significance associated with a lower risk of stroke for both periodontitis and gingivitis groups; the latter one used different measurement metrics focusing on a higher possibility of stroke incidents for patients with intensive treatment or tooth extraction when compared to preventive treatment. Thus, this contrast is explicable since people who have intensive treatment is meaning in the more severe stage of PD. Poor oral conditions raise the risk of ischemic stroke and tooth extraction refers to the final resort in treating the most serious conditions.

Moreover, the study found that the dental prophylaxis and intensive treatment groups had a significantly lower HR for stroke than the group without PD after adjusting for age, sex, and comorbidities in a Cox regression analysis. Combination therapy resulted in a better reduction in stroke events than a single treatment. Dental prophylaxis has as much impact on oral health and reduces the incidence of stroke as an intensive treatment when it does not go as far as irreversible periodontitis^[9].

5. Discussion and future direction

Although the effectiveness of dental therapy being a preventive strategy for stroke has not reached an agreement in the field, the association that could lead to serious consequences is worth exploring. The result of the chronic inflammation may induce vascular dysfunctional endothelium, and promote inflammation in existing atherosclerotic lesions, even stimulating subsequent disease development. To decline the serum of systemic pro-inflammatory mediators, the frequency of tooth brushing is the daily method to improve.

One limitation of this review is that PD and ischemic stroke can separate into more detailed subtypes or levels of disease progression. To evaluate precisely, a classic cohort study applied 7 distinct periodontal contour classes to reflect population disease patterns at the subject and tooth level^[1]. It clarified the association between ischemic stroke subtypes and PD more thoroughly with precise classification. Another limitation consists of potential risks of misdiagnosis of periodontitis and stroke, bias from different oral assessment measures, the influence of other risk factors, patients' lifestyles and so on. The influence of age, sex, comorbidity or smoking habits also needs to consider.

For now, it is time to research the efficacy of dental treatment as an intervention way in the direction of disease progression in clinical trials. An ongoing clinical trial (ClinicalTrials.gov Identifier: NCT04956211), investigates the link between periodontitis and recurrent vascular events in ischemic stroke survivors. They utilize non-pharmacological anti-inflammatory treatment to see if reducing local and systemic inflammation and enhancing vascular endothelium function reduces the risk of ischemic stroke recurrence in patients.

6. Conclusion

Specific dental care is an intervention for PD and ischemic stroke inflammation. People can prevent it in the early stages, maintain good oral hygiene, and appoint prophylaxis regularly. For people with periodontitis, specific treatments to control the inflammation and reduce the hazard of spreading the infection are necessary.

References

- [1] Sen S, Giamberardino LD, Moss K, Morelli T, Rosamond WD, Gottesman RF, et al. Periodontal Disease, Regular Dental Care Use, and Incident Ischemic Stroke. *Stroke*. 2018;49(2):355–62.
- [2] Lafon A, Pereira B, Dufour T, Rigouby V, Giroud M, Béjot Y, et al. Periodontal disease and stroke: a meta-analysis of cohort studies. *Eur J Neurol*. 2014;21:1155–61.
- [3] Hashemipour MA, Afshar AJ, Borna R, Seddighi B, Motamedi A. Gingivitis and periodontitis as a risk factor for stroke: A case-control study in the Iranian population. *Dent Res J*. 2013;10(5):613–9.
- [4] Leira Y, Rodríguez-Yáñez M, Arias S, et al. Periodontitis is associated with systemic inflammation and vascular endothelial dysfunction in patients with lacunar infarct. *J Periodontol*. 2019;90:465–74.
- [5] Aarabi, G.; Heydecke, G.; Seedorf, U. Roles of Oral Infections in the Pathomechanism of Atherosclerosis. *Int. J. Mol. Sci*. 2018;19:1978.
- [6] Hosomi N, Aoki S, Matsuo K, Deguchi K, Masugata H, Murao K, et al. Association of serum anti-periodontal pathogen antibody with ischemic stroke. *Cerebrovasc Dis*. 2012;34(5–6):385–92.
- [7] Stănescu I, Bulboacă AE, Micu IC, Bolboacă SD, Feștilă DG, Bulboacă AC, et al. Gender differences in the levels of periodontal destruction, behavioral risk factors and systemic oxidative stress in ischemic stroke patients: A cohort pilot study. *J Clin Med*. 2020;9(6):1–18.
- [8] Gözl, L.; Memmert, S.; Rath-Deschner, B.; Jager, A.; Appel, T.; Baumgarten, G.; Götz, W.; Frede, S. LPS from *P. gingivalis* and Hypoxia Increases Oxidative Stress in Periodontal Ligament Fibroblasts and Contributes to Periodontitis. *Mediat. Inflamm*. 2014;2014:1–13.
- [9] Lin HW, Chen CM, Yeh YC, Chen YY, Guo RY, Lin YP, et al. Dental treatment procedures for periodontal disease and the subsequent risk of ischaemic stroke: A retrospective population-based cohort study. *J Clin Periodontol*. 2019;46(6):642–9.
- [10] Lee YL, Hu HY, Huang N, Hwang DK, Chou P, Chu D. Dental prophylaxis and periodontal treatment are protective factors to ischemic stroke. *Stroke*. 2013;44(4):1026–30.