Reviewer's report

Title: Periodontitis and COPD - Epidemiological or Causal Association

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Reviewer: Nikos Siafakas

Reviewer's report:

This is an extensive review trying to answer the question if Periodontitis and COPD had an epidemiological or causal association.

Although the evidences that had presented by the authors are in favor of epidemiological association, they support the causal one.

Their theoretical hypothesis that both diseases are due to neutrophilic dysfunction is very weak.

Neutrophils although important cells in the pathogenesis of COPD they are not the only source of oxidative stress in COPD. The main source of oxidants is smoking that causes DNA damage without the “presence” of neutrophils. [DNA damage due to oxidative stress in COPD (Neofytou E. et al: Int J mol Sci 2012;13(12):16853), Oxidative DNA damage and somatic mutations … Tzortzaki E et al: Chest 2012;141(5):1243]. The hypothesis of the authors may be more relevant in the phenotype of COPD of Chronic Bronchitis in association with periodontitis since both represent the “inflammatory”/infectious spectrum of diseases!

This must be clarified in the text, as well as, a brief discussion of the other pathways of the pathophysiology of COPD such as the role of CD8+ cells, of macrophages, of dentritics, and b-cells must be included in the introduction before focusing on the Neutrophils.

In addition the “autoimmune” [New insights into immunology of COPD Brussel GG:Lancet 2011(10);378:1015] part of the disease should also has to be mentioned and discussed.

Thus, the authors should respond to:

1. Neutrophils are not the only players in COPD and not the only source of oxidants.
2. Do imply that periodontitis cause COPD or visa versa, or both have same causative mechanism(s). This must be clear in the text.
3. Since smoking causes COPD and is a significant risk factor for periodontitis why only a fraction of COPD patients showed periodontitis?
4. Although stated, the treatment effect is very weak!! Are there any evidences if treating COPD (antibiotics) could affect periodontitis?

Finally, the text is too long and should be shortening. Figure 1 should be modified to include the other sources of oxidants. Figure 4 should be omitted does not add
relevant information.

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.