**Reviewer's report**

**Title:** Early wound healing outcomes after regenerative periodontal surgery with Enamel Matrix Derivatives or Guided Tissue Regeneration: A Systematic Review

**Version:** 0  **Date:** 13 Feb 2019

**Reviewer:** Gaia Pellegrini

**Reviewer's report:**

Revision of the manuscript entitled "Early wound healing outcomes after regenerative periodontal surgery with Enamel Matrix Derivatives or Guided Tissue Regeneration: A Systematic Review".

In this systematic review, the early wound healing outcomes after two periodontal regenerative procedures have been assessed. In particular guided tissue regeneration (GTR) and application of enamel matrix derivatives (EMD) have been considered.

The topic of this review is very interesting. Clinical trials usually assess medium and long-term outcomes of the surgical procedures, however the critical biological as well as clinical aspects that occurs during the first few weeks after surgery and that guide healing towards a regenerative rather than a reparative pattern are poorly investigated.

The major issue of the manuscript regards the heterogeneity of the GTR treatments included in the study. Authors included regenerative procedures performed with both resorbable and unresorbable membranes, with the graft of bone substitutes or with the membrane alone (without graft), and even membrane+EMD. Thus it is not clear, what is the factor that the authors think can affect the early wound healing (the membrane, the graft,…?). No data are reported about healing outcomes associated to the use of grafting materials (presence/absence, composition…).

Furthermore, in one study (60), EMD is associated to the membrane. It is not clear if data of sites treated with this combination of biomaterials have been assigned to the EMD or to the GTR group.

Conclusion. Since comparative analysis has not been performed between groups, it is not possible to state "there might be a potential beneficial effect of the EMD on the early wound healing outcomes after surgical treatment of periodontal intrabony defects." Results do not support this conclusion.
Minor issues

Table 4: It has been reported "bioresorbable membrane (BM) and collagen membrane (CM)". collagen membranes are resorbable. What is the difference between CM and BM?.

Page 13, line 279. "…angular intrabony defects in the interproximal area ≥4 mm were selected…". Please clarify the concept. Do the authors means ≥4 mm of intrabony component?

Page 18 Defect morphology: please, describe this data separately for GTR and EMD groups.

Page 20, line 436: Please, remove ":." after findings and add the punctuation mark.

Page 20: It is not clear why the frequency of membrane exposure (28%) in GTR group is higher than the frequency of dehiscences (12%). In fact in discussion it has been reported: "if a membrane exposure is present, it means that a dehiscence of the flap has also occurred" . It should be highlighted that percentage of dehiscence and membrane exposure have been computed from data of different manuscripts, and this data should be commented.

Page 21- line 451-452. "minimal amount (3.1%) in the EMD treated sites whereas flap dehiscence/ membrane exposure was observed in the 22% of GTR…". These data (3.1% and 22%) are not reported in the results. Please, report them.

Page 21, line 472: "during the first first post-surgical…"

Page 22, line 490: please, add "of the" after (5/39).

Page 24, line 530: "with antibiotic administration In fact…." Please, add the punctuation mark after "administration".

Page 24, line 542: "especially considered: First, the already mentioned...". Please change First, with first.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

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