Reviewer's report

Title: Chitosan in viscosupplementation: in vivo effect on rabbit subchondral bone

Version: 0 Date: 22 Mar 2017

Reviewer: Stephan Zeiter

Reviewer's report:

In this review the authors investigate the effect of viscosupplementation with hyaluronic acid (HA) alone or combined with chitosan on the subchondral bone in a rabbit OA model.

The manuscript is well written and enough details for replication are provided or referenced. The findings are interesting and of relevance. However, in order to get published two major points and some minor points need to be addressed.

The major limitation of this work is that the untreated, negative control group is missing. In the reviewer`s opinion, this group where saline instead of HA is intraarticularly injected, is needed in order to attribute changes observed to the development of the disease or the effect of HA alone or combined with chitosan. Alternatively, historical data from previous publications could be used.

The contralateral leg provides information on the comparison

Further, the manuscript would be strengthened if histology would be included in the analysis. This could provide additional insight into the pathogenesis of the observed changes.

Minor points:

The reviewer would be interested to know why the authors did not do within animal comparison with the contralateral side - this would be statistically more powerful.

Age/ weight of the rabbits: please include the range of this parameters

The authors should consider to add data on the housing (single vs group housed etc) and feeding (see also comment below on obstipation).
Due to the short acting of buprenorphine it is suggested to repeat injection every 8 to 12 hours. Additionally the use of NSAID should be considered.

What was the rationale for the authors to use metoclopramide and Feligastryl? increased risk of obstipation due to opioid intake?

Since ROI were defined by the operator -was he/ she blinded for the assessment?

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.

No

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

Unable to assess

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.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable
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