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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 59216

Title: Effects of normobaric cyclic hypoxia exposure on mesenchymal stem-cell differentiation–pilot study on bone parameters in elderly

Reviewer's code: 02565385
Position: Peer Reviewer
Academic degree: CCST, FRCS (Ed), FRCS (Hon), MA, MBChB, MSc, PhD
Professional title: Lecturer, Surgeon
Reviewer's Country/Territory: United Kingdom
Author's Country/Territory: Spain

Manuscript submission date: 2020-09-03
Reviewer chosen by: AI Technique
Reviewer accepted review: 2020-09-03 22:08
Reviewer performed review: 2020-09-07 14:51
Review time: 3 Days and 16 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The study suggests that CH can improve bone health in the elderly. In the in vitro experiments, MSC were induced to differentiate in 3% hypoxia. Exposure to hypoxia inhibited MSC differentiation, but increased OPG/RANKL expression in the differentiated cells. In the human experiments, elderly subjects were treated with CH sessions. HC increased total bone mineral density, but not fat content. The authors conclude that HC may improve bone health in elderly, due to its inhibitory effect on bone resorption, by increasing the OPG/RANKL ratio. It is unclear what age patients the MSC used for the in vitro experiments were obtained from. Would it be worth exploring differences in MSCs from patients of different ages? I also find the link between the in vitro and human experiments somewhat tenuous. Why was the drop out rate so high? Are there other factors that could affect bone mineral density other than OPG/RANKL ratio?

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