

PEER-REVIEW REPORT

Name of journal: World Journal of Orthopedics

Manuscript NO: 49724

Title: Effect of clopidogrel in bone healing – experimental study in rabbits

Reviewer's code: 00505755

Reviewer's country: Japan

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-12 00:08

Reviewer performed review: 2019-06-12 01:14

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an important study about the effect of clopidogrel in bone healing. Figure 2 may be revised to indicate or explain the state of the radiographs in each score number. The title of the table 1 may be revised into Secondary histomorphometric parameters shown in mean \pm SD etc. Number of samples may be indicated.



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INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Orthopedics

Manuscript NO: 49724

Title: Effect of clopidogrel in bone healing. Experimental study in rabbits

Reviewer's code: 02728252

Reviewer's country: Egypt

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-11 09:33

Reviewer performed review: 2019-06-12 11:07

Review time: 1 Day and 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is a well written experimental animal study that were performed to evaluate the effect of clopidogrel in bone healing using a calvarial bone defect as a model. The rational of the study was reported in the introduction section and the hypothesis was clear. The study design is sound and the sample size and the statistical analyses were calculated



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with the using appropriate statistical tests. The result section should be extended especially the descriptive one and a scale bar should be calculated on the images. Images with high magnification should be added if possible and I wonder why the authors didn't use Micro-CT to obtain their quantitative data. Tables should follow the format of the journal style. The discussion section was informative and the references are properly cited.

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PEER-REVIEW REPORT

Name of journal: World Journal of Orthopedics

Manuscript NO: 49724

Title: Effect of clopidogrel in bone healing. Experimental study in rabbits

Reviewer's code: 02446061

Reviewer's country: Mexico

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-11 16:12

Reviewer performed review: 2019-06-13 00:43

Review time: 1 Day and 8 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is a simple study regarding the effect of clopidogrel in damaged bone. I suggest some changes before it can be considered to be published. - Please check the entire manuscript to avoid typing and grammar errors. Also spaces should be before to units. - The introduction should be clear about previous studies suggesting a beneficial role of

clopidogrel. You suggest this is a controversial topic, but all sentences suggest it act as a nocive agent. - Discussion is poor. You should analize other articles as the following: a) Jørgensen NR, Schwarz P, Iversen HK, Vestergaard P. P2Y12 Receptor Antagonist, Clopidogrel, Does Not Contribute to Risk of Osteoporotic Fractures in Stroke Patients. Front Pharmacol. 2017 Nov 14;8:821. b) Kim C, Kim T, Yoo J, Sheen DH, Lee SK, Choi EH, Chun TJ, Kang SW, Shim SC, Lim MK. Long-term Treatment with Anti-platelet Agents for Collagen-induced Arthritis Improves Radiological Findings. Osong Public Health Res Perspect. 2017 Jun;8(3):179-184. c) Mediero A, Wilder T, Reddy VS, Cheng Q, Tovar N, Coelho PG, Witek L, Whatling C, Cronstein BN. Ticagrelor regulates osteoblast and osteoclast function and promotes bone formation in vivo via an adenosine-dependent mechanism. FASEB J. 2016 Nov;30(11):3887-3900. d) Coimbra LS, Steffens JP, Alsadun S, Albiero ML, Rossa C Jr, Pignolo RJ, Spolidorio LC, Graves DT. Clopidogrel Enhances Mesenchymal Stem Cell Proliferation Following Periodontitis. J Dent Res. 2015 Dec;94(12):1691-7.

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BPG Search:

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[Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Orthopedics

Manuscript NO: 49724

Title: Effect of clopidogrel in bone healing. Experimental study in rabbits

Reviewer's code: 02544751

Reviewer's country: Slovakia

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-06-11 12:08

Reviewer performed review: 2019-06-20 08:52

Review time: 8 Days and 20 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Recension of manuscript No. 47325: „Effect of clopidogrel in bone healing. Experimental study in rabbits, written by Theodoros Lillis, Alexander Veis, Nikolaos Sakellaridis, Anastasios Tsirlis and Zoe Dailiana“, which will be published in World Journal of Orthopedics. The structure of the manuscript is in keeping with the

standard required criteria. The topic of the work is very actual, because previous studies on the effect of clopidogrel on bone metabolism indicated potential harmful effects, but their results remain controversial. Thus, clopidogrel treatment may also affect bone healing, but it has not been studied yet. Clopidogrel is an antithrombotic drug that inhibits platelet aggregation through inhibition of P2Y₁₂ purinergic receptor on their surface. P2Y₁₂ is also expressed in osteoblasts and osteoclasts, and previous studies raised concerns about clopidogrel's possible effect on bone metabolism. The authors describe the results on the effect of clopidogrel on bone healing using the rabbit calvarial defect model. Their results indicate that clopidogrel treatment not only does not negatively affect bone healing but instead promotes it. Work is legible, brings summarizes new knowledge. The results are documented in graphs that present the review of the obtained data. The citations are actual, and their format respects the usual standards. The conclusion reflects the author's results, and these can be accepted. I recommend the manuscript to be published. Kosice, 20. May 2019 MUDr. Jana Katuchova, PhD. Professor of Department of Surgery Medical Faculty at Safarik University and University Hospital Košice Slovakia

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[Y] No