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World Journal of Cardiology

ESPS Manuscript NO: 18612

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Dear Editor,

Hereby we would like to submit our revised review, entitled:

"Impairment of Aspirin Antiplatelet Effects by Non-Opioid Analgesic Medication" by

Amin Polzin, Thomas Hohlfeld, Malte Kelm, Tobias Zeus.

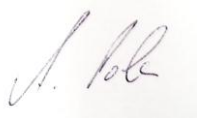
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The manuscript has been improved according to the suggestions of reviewers. Please find the point to point response to the comments of the reviewers below. Changes in the manuscript are clearly marked in blue (reviewer 01293596), yellow (reviewer 00258135) and green (Reviewer 00276417).

Thank you very much in advance for taking the time to consider our submission for publication.

Best regards,



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Point to point response to the comments of the reviewers:

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Reviewer 01293596:

Comment 1:

Thank you for an excellent review for impairment of analgesic medications for aspirin antiplatelet effects. I just recommend to add a table to summarize the benefits/risks of each analgesic medication.

Answer:

We completely agree with the reviewer, added a table summarizing the benefits and risks of the analgesics and thank the reviewer for the rating. (page 26)

Reviewer 00258135:

Comment 1:

The Review submitted deals with a very intriguing topic: the interactions between non-opioid analgesic medications and aspirin, especially in patients with cardiovascular diseases. A huge number of patients rely on analgesic drugs to control the pain but, at the same time, the side effects of aspirin and non-opioid analgesics are well established. The topic is well presented and the revision of the literature is extensive. The Review explores all the analgesic drugs available, suggesting the therapeutic options with the most favourable benefit/risk effect. Obviously, further investigations are required to identify the optimal antiplatelet/analgesic regimen in patients with increased risk of cardiovascular diseases.

Answer:

Thank you very much for this comment. We completely agree, that further investigations are crucial to identify the optimal antiplatelet regimen in patients on analgesic medication.

Comment 2:

I have only few comments: - Page 4 line 14 "ENREF 29" is not specified. - Page 5 line 9 "neither" is not necessary and can be removed. - Page 7 line 24 the reference "Rimon et al., PNAS 2010; 107: 28-33" is not included in the reference list. Please enclose the reference if necessary and correct the order of the list. - Page 9 line 2 "modelling"? - Page 9 line 1, the reference "54" can be removed, as it is inserted at line 2. - Page 10 line 10-11 and page 11 line 4, thromboxane can be abbreviated as TX. - Page 11 line 4, remove bracket.

Answer:

We corrected the manuscript accordingly, clearly marked changes in the manuscript yellow and thank the reviewer for this comments.

Reviewer 00259340:

Comment 1:

The authors present here a review on the effect of common analgesic meds on the antithrombotic properties of aspirin. The topic is interesting. In addition, the text is clear, well written and nicely documented. Thus, my opinion is favourable regarding its publication as is.

Answer:

We thank the reviewer very much for this rating.

Reviewer 00276417:

Comment 1:

I would like to congratulate Dr Polzin on the good review of the topic. The manuscript is written well.

Answer:

Thank you very much for this evaluation.

Comment 2:

I would suggest that the authors correct the following errors: In page 3, line 15: The authors state that HTPR is [This is called high on-aspirin platelet reactivity (HTPR)]. This is inaccurate. HTPR is high on treatment platelet reactivity. In page 4, lines 18-20 state: In the following, we will discuss the most commonly used NSAIDs are discussed with respect to their potential to interfere with platelet inhibition by low dose aspirin. They should have said: In the following, we will discuss the most commonly used NSAIDs with respect to their potential to interfere with platelet inhibition by low dose aspirin. In page 5, lines 25-26: it states: However, data of clinical studies are controversial. Do the authors mean: However, data of clinical studies are contradictory? The trials leading to opposing results, and thus one is uncertain about which one is correct. When one states a trial is controversial that means that there are two opposing views on the assessment of that trial (right or wrong). In page 6, line 2: it states: Naproxen inhibits aspirin antiplatelet effects in-vitro similar like ibuprofen. I would urge the authors to correct this into: Naproxen inhibits aspirin antiplatelet effects in-vitro similar to ibuprofen In page 9, line 8: it states (neither) at the end of a sentence. This should be (either). In page 11, line 4 states: detected in 50% of dipyrrone comedicated patients. 100) Residual platelet thromboxane It should be: detected in 50% of dipyrrone comedicated patients. 100 Residual platelet thromboxane In page 11, line 14 states: analgesics as well. Alternatively, aspirin would be a possible alternative to relief pain and It should be: analgesics as well. Alternatively, aspirin would be a possible alternative to relieve pain and

Answer:

We thank the reviewer very much for these corrections, implemented them in the manuscript and marked the changes in green.