Author’s response to reviews

Title: Risk of new acute myocardial infarction hospitalization associated with use of oral and parenteral non-steroidal anti-Inflammation drugs (NSAIDs): A case-crossover study of Taiwan’s National Health Insurance claims database and review of current evidence

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Author’s response to reviews:

To Editor-in-Chief, BMC Cardiovascular Disorder
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Dear Sir

On behalf of my co-authors, I am submitting the enclosed manuscript entitled “Risk of new acute myocardial infarction hospitalization associated with use of oral and parenteral non-steroidal anti-Inflammation drugs (NSAIDs): A case-crossover study of Taiwan’s National Health Insurance claims database and review of current evidence”, for consideration of publication in BMC Cardiovascular Disorder under the category of “Research”. Neither the submitted paper nor any part of its content has been published and is not currently under consideration by any other journal. All authors have read and approved the manuscript. In case of acceptance of the manuscript, materials described in the manuscript will be freely available to any scientist wishing to use them for non-commercial purposes.

In this population based study, we studied extended number of the most frequently prescribed NSAIDs, and found the risk of new hospitalization for acute myocardial infarction (AMI) was significantly associated with current use of some oral and parenteral NSAIDs in outpatient clinical settings. The risk was significantly elevated with the use of parenteral ketorolac especially, and also significantly associated with oral flurbiprofen, ibuprofen, sulindac and diclofenac.

Few of the previous studies have investigated these drugs. Furthermore, in most of the controlled trials studied these drugs, the numbers of AMI events observed were limited, even the meta-analyses of several trials did not provide sufficient event number, which make it difficult to draw a firm conclusion. Thus large scale
observational studies could provide useful additional information on this topic.

By using the case-crossover design, we managed to reduce the impact of the unmeasured confounding factors between different patients studied, which was a major challenge for observational studies using cohort or case-control designs. To compare the result of the present study, we organized a wide range of evidence, including observational studies as well as review of clinical trials. We found our study results were consistent with the majority of previous studies' results showing trend of increased risk of AMI with current use of some NSAIDs. We believe that the result of this manuscript will make it interesting to general readers of BMC Cardiovascular Disorder.

Thank you very much for your attention to our paper.

Sincerely yours,

Mei-Shu Lai

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