

August, 2014

Dear Editor,

Thank you for the opportunity to revise our submitted manuscript 'Gout: a clinical overview and its association with cardiovascular diseases' according to the comments of the reviewers. The comments of the reviewers were valuable, and have helped us to improve the manuscript. Please find enclosed the revised manuscript in Word format (file name: 12273-Review).

Title: Gout: a clinical overview and its association with cardiovascular diseases

Authors: Laura Kienhorst, Hein Janssens, Matthijs Janssen

Name of Journal: *World Journal of Rheumatology*

ESPS Manuscript No: 12273

The manuscript has been improved according to the suggestions of reviewers.

Reviewer 1:

This is a very nice review article about gout and its association with cv diseases. The article is based on a huge literature and is well-written. It will be of interest for all researchers and clinicians involved in this field.

Reviewer 2:

Kienhorst and colleagues submit a review of the relevant literature on gout, in particular its relation to cardiovascular disease. The paper is well written and extensively referenced. I have a couple of comments.

Page 10 In patients with chronic stable angina allopurinol reduced the time to chest pain and increased the total exercise time.(127, 128) The authors should review this. Reducing the time to chest pain is inconsistent with increasing exercise time. Likely it increased (delayed) the time to chest pain.

Our answer:

We agree with the reviewer that it should have been an increased time to chest pain instead of a reduced time to chest pain. We propose to change this at page 10.

New text:

*In patients with chronic stable angina allopurinol **increased** the time to chest pain and the total exercise time.(127, 128)*

Original text:

In patients with chronic stable angina allopurinol reduced the time to chest pain and increased the total exercise time.(127, 128)

The authors present a very practical paper but then never mention the cost of the various drugs is. A table with cost per dose should be inserted. In addition, in the US colchicine has been rebranded "Colcrys" which now is quite expensive as opposed to \$5 per month which is was when generic. This specific issue regarding colchicine's high cost should be specifically noted in the paper.

Our answer:

We agree with the reviewer that the cost of the various drugs to treat gout are important. However, the cost of the drugs differs between several countries. Therefore we did not mention specific numbers, but we discussed the cost in more general terms. It is a good suggestion of the reviewer to mention the high cost of colchicine after rebranding. Therefore, we propose to add a sentence to the manuscript at page 6.

New text:

*Because of the lack of trials, the choice which anti-inflammatory therapy is prescribed is mainly based on comorbidity and comedications. **In case of no restrictions by comorbidity and comedications, the cost of the therapy can be taken into account. In the United States the cost of colchicine have risen after the rebranding of this therapeutic.** IL-1b blockers such as canakinumab (67), anakinra (68-70), and rilonacept (71-75) are new therapeutic opportunities in patients with gouty arthritis, but their efficacy and safety should be further tested.*

Original text:

Because of the lack of trials, the choice which anti-inflammatory therapy is prescribed is mainly based on comorbidity and comedications. IL-1b blockers such as canakinumab (67), anakinra (68-70), and rilonacept (71-75) are new therapeutic opportunities in patients with gouty arthritis, but their efficacy and safety should be further tested.

References and typesetting were also corrected.

We hope you will consider our revised manuscript for publication in World Journal of Rheumatology.

On behalf of all authors,

Yours sincerely,

Laura Kienhorst