Author's response to reviews

Title: Effect of Tadalafil on blood flow, pain, and function in chronic cold Complex Regional Pain Syndrome: A randomized controlled trial

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Author’s response to the reviewer’s comments

Dear Sir,

We thank the reviewers for their comments regarding our manuscript. The comments of referee 1 have been implemented as follows:

1.2 Original comment Dr Schaller:
For a chronic disease like CRPS, an examination period of 12 weeks seems very low. The authors should at least indicate whether tadalafil medication was continued after the study period or not. Late results providing information about any possible tolerance to the substance or long-term side-effects would be appreciated by the reader.

Reviewer’s comment:
The examination period is low but effects are meaningful. The restrictions on use by the Netherlands needs to be mentioned and certainly could not be circumvented. One sentence to this effect would clarify this point in addition to the sentence added on page 5.

The next sentence has been changed on page 5, 3th alinea, to read: ‘Because, in the Netherlands, the use of Tadalafil has not yet been approved for CRPS, the study medication was stopped after the study period and the patients were seen by FJPMH to discuss further conventional treatment.’

1.4 Original comment Dr Schaller:
In addition to the tables showing start and end figures of the endpoints, it would increase the readability of the data if the authors would add some graphs showing time courses of the data. This would e.g. provide information if data changes are linear/nonlinear or if any plateau was reached at an early phase.

Reviewer’s comment:
I agree with Prof. Schaller’s remarks in regard to the time course of the data. I would add the patient comments as this clarifies the point.”

At the bottom of page 8 the next alinea has been added: ‘Since the outcome data were only assessed at the start and end of the study, we cannot provide information on the time course of these changes. We do know, however, from the remarks of the patients, that most changes in temperature and pain appeared to take place after 4 weeks, after the medication had been doubled from 10 to 20 mg daily.’

We thank the Editorial Board for the opportunity to revise our manuscript. I hope, that the improvements we have made to the manuscript as suggested by the reviewer have now made it acceptable for publication in the BMC Musculoskeletal Disorders.

With kind regards, on behalf of all authors,

George Groeneweg