Reviewer’s report

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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Reviewer: Hans Eberhard Schaller

Reviewer’s report:

The authors present an interesting study concerning the use of a vasodilating agent in the treatment of CRPS of the lower extremity. The study seems very organized and methodologically thorough. However, some points should be critically addressed:

- Regarding the data, significance levels are difficult to achieve with only 12 patients in each study group. We strongly encourage the authors to enclose a higher patient number in further research in this field

- 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.

- It is well known that intensive physiotherapy is crucial in CRPS treatment, so we doubt that one treatment session, which the patients of the study population receive, is effectual. We believe that efficiency of any pharmacotherapy could be strongly enhanced by this basic treatment

- 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.

Due to the new aspects of the submitted work and for stimulus for further studies in this field we recommend to accept the paper if the authors can adequately respond to the above-mentioned points.