Author’s response to reviews

Title: Tolerability of IM Penicillin G Benzathine Diluted or not with Local Anesthetics, or Different Gauge Needles for Syphilis Treatment: A Randomized Clinical Trial

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Thanks to reviewers for their constructive comments.

These are the answers to the reviewer 1 suggestions:

1. When calculating sample size, you expected a mean pain intensity of 7.6 in the 19G without anaesthetic and 8.6 in the 21G without anaesthetic but in reality you saw much lower levels of pain (5.56 and 5.06 respectively). Can you comment on this?

   The sample size was estimated using a pilot sample of 22 patients treated at Hospital Clínico, and four groups composed of 5 or 6 patients were used. There is no clear explanation for the differences found between this sample and the full study group, and we believe that they are only due to a random error since the same methods of pain measurement were used, the same researchers participated, and the patients were recruited from one the centers of the full study. However, even considering this error in the estimation of the sample size, our study has enough statistical power; the comparisons of the groups with and without anaesthesia (Anaesthesia/long19G vs No anaesthesia/long19G N) and (Anaesthesia/short21G vs No anaesthesia/short 21G) show a statistical power of 95% and 87%, respectively.
2. Do you have outcome data for these patients? i.e., did a similar number have serological cure / serofast / increase in titers. I ask simply because you mention previous studies in MDRTB that have found co-administration with anaesthetic did not impact effectiveness.

This relevant point was not an objective of the study. However, we have complete information on the serological evolution at 6 months of 79 patients (73.1%), and in all cases, a reduction in the RPR value compatible with adequate treatment response was observed. If the reviewer or the editor considers it, we can include this information in the results.

3. Figure 2 - could you consider also adding graphical representation comparing all participants with anaesthetic versus all without?

We have included a new figure (Fig 3) with the results of pain depending on the use or not of anesthesia.