Author’s response to reviews
Title: Manual therapy in the treatment of patients with hemophilia B and inhibitor. A case report

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Author’s response to reviews:
Commentaries ‘Editor:

I agree with the reviewer that the manuscript is good and worthy. However, there are some issues, which need to be revised to improve the quality of the manuscript. In addition to comments of both the reviewers, below are my comments:

1. First three paragraph in the background section required references to support the statements. We have added 6 references that support the text [1-6].

2. Please discuss the patient description in details. To clarify the description of the patient, we have included the following text: “The patient reports to have had moderate-severe pain for more than 3 years, requiring painkillers on a daily basis for 3 years. In the 6 months prior to the study he developed 6 hemarthrosis in the lower limbs (1 in the right knee, 1 in the left knee, and 4 in the left ankle). The patient is on the waiting list to undergo orthopedic surgery for total right knee replacement. In the months prior to the study, he underwent two radiosynovitis interventions (in his right elbow and left ankle joints). His clinical and functional situation is currently affecting his work performance, with a moderate amount of time away from work. The pharmacological treatment received is based on a prophylaxis regime (5 IU of Novoseven, every 48 hours). Figure 1 shows the lower limbs and their radiological image (Figure 1)”.

3. What other interventions were given in addition to manual therapy? No intervention was not performed during the treatment period. To avoid any doubt, we have added in the text the following paragraph: “In addition to the physiotherapy treatment using manual
therapy, no further intervention was performed. Moreover, the patient continued with his normal everyday activities throughout the treatment period”.

4. Explain the procedure in details for example assessment procedure. We have included the following text to explain the use of different measurement instruments: “Range of motion of dorsal and plantar ankle flexion and flexion and knee extension were measured using a universal goniometer. The anatomical references used were those identified by Querol [10], using the zero-reference method for the mobile arm of the goniometer, as described by Norkin et al. [11]. Pain perception was measured using the visual analog scale, VAS, with scores ranging from 0 to 10 points (from no pain, to the maximum pain imaginable). Joint condition was evaluated using the Hemophilia Joint Health Score [12]. This scale consists of 8 items per joint (plus Gait being analyzed globally), evaluating joint swelling, duration of swelling, muscle atrophy, strength, crepitus on motion, flexion and extension loss, and pain. The total scores of the updated version of HJHS range from 0 to 124 points (0-20 points for each of the six joints evaluated, plus 4 points for the overall assessment of gait). At baseline, patient was given a self-record of bleeding and a telephonic follow-up was carried out over the 48 hours following each treatment session. In this way, intervention safety was assessed, in terms of the occurrence of muscle and joint bleeding in the treatment area.”

5. Provide information about Hemophilia Joint Health Score. We have added the following paragraph to explain the HJHS features: “Joint condition was evaluated using the Hemophilia Joint Health Score [12]. This scale consists of 8 items per joint (plus Gait being analyzed globally), evaluating joint swelling, duration of swelling, muscle atrophy, strength, crepitus on motion, flexion and extension loss, and pain. The total scores of the updated version of HJHS range from 0 to 124 points (0-20 points for each of the six joints evaluated, plus 4 points for the overall assessment of gait)”.

Breanne Bovee, DC (Review 1):

Great article, I learned a lot and found it to be interesting with useful information for helping patients.
1. Adding what inhibitors are in the abstract would be helpful. We have added in the abstract: “(antibodies against FVIII/FIX concentrates)”.

2. There are no references until the 4th paragraph, it would be beneficial to include references sooner. We have added 6 references that support the text [1-6].

3. Include more details on the case presentation such as the patients original pain levels, chronicity of pain, impact the condition has on his quality of life. We have added the following text: “The patient reports to have had moderate-severe pain for more than 3 years, requiring painkillers on a daily basis for 3 years. In the 6 months prior to the study he developed 6 hemarthrosis in the lower limbs (1 in the right knee, 1 in the left knee, and 4 in the left ankle). The patient is on the waiting list to undergo orthopedic surgery for total right knee replacement. In the months prior to the study, he underwent two radiosynovitis interventions (in his right elbow and left ankle joints). His clinical and functional situation is currently affecting his work performance, with a moderate amount of time away from work. The pharmacological treatment received is based on a prophylaxis regime (5 IU of Novoseven, every 48 hours). Figure 1 shows the lower limbs and their radiological image (Figure 1).

4. Add rationale for treatment decisions and references, possibly include a picture of it or elaborate on the explanation of the treatment. We have added the following text, explaining the intervention more in detail: “The treatment involved 15 minutes of joint traction in ankles and another 15 minutes in knees (grade I–II). The distal tibia and fibula were fixation with straps and the proximal talus was held in place manually with the patient in supine position and the traction was carried out in the submaximal ranges of dorsal and plantar flexion to traction the ankle. For knee joint traction, we placed the patient in the prone position, performing traction (grade I-II) in submaximal flexion and knee extension, using a strap and manually securing the distal part of the femur. Traction was maintained for 15 seconds, with a 20-second interval between each joint traction [9]”

5. The goal of the article is to evaluate the safety of manual physiotherapy, include how you evaluated safety. We have added the text: “At baseline, patient was given a self-record of bleeding and a telephonic follow-up was carried out over the 48 hours following each treatment session. In this way, intervention safety was assessed, in terms of the occurrence of muscle and joint bleeding in the treatment area”.
6. Elaborate on line 46 page 6 or add it to the next paragraph.

Overall, great job.

Karen Barker, PhD, FCSP (Review 2):

1. Background… state what the prevalence of inhibitors is? We have added data for the prevalence of inhibitors: “The reported prevalence of inhibitors in unselected haemophilia populations is generally reported to be about 5–7% [2]”.

2. Useful to know bleed history (number and site) in the 6 months prior to intervention and 6 months after to see if any change. Hemos añadido los datos en el texto: “In the 6 months prior to the study he developed 6 hemorrhages in the lower limbs (1 in the right knee, 1 in the left knee, and 4 in the left ankle)”.

3. Why grade 1 and 2 for mobs? need a rationale for choice of technique and how many treatments offered? what therapeutic benefit was expected to occur with a grade I mobilisation - this section poorly referenced suggest refer to latest edition Grieve's Modern Musculoskeletal Therapy or similar When performing a grade I traction, we do not stress the joint capsule, because we work up to a grade II (until we reach the slack of the capsule). In grade III we would put the joint structures at maximum tension: for this reason, and in order to avoid irritating the synovial membrane, we work in the I-II range of knee and ankle traction [Kaltenborn FF, Evjenth O. Fisioterapia manual: extremidades. 10ª ed. S.A. McGraw-Hill/Interamericana de España. 2004; Cuesta-Barriuso R, Gómez-Conesa A, López-Pina JA. Effectiveness of two modalities of physiotherapy in the treatment of haemophilic arthropathy of the ankle: a randomized pilot study. Haemophilia. 2014;20:e71–e78].

4. More info about positioning and technique and why choose that technique…perhaps a picture? We have added figure 2 with an image and the following text to better explain the methodology of the intervention: “The treatment involved 15 minutes of joint traction in ankles and another 15 minutes in knees (grade I–II). The distal tibia and fibula were
fixation with straps and the proximal talus was held in place manually with the patient in supine position and the traction was carried out in the submaximal ranges of dorsal and plantar flexion to traction the ankle. For knee joint traction, we placed the patient in the prone position, performing traction (grade I-II) in submaximal flexion and knee extension, using a strap and manually securing the distal part of the femur. Traction was maintained for 15 seconds, with a 20-second interval between each joint traction [9].”

5. Justify time span for Intervention. The periodicity of previous studies of manual therapy using traction joint in patients with psoriasis hemophilia is two sessions per week. For this reason, we have employed in the present study the same periodicity. In addition, to have the patient inhibiting, a major exhibition to articulate to technologies of traction to articulate might provoke major stress articulate and with it, it increases the risk of bled in knees and ankles [Cuesta-Barriuso R, Gómez-Conesa A, López-Pina JA. Manual therapy in the treatment of ankle hemophilic arthropathy. A randomized pilot study. Physiother Theory Pract. 2014;30(8):534–9; Cuesta-Barriuso R, Gómez-Conesa A, López-Pina JA. Effectiveness of two modalities of physiotherapy in the treatment of haemophilic arthropathy of the ankle: a randomized pilot study. Haemophilia. 2014;20:e71–e78].

6. Not a clinical significant difference in pain response. We have not calculated the statistical correlation and t test because the sum of the weights of the cases is less than or equal to 1. Therefore, to obtain numerical results, we have calculated the percentage of improvement in each of the dependent variables.

7. HJHS score has many criteria to make up the score swelling, pain muscle strength ROM any of these could have changed from the tiny change of score, or even operator error in recording it. A difference of under 6 is generally consider what can happen due to chance. A score over 6 considered useful. The patient with hemophilia and inhibitor included in the study had a score of 9 to 11 points, knees and ankles. Taking into account the radiological image shown in Figure 1 and the situations of the HJHS, we can not speak of improvement due to chance. In fact, after the intervention, as indicated in Table 1, the score varied very little (range 0-2 points).

8. ROM the error of measurement will account for most of the changes. Percentage change is not a useful analysis. We have not calculated the statistical correlation and t test because the sum of the weights of the cases is less than or equal to 1. Therefore, to obtain numerical results, we have calculated the percentage of improvement in each of the
dependent variables. Although the calculation of the range of motion with goniometer can be subject to measurement errors, to both assessments be performed by the same physical therapist, with the same measurement protocol, we have minimized the possibility of error.

9. Also the base line and post treatment at 3 months, when did the minimal changes occur? After the first treatment?? Although the patient perceived improvement in pain and joint mobility from the first session, no measurements of the dependent variables were taken until the third month. The design of the study was pretest-posttest and therefore no measurements were made at the end of each session.

10. Not sure that the summing up that grade 1 and 2 mobs can help the severely arthritic joints as there was no proof from his results. When there is an important joint limitation, joint traction helps to improve mobility parameters related to the joint capsule only. Obviously, the difference of the prestest-posttest mobility in severe cases of hemophilic arthropathy will be less, the more deteriorated the joint is. Reference 10 indicates the efficacy of orthopedic manual therapy in the improvement of joint mobility of patients with ankle hemophilia without inhibitor.