Author's response to reviews

Title: A positioning pillow to improve lumbar puncture in paediatric haematology-oncology patients: A randomized controlled trial.

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Author's response to reviews: see over
Dear Melissa Norton, Editor-in-Chief

We are happy to submit to BMC Cancer our revised manuscript entitled:

"A positioning pillow to improve lumbar puncture in paediatric haematology-oncology patients: A randomized controlled trial".

1. An Authors’ contributions section is included before the Acknowledgements and Reference list.

2. The trial was registered with Clinical Trials.gov (number NCT00775112).

3. The paper was copyedited using ErrNet™ services.

4. The manuscript was checked and formatted according to BMC medicine journals - Authors' checklist for manuscript formatting

Reviewer: Lise Nigrovic

Major compulsory revisions.
The investigators should not report non-significant differences between groups as showing groups are being different in any way (for example see page 11 of discussion).

We clearly state in the new version that our results on the main outcome are inconclusive.

I would caution the investigators against making clinical recommendation base on their post-hoc sub-group analysis because of the risk of chance explaining the associations seen. This finding should instead be hypothesis generating for further study although there is a clinical sensibility to this finding (younger children are less likely to be able to use the pillow effectively or pillow as not sized for younger patients).

We amended this paragraph and added that this post hoc sub-group analysis needs confirmation by a new trial.

Were most LPs performed in the sitting position?

Were non pillow LPs required to be done in the sitting position. Please add LP position for first attempt to Table 1 (done). At my institution, most LPs are done in the lateral recumbent position not the sitting position. If, in the observation group, clinicians were allowed to select patient position (sitting or lateral recumbent), position is a potential confounder of LP success rates. This needs to be specifically addressed by the investigators.

All LPs were performed in sitting position, in both groups according to the usual practice in these clinical services. Details have been added page 5 and Table 1.

Minor compulsory revisions
The intervention could not be blinded for the patient or the person performing the procedure. This should be explored further in the limitations, with reference to the subjective secondary outcomes.

An explanation has been added page 8.

Small points
1. How was the pillow sterilized between uses or were they single use? This represents a potential limitation to this technology, even if demonstrated to be effective.

Sterilization was performed using surface disinfection after each use. This has been added page 5.
2. Please further discuss why a single size pillow was used for children age 2 years to 16 years. This issue could potentially explain the lack of benefit in the youngest patients (< 6 years of age).

**Four LP pillow sizes were available for the study (for 2-6 years, 6-10 years, 10-15 years and 15-18 years). ("Methods" Section page 5).**

**Reviewer:** Johann Hitzler

Major compulsory revisions

1. Some inconsistencies in the data need to be corrected or clarified.
   a. Three patients without analyzable CSF specimens were excluded from the analysis of the primary outcome. It is not clear whether they were randomized to the experimental and control group.

   **Two were in the group control and 1 in the pillow group. This has been specified page 7**

   b. Why are the cohort sizes and results of the analysis of children’s satisfaction in the age group >6 years different in table 2 and 3?

   **Corrections have been made.**

   c. The percentages calculated for primary outcomes and child satisfaction in both control and pillow group in table 3 are incorrect if calculated based on the data provided (e.g. successful LP, pillow group: 24/38 = 63% not 58.3%; 17/34=50% not 41.5% etc.)

   **Corrections have been made.**

   d. The overall success rate of lumbar puncture is described as 62%. Yet 19% required more than one attempt, 21% had a traumatic LP and in an additional 3% the LP goal was not achieved, accounting together for 43% without success (page 9, third paragraph).

   **Some LPs have more than one cause of failure. Numbers have been verified.**

   e. In table 1, 7 patients in the pillow group and 5 in the control group had no prior LP. Yet in both groups 7 patients are listed under diagnostic LP (presumably without prior lumbar punctures).

   **Diagnostic LPs can be performed for diagnosing relapses. It is therefore possible for children to have a diagnostic LP and several previous LPs.**

2. The tables describing outcomes mention the absence of differences between control and experimental group with regard to the patient’s pain, anxiety and satisfaction as well as the nursing team’s and physicians’ satisfaction. Why is the perception by parents (see page 10, second line before last) of a higher level of pain and anxiety in the experimental group omitted from table 2?

   **Perception of parents has been added to table 2 (available when parents were present).**

3. A pertinent comparison of LP success for this study are LPs performed under deep sedation. Some information and discussion is warranted to be able to decide how best to improve outcomes.

   **We did not find articles giving the rate of success in LP performed under deep sedation. Furthermore, because repeated deep sedation could cause side effects, a comparison of success rates in patients receiving conscious sedation or no sedation seems relevant. Deep sedation is not recommended in France when performing LPs (REF).**

Minor essential revisions

1. Why did the authors use a red cell concentration of 50/mm3 to define a traumatic lumbar puncture rather than the 10/mm3 used in large trials (e.g. Gajjar 2000, Burger 2003)?
This threshold was routinely used by the biologist in our hospital to determine CSP samples difficult to interpret.

2. How was post-LP syndrome defined for the purpose of the study?
Post LP syndrome has been defined according to clinical criteria as described by Spencer et al. The reference has been added in the text page 6
- Onset during the first 24 or 48 hours
- Headache with bifrontal, occipital, neck, or upper shoulders location
- Characterised by postural worsening in upright position, coughing, straining and which alleviates while lying down).
- Of mild intensity to prostrating
- With possible Associated symptoms: photophobia, nausea, loss of appetite, diplopia.

3. ‘LP duration’, ‘number of attempts’ and ‘number of attending persons’ in table 1, base line characteristics, appear to be outcomes and should be moved to table 2. Done.
P values are provided for LP duration but not for use of EMLA, N2O, number of attempts, number of attending persons and CSF amount collected.
Done

4. “Caregiver” is used ambiguously and sometimes seems to denote nursing staff and sometimes parents.
“Caregivers” is used for nursing staff. This has been checked in the article.

5. A reference should be given for the success rate of LPs performed without deep sedation (page 10, third paragraph, line 6).
Two references have been added: references 13 and 14, page 12.

6. The discussion states there was less bleeding in the experimental group. Was this defined as macroscopic or microscopic haemorrhage? No data are provided for this in the result section.
The components of “success” have been added in table 2.

7. The photo is very helpful. It appears to show a lumbar puncture. The misleading and unfortunate part is that the operator wears neither mask nor gloves in the picture.
The picture was replaced.

8. suggested edits: all done
- “cytological” for “biochemical” analysis (page 6, first paragraph, line 3);
- “that the LP pillow ...could not only increase ...but would decrease pain” in stead of “that the LP pillow ...could not only increase ...but would be less painful” (page 8 first paragraph of Discussion section;
- “traumatic” for “hemorrhagic” LP (page 8, third paragraph, of Discussion section;
- table 2 , second line, operating physician % satisfaction in control group “(84)” instead of “(8)”: table 2 was totally revised;
- clarify and correct “carer” (page 11, third paragraph, line 3): carer was replaced by care givers;
- table 2, remove “a” in “0.85 a “(fourth row); define or remove “nb” for number in tables: table 2 was totally revised;
- define or remove “*” in figure 1: * and ** were defined.

Discretionary revisions
1. The presence of a parent during the procedure was significantly less frequent in centre 2 than centre 1. Did the parent’s presence have an effect on technical success and anxiety level/self perception of pain of the patient? If so, were the effects in both areas concordant?

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Nigrovic et al\(^2\) reported that Family-Member presence doesn’t influence Lumbar puncture success rate. In our sample, this is also true in our sample. Family attendance does not influence the child’s anxiety, pain, satisfaction, nor the nursing staff’s satisfaction, nor the primary criterion.

2. It is interesting that the LP success rate dropped from 70% during the preceding two years to 56% in the study setting (control group). Is it possible that the study setting itself has a negative impact on LP success rates?

As the 70% success rate is usually found in literature data, we can imagine and discuss on the negative impact of that study.

The expected rate of success of 70% was based on literature data. The rate of haemorrhagic LPs (RBC > 10/mm\(^3\)) was 20% in the preceding year, in centre 1, a centre for paediatric oncology. Rates of success reported in the literature were evaluated mostly in emergency rooms (Nigrovic et al, Ann Emerg. Med 2007, Pediatrics 2007), whereas most patients in this study were children with haematological disorders (centre 2). This might have influenced the overall rate of success, since these children are more likely to have a reduced platelet number. The platelet count is actually lower in centre 2 compared to centre 1: 305.08 (SD 166.7), vs

177.09 (SD 106.9), p=0.0011.

3. Information regarding the diagnoses among participating patients, the minimal required platelet count prior to LP, the consent rate and identification of participating centres would be useful.

These information were added in the text:

- Diagnoses among participating patients and identification of participating centres: page 7, Results section, lines 26-27. Individual diagnoses are not available, but the specialty of participating centres is informative to this respect.
- the minimal required platelet count prior to LP was 50,000/mm\(^3\) in each centre.

Reviewer: Jacqueline Ellis

The justification for the study needs to be better described. It is not clear why a pillow is needed and why sedation is not used in France. The standard for LP performance is conscious sedation with local analgesia. The authors need to make a case for why this is not done in France and why it is then useful to have some sort of restraining or comfort device to aid in the performance of the LP.

The justification for the study has been better described: recommendations for performing LPs in France and the need for a restraining or comfort device have been added to the text page 4, line 4. Anaesthesia or deep sedation is not recommended in France for lumbar punctures [1].

Since the outcome of the study was largely negative and there was no significant difference between the control and the intervention group it is not clear why you are trying to publish the results. Is this a pillow that is used widely in France but has never been tested? Is this something that the authors developed or have used in the past and found helpful. The basic premise for the study needs to be better developed in the introduction.

The pillow had been used before the study in centre 1, where it was found useful, but not in centre 2. We have added this information page 4, line 24-25. The study was performed to demonstrate the benefit of this device on the quality of the LP success rate, and favour the dissemination of the device. The device - a prototype- was left to the centre use after the study, and is still in use since then.

It is not clear what the ‘usual procedure’ is for the LP. The control group needs to better described with respect to how their LPs were performed? Were they sitting or lying down? Restrained in any way?

\(^2\) Lise E. Nigrovic, Alisa A. McQueen and Mark I. Neuman. Lumbar Puncture rate is not influenced by family-Member presence. Pediatrics 2007;120;e777-e782
The ‘usual procedure’ for the LP and how it was performed in the control group has been added page 5, lines 14-16.

Can you include a section on measures so that we know the psychometrics of the measures that you used and the justification for choosing those measures. What is the LeBaron score, Lansky score, why did you use a VAS instead of numerical or facial pain scale (for the 2-6 year olds)?

The Le Baron scale is a 8-item scale which is rated by an observer to evaluate the child’s anxiety based on the child’s behaviour. The Lansky\(^3\) score is a Performance Status - Rating scale for patient function, used in children (the Karnofsky score is used in adults). Details have been added page 6 line 12 and 19 respectively.

The discussion needs to be restructured

The discussion was structured according to the recommendations of the editors of biomedical journals: key findings, comparison with previous studies, strengths and weaknesses, implications for practice and research.

The title could be more specific as to what you are trying to improve with LP. The accuracy and comfort might be added to the title.

The title has been changed to ""A positioning pillow to improve lumbar puncture success rate in paediatric haematology-oncology patients: A randomized controlled trial"".

The writing needs some fine tuning and editing.

Editing was performed.

The picture is misleading as it looks like the person behind the patient is actually performing the LP. I am assuming that she was posed for the picture and not actually performing an LP. She has no mask, hat, gloves or gown and has hair falling in her eyes. You would not want your readers to think that this is how you do your LPs on cancer patients.

The picture was replaced.

\(^3\) http://www.fda.gov/cder/cancer/oncrefto.htm