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

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Short title: Pillow for lumbar puncture

Key words: supportive care, lumbar puncture, child, cancer, hood disease, randomized trial
Abstract (275 words, max 300)

Objectives

Lumbar punctures (LPs) are common in children with cancer. Although pain management during the lumbar puncture has been well standardized, dealing with stress and anxiety is not well addressed yet. Our objective was to evaluate the potential improvement of the LPs success rate using a positioning pillow, thus to ensure maximum lumbar flexion, and while allowing paravertebral muscles to relax, in children who are awake, with either conscious sedation or no sedation, or a conscious sedation.

Patients and Methods

Children aged 2-18 years undergoing LPs were randomly assigned to a positioning pillow or no intervention. The primary outcome was the rate of success, i.e. achieving the LPs achieving their objective (sampling or injection) at the first attempt, without bleeding (RBC < 50/mm³). The secondary outcomes included: the child's pain, assessed by a self-administered visual analogue scales (VAS) for children over 6 years of age; the parents' and caregivers' perception of the child’s pain; satisfaction of the children, the parents, the caregivers and the physician. The child’s cooperation and the occurrence of post-LP syndrome were also evaluated.

Results

124 children (62 in each group) were included. The LP pillows tended to increase the success rate of LPs (67% vs. 57%, p = 0.23), and decreased post-LP syndromes (15% vs. 24%, p = 0.17) but the differences were not statistically significant. In children over 6-year of age (n = 72), the rate of success was significantly higher in the pillow group (58.5% vs. 41.5 %, p = 0.031), with a tendency to feel less pain (median VAS 25 vs. 15 mm, p = 0.39) and being more satisfied (84.4 % vs. 75.0 %, p = 0.34).

Conclusions

Even if the overall results presented here are not as optimistic as we might have wished, we can confirm that there is do not demonstrate a benefit in using this pillow for lumbar
punctures... This study results also suggest a benefit. It is especially using a positioning pillow should help performing LPs when deep sedation or anaesthesia is not available. Using the pillow does not improve the rate of success of LPs. It might however be promising in the sub group of children over 6-year of age.
INTRODUCTION (321 words, max. 500 words)

Lumbar punctures (LP) are commonly performed for diagnosis or treatment purposes in children with cancer or haematological diseases. Anaesthesia or deep sedation is not recommended in France for lumbar punctures. In this situation, because of lack of anaesthesia, appropriate body posture, muscle relaxation, and quietness (or calmness?) of the child are important determinants of the success of the LP. When LPs are performed in a good position, pain is well controlled by local anaesthesia. A good positioning requires the presence of at least 3 attendees: one for maintaining to hold the child, one for performing the LP, and a third person to serve, or help the performer.

In a paediatric population, LP causes anxiety and stress [1], leading to a high rate of traumatic samples being traumatic or hemorrhagic samples. Repeated attempts to obtain a successful LP will, in turn, aggravate anxiety [2]. Evans et al. have shown that 70% of patients undergoing LP have post traumatic haemorrhage with a red blood cell counts (RBC) ranging from 1-5/mm$^3$ (27%) to more than 50/mm$^3$ (24%) [3]. Needle size, thrombocytopenia, repeated or recent LPs are among factors that affect its quality [2, 4, 5]. The rate of successful LPs in our hospital within the last 2-year reached 70%. Success was defined as a LP achieving its objective at the first attempt (sampling or injection) sampling and/or injection objective at first attempt, and a RBC ≤ 50/mm$^3$.

Although awareness of controlling pain during invasive procedures has increased, evidence based pain management remains insufficient. Non pharmacological, cognitive, and behaviour-based techniques such as hypnosis, comfortable environment and distractions are currently used to control pain [6-9].

To decrease discomfort and apprehension, and to improve the position of the patient during the LP (working LP position pas clair??? for caregivers ????? est ce le soignant ou l'enfant?), we have developed a positioning pillow. This pillow allows children to remain lax in an appropriate position throughout the LP procedure, and to be relaxed. We performed a randomized controlled study to estimate the success rate of LPs using the
LP pillow compared to with the usual procedure. Secondary outcomes were pain, anxiety, post-LP syndrome, and the satisfaction of the children, the parents and the caregivers. 

Patients and methods

Participants

Children aged 2 to 18 years undergoing an LP were eligible for inclusion. Children who had already participated or used the LP pillows, who had a medical condition (orthopaedic anomaly) contraindicating the use of the LP pillows or whose parents refused consent were excluded.

Participants undergoing LPs were randomly assigned to “LP pillow” or “no intervention”. A permuted-block algorithm was used for randomization, and with participants were stratified according to allocation centre. Concealed allocation was centralized by a phone call to the coordination centre after eligibility check and baseline data collection.

Intervention

The LP pillow was made of polyethylene microcellular foam, coated with rubber to facilitate decontamination. It was placed on the thighs of the child who was sitting with his trunk leaning forward. This position ensures a maximum lumbar flexion. The trunk can rest on the pillow allowing paravertebral muscles relaxation. The body axis and the spinal column are perfectly maintained symmetrical in the sagittal plane (see illustration). The pillow included side supports for the head; the face remained uncovered in order to allow the child to breathe, speak comfortably and to facilitate nitrous oxide administration. Aides hold patient's arms along the cervical column in a neutral position and an opening allows parents to touch their child's hands and forearms. To ensure an effective stabilization, splints positioned at the bottom side of the LP pillows immobilized the child’s thighs.
Two sets of pillows were available for the study (for 2-6 year, 6-10 year, 10-15 year and 15-18 year). For this study we made four sets of pillows for different age groups:

The study was performed with required experienced operators to perform LP, i.e., having performed more than 50 LPs before.

**Outcomes**

The primary outcome was the success or the failure of the LP. LP was rated successful when it achieved its purpose (sampling and/or treatment) at the first attempt, without visible haemorrhage or with RBC < 50/mm³ in the cerebrospinal fluid (CSF) sample (biochemical analysis). When one of these criteria was missing, LPs were rated as failure.

Secondary outcomes included: the child's pain, evaluated by self-administered visual analogical scales (VAS) for children over 6 years of age; the parents' and caregivers' perception of the child's pain; the satisfaction of the children, the parents, the caregivers and the physician who has performed the LP; the child cooperation of the child rated with the “LeBaron Scale” [10]; the incidence, the symptoms and the length duration of the post-LP syndrome assessed after 48 hours after the LP by a phone interview. To be able to estimate if the pillow seemed convenient or not, we also counted the number of attendees (parents and/or caregivers) in present and the length of the LP procedure. In order to estimate the convenience of LP pillow use, we measured the number of attendees (parents and/or caregivers), and the duration of LP procedure.

The data collection included the drugs used (anaesthetic, sedative and analgesic drugs); the needle size (19G, 20G, 22G); the general medical state of the child evaluated with Karnofsky or Lansky score [11] of the child general medical state of the child; the platelet count; the number of previous LP; the date of the LP and the satisfaction with the last LP (verbal scale); the practitioner’s experience in performing LP, the presence of the parents, the aim of the LP (diagnosis, therapeutic monitoring, treatment injection) and the amount of CSF removed (drops).
The study protocol was approved by the institutional review board of Lyon A - Hôtel-Dieu on the 8th June 2004, and was conducted in accordance with the Helsinki Declaration. All parents gave a written informed consent before their children participated in the study. Children were asked to give written consent when fully able to understand the proposed procedure. Data management and quality control were performed by CLININFO S.A. (France).

**Sample size and statistical analysis**

The protocol initially included a total of 80 children. The sample size calculation was based on a 70 % success rate in the control group and 95% in the LP pillow group, with 80%-power and 0.05 two-sided significance level. After inclusion of the 40th children and based on the success rate in the control group, the sample size and was re-estimated and increased to 124 children (62 per group). In order to achieve this sample size, inclusion period was extended from 12 to 24 months.

Analyses were performed according to the intention to treat principle. All patients were kept in their randomization group, regardless of subsequent protocol deviations. Depending on the nature of the variable, Wilcoxon rank or Fisher's exact tests were used to compare results between groups. A logistic regression model was fitted to the platelet count and the number of LPs prior to entering the study. An exploratory subgroup analysis was performed in children over 6 years of age. For the main outcome, comparisons with p-value <= 0.05 were considered significant. The STATA 9.2 software (SatatCorp 2005. Stata Statistical Software: Release 9.0 College Station, TX: Satat Corporation) was used to perform statistical analyses. Statistical analyses, sample size calculation and generation of the sequence of allocation were performed at the Lyon University Hospital Department of Biostatistics.

**RESULTS**

Between July 2004 and September 2006, 124 children, 62 in the pillow group and control group were included. 24 children were included in Centre 1, and 100 children in
Because of technical problems, cerebrospinal fluid samples could not be analyzed in three patients. One participant in the control group was given a pillow (protocol deviation).

Analysis of the baseline characteristics of participants (table 1) did not show major differences between randomized groups. Concomitant therapies to alleviate pain or stress were identical in both groups: 30 % received premedication with Hydroxyzine 1 mg/Kg, 98% received local anaesthesia with a lidocaïn / prilocaïn patch, and 94% received NO-N2O-02 therapy.

There was no statistically significant difference between groups for the primary or secondary outcomes (table 2). The rate of success, the patient’s pain, the satisfaction of the child, the parent’s and the caregivers, the LP duration and the number of attending persons did not differ between groups.

The overall rate of success was 62%; reasons for failure included i) need for more than one attempt to achieve the LP objective (19%), ii) LP objective or goal not reached (3%), and iii) CSF haemorrhage (21%, either microscopic or macroscopic).

Nine (7%) patients who were in received the pillow group had the pillow removed when difficulties occurred while performing the LP. These difficulties occurred mostly in very young patients, since eight of them were aged less than 6 years of age. Theses patients were all and eight occurred in centre 1. This centre had little experience of the pillow before the study, and recruited most patients (non seulement 24??).

Few children received premedication (33% in centre 1 and 28% in centre 2), 100% received local anaesthesia using an EMLA® patch in centre 1 and 98% in centre 2; 79% of children received nitrate monoxide nitrous oxide (ENTONOX®) est ce bien ce que tu veux dire?? in centre 1 and 98 % in centre 2. Practices were different differed between the two centres regarding the attendance of caregivers: 3 persons on average in centre 1, and 4 persons on average in centre 2. In centre 1, One parent was present one parent is present in 79% of cases in centre 1, and in 57% of cases in centre 2 (p=0.004).
We performed a post-hoc analysis in the subgroup of 72 children aged over 6-year (58%). This cut-off was chosen because the pain and anxiety questionnaires we used were validated in this age range, and because the feeling of care givers was that the pillow was less useful for smaller children. In this sub-group, LP success rates were significantly higher with the LP pillow (58.5% vs. 41.5 %, p = 0.031). This subgroup also seem more satisfied (84.4 % vs. 75.0 %, p = 0.344) with the pillow.

**DISCUSSION**

We performed a randomized controlled trial to estimate the benefit of the LP pillows in improving the success rate of LPs and in by-reducing patient discomfort. Our hypothesis was that the LP pillow by, improving the child’s position, could not only increase the rate of successful LPs, but would be less painful especially when LPs are performed without deep sedation.

Because it was not possible to warrant blind intervention and in order to avoid evaluation bias, RBC < 50/mm³ in the cerebrospinal fluid sample was added to the primary outcome.

We based our power calculation on the successful-LPs rate of success reported in literature [3-5]. At our hospital the rate of haemorrhagic LPs (20% within the last two-year) was consistent with those reported in the literature. We expected a 70% success rate in our centre which is very similar to the rate of success described in the literature when LPs are performed without deep sedation / anaesthesia. But only 60% of LPs succeeded in the control group. With this rate of success, and an 11% difference between groups, more than 300 patients per group would have been required to provide an 80 % statistical power to the study.

There was a great consistency between endpoints in favour of the pillow, although non significantly. The rate of successful LPs was non significantly higher in the pillow group (68% vs. 57%, p = 0.23), there was less bleeding (19% vs. 23%, p = 0.48), and fewer post-LP syndromes (15% vs. 24 %, p = 0.17). Children seemed to declare less pain with the pillow (median VAS 15 vs. 25 mm, p = 0.39), whereas caregivers seemed to declare more pain (median VAS 17.5 vs. 10 mm, p = 0.16) and more anxiety (median score 4 vs. 3.5, p =
0.28) in children treated with the pillow. It is important to spot that the pain score evaluated for lumbar punctures with local topical anaesthesia and sedation with MEOPA® is usually fairly low. That could contribute to the fact that the expected difference, with the pillow, in terms of pain scores is low.

Children seem to be more satisfied (84% vs 75%, NS), caregivers equally satisfied (81% vs 79%, NS), and operators less satisfied (79 % vs 84 %, NS) with the pillow.

Nine (7%) patients who were in the pillow group had the pillow removed when difficulties occurred while performing the LP. These difficulties occurred mostly in very young patients, since eight of them were less than 6 years of age. Theses patients were all in centre 2. This centre had little experience of the pillow before the study, and recruited most patients.

Decreasing the number of attendees during LP procedure was a potential advantage of the pillow. However, the number of attendees was not modified during the study in any group. The reason might be that the centre who recruited most of the patients was not used to the pillow use, and maintained an equal number of attendees, for security reasons, or due to internal procedures.

The rate of success with LP pillows was significantly higher in the subgroup of children over 6-year. The analysis in children over 6 years of age was post hoc, and the study was not stratified on children’s age. Sub group analysis was planned after the carer reported that the pillow appear not to be very useful for young children. The cut-off age was fixed at 6 years since it was the cut-off for validated pain and satisfaction scales. This subgroup was characterized by investigators and nurses when the study was still ongoing (comprend pas !!!). The shape, size or smoothness of the device might be insufficiently adapted to smaller children. For younger children, the device seems too large and too hard, and technical improvements are necessary. Moreover, LPs might be easier in younger children without supporting devices.

Conducting clinical trials to evaluate interventions to alleviate pain in children with cancer is
Conclusions: difficult, because of the very limited numbers of patients. Our study shows the difficulties encountered in paediatric clinical research on paediatric pain. Indeed, the pillow has been routinely used for 4 years in centre 1; it illustrates that carers seem to find an advantage in using the pillow. The children themselves request its use when undergoing a LP. We wished to formally demonstrate the benefit gained from using the pillow. Recruiting 124 patients was therefore quite difficult, and demonstrating a significant difference was very challenging. Moreover, the pain score evaluated for lumbar punctures with local topical% anaesthesia and sedation with MEOPA® is usually fairly low, hence The expected difference, with the pillow, in terms of pain evaluations scores is low, but this was not the principal objective of this trial.

Conclusion:

Even if the overall results presented here are not as optimistic as we might have wished, we can confirm that there is do not demonstrate a benefit in using this pillow for lumbar punctures. This study results also suggest a benefit. It is especially Using a positioning pillow should help performing LPs when deep sedation or anaesthesia is not available. Using the pillow does not improve the rate of success of LPs. It might however be promising in the sub group of children over 6 year of age. Should further studies be performed, they should target this age range. are able to can confirm that there is a benefit in using this pillow for lumbar punctures. The use of the LP pillow offers a real benefit in children over 6 years. For younger children, the device seems too large and too hard, and technical improvements are necessary. A confirmation study should be performed in both age group. However, caregivers continue using it in routine after 2 years in ours units. This device could also help improve the comfort of paediatric patients undergoing LP for infectious diseases or emergency conditions, or of adult patients undergoing obstetric spinal analgesia or kidney puncture.
According to our experience and the adherence of care givers to the device are good indicators that this device could be helpful in clinical practice. A larger study is required to confirm these results.
Acknowledgements:

This study was financially supported by the Fondation de France. The Centre Léon Bérard, sponsored the study.

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Conflict of interest: The Centre Léon Bérard holds the licence of the Pillow.

Participating entities:

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Investigating centres: Hôpital Debrousse, Kamila Kebaïli, MD, Sophie Dupuis, Corinne Pondarre, Eric Dore, Carine Marcellin; Centre Léon Bérard: Perrine Marec-Bérard, Mathias Schell, Florence Goy; Lyon Clinical Research Centre: Catherine Cornu, Martine Pelosse, Françoise Aubert, Ségolène Gaillard, Corine Carré, Ahmed Arkhis, Sandrine Théron

Statistics: Alvine Bissery, Michel Cucherat, Muriel Rabilloud.

Database management: CLININFO SA, Lyon, France.

Pillow: designer Serge Rochatte, prototype manufacturer: Roger Faure, PROTEOR SA
Table 1: Baseline characteristics of the participants

<table>
<thead>
<tr>
<th></th>
<th>Pillow group n = 62</th>
<th>Control group n = 62</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>median (min, max)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>6.63 (2.18-17.48)</td>
<td>7.70 (2.02-16.68)</td>
<td>0.60</td>
</tr>
<tr>
<td>Status, Lansky or Karnofsky score (%)</td>
<td>100 (40-100)</td>
<td>100 (40-100)</td>
<td>0.86</td>
</tr>
<tr>
<td>Platelet count</td>
<td>189.5 (11-660)</td>
<td>201.5 (24-609)</td>
<td>0.63</td>
</tr>
<tr>
<td>Number of previous LP</td>
<td>4 (0-16)</td>
<td>3 (0-16)</td>
<td>0.82</td>
</tr>
<tr>
<td>Male</td>
<td>38 (61.3)</td>
<td>37 (59.7)</td>
<td>0.85</td>
</tr>
<tr>
<td>Previous LP</td>
<td>55 (88.7)</td>
<td>57 (91.9)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

**Description of the LP**

<table>
<thead>
<tr>
<th></th>
<th>(n, %)</th>
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</thead>
<tbody>
<tr>
<td>Premedication</td>
<td>21 (33.9)</td>
</tr>
<tr>
<td><strong>EMLAC</strong></td>
<td>61 (98.4)</td>
</tr>
<tr>
<td>Entonox</td>
<td>57 (91.9)</td>
</tr>
<tr>
<td>Purpose of LP</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>7 (11.3)</td>
</tr>
<tr>
<td>Disease follow-up</td>
<td>10 (16.1)</td>
</tr>
<tr>
<td>Treatment injection</td>
<td>45 (72.6)</td>
</tr>
<tr>
<td>LP duration (minutes)</td>
<td>4 (1-33)</td>
</tr>
<tr>
<td>Number of attempts</td>
<td>1.34 (1-5)</td>
</tr>
<tr>
<td>Amount of CSF* withdrawn (drops)</td>
<td>20 (10-34)</td>
</tr>
<tr>
<td>Number of attending persons</td>
<td>3.77 (2-7)</td>
</tr>
</tbody>
</table>

* CSF = cerebrospinal fluid
Table 2: Outcome, intention to treat analysis

<table>
<thead>
<tr>
<th></th>
<th>Pillow group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 62</td>
<td>n = 62</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary outcome: successful LP (n, %, n=121)</strong></td>
<td>41 (67.2)</td>
<td>34 (56.7)</td>
<td>0.23</td>
</tr>
<tr>
<td>Operating physician satisfaction: nb very satisfied or satisfied (n, %, n = 124)</td>
<td>49 (79)</td>
<td>52 (8)</td>
<td>0.44</td>
</tr>
<tr>
<td>Child anxiety (LeBaron scale): median (min.-max, n = 124)</td>
<td>4 (0-33)</td>
<td>3.5 (0-23)</td>
<td>0.28</td>
</tr>
<tr>
<td>Child satisfaction: nb very satisfied or satisfied (n, %, children over 6 years, n=47, 46)</td>
<td>37 (80)</td>
<td>35 (74)</td>
<td>0.85a</td>
</tr>
<tr>
<td>Nursing team satisfaction: nb very satisfied or satisfied (n, %, n = 124)</td>
<td>50 (81)</td>
<td>49 (79)</td>
<td>0.69</td>
</tr>
<tr>
<td>Post-LP syndrome (n, %, n = 124)</td>
<td>9 (14.5)</td>
<td>15 (24.2)</td>
<td>0.17</td>
</tr>
</tbody>
</table>
Table 3: Subgroup analysis, outcome in children over 6 years of age

<table>
<thead>
<tr>
<th></th>
<th>Pillow group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 38</td>
<td>N = 34</td>
<td></td>
</tr>
<tr>
<td>Primary outcome: successful LP (n, %)</td>
<td>24 (58.5)</td>
<td>17 (41.5)</td>
<td>0.031</td>
</tr>
<tr>
<td>Children’s pain (Visual analogical scale*, mm, median (min-max)*</td>
<td>15 (0-91)</td>
<td>25 (0-90)</td>
<td>0.39</td>
</tr>
<tr>
<td>Child satisfaction*, nb satisfied (n, %)</td>
<td>27 (84.4)</td>
<td>27 (75.0)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*: this scale has been validated for children above 6 years only
Illustration: The LP pillow is placed on the thighs of the child; it includes side supports for the head, openings to allow the child to breathing and speaking for the child, to touching the child’s hands and forearms and be able to administrate nitrous oxide, N2O-O2 administration. Props supporting the patient's arms maintain the cervical column in a neutral position.
Figure 1: Flow diagram of the progress through the study.

* Child refusal (2), pillow positioning difficulty (2), pillow judged too large (2), pillow removal after failure of first attempt (2)

** One child of this group received the pillow
References


