Levobupivacaine for Spinal Anesthesia in Children: Cerebrospinal Fluid Aspiration Before the Injection Does not Affect the Spread or Duration of the Sensory Block

Merja Kokki,1,2,* Marja Heikkinen,3 Elina Kumpulainen,2 Aura Vähäoja,2 and Hannu Kokki2

1 Department of Anesthesia and Operative Services, Kuopio University Hospital, University of Eastern Finland, Kuopio, Finland
2 Department of Anesthesiology and Intensive Care, School of Medicine, University of Eastern Finland, Kuopio, Finland
3 Department of Pediatric Surgery, Kuopio University Hospital, University of Eastern Finland, Kuopio, Finland

* Corresponding author: Merja Kokki, Department of Anesthesia and Operative Services, Kuopio University Hospital, University of Eastern Finland, Kuopio, Finland. Tel: +358-447174764, E-mail: merja.kokki@kuh.fi

Received 2015 December 02; Revised 2016 March 05; Accepted 2016 April 04.

Abstract

Background: Several factors are thought to affect the spread and duration of spinal anesthesia (SA) in adults. These include the volume of cerebrospinal fluid (CSF) in the lumbar spinal canal, which has a negative correlation with both the spread and duration of the sensory block.

Objectives: We evaluated whether CSF aspiration before an injection of levobupivacaine affected the spread or duration of SA in children.

Patients and Methods: SA was induced by levobupivacaine (5 mg/mL, 0.25 - 0.5 mg/kg) in 186 children aged 10 months to 18 years (mean of 7.5 years). Two groups were analyzed prospectively: 93 children from which 1 - 3 mL of CSF (CSF-aspiration group) was aspirated before the injection of levobupivacaine to induce SA and 93 children from which no CSF was aspirated (no-CSF-aspiration group) prior to the injection of levobupivacaine. The main outcome measure was regression of the sensory block below T10, cephalic spread of the block, and postpuncture complications after SA.

Results: There were no between-group differences in the time to regression of the block below T10 or in the cephalic spread of the sensory block: 94 (27) minutes and T4.4 (SD 2.2) in the CSF-aspiration group, respectively, vs. 97 (29) minutes and T4.3 (1.8), respectively, in the no-CSF-aspiration group. Position-dependent headaches developed in 4 of 91 children in the CSF-aspiration group and 5 of 86 children in the no-CSF-aspiration group, but no epidural blood patches were required.

Conclusions: The aspiration of 1 - 3 mL of CSF before an injection of levobupivacaine did not seem to affect the spread and duration of the sensory block or postpuncture complications in children following SA.

Keywords: Anesthesia, Spinal, Levobupivacaine, Child, Preschool, Adolescent, Postdural Puncture Headache, Cerebrospinal Fluid

1. Background

Spinal anesthesia (SA) produces profound and uniformly distributed analgesia, with rapid onset and good muscle relaxation. SA also provides enhanced control of cardiovascular and stress responses, is simple to perform, and results in a lower incidence of epinephrine episodes than epidural or opioid anesthesia (1). Recently, concerns have been raised about the neurotoxicity of general anesthetics in infants and young children. Thus, potential alternatives to general anesthesia, such as SA, have attracted interest.

Several factors are thought to affect the spread and duration of SA in adults. These include the volume of cerebrospinal fluid (CSF) in the lumbar spinal canal, which has a negative correlation with both the spread and duration of sensory block (2, 3). A reduced lumbar volume of CSF may explain why normal doses of local anesthetics produce high levels of anesthesia in obese, parturient, and spinal stenosis patients (4, 5). In adult patients, the onset time to maximum spread of analgesia is slower following CSF aspiration (6, 7). If the volume of CSF aspirated is greater than that of the intrathecal injectate, the cephalad spread of anesthesia is significantly higher than in patients from which CSF is not aspirated (7). Less is known about pediatric SA. On a per weight basis, the CSF volume and surface area of the spinal cord are larger in children than in adults (8). Thus, higher doses of local anesthetic per body weight are required in children (9). We are unaware of any attempts to correlate the spread and duration of SA in children with the volume of lumbosacral CSF.

2. Objectives

The aim of the present study was to evaluate whether the aspiration of 1 - 3 mL of CSF before an intrathecal in-
jection of isobaric levobupivacaine (5 mg/mL) affected the spread and duration of SA in children undergoing surgery on the lower part of the body. The primary outcome was the regression of the sensory block below T10, and the secondary outcome were the cephalic spread of the block and postpuncture complications during the first week after SA.

3. Patients and Methods

The study population was constructed from three prospective studies. The subjects were assigned to two groups: a CSF-aspiration group and a no-CSF-aspiration group. In the CSF-aspiration group, a CSF-sample of 1 - 3 mL was obtained (equal to the volume of the intrathecal injectate) during a lumbar puncture for SA to investigate the CSF permeation of paracetamol and nonsteroidal anti-inflammatory analgesics (NSAIDs) (10) or as control samples from healthy children for our research project on autism (11). From the autism study, consent and data were available for the evaluation of SA performance and outcome for all 16 children and from the CSF permeation study for 77 out of the 160 children included in that study. In the no-CSF-aspiration group, children had SA with no CSF aspiration before local anesthetic injection (12). The studies were conducted in accordance with the declaration of Helsinki. Ethical approval for the study was provided by the research ethics committee of the hospital district of northern Savo, Kuopio, Finland (No. 120/2004), and it was registered in the EudraCT database (No. 2004-001702-27). The parents and children were informed, and the parents then gave written consent and children were assented.

One hundred eighty-six healthy children aged 10 months to 18 years who were scheduled for surgery below the umbilicus at Kuopio University Hospital with SA were enrolled. All children with physical status classification 1 or 2 according to the American Society of Anesthesiologists were included, unless they had any contraindications for lumbar punctures or levobupivacaine. Children were excluded if they had any neurological, neuromuscular, psychiatric, or bleeding disorders; seizures; or a known allergy to local anesthetics, paracetamol, or NSAIDs.

Premedication of younger children consisted of 0.375 mg/kg (up to 7.5 mg) of buccal midazolam (Midazolam Hameln, Hameln Pharmaceuticals, Hameln, Germany) 0 and 1.25 mg/kg (up to 25 mg) of ketamine (Ketalar, Pfizer AB, Taby, Sweden). Adolescents received 10 mg of diazepam by mouth. Intravenous thiopental (Pentothal Natrium, Abbott Scandinavia AB, Solna, Sweden) was administered intravenously (i.v.) as supplementary analgesia. Patients without signs of sensory or motor block within 10 minutes of the injection were given general anesthesia.

After the surgery, all the children were transferred to the postanesthesia care unit (PACU) for continuous monitoring of vital signs and regression of the block. In the PACU, the time for regression of the sensory block by two segments and to T7 (processus xiphoideus) and T10 (umbilicus) was tested using a transcutaneous electric stimulator every 5 minutes. One of two trained research nurses or one of the researchers (MK, EK, or HK) conducted the tests. If the child was in pain, 1 µg/kg of fentanyl or 0.05 mg/kg of oxycodone (Oxanest, Oy Leiras AB, Helsinki, Finland) was administered i.v. as rescue analgesia, and the time was recorded. All analgesics in the PACU were given i.v.

The children were discharged when they were awake, able to walk unaided, had stable vital signs at least for 1 hour, had no or only mild pain, had no nausea/vomiting, and were able to tolerate clear fluids.
Follow-up of the children after discharge was recorded by means of a diary, which was to be returned in a prepaid envelope one week after the surgery. Nonresponders were contacted by telephone.

No formal sample size calculation was performed. The sample size was based on the available children from the other studies (10, 11) who had undergone CSF aspiration, and those data were compared with a similar sample of controls who had SA with levobupivacaine without CSF aspiration (12). A sample size of 93 children in each group was calculated to provide a study power of over 0.9 to detect a 15-min between-group difference in the regression of the sensory block below T10, with a probability alpha error of 0.05 or less.

Statistical comparisons between the two groups were carried out with Chi-squared and Fisher’s exact test for proportions. A t-test was used for continuous data, and the Mann-Whitney test was applied for ordinal data. A two-sided P value of 0.05 or less was considered statistically significant. The results are given as the mean (SD), range, or number of patients, as appropriate. All the statistical analyses were performed with the statistical package for social sciences (SPSS), version 22.0 software (IBM Corp., Armonk, NY, USA).

4. Results

Table 1 shows the baseline patient, surgical, and lumbar puncture data. There were no dropouts or protocol deviations likely to interfere with the results. The response rate of the follow-up diaries was 95% (177 of 186).

There were no between-group differences in the characteristics of sensory and motor blocks, and CSF aspiration did not affect the success rate of SA, with 89 of 93 children in the CSF-aspiration group and 90 of 93 children in the no-CSF-aspiration group not requiring any supplementation to complete the surgery (Table 2). In a post hoc analysis, the age of the children, < 12 years (n = 133) vs. 12 years or older (n = 53), did not affect the success rate or characteristics of the spinal block. A post hoc analysis indicated that the puncture level, L3-4 vs. L4-5, did not affect the spread of the sensory block, T4.5 (1.9) vs. T4.4 (2.1) (P = 0.67) or the regression of the sensory block below T10, 98 (26) minutes vs. 92 (24) minutes (P = 0.13).

Seven children in the CSF-aspiration group developed nine adverse events vs. seven children in the no-CSF-aspiration group, with seven adverse events during the surgery. Nausea and vomiting were the most common events during surgery. In the CSF-aspiration group, two had nausea and one vomited, and four had nausea and three had vomiting in the no-CSF-aspiration group. Four children had bradycardia and were given atropine, one had shivering, and one was restless. Of the 14 patients who experienced adverse events during the surgery, 12 were adolescents (aged 12 years or older), and two were young children (aged 30 months and 50 months, respectively).

After surgery, in the PACU, 27 of 93 (29%) children in the CSF-aspiration group developed 28 adverse events vs. 40 of 93 (43%) children in the no-CSF-aspiration group, with a total of 51 adverse events (P = 0.047). Emetic episodes were less common in the CSF-aspiration group (n = 10) than in the no-CSF-aspiration group (n = 24) (P = 0.008). There were no differences in the incidence of other adverse events in the CSF-aspiration group and no-CSF-aspiration group: shivering (14 vs. 15), agitation (3 vs. 1), hypotension (0 vs. 1), and hiccups (0 vs. 1). In a post hoc analysis, the mean age of the children (n =103, 52 months) with adverse events was significantly higher than the mean age of the children (n = 87, 48 months) without adverse events (P = 0.038). In the PACU, 24 of 53 adolescents compared to 43 of 133 younger patients (P = 0.097) had adverse events.

There were no between-group differences in postpuncture complications after discharge, with 35 of 91 (38%) children in the CSF-aspiration group developing 61 adverse events and 32 of 86 (37%) children in the no-CSF-aspiration group experiencing 61 adverse events. A headache was the most common complaint. In the CSF-aspiration group, 19

| Parameter                  | CSF-Aspiration Group (n = 93) | No-CSF-Aspiration Group (n = 93) | P Value |
|----------------------------|-------------------------------|-----------------------------------|---------|
| Gender (male/female)       | 28/65                         | 36/57                             | 0.22    |
| Age, mo                    | 85 (47)                       | 100 (52)                          | 0.02    |
| range                      | 11 - 225                      | 10 - 214                          |         |
| Weight, kg                 | 28 (16)                       | 35 (20)                           | 0.01    |
| range                      | 8 - 86                        | 8 - 86                            |         |
| Height, cm                 | 122 (25)                      | 110 (29)                          | 0.034   |
| range                      | 68 - 179                      | 72 - 176                          |         |
| ASA I/II                   | 82/11                         | 80/13                             | 0.66    |
| Puncture level (L3-4/L4-5) | 24/59                         | 42/51                             | 0.01    |
| Surgery                    | 0.011                         |                                   |         |
| Herniotomy                 | 40                            | 25                                |         |
| Orthopedic                 | 22                            | 39                                |         |
| Genitourinary              | 27                            | 20                                |         |
| Other                      | 4                             | 9                                 |         |

*Values are expressed as No. or mean (SD).
of 91 children developed headaches, four of which were position dependent. In the no-CSF-aspiration group, 15 of 86 children experienced headaches, five of which were position dependent. No epidural blood patches were required in any of these cases. Two of the patients in the CSF-aspiration group who developed position-dependent headaches were adolescents. Seven of the patients who developed headaches were younger than 12 years: three in the no-CSF-aspiration group and four in the CSF-aspiration group. Thirteen children in the CSF-aspiration group developed severe low back pain, radiating to the buttocks. However, in all three children who developed position-dependent headache after discharge, and one had nausea in the PACU but uneventful SA and recovery.

5. Discussion

Data indicate that the aspiration of CSF less than or equal to the volume of the intrathecal injection of local anesthetic does not affect the spread, duration, success rate, or outcome after SA in children. In the present study, the success rate was high in both groups: 96% of children in the CSF-aspiration group and 97% of children in the no-CSF-aspiration group did not need any supplementation to complete the planned surgery. This finding is similar to our experience with pediatric SA (9). All three children who required general anesthesia were in the no-CSF-aspiration group, whereas the supplementation required in the CSF-aspiration group was a single intravenous dose of fentanyl.

The results of the present study also indicate that the aspiration of a small amount of CSF does not seem to affect the incidence of perioperative or postpuncture complaints. In the present study, the incidence of PONV was higher in the no-CSF-aspiration group (31%) than in the CSF-aspiration group (16%). This finding was unexpected, as there were no between-group differences in known risk factors for PONV, with 35 vs. 33 patients reporting a positive history of PONV or motion sickness in the no-CSF-aspiration group and CSF-aspiration group, respectively (16). After discharge, reports of lower back pain were two times more common in the CSF-aspiration group than in the no-CSF-aspiration group. However, the difference was not significant. Therefore, it seems that in children, a small amount of CSF, less than or equal to the volume of the intrathecal injection, can be obtained during SA, without compromising the patients’ safety or outcome, which was our concern when planning these trials in children (10, 11).

In contrast to the findings of the present study, studies of children with diagnostic or therapeutic lumbar puncture found no relation between the aspiration of small
amounts of CSF and the incidence of postpuncture complications (17,18). Thus, the lumbar puncture per se, and not the small amount of CSF aspiration, seems to be the major determinant in the occurrence of postpuncture complications.

Headaches were the most common complaint, with 4 of 91 children in the CSF-aspiration group developing position-dependent headaches vs. 5 of 86 children in the no-CSF-aspiration group. This incidence is significantly lower than that observed in adults following SA for orthopedic surgery, where 10% of patients may develop position-dependent headaches, and some need an epidural blood patch to relieve the symptoms (19). In children with position-dependent headaches, with conservative treatment, the recovery is often uneventful (20-22). This was the case in the present study, as none of the nine children with headaches needed to be hospitalized or required epidural blood patches.

The main limitation of the present study is its non-randomized and non-blinded design. Thus, the distribution of the patients in the two groups was unequal, and the researchers evaluating the outcomes were aware of the group allocation. In addition, the age distribution was large in both groups. This is a concern because the patient’s age may have influenced the assessment of sensory and motor block, as well postoperative complaints. Such assessments are much more subjective in preverbal noncooperative children than in older children and adolescents. However, in the present study, only the intraoperative adverse events were little more common in adolescent than in younger children. The outcomes for the other parameters were quite similar across the age groups.

5.1. Conclusions

In conclusion, the data indicate that the aspiration of CSF equal to the volume of an intrathecal injection of levobupivacaine does not seem to affect the spread, duration, or outcome of SA in children.

Footnote

Authors’ Contribution: Merja Kokki and Marja Heikkinen contributed equally to this study. Study concept and design: Hannu Kokki; acquisition of data: Merja Kokki, Marja Heikkinen, Elina Kumpulainen, Aura Vähäoja, and Hannu Kokki; analysis and interpretation of the data: Merja Kokki, Marja Heikkinen, Elina Kumpulainen, Aura Vähäoja, and Hannu Kokki; drafting of the manuscript: Hannu Kokki; critical revision of the manuscript for important intellectual content: Merja Kokki, Marja Heikkinen, Elina Kumpulainen, Aura Vähäoja, and Hannu Kokki; statistical analysis: Hannu Kokki; administrative, technical, and material support: Merja Kokki and Hannu Kokki; study supervision: Hannu Kokki.

References

1. Wolf AR, Doyle E, Thomas E. Modifying infant stress responses to major surgery: spinal vs extradural vs opioid analgesia. Paediatr Anaesth. 1998;8(4):305–11. [PubMed: 9672928].
2. Carpenter RL, Hogan QH, Liu SS, Crane B, Moore J. Lumbosacral cerebrospinal fluid volume is the primary determinant of sensory block extent and duration during spinal anesthesia. Anesthesiology. 1998;89(1):24–9. [PubMed: 9667280].
3. Higuchi H, Adachi Y, Kazama T. The influence of lumbosacral cerebrospinal fluid volume on extent and duration of hyperbaric bupivacaine spinal anesthesia: a comparison between seated and lateral decubitus injection positions. Anesth Analg. 2005;101(2):555–60. doi: 10.1213/01.ANE.0000186865.57437.F7. [PubMed: 16037751].
4. Sullivan JT, Grouper S, Walker MT, Parrish TB, McCarthy RJ, Wong CA. Lumbosacral cerebrospinal fluid volume in humans using three-dimensional magnetic resonance imaging. Anesth Analg. 2006;103(5):1306–10. doi: 10.1213/01.ane.0000240886.55044.47. [PubMed: 17056974].
5. Greene NM. Distribution of local anesthetic solutions within the subarachnoid space. Anesth Analg. 1985;66(7):715–30. [PubMed: 3893222].
6. Pitkanen M, Tuominen M, Asantila R, Rosenberg PH. Effect of aspiration of cerebrospinal fluid on spinal anaesthesia with 0.5% bupivacaine. Acta Anaesthesiol Scand. 1985;29(6):590–3. [PubMed: 4060800].
7. Jawan B, Lee JH. The effect of removal of cerebrospinal fluid on cephalad spread of spinal analgesia with 0.5% plain bupivacaine. Acta Anaesthesiol Scand. 1990;34(6):452–4. [PubMed: 223916].
8. Porter RW, Hibbert C, Wellman P. Backache and the Lumbar Spinal Canal. Spine. 1980;5(2):299-105. doi: 10.1097/00007632-198003000-00001.
9. Kokki H. Spinal blocks. Paediatr Anaesth. 2002;12(4):56-64. doi: 10.1046/j.1460-9592.2001.03693.x. [PubMed: 12899656].
10. Kumpulainen E. Central Nervous System Permeation of Non-Steroidal Anti-Inflammatory Drugs and Paracetamol in Children University of Eastern Finland; 2010. Available from: http://epublications.uef.fi/pub/urn_isbn_978-952-952-952-101-0117-0/urn_isbn_978-952-61-61-0117-0.pdf.
11. Rikonen R, Makkonen I, Vanhala R, Turpeinen U, Kuikka J, Kokki H. Cerebrospinal fluid insulin-like growth factors IGF-1 and IGF-2 in infantile autism. Dev Med Child Neurol. 2006;48(9):751-5. doi: 10.1034/j.1469-8749.2006.00605.x. [PubMed: 16904022].
12. Kokki H, Ylonen P, Heikkinen M, Reinkainen M. Levobupivacaine for pediatric spinal anesthesia. Anesth Analg. 2004;99(1):56-74. [PubMed: 14695856].
13. Kokki H, Turunen M, Heikkinen M, Reinkainen M, Laisalmi M. High success rate and low incidence of headache and neurological symptoms with two spinal needle designs in children. Acta Anaesthesiol Scand. 2005;49(9):4367-72. doi: 10.1111/j.1399-6576.2005.00837.x. [PubMed: 16146477].
14. Kokki H, Tuovinen K, Hendolin H. Spinal anesthesia for paediatric day-case surgery: a double-blind, randomized, parallel group, prospective comparison of isobaric and hyperbaric bupivacaine. Br J Anaesth. 1998;81(4):502-6. [PubMed: 9924420].
15. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965;16:55-69. [PubMed: 5322004].
16. Eberhart LH, Geldner G, Kranke P, Morin AM, Schauffelen A, Treiber H, et al. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. Anesth Analg. 2004;99(6):1630–7. doi: 10.1213/01.ANE.0000135639.57715.6C. [PubMed: 15562045]

17. Kokki H, Salonvaara M, Herrgard E, Onen P. Postdural puncture headache is not an age-related symptom in children: a prospective, open-randomized, parallel group study comparing 22-gauge Quincke with a 22-gauge Whitacre needle. Paediatr Anaesth. 1999;9(5):429–34. [PubMed: 10447907]

18. Ebinger F, Kosel C, Pietz J, Rating D. Headache and backache after lumbar puncture in children and adolescents: a prospective study. Pediatrics. 2004;113(6):1588–92. [PubMed: 15173478]

19. Mosaffa F, Karimi K, Madadi F, Khoshnevis SH, Daftari Besheli I, Ejaiz A. Post-dural Puncture Headache: A Comparison Between Median and Paramedian Approaches in Orthopedic Patients. Anesth Pain Med. 2011;1(2):66–9. doi: 10.5812/kowsar.22287523.2159. [PubMed: 25729658]

20. Ylonen P, Kokki H. Epidural blood patch for management of postdural puncture headache in adolescents. Acta Anaesthesiol Scand. 2002;46(7):794–8. [PubMed: 12139533]

21. Ylonen P, Kokki H. Management of postdural puncture headache with epidural blood patch in children. Paediatr Anaesth. 2002;12(6):526–9. [PubMed: 12139594]

22. Kokki M, Sjovall S, Kokki H. Epidural blood patches are effective for postdural puncture headache in pediatrics-a 10-year experience. Paediatr Anaesth. 2012;22(12):1205–10. doi: 10.1111/j.12004. [PubMed: 2301060].