Reduction of cerebral mean blood flow velocity and oxygenation after high-volume (1.5 ml kg\(^{-1}\)) caudal block in infants†

M. Lundblad†*, J. Forestier1, D. Marhofer5, S. Eksborg4, P. Winberg2 and P. A. Lönnqvist1,3

1 Department of Paediatric Anaesthesia, Intensive Care & ECMO and 2 Department of Paediatric Cardiology, Astrid Lindgrens Children’s Hospital/Karolinska University Hospital, Stockholm, Sweden
3 Department of Physiology & Pharmacology, Section of Anaesthesiology & Intensive Care and 4 Department of Women’s and Children’s Health, Childhood Cancer Research Unit, Karolinska Institutet, Stockholm, Sweden
5 Department of Anaesthesiology & Intensive Care, AKH/Medical University of Vienna, Vienna, Austria

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Editor’s key points

- The authors previously used lumbar ultrasonography to show that caudal injection causes bi-directional cerebrospinal fluid shifts in infants.
- The current study assessed cerebral haemodynamics using transcranial Doppler ultrasonography and near-infrared spectroscopy.
- High-volume caudal injection caused short-lived but significant perturbations of cerebral blood flow velocity and oxygenation.

Background. We have recently described a bi-directional bulk flow of cerebrospinal fluid (CSF) (coined ‘the CSF rebound mechanism’) after the use of high-volume caudal block in infants, which may explain the secondary longitudinal spread of the block. If important the initial cephalad transfer of CSF should be of such a magnitude that it would cause a transient reduction in cerebral blood flow (CBF) and cerebral oxygenation. The primary aim of this observational study was to delineate the magnitude of the reduction of CBF velocity (CBFV) associated with high-volume caudal block in infants.

Methods. Ultrasound Doppler measurements of CBFV in the middle cerebral artery and also haemodynamic parameters and cerebral regional oxygenation (CRSO\(_{2}\)) were followed during 5 min after the initial caudal injection (1.5 ml kg\(^{-1}\), ropivacaine 0.2%) in 12 infants, 3 months of age.

Results. The caudal injection was associated with immediate and major reductions in CBFV indicating a concomitant reduction in CBF. A significant reduction of cerebral regional oxygenation CRSO\(_{2}\) was also observed. Systemic haemodynamic parameters were unchanged during the observation period.

Conclusion. High-volume caudal block causes a biphasic change in CBFV and was also found to affect cerebral oxygenation. Our findings lend further support to ‘the CSF rebound mechanism’ for secondary spread of high-volume caudal block.

Keywords: anaesthesia, paediatric; anaesthetic techniques, regional, caudal; ICP (intracranial pressure) increase; measurement techniques, ultrasound

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Caudal block has become the most frequently performed nerve block in paediatric anaesthesia since its first description for use in children in 1933.\(^1\)\(^2\) A review regarding the clinical and scientific aspects of the technique has recently been published by Jöhr and Berger.\(^3\) However, certain fundamental aspects of this block still need further study.

One such aspect is the striking difference concerning the cranial spread of high-volume caudal block between earlier predictive equations/dosage guidelines\(^4\)\(\text{–} 6\) and objective imaging techniques (e.g. radiography and ultrasound visualization).\(^7\)\(\text{–} 11\) Thus, whereas earlier dosage guidelines indicate an approximately mid-thoracic spread of a caudal injection of 1.25–1.5 ml kg\(^{-1}\),\(^5\)\(\text{–} 6\) ultrasound imaging can only identify cranial spread up to the thoraco–lumbar junction.\(^10\)\(\text{–} 11\)

To explain this difference, one or more mechanisms of secondary spread that will follow during the time period after the initial injection are required. As the difference in cranial level between the predictive equations and what can be seen by ultrasound is substantial (four to six spinal segments) we have postulated that secondary spread must involve a mechanism associated with an additional wave of bulk flow of the local anaesthetic (LA).\(^12\)\(\text{–} 13\) In a...
previous study, we have identified that the primary caudal injection will produce a bidirectional movement of cerebrospinal fluid (CSF), coined ‘the CSF rebound mechanism’, which eventually will cause secondary cranial spread of the LA. This shift in CSF has been ~15–20% of the initially injected volume of LA, which based on the Takasaki equation would result in an additional cranial spread of four spinal segments.12 13

If our hypothesis is true, ‘the CSF rebound mechanism’ should result in an initial transfer of CSF from the spinal canal to the intracranial space of such a magnitude that it would result in alterations of cerebral blood flow (CBF). If the transfer of CSF is substantial, this should result in a reduction of CBF and cerebral oxygenation. Changes in CBF can be approximated by ultrasound Doppler measurements of CBF velocity (CBFV) where changes in the mean flow velocity (MFV) is the parameter that best reflects changes in CBF.14 15

Thus, the primary aim of the present study was to observe whether a high-volume caudal block in fact does cause a reduction of CBFV and, if so, of what magnitude. A positive finding in this regard would lend further support to ‘the CSF rebound mechanism’.

Methods

The study was approved by the Regional Ethics Review Board of Stockholm, Sweden (DNr 2012/1928-31/3). Written informed consent was obtained from the parents of all children.

Infants < 6 months of age (ASA Physical Status I–III) undergoing surgery requiring caudal anaesthesia for intra- and postoperative analgesia were eligible for inclusion in this prospective observational study.

Known contraindications to regional anaesthesia (e.g. coagulation disorders, allergy to amide LAs, or local infection at the planned injection site) or anatomical abnormalities of the lumbosacral spine were defined as exclusion criteria.

Biometric data

According to established clinical routine, the children were weighed on admission. Patient height was measured with the patient lying supine on the operating table after induction of anaesthesia, using a regular measuring tape.

Anaesthetic protocol

A peripheral venous cannula was inserted already on the general paediatric ward after prior EMLA cream application. General anaesthesia was thereafter induced by propofol (3 mg kg⁻¹), subsequently followed by insertion of a laryngeal mask airway to secure the airway. In patients undergoing laparoscopic surgery tracheal intubation was performed and was facilitated by prior administration of atracurium (0.5 mg kg⁻¹). Anaesthesia was thereafter maintained by sevoflurane–air (FiO₂ 0.3%, end-tidal sevoflurane concentration 2.5%) with the patient breathing spontaneously. Standard monitoring devices [ECG, pulse oximetry, end-tidal CO₂, and non-invasive arterial blood pressure (NIBP)] were used throughout the anaesthetic.

Haemodynamic data

Heart rate, NIBP, and C₃SO₂ were recorded after turning the patient to the left lateral decubitus position for performance of the caudal block (baseline). Heart rate and NIBP were also registered immediately after surgical skin incision, to determine block success/failure, see below.

Caudal block procedure

The caudal injection was made with the child positioned in the left lateral decubitus position. After sterile preparation of the injection site, the sacral cornuae and sacro-coccygeal membrane were palpated. The caudal space was subsequently cannulated using a 25 G paediatric caudal-epidural needle (Epican® Paed caudal, B Braun, Melsungen, Germany). An aspiration test was performed to exclude inadvertent intravascular or intrathecal placement. The LA solution was then manually injected at a rate of ~0.5 ml s⁻¹. A total volume of 1.5 ml kg⁻¹ of 0.2% ropivacaine (Narop®, AstraZeneca, Södertälje, Sweden) was used, representing the upper limit of safe dosage (3 mg kg⁻¹) as described by Bösenberg.16

Transcranial Doppler flow measurements

A duplex ultrasound Doppler equipment (Acuson SC 2000, Siemens, Mountain View, CA, USA) was used for the CBFV measurements. Through the temporal window, the right middle cerebral artery (MCA) was identified by colour Doppler. The pulsed Doppler sample volume was placed in the vessel and the probe position was adjusted to obtain an angle <20°, thus minimizing the angle error to record the highest possible velocities. The probe was held in the same position during the study and the position of the Doppler sample volume was checked before each recording. Recordings were made before the caudal injection as baseline values, at the start of caudal injection, after complete injection, and at 1 min intervals after the start of caudal injection for a total of 5 min (Fig. 1).

In each recording, three consecutive high-quality waveforms were selected for analysis and the average peak systolic and end-diastolic velocities were calculated. The velocity time integral (VTI) of the three cycles was determined and the MFV was calculated according to the formula: VTI/3 × HR/60. Pulsatility index (PI) and resistivity index (RI) were calculated according to the formulas: PI = (peak systolic velocity – end-diastolic velocity)/mean systolic velocity; RI = (peak systolic velocity – end-diastolic velocity)/peak systolic velocity. All examinations were performed by a single investigator (P.W.) well experienced in Doppler sonography.

After the completion of the transcranial flow velocity measurements, the child was again carefully placed in the supine position.

Measurements of cerebral oxygenation

After induction a near-infrared spectroscopy (NIRS) sensor (Oxy Alert™ Cerebral-Neonatal, Covidien, Mansfield, MA, USA) was placed on the left side of the forehead and connected to the INVOS® oximeter for monitoring of cerebral regional oxygenation C₃SO₂.
The sole purpose of adding C\textsubscript{RSO2} to the protocol was to estimate the magnitude of the expected change in cerebral circulation caused by the caudal injection (no significant change in C\textsubscript{RSO2}=no or only minor effect of the measured changes on cerebral circulation; significant reduction in C\textsubscript{RSO2}=major effect of the measured changes on cerebral circulation). This parameter was not intended to be used as support for any biphasic changes of CBFV.

Skin incision was performed not earlier than 15 min after the caudal block. The caudal block was considered a failure if one or more of the following were noted: (1) movement of the limbs in association with skin incision, (2) an increase in heart rate, NIBP, or both of >15% compared with baseline in association with skin incision, (3) intra-operative need for supplemental administration of fentanyl (1 \(\mu\)g kg\(^{-1}\)), as judged by the attending anaesthetist.

**Statistics**

Changes in CBFV and haemodynamic parameters with time were established by the Wilcoxon matched-pairs signed-ranks test.

The data in the figures are expressed by mean values and 95% confidence intervals (95% CIs).
Results

A total of 12 male infants were enrolled in the study. The patients were 8 weeks old (median value; range: 2–18 weeks) at the time of surgery and were born at 37.5 gestational week (median value; range: 33–40 gestational weeks). Patient weight and height was 4.95 kg (median value; range: 2.9–7.5 kg) and 56.5 cm (median value; range: 51–67 cm), respectively.

Eleven patients underwent elective inguinal hernia repair either by the laparoscopic (n=10) or by traditional open (n=1) techniques and one patient had surgery of pyloric stenosis. All blocks were judged to be clinically successful according to the criteria outlined in the Methods section.

Transcranial Doppler flow measurements

The results of the repeated CBFV measurements are shown in Figure 2A–E. No significant changes in haemodynamic parameters were noted during the observation period (Fig. 2F). Diastolic blood pressure at 1-min post-injection was 31 mm Hg (median value; range: 12–45).

Immediately after completed injection

The peak systolic CBFV was reduced by 3% (median value; range: –4–23%) compared with baseline values. This finding did only reach borderline significance (P=0.0522).

Fig 2 Changes in peak systolic CBFV (A), end-diastolic CBFV (a), MFV (c), PI (o), RI (e), and haemodynamics (r) in association with a caudal injection of 1.5 ml kg⁻¹ ropivacaine 0.2% in infants < 3 months of age. HR, Red star; Syst NIBP, Blue circle; Diast NIBP, Green circle. Data are given as mean and 95% CI.
The end-diastolic CBFV was reduced by 89% (median value; range: 43–100%) compared with baseline values ($P=0.0005$). In 6 of the 12 patients, the end-diastolic CBFV was completely abolished.

The MFV was reduced by 26% (median value; range: 15–40%) compared with baseline values ($P=0.0005$).

**At the end of the observation period**

At 5 min after the start of the injection, the peak systolic CBFV had recovered to 94% (median value; range: 83–105%) compared with baseline values. The peak systolic CBFV was at this time point statistically reduced compared with baseline ($P=0.0068$), Figure 2a.

At 5 min after the start of the injection, the end-diastolic CBFV had recovered to 70% (median value; range: 50–113%) compared with baseline values. The end-diastolic CBFV was at this time point still statistically reduced compared with baseline ($P=0.0024$), Figure 2b.

At 5 min after the start of the injection the MFV had recovered to 85% (median value; range: 71–103%) compared with baseline values. The MFV was at this time point still statistically reduced compared with baseline ($P=0.0024$), Figure 2c.

PI and RI values are shown in Figure 2b and e.

There was no correlation between the reduction of end-diastolic CBFV and patient weight, length, or diastolic NIBP (data not shown).

**NIRS measurements**

A significant reduction of cerebral regional oxygenation $C_r$SO$_2$ was observed immediately after the end of injection ($P=0.0020$). No recovery of $C_r$SO$_2$ could be seen during the post-injection period ($P=0.0020$ at 5 min post-injection), Figure 3.

There was no correlation between the reduction of $C_r$SO$_2$ and patient weight, length, or diastolic NIBP (data not shown).

**Discussion**

The main finding of the present study was that a high-volume (1.5 ml kg$^{-1}$) caudal block in young infants is associated with significant reductions of transcranial Doppler flow velocity indices of cerebral perfusion. The reduction in cerebral perfusion appeared immediately after the injection and a partial, but significant reduction was still present at 5 min post-injection. These findings provide supportive evidence for the ‘CSF rebound mechanism’ causing secondary spread of caudal block.

In a previous study, we have been able to show that a high-volume caudal block is associated with two different patterns of secondary spread: horizontal intra-segmental redistribution and longitudinal cranial spread. Based on the magnitude of secondary longitudinal cranial spread, it can be postulated that the observed increased cranial spread cannot only rely on mechanisms such as diffusion or capillary forces but must be the result of a secondary wave of bulk flow of LA.

In a recent study, we did find ultrasonographic evidence of a bidirectional movement of CSF, coined ‘the CSF rebound mechanism’, that may be the cause of such secondary cranial bulk flow of LA. For this mechanism to be of major importance, the volume of this bidirectional shift of CSF must be substantial. In our previous study, we have estimated this volume to equal $\sim 15\%–20\%$ of the injected volume of LA.

When such a considerable volume is shifted from the spinal canal to the intracranial space, this volume should increase intracranial pressure (ICP) to such a degree that it will affect cerebral perfusion. As CSF subsequently is rebounded from the intracranial space to the spinal canal, the cerebral perfusion should return towards baseline levels. Thus, the main reason for the present observational study was to investigate whether such changes in cerebral perfusion are associated with a high-volume caudal block, thereby generating support for the importance of the ‘CSF rebound mechanism’.

Before commenting on our own results, we would like to draw the reader’s attention to a previous seminal publication in this domain. In a porcine study mimicking epidural anaesthesia in adults, Grocott and Mutch measured ICP (by use of an intracranial catheter) and CBF (microsphere technique) after an epidural injection of 0.33 ml kg$^{-1}$ of lidocaine. Their main findings were a rapid increase of ICP (baseline: 10 mm Hg; immediately post-injection: 54 mm Hg) that slowly normalized over a 30-min period and a rapid reduction of CBF to $<10\%$ of baseline values during the 0–60 s post-injection period, followed by a much faster recovery compared with the ICP response.

**Changes in CBFV**

The caudal injection was associated with immediate and major reductions in end-diastolic CBFV and MFV. Although the ultrasound Doppler technique measure blood flow velocity and not CBF, it has long been established that changes in CBFV, especially MFV, reflect CBF changes. The observation that our CBFV recordings were found to be virtually identical to the true CBF changes measured by Grocott and Mutch in their porcine study does in our opinion provide firm support for the notion that our CBFV measurements in fact reflect actual changes in CBF.

As the haemodynamic parameters were unchanged during the entire observation period, the dramatic reductions in CBFV...
caused by the caudal injection could only be caused by either a rapid increase in the resistance to CBF (i.e. by an increase in ICP causing compression of the cerebral vasculature, thereby increasing vascular resistance causing reduced flow) or pronounced dilatation of the MCA at the point of investigation. The ultrasound Doppler technique cannot determine the magnitude of flow changes as the flow velocity also will be affected by a concomitant change in vessel diameter at the recording site which is difficult to assess. However, the technique has been proved to correctly identify the direction of flow changes. Thus, the reduced CBFV do indicate a true reduction in CBF. This is further corroborated by the fact that in 6 of the 12 infants there was no detectable diastolic flow at all directly after injection. A sudden increase in ICP thus represents a much more likely explanation and is in line with the data published by Grocott and Mutch.

The observation that end-diastolic CBFV was completely abolished in 50% of the patients requires an increase in ICP to a level equal to or above the diastolic blood pressure. In these patients, the diastolic NIBP ranged 26–37 mm Hg (median 29.5 mm Hg) at the time point when end-diastolic CBFV was abolished. Hence the resulting ICP caused by the caudal injection in these patients must be at or above this range and an ICP level of this magnitude immediately after the completion of the injection is also in agreement with the findings of Grocott and Mutch. Furthermore, as complete abolishment of end-diastolic CBFV must equal a no-flow situation, this subgroup of patients provide further support to the notion that our CBFV measurements reflects actual changes in CBF.

The immediate and profound reduction in CBFV was followed by a rapid and partial recovery of end-diastolic CBFV and MFV during the first 2–3 min. However, at the end of the observation period, all recorded parameters were still slightly but significantly reduced compared with baseline.

The observation of an immediate reduction, followed by a rapid recovery of CBFV, provides additional support for the CSF rebound mechanism. The substantial reductions in CBFV-related parameters indicate that the volume of CSF shifted from the spinal canal to the intracranial space is substantial and may, thus, be in agreement with our previous estimate (15–20% of the injected volume of LA). In our recently published study, we have shown that intra-spinal pressure is gradually normalized after a high-volume caudal injection and only a marginal increase, compared with baseline, is still present at 15 min post-injection. However, at 5 min post-injection, the intra-spinal pressure was still noticeably increased (8–10 mm Hg), and represents the most probable reason why cerebral perfusion was not fully recovered at 5 min post-injection. Based on our earlier data, it appears reasonable to expect full recovery of cerebral perfusion by ~15 min.

Changes in cerebral oxygenation

The caudal injection of 1.5 ml kg⁻¹ was associated with a rapid and significantly reduction of CᵦSO₂ compared with baseline values. Based on the definition in the Methods section, we therefore conclude that the effects on the cerebral circulation associated with a high-volume caudal block is of a major magnitude. This does in our opinion provide support for the notion that the postulated volume of CSF shifted from the spinal canal to the intracranial space is sizeable and potentially in line with our previous approximation of 0.2–0.3 ml kg⁻¹.

Somewhat surprisingly no recovery of oxygenation was observed during the recovery phase of cerebral perfusion indices. The reason why the NIRS values did not show the same recovery pattern as the CBFV measurements is thought-provoking. A number of reasons for this observation may be speculated. First, in the Grocott and Mutch study, the significantly elevated ICP was associated with a quite slow recovery phase (30 min) compared with a relatively rapid recovery of CBF. Thus, NIRS measurements may be more influenced by ICP than CBF. Secondly, although CBFV and NIRS both will react to substantial reductions of CBF, they cannot be viewed as synonymous or entirely interchangeable as CBFV is more linked to CBF and NIRS more linked to cerebral metabolism/oxygen extraction. Furthermore, the response time for CBFV changes associated with alterations in CBF is almost instantaneous whereas the response time for NIRS measurements will comparatively be more delayed. Bearing the above in mind it may not be surprising that the recovery curves of CBFV and CᵦSO₂ are not identical.

In this context it may be prudent to discuss the potential effect on brain geometry that the initial intracranial CSF volume might have. Of the average 7.5 ml (median weight 5 kg, injected volume 1.5 ml kg⁻¹) that was injected into the caudal space, we have made a previous estimation that the volume that is shifted from the spinal canal into the intracranial space is maximally half the injected volume (3.75 ml). Thus, in the specific context of neonates and young infants, this volume would in fact represent <1% of the total intracranial volume (425 ml). Against this background it appears quite unlikely that such a minor added volume would be able to result in any appreciable change of intracranial geometry, thus, causing any relevant interference with the NIRS measurements unlikely.

Safety aspects of high-volume caudal block

The reduction of CBFVs and cerebral oxygenation is not of such a magnitude or duration to cause concern in otherwise healthy babies but do raise concern with regard to the use of high-volume caudal block in children with intracranial pathology and associated risk factors. Thus, caution is advised when contemplating the use of high-volume caudal block in patients with known intracranial conditions, for example hydrocephalus, arterio-venous malformations, tumours, or cysts.

In conclusion, high-volume caudal block causes a dramatic initial reduction of CBFV, followed by a 70–95% recovery within 5 min. These changes are in agreement with previous published animal data, showing that epidural injections are associated with a drastic increase in ICP and pronounced reduction of CBF. Our findings support the existence and importance of ‘the CSF rebound mechanism’ for secondary spread of high-volume caudal block. The magnitude of the
observed changes in CBFVs and oxygenation raises concerns with regard to the use of high-volume caudal block in children with known intracranial pathology.

**Authors’ contributions**

M.L.: conception of the study, ethics application, data acquisition, data handling, and manuscript writing. J.F.: data handling, statistical analysis, and writing the manuscript. D.M.: data acquisition, coordination, and responsible for NIRS technology. P.W.: ultrasonographic measurements of CBFV parameters and manuscript writing. S.E.: study design, statistical analysis, and manuscript writing. P.A.L.: fundamental conception of the study, funding application, data acquisition, and senior supervisor of study and manuscript writing. All authors have accepted the final version of the original manuscript.

**Declaration of interest**

None declared.

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