Sedation during spinal anaesthesia in infants

H. Hermans, M. F. Stevens*, R. Werdehausen, S. Braun, P. Lipfert and M. Jetzek-Zader

Department of Anaesthesiology, University Hospital Düsseldorf, Germany

*Corresponding author: Department of Anaesthesiology, University Hospital Düsseldorf, Moorenstrasse 5, Postfach 101007, 40225 Düsseldorf, Germany.
E-mail: markus.stevens@med.uni-duesseldorf.de

Background. Neuraxial anaesthesia in adults decreases the dose of i.v. or inhalational anaesthetic needed to reach a desired level of sedation. Furthermore, spinal anaesthesia alone has a sedative effect. The mechanism behind this phenomenon is presumed to be decreased afferent stimulation of the reticular activating system after sympatholysis. We hypothesized that this mechanism is equally active in infants undergoing spinal anaesthesia.

Methods. In total, 20 unpremedicated former preterm infants underwent surgery under spinal anaesthesia with hyperbaric bupivacaine 0.5% 1 mg kg\(^{-1}\) with epinephrine 10 \(\mu\)g kg\(^{-1}\). No additional sedatives or anaesthetics were administered. Sedation was evaluated using the bispectral index (BIS) score and the 95% spectral edge frequency (SEF\(_{95}\)).

Results. After spinal anaesthesia, mean (SD) BIS began to decrease significantly from baseline 97.0 (1.1) to 83.9 (14.4) after 15 min (P=0.006). BIS decreased further, reaching the lowest values after 30 min [62.2 (14.0); P<0.00001]. Mean (SD) SEF\(_{95}\) declined from baseline 26.1 (1.8) Hz to 24.3 (3.1) after 5 min (P=0.02) and further to 9.9 (3.8) after 30 min (P<0.00001). Mean arterial pressure also decreased significantly from 66.5 (4.7) mm Hg within 10 min to 56.1 (5.6) after spinal anaesthesia (P=0.0002), while heart rate remained stable.

Conclusions. These results suggest that sedation after spinal anaesthesia in infants is at least as pronounced as in adults. The sedative effect of spinal anaesthesia should be kept in mind when additional sedatives are administered, especially in former preterm infants.

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Subarachnoid blockade has been shown to decrease hypnotic requirements for thiopental sodium and midazolam in adults. This finding has been confirmed for other anaesthetics, such as isoflurane, enfurane and sevoflurane. In spinal anaesthesia without supplemental anaesthetics, significant sedation has been observed by means of objective sedation scores, assessment of brainstem evoked potentials and bispectral index (BIS) values. The presumed underlying mechanism for this phenomenon is that spinal anaesthesia blocks afferent somatosensory transmission to reticulo-thalamo-cortical projection pathways, reducing their excitability and consequently decreasing the arousal level of the brain.

Our own observations and findings from previous studies indicate that infants undergoing procedures in spinal anaesthesia commonly fall asleep or are at least into a drowsy state. We hypothesized that sedation after spinal anaesthesia develops in infants as it does in adults. Therefore we compared the BIS score and the 95% spectral edge frequency (SEF\(_{95}\)) before and up to 60 min after initiation of spinal anaesthesia.

Methods

After approval from the local ethics committee and informed parental consent, spinal anaesthesia was performed in 20 infants and no premedication was given; 17 of them were undergoing repair of inguinal hernia, two infants required resection of ileostoma and in one case, a sacral teratoma was removed. The median (range) gestational age at birth was 34.5 (24–40) weeks, the median postnatal age at the time of the operation was 10 (5–24) weeks, and the median weight was 3.5 (2.2–5.2) kg. All patients had an increased risk of respiratory complications.
or postoperative apnoea because of a history of hyaline membrane disease or prematurity. Patients were excluded if they had significant cardiovascular or neurological disease. No sedatives, anticholinergic drugs or fluids were administered before spinal anaesthesia. The infants were fasted for 4 h for solids and for 2 h for fluids before anaesthesia. Crystalloids were infused at 6 ml kg\(^{-1}\) h\(^{-1}\) perioperatively.

Spinal anaesthesia was induced in lateral or sitting position at the L4/L5 interspace with hyperbaric bupivacaine 0.5% 1 mg kg\(^{-1}\) with epinephrine 10 \(\mu\)g kg\(^{-1}\) added using a 25 G neonatal spinal cannula (Becton Dickinson, Franklin Lakes, USA). Successful anaesthesia was indicated by sudden loss of leg movement while normal tonus in the arms proved that anaesthesia level was below C8. Surface ECG, cuff arterial pressure and oxygen saturation were measured before, during and after the operation. The BIS and SEF\(_{95}\) were monitored continuously using BIS sensor electrodes applied to the forehead (Aspect Medical Systems, Natick, MA, USA). SEF\(_{95}\) of the EEG is the frequency below which 95% of the power spectrum resides. It was one of the first electroencephalographic-derived values used to monitor anaesthetic depth.\(^5\) SEF values correlate with prematurity.\(^6\)\(^\text{-}^8\) BIS values were only considered valid when the signal quality index was above 50%. Two baseline values were recorded 20 and 10 min before spinal anaesthesia was performed. After the operation, the infants were transferred to the postanaesthetic care unit where they remained until hip flexion was noted.

We considered a decrease in BIS and SEF\(_{95}\) values of 20% as clinically relevant and estimated a 30% SD for the BIS and SEF\(_{95}\) values. We estimated these values from those reported in adults\(^5\) and made the assumption that BIS values are more sensitive and more variable in infants.\(^9\) With an \(\alpha\) error of 0.05 and a power of 0.8 at least 20 infants were needed (power analysis). Data are presented as means (SD) or median (and range). Blood pressure measurements before and after spinal anaesthesia were compared by paired \(t\)-tests, corrected for multiple comparisons (Bonferroni). All BIS and SEF\(_{95}\) data at each point in time were tested for normal distribution by Kolmogorov–Smirnov test and further parametric analysis was only made, if normal distribution was assured. Comparisons were made between baseline BIS and SEF\(_{95}\) values and those after spinal anaesthesia by repeated measurement ANOVA and, if significant, each time point was compared with baseline by paired \(t\)-test corrected for multiple comparisons (Bonferroni). \(P\)-values <0.05 were considered significant.

### Results

Spinal anaesthesia was performed successfully and without complications in all 20 infants, resulting in a complete sensory and motor block. Patient characteristics are reported in Table 1. One infant was so agitated initially, that it had to be sedated with propofol. The patient was excluded from further analysis.

Systolic and diastolic arterial pressure decreased significantly within 10 min compared with values 5 min before spinal anaesthesia in all infants while heart rate did not change significantly (Table 2).

The two baseline BIS and SEF\(_{95}\) values before the procedure remained stable. BIS values began to decrease significantly 15 min after spinal anaesthesia (\(P<0.01\)). In all 19 infants included, a significant change from baseline was observed during the operation. The mean BIS fell below 70 after 25 min. The lowest values were observed between 30 and 45 min after spinal anaesthesia (Fig. 1). The lowest mean (SD) BIS 62.2 (14.0) was noted after 30 min. Mean (SD) SEF\(_{95}\) declined significantly from baseline 26.2 (1.8) Hz to 24.3 (3.1) Hz after 5 min (Fig. 2). The lowest values also occurred after 30 min [9.9 (3.8) Hz].

BIS and SEF\(_{95}\) returned to baseline values after 60 min, when most procedures had finished. Motor block lasted 96.6 (23.0) min. Peripheral oxygenation was monitored for 24 h after operation. Neither episodes of desaturation or apnoea, nor any other respiratory or haemodynamic problems were observed.

### Discussion

Our study demonstrates that spinal anaesthesia in infants has a significant sedative effect, as confirmed by high-order spectral analysis in the form of bispectral EEG. There is some controversy about the reliability of BIS monitoring in infants, as the central nervous system is functionally immature at birth. In comparison with

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**Table 1** Infant characteristics and clinical variables presented as median and range

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>14/6</td>
</tr>
<tr>
<td>Birth term (weeks)</td>
<td>34.5 (24–40)</td>
</tr>
<tr>
<td>Postnatal age (weeks)</td>
<td>10 (5–24)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>3.5 (2.2–5.2)</td>
</tr>
<tr>
<td>Ex-preterm (n)</td>
<td>17</td>
</tr>
<tr>
<td>Time between spinal anaesthesia and onset of surgery (min)</td>
<td>15 (9–24)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>40.5 (20–115)</td>
</tr>
</tbody>
</table>

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**Table 2** Haemodynamic parameters 5 min before and 10 min after spinal anaesthesia. Values are mean (SD). **\(P<0.001\) (paired samples \(t\)-test)

<table>
<thead>
<tr>
<th>Haemodynamic variables</th>
<th>5 min before spinal anaesthesia</th>
<th>10 min after spinal anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>93.7 (6.4)</td>
<td>81.4 (7.3)**</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>66.5 (4.7)</td>
<td>56.1 (5.6)**</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>54.1 (5.6)</td>
<td>42.6 (6.7)**</td>
</tr>
<tr>
<td>Heart rate (min(^{-1}))</td>
<td>160 (16)</td>
<td>157 (17)</td>
</tr>
</tbody>
</table>

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adults and older children, BIS in infants has poorer correlation with concentration of volatile anaesthetic and lower values at awakening.\textsuperscript{12,13} This may be related to the higher anaesthetic requirements of infants undergoing inhalation anaesthesia.\textsuperscript{14,15} Despite this, Kim and colleagues\textsuperscript{16} were able to obtain reliable BIS values from infants and from children under general anaesthesia with sevoflurane, indicating the principal applicability of the BIS score in infants.

Some studies found lower BIS values at similar clinical levels of anaesthesia in infants compared with older children,\textsuperscript{12,17} which may be explained by differences in EEG reflecting cerebral maturation processes. This may be the reason why the BIS values observed in our study are considerably lower than those seen in unmedicated adult volunteers after spinal anaesthesia.\textsuperscript{5}

Although it was not the aim of this study to compare BIS and SEF\textsubscript{95} values, it seems that the SEF\textsubscript{95} is a more sensitive variable during sedation caused by spinal anaesthesia, as it changed earlier and decreased to relatively lower values than BIS. This is in contrast to BIS and SEF values during general anaesthesia, where BIS was reported to be the more sensitive variable.\textsuperscript{18,19} This may be related to the different mechanisms of sedation during general anaesthesia (cerebral desensitization) and neuraxial anaesthesia (peripheral deafferentiation).

Interestingly, the infant who underwent resection of a sacral teratoma in the prone position reached the lowest
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BIS values (a minimum of 32). This incidental finding is in line with studies demonstrating that prone sleeping in low birth weight infants promotes a shift in EEG activity towards slower frequencies and therefore may be related to mechanisms associated with decreased arousal and increased risk of sudden infant death syndrome.

One could speculate that the observed decrease in arterial pressure is responsible for the reduced consciousness especially because in former preterm infants cerebral blood flow after spinal anaesthesia was found to decrease similarly. Nevertheless, the arterial pressure after spinal anaesthesia of all infants was within the normal range. Furthermore, infants and neonates seem to tolerate even much lower levels of systemic blood pressure without serious sequelae. Additionally, no episodes of severe hypotension were noted in our study.

One may argue that the decrease in BIS and SEF95 values might have occurred over time even without spinal anaesthesia, but this is highly unlikely, as the baseline values were stable over a period of 20 min in the same surroundings.

The presumed mechanism for sedation after spinal anaesthesia is a diminished afferent conduction to reticulo-thalamo-cortical projection pathways, reducing their excitability and hence decreasing the arousal level of the brain. This assumption is supported by recent animal studies. Our results suggest that this mechanism is equally present or potentially even more pronounced in former preterm infants.

In adults there is conflicting literature as to whether a higher level of spinal anaesthesia leads to higher degrees of sedation. In our study we only roughly quantified the level of block by observing loss of motor tone in the legs while the arms could still be moved. Pinprick testing or any other painful sensory testing such as a neuromuscular block monitor as used in previous studies may have artificially increased BIS values and/or arterial pressure. For the same reason we did not use clinical sedation scores. The common scores such as the University of Michigan sedation scale (UMSS), or the Ramsay score are partially based on responsiveness to defined stimuli. We omitted stimulation such as stroking the face, massaging the upper back (UMSS), glabellar tap or loud auditory stimuli (Ramsay score) because these would have artificially increased the measured BIS and SEF values. Moreover, the correlation between BIS and the Ramsay and UMSS scores has been assessed in previous studies.

As we abstained from any sensory testing, the level of sympathetic blockade might have varied in the thoracic region (Th1-8) as observed by Rochette and colleagues with the same dose of bupivacaine. Therefore, we cannot make an assertion about the influence of block height on sedation in this case.

Pollock and colleagues found that in adults the largest deviations in BIS from baseline occurred at 30 and 70 min after the initiation of spinal anaesthesia. In contrast, we did not observe a second decrease in BIS or SEF95 levels. The most likely explanation is the much shorter duration (96.6 min) of spinal anaesthesia in infants compared with adults.

In conclusion, spinal anaesthesia in infants is accompanied by significant sedation as seen in adults with a noticeable trend towards even lower BIS values. The sedative effect of neuraxial blockade in infants should be considered when supplemental pharmacological sedation is performed.

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