To the Editor.—We read with interest the case report by Albertin et al.1 regarding a spontaneous arachnoid postpartum leak and headache. In the case report, the authors state that the magnetic resonance imaging scanning was done without contrast because the patient was breast-feeding. However, current recommendations suggest that the use of radiographic contrast media is compatible with breast-feeding.2 Although the proper diagnosis was made in the case by Albertin et al., it is important for physicians to be aware of current recommendations regarding the safety of various medications during lactation to allow for optimal treatment options or, in this case, optimal imaging.

In Reply.—In our case report, we state that the magnetic resonance imaging scanning was performed without contrast because the patient was breast-feeding.1 As Camann and Stuebe wrote, current recommendations suggest that the use of radiographic contrast media is compatible with breast-feeding.2 However, the informative sheet of all three contrast brands in use at our hospital state that breast-feeding is a relative contraindication to contrast medium use. One contrast medium producer recommends a 24-h suspension of breast-feeding for lactating women in case of contrast medium administration. Kubik-Huch et al.3 have demonstrated that small amounts of radiographic contrast medium are excreted into human breast milk during lactation, but the amount transferred to a nursing infant orally is so small that the authors state that the recommendation of a 24-h suspension of breast-feeding for lactating women should be reconsidered.

The clinical relevance of contrast medium excretion into human breast milk is not known. But because magnetic resonance imaging scanning without contrast gave us a satisfactory diagnostic certainty, we decided not to expose the patient to an avoidable risk.

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References


Is Bilateral Cerebral Subdural Hematoma More Frequent after Epidural Anesthesia than Spinal Anesthesia?

To the Editor.—We read with interest the case report of Mashour et al.,1 who reported a bilateral subdural hematoma (SDH) in a parturient after epidural anesthesia. In a previous report,2 we reviewed 47 cases of cerebral hemorrhage after spinal (26 cases) and/or epidural (21 cases) anesthesia (table 1). Almost half of the patients developed bilateral subdural hematoma after dural puncture by an epidural needle. In contrast, subdural hematoma after spinal anesthesia occurred most frequently on the left side of the brain. It is possible that the increased incidence of bilateral subdural hematoma after epidural (11 of 21) versus spinal anesthesia (4 of 26) can be attributed to the greater loss of cerebrospinal fluid volume after inadvertent dural puncture with a large-bore epidural needle. Cerebrospinal fluid leak through a large dural hole might lead to marked cerebral hypotension associated with excessive traction on the bridging veins on both sides of the brain, resulting in bilateral subdural hematoma formation.

Table 1. Cerebral Subdural Hematoma after Spinal versus Epidural Anesthesia

<table>
<thead>
<tr>
<th></th>
<th>Spinal Group</th>
<th>Epidural Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>Bilateral subdural hematoma</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Left subdural hematoma</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Right subdural hematoma</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Intracerebral hematoma</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pregnant patients</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Blood patch</td>
<td>—</td>
<td>8</td>
</tr>
</tbody>
</table>

Further analysis of the 47 cases of SDH showed that half of the published cases were in obstetric patients (22 of 47 cases); 6 cases were reported after spinal anesthesia, and 17 cases followed epidural...
Anesthesiology. V 105, No 6, Dec 2006

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(Accepted for publication August 17, 2006.)

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References


(Accepted for publication August 17, 2006.)

To the Editor.—Plourde et al. proposed that the subjects in the study of Plourde et al. were awake and sedated during recovery, because they remembered some 60% of the stimuli presented to them. Therefore, the phenomenon of increased statistical significance seems to be a marker of the effect of a sedative drug on auditory stimulation in an awake cortex. The new, paradoxical finding in the study of Plourde et al., however, is that this situation is absent in the initial “sedation” condition, where both blood oxygenation level-dependent signal and significance are similar to the anesthesia condition. The only behavioral measure prospectively collected in this study is memory performance, and it too is noticeably absent in the initial “sedation” condition, being the same as during anesthesia. However, at recovery, the memory performance is at the expected 60% of control. As noted by Plourde et al., these sedative concentrations of propofol should produce performance of approximately 50% of baseline/control, as we have documented in our studies.

The most parsimonious explanation of the paradoxical findings during the initial “sedation” condition is that the subjects were indeed asleep, whereas they were awake and truly sedated in the recovery condition. The contention that sedation was equivalent at the begin-
niging and at recovery is based solely on measured concentrations of propofol, not on behavioral state. Clear interpretation of the imaging findings is difficult because volunteers were performing no active behavioral task (e.g., button press to hearing a word) to measure their degree of sedation and responsiveness while inside the scanner. Although the authors state that “it is difficult to fall asleep in the cramped and noisy scanner environment,” our experience has been that, even without drug, it is actually easy to fall asleep in a 3-T magnetic resonance scanner in the absence of an active task. Other investigators at our institution have had similar experiences; being confined in a constant position with the arms tucked in under warm blankets, particularly if the eyes are closed, is a situation similar to swaddling a baby to induce sleep. The “close monitoring” of the subjects is not defined, and an “impression” of whether the subject is awake or asleep is difficult to assess while in the scanner, particularly in retrospect. Any subjects sleeping after initial sedation would wake up when moved out of the scanner in preparation for induction of anesthesia.

On another point, some caution must be exercised regarding which auditory processes are affected most by propofol. The authors state that higher level processing for speech and voice is abolished during anesthesia, whereas the response to nonspecific auditory stimuli is not. However, the cortical response to nonspecific auditory stimuli was determined using all measured data versus a rest condition, whereas response to speech and voice were measured using only a subset of the data collected, with the comparison being between two active conditions. The effect of this change in data handling is evident in baseline. Whereas maximal t values for the nonspecific auditory stimulation are on the order of 14, those of the speech- and voice-related activation are only approximately 3.5 (the significance threshold is 3.2). Concomitantly, blood oxygenation level-dependent signal magnitudes at baseline for nonspecific auditory stimuli are approximately 30, whereas for speech and voice they are approximately 5. Therefore, the presence of decreased but still present brain activity in response to voice or speech during anesthesia would not likely be detected in this study.

Plourde et al. have presented a more refined evaluation of auditory processing during sedation and anesthesia than has heretofore been published. The interesting questions raised by these findings clearly elucidate paths for further study. However, the conclusions drawn from the current study are limited by lack of behavioral data and by issues of statistical significance. I would suggest that the evidence for acute tolerance to propofol is confounded by sleeping subjects. The issue of inhibition of higher order but not general auditory processes by propofol is still an open one. It seems likely that decoding of auditory stimuli during anesthesia is still functioning at some level, because numerous studies have demonstrated at least an implicit form of memory for these stimuli, albeit in much larger sample sizes (e.g., Deeprose et al.4).

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(Accepted for publication August 17, 2006.)
our conclusion is consistent with electrophysiologic data from higher order visual cortex in monkeys.

Second, and perhaps more important, we successfully demonstrated significant negative activation during anesthesia in the words-versus-scrambled words contrast. This suggests that the protocol had adequate sensitivity, because with the same number of trials, we picked up an atypical response difference between the two stimulus classes. If the lack of normal positive response to words or voice stimuli were simply due to low signal and/or high noise, we would not have detected the unusual negative response either.

Third, the reduced level of significance for the words versus scrambled words and vocal versus nonvocal stimuli was expected because we were comparing activations produced by different classes of stimuli (instead of a stimulus vs. silent baseline). This is therefore not an indication of inadequate signal acquisition.

We look forward to additional research on this topic from Dr. Veselis’ group and others, because much clearly remains to be learned from the study of neural responses during anesthesia.

In his letter, Dr. Eisenhut suggests that tumor necrosis factor – and interleukin 1–dependent formation of pulmonary edema might be primarily responsible for lipopolysaccharide-induced lung damage and that nuclear transcription factor KB might be the main target for the antiinflammatory effects of isoflurane observed in our study.

Although increased vascular permeability and PMN recruitment are two key factors in lung injury, there is evidence that regulation of both is different and one might occur without the other. For example, vascular protein leakage is dependent on inducible nitric oxide synthase with the general anesthetic propofol. ANESTHESIOLOGY 2006; 104:448–57

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(Accepted for publication August 17, 2006.)
thase from alveolar macrophages; however, PMN recruitment is not.3 In our model, lipopolysaccharide inhalation results in a rapid PMN accumulation in the vascular bed within 1 h,4 whereas vascular protein leakage is not seen until 6 h after lipopolysaccharide exposure. Lung injury in our model is completely dependent on PMN recruitment as demonstrated in CXCR2-deficient mice,5 suggesting that vascular leakage might be a secondary event.

Chemokactants are essential in acute lung injury. Functional blocking of chemokines or their receptors curbs lung damage.6 In our model, CXCL1 and CXCL2/3 account for approximately 70% of the chemotactic activity in lipopolysaccharide-exposed bronchoalveolar fluid.7 Tumor necrosis factor α and interleukin 1 may also contribute, although tumor necrosis factor α- and interleukin 1-independent production of CXCL1 and CXCL2/3 has been reported.7 Although type II cells are involved, alveolar macrophages seem to be the major source of chemokines in the lung as shown by depletion studies. Our data do not allow distinguishing between effects of isoform on either cell type. The concept of cytokine-dependent fluid transport across alveolar epithelial cells is interesting and may well promote lung damage. This pathway could involve nuclear transcription factor-KB activation and might be particularly relevant for the delayed, CXCL1- and CXCL2/3-independent protection observed in our study.

We agree that future studies should further characterize the mechanisms underlying the antiinflammatory effects of isoflurane in lung injury.

To the Editor—The elegant studies by Hanss et al.1,2 demonstrate that alterations in heart rate variability (HRV) may predict hypotension after spinal anesthesia. The authors found a significant association between an increased ratio of low-frequency HRV (LF) to high-frequency HRV (HF) (i.e., LF/HF) and subsequent hypotension. A less predictive but still significant relation was found between decreased HF and subsequent hypotension.1

In their discussion, the authors briefly compare their results with our previous results3 investigating altered autonomic function and hypotension after induction of general anesthesia. Both of these studies demonstrated an association between decreased HF and subsequent hypotension. Although the stronger relation that we found with decreased HF and subsequent hypotension may simply reflect obvious differences in the study conditions (e.g., general anesthesia vs. spinal anesthesia, different patient populations), it might also relate to the different methods used to quantify HF.

Heart rate variability measurements in the study by Hanss et al.1 are presented using normalized units, where the power in a specific frequency band (e.g., HF) is normalized by the total power in the HRV spectrum (total HRV) for that patient (i.e., HF in normalized units = HF in absolute units/total HRV in absolute units). A patient with decreased HF expressed in absolute units might have a normal value of HF when expressed in normalized units if the total HRV in his or her HRV power spectrum is also reduced (which is often the case in patients with autonomic dysfunction from multiple causes). For this reason, we used absolute measurements of HF in our study. We found both a significant predictive value of decreased HF for postinduction hypotension and a strong correlation between HF and other measures of autonomic dysfunction. Historically, both absolute and normalized measurements of HF have been used by different investigators.8 Normalized units have advantages when HRV is used to examine “sympathovagal balance” (a major focus of the study of Hanss et al.1), whereas absolute units have advantages when reflex integrity or “gain” (a major focus of our study) is examined.

REFERENCES


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Accepted for publication August 18, 2006.
In Reply.—We thank Dr. Latson for and appreciate his interesting comment on our study. As he stated, we demonstrated that the ratio of low frequency (LF) to high frequency (HF) of heart rate variability (HRV) predicts postspinal hypotension with high sensitivity and specificity.\(^1\,\,2\) These findings were confirmed in the control group of another study.\(^3\) In addition, we demonstrated significant differences of normalized HF spectral power before subarachnoid block. These results may indicate that baseline HF is of predictive value as well, confirming the conclusions of Latson et al.\(^4\)

We agree with the author that the type of HRV analysis may crucially influence the results. Latson et al. investigated absolute values, whereas we analyzed the different frequency bands of the power spectrum as normalized units.

Currently, HRV-derived data are processed and presented in different ways. First, absolute HRV values are frequently analyzed and, as the author stated, may have advantages in the analysis of autonomic reflex integrity. Nevertheless, total power of HRV and its different parts decrease with increasing age, underlying cardiovascular disease, and impaired autonomic regulation.\(^3\,\,4\,\,5\) Thus, an absolute HF of, for example, 1,000 ms\(^2/\)Hz may be considered as below normal in young and healthy patients, normal in older healthy patients, and even above normal range in patients with coronary artery disease. Therefore, absolute values do not reflect the specific impact of the parasympathetic or the sympathetic activity of the autonomic regulation. Second, HRV data are normalized to total power. If the total power is high (e.g., 10,000 ms\(^2/\)Hz), an HF of 1,000 ms\(^2/\)Hz is only 10\%, reflecting a low parasympathetic activity in the individual. If the total power is only 2,000 ms\(^2/\)Hz, the same absolute HF value would reflect a considerably higher parasympathetic activity. The aim of our studies was to identify a general predictor of postspinal hypotension; therefore, we investigated the different frequencies in normalized units and cannot comment on absolute HF values in our patients. Absolute values were analyzed as well, but demonstrated only a trend toward higher HF in normotensive patients compared with hypertensive patients. Therefore, we cannot recommend the analysis of absolute values for prediction of postspinal hypotension based on our data.

The guidelines of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology do not favor any one of the mathematical techniques, and each may have advantages and disadvantages.\(^6\)

However, the ratio of LF to HF was demonstrated to be the most valuable parameter of HRV in terms of prediction of postspinal hypotension.\(^1\,\,3\,\,5\) This parameter reflects the balance of the autonomic nervous system and is independent of relative or absolute values because the ratio of absolute and normalized values is mathematically identical. Risk stratification based on the analysis of this autonomic balance was demonstrated to successfully guide prophylactic therapy.\(^5\)

We conclude that in a homogenous group of patients, analysis of absolute values of HRV parameters is probably the best method to determine reflex integrity or “gain.” If the trial’s patient population demonstrates a large variation with respect to age, sex, and underlying diseases, relative values may be more appropriate. LF to HF ratio may be particularly useful for HRV analysis because it is independent of this difference.

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(Accepted for publication August 18, 2006.)

To the Editor.—I read with great interest the article by Hanss et al.\(^1\) in which the authors elegantly demonstrate a relation among heart rate variability, the risk of hypotension after spinal anesthesia for cesarean delivery, and the effectiveness of prophylactic measures such as prehydration and vasopressor use in terms of heart rate variability as well as clinical outcome.

However, I am puzzled by the fact that there was no control for the time of day when the experiments were performed. The authors did their baseline assessments between 18:00 and 20:00, which might be totally different from the values obtained during the experiments. Chassard and Bruguerolle\(^2\) recently reviewed the effects of time of day as a synchronizer for different processes and bodily functions such as drug metabolism, cortisol levels, and hepatic blood flow. Therefore, it should not be surprising to see different results depending on the time of day when the experiments were performed. A clinical observation is that early morning elective cesarean deliveries tend to have a higher incidence of hypotension than afternoon deliveries. This may represent a multifactorial problem, however, after the results of Hanss et al.\(^1\,\,3\) Heart rate variability might be a good representation of one of the main factors influencing postspinal hypotension: sympathetic relative overactivity, which might be synchronized with the time of day.

What Sunrise Might Reveal

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In Reply.—We thank Dr. Lacassie for and appreciate his valuable comment on our study.1 We agree with his statement that if prophylactic treatment of postspinal hypotension is based on measurement of heart rate variability (HRV), timing of the analysis is crucial. Measurement of HRV is performed to analyze autonomic nervous system regulation. It was clearly demonstrated by Chassard and Bruguerolle2 as well as Takase et al.3 that autonomic nervous system activity demonstrates circadian rhythm. Therefore, timing of the measurement is important and should be comparable in all patients. In our previous studies, baseline analysis of HRV on the day of surgery directly before volume preload and regional block was demonstrated to identify patients at risk of hypotension in the course of subarachnoid block,4,5 whereas the analysis on the day before surgery did not correlate with postspatial hypotension.

Events of the current study were defined based on these findings. Baseline analysis identifying patients at risk was the analysis on the day of surgery before volume preload and anesthesia. Because cesarean deliveries were performed at 8:00 AM, all analyses were performed at the same time. The measurement on the day before surgery was performed according to our previous studies and confirmed that there was no correlation between HRV parameters at that event and postspinal hypotension. We conclude that HRV changes during a 24-h period. Therefore, under study conditions, analyses should be performed at the same time to secure comparability of results, as was done in our study.

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Accepted for publication August 18, 2006.)

To the Editor.—The ProSeal™ laryngeal mask airway (PSLMA; Laryngeal Mask Company Limited, Mahe, Seychelles) is not designed as an intubation device. However, we may need to intubate the trachea with a PSLMA in place, using it as an intubation conduit with fiberoptic guidance. This situation may occur in an unanticipated difficult intubation device. However, we may need to intubate the trachea with a PSLMA when a potentially full diameter being the same. In our opinion, this misinformation on the LMA North America Web site should be corrected because many anesthesiologists transcribe it on their difficult airway chart for emergency airway management.

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(Accepted for publication June 28, 2006.)