Epidural Anesthesia and Acutely Increased Intracranial Pressure

Lumbar Epidural Space Hydrodynamics in a Porcine Model

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Background: The effects of epidural injection on intracranial pressure (ICP), lumbar epidural pressure, cerebral blood flow (CBF), and spinal cord blood flow (SCBF) were studied after acutely increased ICP in swine.

Methods: Twenty pigs, anesthetized with isoflurane and mechanically ventilated to maintain normocarbia, had two Tuohy needles placed in the lumbar epidural space. The ICP, lumbar epidural pressure, heart rate, mean arterial pressure, and central venous pressure were monitored. All animals had a Fogarty catheter placed in the parietal epidural space. Six pigs were randomized to a normal ICP group (group N) and eight pigs to an increased ICP group by inflation of the Fogarty catheter balloon (group R). Each pig had 0.33 ml · kg⁻¹ of 2.0% carbonated lidocaine injected over 20 s via an epidural needle placed at L3. The ICP and lumbar epidural pressure were then monitored continuously for 30 min. Pressure–time data were fit to traditional compartmental models. Epidural elastance and resistance were calculated using a derivation of the Windkess theory. An additional six pigs had ICP elevated as in group R and CBF and SCBF measured using radioactive microspheres at five time periods: baseline, 0–60 s, 100–160 s, 200–260 s, and at 30 min after epidural injection.

Results: The animals did not differ with respect to heart rate, central venous pressure, or mean arterial pressure at baseline. The ICP was 10 ± 2 mmHg in group N, and 24 ± 2 mmHg after balloon inflation in group R. After epidural injection, peak ICP was significantly greater in group R (76 ± 22 vs. 54 ± 17 mmHg) but not different by 30 min (17 ± 5 vs. 11 ± 1 mmHg). Epidural elastance in group N was 8.3 ± 3.1 mmHg · ml⁻¹ and 12.8 ± 3.0 mmHg · ml⁻¹ in group R (P = 0.045). Epidural resistance was 1,330 ± 590 mmHg · s · ml⁻¹ in group N and 2,220 ± 660 mmHg · s · ml⁻¹ in group R (P = 0.038). The CBF and SCBF were less than 10% of baseline during the 0–60 s time period after epidural injection. Thereafter, CBF and SCBF did not differ from baseline values.

Conclusions: In this porcine model, epidural injection increased ICP. With increased ICP at baseline, more pronounced increases in ICP followed epidural injection. With increased baseline ICP, both epidural elastance and resistance increased compared with controls. The CBF and SCBF were markedly reduced immediately after local anesthetic injection into the epidural space. (Key words: epidural anesthesia; intracranial hypertension; spinal cord; cerebral blood flow.)

The effects of lumbar epidural pressure on intracranial pressure (ICP) has been studied both in animals1 and humans.2–4 It is known that epidural injections, at least transiently, increase ICP. Intracranial hypertension has long been considered a contraindication to epidural anesthesia. However, there are only two case reports where ICP was measured during epidural anesthesia in patients with increased ICP.5 As such, very little data exist, from controlled experiments, that compare epidural injection into the lumbar epidural space under basal conditions versus conditions raised ICP. For instance, measurement of the hydrodynamic characteristics, specifically the elastance and resistance, of the epidural space have been documented,6 but not in subjects with increased ICP. In this experiment, using a porcine model, we studied the effects of epidural injection on epidural hydrodynamics in animals with normal and increased ICP. We also studied how craniospinal blood flow was altered when epidural injection occurs in the presence of intracranial hypertension. Cerebral blood flow (CBF) and spinal cord blood flow (SCBF) were measured during and immediately after local anesthetic injection into the epidural space in the setting of increased ICP.

Materials and Methods

After University of Manitoba Animal Care Committee approval, 20 pigs (22 ± 3 kg; mean ± SD), were premed-
licated with atropine (0.03 mg/kg) and ketamine (10 mg/kg), and anesthetized with 1 minimum alveolar concentration isoflurane* (1.5 vol% end-tidal), intubated tracheally, paralyzed with pancuronium (1.5 mg/kg) and had their lungs mechanically ventilated to maintain normocarbia (Paco2, 38 ± 2 mmHg). Temperature was maintained at 37 ± 1°C with the use of a heating blanket and lamp, as necessary. A right inguinal incision was made and the femoral artery cannulated with a 3 Fr catheter for direct arterial pressure monitoring and blood sampling. For animals undergoing regional blood flow measurements (discussed later), a left inguinal incision was made and the femoral artery cannulated with a 7 Fr pig-tail catheter. This catheter was advanced into the left ventricle by pressure monitoring, and was used for subsequent injection of radioactive microspheres. A 7.5 Fr flow directed catheter was positioned, via the femoral vein, in the right atrium, to continuously monitor central venous pressure. With the pig in the right lateral decubitus position, the head was secured in a stereotactic frame. The scalp was incised, and burr holes were placed in the left and right parietal crania, 1 cm posterior and 1 cm lateral to the coronal and sagittal sutures. Using a micromanipulator, a 22-gauge spinal needle was advanced into the left lateral ventricle to monitor ICP. An 8.5 Fr Fogarty catheter was placed, via the right burr hole, into the cranial epidural space. Both burr holes subsequently were filled with bone wax. The catheter was inflated with saline, at the appropriate time, to increase ICP to 25 mmHg, and were maintained at this level for the next 30 min by graded inflation or deflation of the catheter balloon. Two 16-gauge Tuohy epidural needles were placed, via a parietal approach, into the lumbar epidural space at L1 and L3. The epidural space was identified by tactile feel and with a 20-gauge epidural catheter that was used intermittently as a probe. As such, no saline or air was introduced into the epidural space (as would happen with loss of resistance techniques) that might influence epidural pressure. Needle placement was confirmed, at the conclusion of the experiment, by direct dissection into the epidural space.

The first 14 pigs were randomized into one of two groups after a 30-min period of stabilization. Six pigs had normal ICP (group N) and eight had increased ICP (group R). An additional six pigs were not randomized, but assigned to group R for regional blood flow determination.

Fig. 1. Application of the Windkessel theory to determine lumbar epidural space elastance and resistance, where P1 = peak epidural pressure and ΔS = area under the pressure–time curve from start until finish of injection. See text for further details.

nations. Physiologic measurements were recorded by chart recorder and a computerized data acquisition system (CODAS, Datag Instruments, Akron, OH). Heart rate, mean arterial pressure (MAP), central venous pressure, ICP, and lumbar epidural pressure (LEP; at the L1 site) were measured at baseline (before inflation of the Fogarty catheter in group R), after inflation of the Fogarty catheter in group R, at the start of the epidural injection continuously for approximately 2 min, and at 60-s intervals thereafter for 30 min. From these data, cerebral perfusion pressure (CPP; CPP = MAP - ICP) was calculated for the same time periods. Pigs in both groups then had 0.33 ml·kg⁻¹ of carbonated lidocaine injected via the L3 epidural needle by syringe pump, at a rate of 0.33 ml·s⁻¹.

Comparisons were made between the two groups with respect to heart rate, MAP, central venous pressure, ICP, LEP, CPP, epidural elastance, and resistance.

The epidural elastance was calculated using a derivatization of the Windkessel theory: 

\[
E = \frac{P_1 + (T^{-1} \cdot \Delta S)}{V}
\]

(1)

where E = epidural elastance, V = volume of local anesthetic injected, P_1 = peak epidural pressure, T = first order time constant for the epidural space pressure–time curve, and ΔS = area under the pressure–time curve from start until finish of injection (fig. 1).

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Resistance of the epidural space was determined from the relation:

\[ T = \frac{R}{E} \]  

where \( T \) = time constant, \( E \) = elastance, and \( R \) = resistance. Algebraic manipulation of equations 1 and 2 allows for the solving of epidural resistance:

\[ R = \frac{(T \cdot P_t + \Delta P)}{V} \]  

The six additional pigs assigned to group R had radioactive microspheres injected to determine CBF and SCBF before, during, and after epidural injection. The details of this technique have been described elsewhere. This involved injection of isotopically distinct microspheres into the left ventricle at baseline, at 3 time periods immediately after epidural injection (0–60 s, 100–160 s, 200–260 s), and at 30 min after epidural injection. Blood was withdrawn from the right femoral artery at a constant rate immediately before, during, and after each isotopic microsphere injection to serve as the “reference organ.” At the conclusion of the experiment, the animals were killed, and the brain and spinal cord were removed and weighed. After gamma counting of the tissue and blood samples, regional blood flows were determined, using standard equations.

With the use of regression analysis and mathematical curve fitting, pressure-time curves for the epidural space were determined for each experiment and fit to one or two compartment models. More than 40 pressure-time points (\( P_t \), considered as time 0) were analyzed per experiment. The models were compared for goodness of fit by comparing the respective \( F \)-statistic and \( P \) values. Statistical analysis of the elastance and resistance calculations were by unpaired Student’s \( t \) test, with a \( P \) value \( \leq 0.05 \) considered significant. Changes over time for the various pressures and regional blood flows measured were evaluated by analysis of variance for repeated measures within group and between groups. When analysis of variance was significant, comparisons were made with the least squares means test. Bonferroni’s correction was applied \( (P < 0.05/n, \text{ where } n = \text{number of comparisons}) \) when multiple comparisons were made within groups. The corrected \( P \) value was considered statistically significant.

Results

The animals in the two groups did not differ at baseline with respect to ICP, LEP, heart rate, central venous pressure, MAP, or CPP (table 1). The ICP was increased in group R from 11 ± 2 mmHg to 24 ± 2 mmHg after the injection of 2.4 ± 0.7 ml saline into the epidural balloon. After epidural injection, peak ICP was significantly greater in group R \((76 ± 22 \text{ vs. } 54 ± 17 \text{ mmHg})\) but not different by 30 min \((17 ± 5 \text{ vs. } 11 ± 1 \text{ mmHg})\. There was a very close relation between ICP and LEP during and after the epidural injection (fig. 2).

The epidural pressure-time data in all experiments fit a biexponential regression model better than a monoeXponential one. The mean decay curves were:

\[ \text{LEP}_N = 41e^{-0.16t} + 13e^{-0.076t} \]

\[ \text{LEP}_p = 69e^{-0.108t} + 14e^{-0.071t} \]  

where \( \text{LEP}_N \) = epidural pressure at time \( t \), in group N, and \( \text{LEP}_p \) = epidural pressure at time \( t \), in group R. The standard deviations for the coefficients and exponential terms for the two groups are shown in table 2. The exponential terms were not significantly different between the two groups.

The elastance of the epidural space was 8.3 ± 3.1 mmHg ∙ ml⁻¹ in group N and 12.8 ± 3.0 mmHg ∙ ml⁻¹ in group R \((P = 0.045)\. The resistance of the epidural space was 1,350 ± 590 mmHg ∙ s ∙ ml⁻¹ in group N and 2,220 ± 600 mmHg ∙ s ∙ ml⁻¹ in group R \((P = 0.038)\. \)

The CBF and SCBF results are presented in table 3. The CBF and SCBF were significantly reduced during the 0- to 60-s time period as compared with baseline, but not significantly different from baseline at the other measurement periods.

Discussion

Although the effects of epidural injection on ICP were documented previously, this is the first time that the effects of epidural injection in animals with increased ICP were studied. Elastance characteristics (reported as compliance) of the epidural space in dogs with normal ICP were determined by Bengis and Gunton. In humans, using the Windkessel theory, Hirabayashi et al. found epidural space compliance and resistance to be 0.39 ± 0.13 ml ∙ mmHg⁻¹ and 27 ± 15 mmHg ∙ s ∙ ml⁻¹, respectively. In their experiment, epidural elastance would be 2.6 ± 0.9 mmHg ∙ ml⁻¹. Frank, in his classic description, used the Windkessel theory to analyze the arterial waveform, and, using the decay of the arterial pulse, calculated the elastance of the system in which the blood was being “pumped.” Hirabayashi applied this analysis to the situation where an injection
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Table 1. Pressure Measurements from the Experiments

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Start</th>
<th>Stop</th>
<th>60 s</th>
<th>30 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>8 ± 2</td>
<td>8 ± 2</td>
<td>57 ± 21†</td>
<td>25 ± 11†</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>Increased</td>
<td>7 ± 2</td>
<td>10 ± 5</td>
<td>87 ± 20†</td>
<td>43 ± 14†</td>
<td>8 ± 2</td>
</tr>
<tr>
<td>ICP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>10 ± 2</td>
<td>10 ± 1</td>
<td>54 ± 17†</td>
<td>26 ± 12†</td>
<td>11 ± 1</td>
</tr>
<tr>
<td>Increased</td>
<td>11 ± 2</td>
<td>24 ± 2†</td>
<td>76 ± 22†</td>
<td>48 ± 11†</td>
<td>17 ± 5</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>75 ± 5</td>
<td>75 ± 4</td>
<td>77 ± 5</td>
<td>75 ± 5</td>
<td>73 ± 9</td>
</tr>
<tr>
<td>Increased</td>
<td>82 ± 12</td>
<td>81 ± 8</td>
<td>81 ± 6</td>
<td>78 ± 8</td>
<td>60 ± 15</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3 ± 2</td>
<td>3 ± 2</td>
<td>3 ± 2</td>
<td>4 ± 1</td>
<td>4 ± 2</td>
</tr>
<tr>
<td>Increased</td>
<td>2 ± 3</td>
<td>3 ± 3</td>
<td>3 ± 3</td>
<td>3 ± 3</td>
<td>3 ± 3</td>
</tr>
<tr>
<td>CPP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>65 ± 6</td>
<td>65 ± 5</td>
<td>23 ± 16†</td>
<td>49 ± 14†</td>
<td>62 ± 10</td>
</tr>
<tr>
<td>Increased</td>
<td>71 ± 12</td>
<td>58 ± 9</td>
<td>12 ± 17†</td>
<td>30 ± 12†</td>
<td>64 ± 15</td>
</tr>
</tbody>
</table>

Mean ± S.D.
* P < 0.05 between groups.
† P < 0.05 within groups.
Group N, n = 6, normal ICP; Group R, n = 8, increased ICP.
CPP = cerebral perfusion pressure; CVP = central venous pressure; ICP = intracranial pressure; LEP = lumbar epidural pressure; MAP = mean arterial pressure.

The injection of local anesthetic into the epidural space is like a single pulse from the injectate needle, and its pressure decay over time has characteristics of a Windkessel. Using a similar analysis, in this porcine model, we demonstrated elastance values approximately 5 times and resistance values approximately 50 times higher than those seen in humans. These findings may relate, in part, to species difference, but also to the fact that the pigs were anesthetized with isoflurane, with its known effects on intracranial blood volume, whereas the patients examined by Hirabayashi were awake. As well, the greater resistance and elastance may be a consequence of the longer sampling time of the pressure-time data (30 min vs. 1 min). Hudson demonstrated prolonged elimination half-times with longer sampling periods in pharmacokinetic studies. An analogous situation exists here.

In the animals with increased ICP, we demonstrated an increase in both elastance and resistance compared with the control animals. We suggest that the explanation for this hydrodynamic relation lies in the translocalization of the ICP and the LEP.

Table 2. Two-compartment Model for Lumbar Epidural Pressure with Normal and Increased Intracranial Pressure (ICP), where LEP = Ae⁻ᵀ₁ + Be⁻ᵀ₂

<table>
<thead>
<tr>
<th></th>
<th>A (mmHg)</th>
<th>T₁ (s)</th>
<th>B (mmHg)</th>
<th>T₂ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal ICP</td>
<td>41 ± 17</td>
<td>146 ± 53</td>
<td>13 ± 2</td>
<td>5,076 ± 1,953</td>
</tr>
<tr>
<td>Increased ICP</td>
<td>68 ± 18</td>
<td>168 ± 30</td>
<td>14 ± 2</td>
<td>2,741 ± 1,344</td>
</tr>
</tbody>
</table>

Mean ± S.D.
Group N, n = 6, normal ICP; Group R, n = 8, increased ICP.

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tion of cerebrospinal fluid out of the cranial vault down the spinal cerebrospinal fluid space when the ICP is increased as a compensatory mechanism suggested by the Munro-Kellie doctrine. We speculate that such a caudal translocation would result in an outward displacement of the spinal dura mater into the epidural space, reducing the volume of the epidural space and, as a result, increasing its elastance. The marked elevation in epidural resistance is also consistent with an outward bulging of the spinal dura into the epidural space. Because the first order time constant for the epidural space is the quotient of resistance and elastance, outward displacement of the spinal dura mater with increased ICP would effect the epidural elastance and resistance in a similar manner. This observation may explain why there is no statistical difference between groups for the first and second order time constants irrespective of ICP.

Other researchers established that epidural space compliance correlates (and, therefore, elastance inversely correlates) with the level of anesthesia. An increase in elastance, therefore, results in a lower level of anesthesia for similar injected volumes. The reason for this may be the higher resistance to flow of fluid in the epidural space that accompanies the greater elastance. In the situation of increased ICP, greater volumes of local anesthetic would be needed to attain the same level of anesthesia. As such, epidural anesthesia would potentially be even more hazardous, because of the need to inject greater volumes than would normally be required to obtain an adequate level of neural blockade, with resultant marked increases in ICP. In the clinical situation, an increase in epidural elastance may be problematic if epidural anesthesia is considered in patients with possible or proven increased ICP. Two case reports in patients undergoing orthopedic procedures who had elevated ICP demonstrated marked increases in ICP as measured by cranial epidural pressure transducers after the institution of lumbar epidural anesthesia.

We demonstrated a greater than 90% reduction in CBF and SCBF after epidural injection in pigs with increased ICP. The marked decrease in flows correlates well with the decrease in CPP coincident with epidural injection in this setting. The prompt return of CBF and SCBF to baseline values by 100-160 s after epidural injection suggests preserved autoregulatory mechanisms.

A porcine model has been used by others for study of the effects of epidural analgesia, validating our use of this species to study the effects of epidural injection. Our method to increase ICP by inflation of an intracranial epidural balloon has also been used by others to successfully create a model of acutely increased ICP. Use of barbiturates may have been superior to the use of isoflurane for a more meaningful model to examine the risk of epidural anesthesia for patients with increased ICP. However, the significant differences in epidural elastance and resistance seen between healthy pigs and those with increased ICP with the same anesthetic management suggests that proportional changes would be expected independent of the anesthetic chosen.

In summary, in a porcine model of epidural anesthesia, we showed the time course of the increase in ICP when an epidural injection occurs, both in pigs with normal and increased ICP. The elevation in ICP after epidural injection was significantly greater in the presence of intracranial hypertension. The epidural space, when modelled mathematically, best conformed to a two-compartment model. Epidural space elastance and resistance both increase when ICP is acutely increased. A reduction in CBF and SCBF that correlates to the acute reduction in CPP also occurs with epidural injection.

References

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7. Manohar M, Parks C: Regional distribution of brain and myocardial perfusion in swine while awake and during 1.0 & 1.5 MAC isoflurane anesthesia produced without or with 50% nitrous oxide. Cardiovasc Res 1984; 18:544-53
11. Archer DP, Labrecque P, Tyler JL, Meyer E, Trop D: Cerebral blood volume is increased in dogs during administration of nitrous oxide or isoflurane. Anesthesiology 1987; 67:642-8