Region of Epidural Blockade Determines Sympathetic and Mesenteric Capacitance Effects in Rabbits

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Background: The mechanisms producing hemodynamic changes during epidural anesthesia are incompletely understood. The role of capacitance changes in the splanchic venous bed can be clarified by comparing blocks of differing segmental distributions. Specifically, we speculated that blocks that include the innervation to the mesenteric circulation alter hemodynamics, sympathetic activity, and venous capacitance to a greater extent than blocks without blockade of sympathetic nerves to this critical vascular bed.

Methods: Rabbits were studied during a-chloralose anesthesia and mechanical ventilation. Sympathetic efferent nerve activity to the mesenteric vessels was measured by surgically placed electrodes, and mesenteric vein diameter was measured by videomicroscopy. Heart rate and mean arterial pressure were monitored by intraarterial cannulation. Responses were compared after administration of epidural lidocaine using a dose and catheter level that limited sympathetic to lumbar levels (lumbar group) or thoracic levels (thoracic group). In addition, hemodynamic responses were recorded after thoraco-lumbar block in animals receiving a-chloralose but breathing spontaneously (spontaneous ventilation group) and in awake animals (awake group).

Results: Mean arterial pressure decreased 38.3 ± 5.8% in the thoracic group but only 16.5 ± 2.8% in the lumbar group. Sympathetic efferent nerve activity decreased in the thoracic group but increased in the lumbar group. An increase in vein diameter followed thoracic epidural anesthesia, but venoconstriction was observed after lumbar epidural block. The addition of intravenous sedation with a-chloralose did not increase the hydropoetic effect of epidural anesthesia in this model.

Conclusions: Block of sympathetic fibers to the splanchic circulation with thoracic epidural lidocaine produces mesenteric venodilatation that contributes to hypotension in rabbits. Although a lesser decrease in blood pressure follows blocks limited to lower segments, because baroreceptor stimulation produces increased splanchic sympathetic activity and mesenteric venoconstriction. Responses in this model are comparable with and without general anesthesia and mechanical ventilation. To minimize hemodynamic consequences, epidural blockade should ideally be confined to the fewest necessary segments, avoiding splanchic innervation if possible. (Key words: Anesthetics, local; Lidocaine. Anesthetic techniques: epidural. Blood vessels: venous capacitance. Sympathetic nervous system: efferent nerve activity.)

CIRCULATORY changes during epidural anesthesia are related to the extent of blockade, but not in a simple way. Lumbar injections with interruption of sympathetic fibers originating in spinal segments T10 and below typically produce minimal hemodynamic alterations. 1 Capacitance changes are minor with these lower extremity blocks because veins in skeletal muscle have negligible baseline sympathetic activity and so are unaffected by sympathetic withdrawal. 2 Also, arterial dilatation in the blocked segments is balanced by increased resistance in unblocked areas. 3 Anesthesia limited to segments providing cardiac innervation (T1–T5) similarly causes only slight blood pressure and heart rate (HR) changes 4–7 because cardiac performance at rest is not dependent on sympathetic tone, and because the block affects sympathetic nerves to only a small perfusion bed. In contrast, extensive thoraco-lumbar anesthesia interferes with nearly all sympathetic outflow and often results in hypotension 8–10 because complete sympathetic block produces the

Materials and Methods

Preparation

The preparation was similar to that previously reported. 12 In brief, after approval by the Institutional Care Committee, anesthetized New Zealand White rabbits (1.0–1.5 kg) were used for local infiltration of the epidural space. After administration of the local anesthetic, the animal was placed in the supine position, and the lumbar spinous process was exposed and dissected in the midline (at T11) in sterile fashion. The dermatome and spinous processes were exposed, and an incision was made over the lumbar region. A 22-gauge polyethylene catheter (PE-50) was inserted into the epidural space through a 24-gauge needle. The contents of the catheter were taken up by introducing 0.5 ml of 2% lidocaine solution. The catheter was then attached to a 5-ml syringe and 0.5 ml of 2% lidocaine solution was administered. This was repeated three times, with a total of 4 ml of 2% lidocaine solution administered. The catheter was then disconnected from the syringe and the needle was removed. The incision was closed with sterile suture material, and the animal was allowed to recover.

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The thoracic group of intercostal arteries is more extensive arteriolar dilatation and little area for compensatory changes. In addition, epidural blockade of thoracic neural segments may produce mesenteric venodilatation \(^{11}\) that contributes to hypotension by decreasing venous return. The importance of splanchic venous dilatation during epidural anesthesia in general is uncertain because contributions of this mechanism have been observed only in humans after extensive blockade \(^{11}\) and in rabbits after full thoracolumbar epidural anesthesia. \(^{12}\)

Although widely differing segmental regions of epidural blockade are used clinically, splanchic venous changes during segmental blocks of thoracic or lumbar neural outflow have not been investigated. We speculate that inclusion of segments in the block that contribute preganglionic fibers to the mesenteric bed amplifies hemodynamic depression during epidural anesthesia by decreasing mesenteric sympathetic activity and thereby increasing mesenteric venous capacitance. Using a rabbit model comparable to that used in a previous study of extensive thoracolumbar blockade, \(^{12}\) the current study examined the effects of lumbar and thoracic segmental epidural anesthesia on directly measured sympathetic activity and mesenteric venous capacitance. In addition, to determine more carefully the relevance of findings with this preparation to clinical situations, we also examined the influence of background systemic anesthesia and mechanical ventilation.

Materials and Methods

Preparation

The preparation was similar to one that we have previously reported. \(^{12}\) In brief, after approval by the Animal Care Committee, anesthesia was induced in male New Zealand White rabbits (1–2 kg) with thiobental (10–25 mg/kg) via an ear vein. Lidocaine (5 mg/kg) was used for local infiltration of the surgical sites. An epidural catheter was placed by removing the first or sixth lumbar spinous process. The ligamentum flavum was exposed and dissected in the midline, and a catheter (0.965 mm OD) was inserted gently through the gap so as not to puncture the dura and was advanced 1 cm into the spinal canal. The trachea, femoral artery and femoral vein were cannulated for ventilation, blood pressure and HR measurement and blood sampling, and administration of fluids and drugs, respectively. Systemic mean arterial pressure (MAP) was measured with the femoral arterial catheter, and HR was determined from the arterial pressure signal. A midline laparotomy was made and a postganglionic splanchic nerve was dissected from the adjacent tissue maintaining continuity proximally and distally. A bipolar recording electrode, composed of two single-strand coated stainless steel wires (0.25 mm OD) in silicone elastomer tubing, was fixed to the nerve with Silgol (tissue-inert silicone polymer; Wacker-Chemie, Munich, Germany) for direct measurement of sympathetic efferent nerve activity (SENA). \(^{13}\)

Rabbits were placed on a specially constructed transparent and movable microscope stage. A 13-cm loop of ileum was externalized through the laparotomy and mounted in a temperature-regulated plastic chamber. The ileum and associated mesentery were superfused continuously with physiologic salt solution formulated to simulate peritoneal fluid. \(^{14}\) This solution was maintained at 37°C and pH between 7.35 and 7.45, and continuously aerated with a gas mixture of 5% O2, 5% CO2, and 90% N2. The mesentery was pinned to the Silastic floor of the chamber and in situ segments of mesenteric vein 500–800 μm in diameter were cleared of excess fat tissue if their margins were not clearly visible to prepare them for vein diameter (VD) measurement. An on-line videomicroscopy system provided a continuous measurement of mesenteric VD. \(^{15}\) To verify an adequate preparation of the vessel and nerve, the animals were exposed to hypoxia (fraction of inspired O2 = 0 for 40 s) \(^{16}\) before and after the protocol. Data were included only for studies in which SENA and VD were confirmed to be responsive to hypoxia both before and after the full protocol. Rectal temperature was measured continuously by a thermistor probe and maintained between 36.5°C and 37.5°C by a warming pad.

Experimental Protocol

Before the protocol was begun, an interval of at least 1 h followed the preparation of the animal to minimize the effect of the initial thiobental administration and to allow stabilization of body temperature and measured parameters. Warmed (37°C) normal saline 25 ml/kg was administered intravenously over 10 min. Five minutes later, lidocaine was injected epidurally. Normal saline (30 μl) was injected to flush the catheter. Blood pressure, HR, VD, and SENA measurements were collected for 1 h after the lidocaine injection. Sampled blood was replaced by twice as much normal saline. The ganglionic blocker hexamethonium (10 mg/kg intravenously) was injected at the end of the protocol to

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produce complete sympathetic blockade, confirming postganglionic site of monitoring. SENA measurements were made in reference to the baseline established after hexamethonium administration.

The rabbits were divided into four groups that differed in the sites and doses of lidocaine injection and concurrent systemic medication and ventilation. In two groups, saline 0.4 ml/kg was injected intramuscularly (for comparability with previously studied control groups), and lidocaine 1.0% was injected epidurally in doses and at sites determined in preliminary tests to produce a desired epidural distribution of injectate: thoracic block was produced by injection of 0.2 ml/kg through an epidural catheter inserted at the T12–L1 interspace (thoracic group, n = 6); and lumbar block was produced by the injection of 0.2 ml/kg through a catheter inserted at the L5–L6 interspace (lumbar group, n = 6). Rabbits in these groups had general anesthesia maintained by infusion of α-chloralose (25 mg/h) and vecuronium (0.3 mg·kg⁻¹·h⁻¹). Ventilation was controlled with an animal respirator (655, Harvard Apparatus, South Natick, MA). Normal arterial CO₂ tension (35–40 mmHg) and pH (7.35–7.45) were maintained by ventilator adjustments and NaHCO₃ administration guided by arterial blood gas determination (ABL 1, Radiometer Copenhagen, Copenhagen, Denmark) every 15 min and by the continuous monitoring of end-tidal CO₂ tension (1100, Perkin-Elmer, Norwalk, CT).

Two other groups were studied to investigate the effects of mechanical ventilation and general anesthesia during thoracolumbar epidural anesthesia (lidocaine 1%, 0.4 ml/kg, injected at the thoracolumbar junction). General anesthesia was maintained in one group by the infusion of α-chloralose (25 mg/h) as in the other groups, but no vecuronium was administered and the animals breathed spontaneously (spontaneous ventilation group, n = 8). Reliable measurements of nerve activity and ventilation did not occur because of electrical interference from diaphragmatic activity and movement artifact in the spontaneously breathing animals. Finally, in another group, neither vecuronium nor α-chloralose were administered, and epidural anesthesia was induced only after the animals had fully awakened from the thiopental anesthesia used during surgical preparation (awake group, n = 6). The animals were loosely confined in a box just small enough to prevent turning and also breathed spontaneously but had no tracheostomy or laparotomy incisions. In the awake and spontaneous ventilation groups, respiratory rate and arterial blood gases were measured before and 10 min after epidural injection. To examine further the contribution of mechanical ventilation to circulatory changes, MAP, HR, and VD were monitored during brief (15-s) mechanical ventilation imposed on the spontaneous ventilation group during epidural blockade.

At the completion of each experiment, the rabbit was killed with intravenous thiopental and the spine dissected to confirm that the catheter was properly placed in the epidural space. The extent of epidural solution spread was identified by the stain of ink (particulate black, 25 μl) included with the injectate, and the segmental level of the tip of the catheter was located. Spread within the epidural space was confirmed by ink staining the canal but not the spinal cord.

Statistics
HR, MAP, SENA, and VD were measured from the recorded printout at 0, 2, 5, 10, and 15 min, and every 15 min thereafter. Data were evaluated by multiple analysis of variance for repeated measures comparing least-squares means (Super ANOVA, Abacus, Berkeley, CA). Results are reported as means ± standard error. Findings are considered significant if P ≤ 0.05.

Results
There were no differences between groups in NaHCO₃ administration. Maximum changes in HR, MAP, SENA, and VD for each group are listed in table 1. Percentage changes over time are illustrated in figure 1, which compares lumbar and thoracic groups, and in figure 2, which compares the spontaneous ventilation and awake groups.

Extent of Injectate Spread
On average, the catheter tip was located at the L4–L5 disc in the lumbar group and at the T11–T12 disc in the others. The median segmental extent of solution distribution within the vertebral canal (fig. 3) was T11 to L7 for the lumbar group (range T7–T12 cephalad, L6–L7 caudal), T4 to L1 for the thoracic group (range T1–T6 cephalad, T12 to T2 caudal), and T1 to L4 for the spontaneous ventilation and awake groups (range T1–T2 cephalad and L3–L5 caudal).

Mean Arterial Pressure
MAP decreased after lidocaine administration in all groups. Recovery was complete by 60 min. There was
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Table 1. Maximum Percentile Changes of Measured Parameters after Lidocaine Injection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MAP</th>
<th>HR</th>
<th>SENA</th>
<th>VD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar</td>
<td>-16.5 ± 2.8*</td>
<td>-3.5 ± 2.2</td>
<td>23.0 ± 13.0*</td>
<td>-5.3 ± 2.3*</td>
</tr>
<tr>
<td>Thoracic</td>
<td>-38.3 ± 5.8*</td>
<td>3.9 ± 3.6</td>
<td>-47.3 ± 18.7*</td>
<td>8.6 ± 3.6*</td>
</tr>
<tr>
<td>Spontaneous ventilation</td>
<td>-48.0 ± 5.0*</td>
<td>-14.2 ± 4.2*</td>
<td>-6.6 ± 4.2*</td>
<td>-1.2 ± 2.0</td>
</tr>
<tr>
<td>Awake</td>
<td>-41.3 ± 8.4*</td>
<td>-8.0 ± 6.7</td>
<td>-8.6 ± 14.1*</td>
<td>7.5 ± 1.8*</td>
</tr>
<tr>
<td>IM</td>
<td>-6.9 ± 3.2</td>
<td>4.1 ± 2.3</td>
<td>-6.6 ± 6.7</td>
<td>-1.2 ± 2.0</td>
</tr>
<tr>
<td>Thoracolumbar</td>
<td>-56.9 ± 4.3*</td>
<td>-13.1 ± 4.3*</td>
<td>-8.6 ± 14.1*</td>
<td>7.5 ± 1.8*</td>
</tr>
</tbody>
</table>

The bottom two rows present data for comparison from a previous study with an identical preparation, including mechanical ventilation and α-chloralose sedation. In the IM group (n = 7), lidocaine 1.5% 0.4 ml/kg was injected intramuscularly. In the thoracolumbar group (n = 8), lidocaine 1.0% 0.4 ml/kg was injected at the T12/L1 interspace to produce full thoracolumbar blockade.

* P < 0.05 versus baseline measurement.

Heart Rate
HR decreased only in the animals receiving thoracolumbar epidural anesthesia (spontaneous ventilation and awake groups). The decrease was significantly less in the awake group at 10 min.

Sympathetic Efferent Nerve Activity
A marked decrease followed injection in the thoracic group. SENA increased at the onset of lumbar epidural anesthesia.

Vein Diameter
VD increased in the thoracic group. Venoconstriction accompanied lumbar epidural lidocaine injection.

Ventilatory Changes
In both the spontaneous ventilation and awake groups, respiratory rate, and arterial CO₂ tension did not change with epidural blockade (spontaneous ventilation: 50.0 ± 50.3 s⁻¹ and 32.5 ± 26 mmHg before block. 49.1 ± 3.5 s⁻¹ and 33.6 ± 4.2 mmHg after; awake: 90.3 ± 13.1 s⁻¹ and 25.5 ± 1.8 mmHg before block. 89.0 ± 12.4 s⁻¹ and 23.5 ± 0.7 mmHg after). Brief mechanical ventilation imposed on spontaneous ventilation group animals had no effect on HR, MAP, or VD (data not shown).

Discussion
Studies in humans have documented greater hemodynamic consequences of extensive epidural anesthesia compared with more limited neuraxial blockade. It is well accepted that hemodynamic changes with spinal and epidural anesthesia are influenced by the extent of sympathetic blockade produced by the block. However, attempts to delineate this relation have been limited by a lack of consistent evidence on the extent and intensity of sympathetic blockade when various measures of sympathetic activity are used. Skin blood flow may increase in areas more extensive than the somatosensory blockade, or may increase with a limited segmental distribution and even paradoxically decrease in the center of thoracic segmental blocks. Elimination of the skin conduction response is unpredictable and incomplete. Global norepinephrine production decreases partially or not at all with extensive block. Not only do these observations fail to produce a clear picture of sympathetic blockade with spinal and epidural anesthesia, but the sites of measurement may not be those important to hemodynamic changes. Sympathetic system activity is heterogeneous and fibers to different tissues exhibit specific patterns of basal and reflex activity. Because neuraxial blockade is an incomplete process, uniform effects on sympathetic activity to various organs can not be assumed. Changes in skin blood flow, circulating norepinephrine, and sweat gland function have minimal influence on hemodynamics, giving impetus to direct measurement of activity in sympathetic fibers supplying large vascular beds. Microneurographic monitoring of sympathetic fibers to lower extremity muscle vasculature has shown prompt and complete termination of activity with onset of epidural anesthesia in humans.

We monitored the sympathetic innervation of the splanchnic circulation because of the unique role of splanchnic veins in regulating circulatory capacitance. The importance of these vessels during spinal

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and epidural anesthesia is supported by abrupt hemodynamic collapse in humans when abdominal vasodilatation accompanies the onset of epidural anesthesia.\textsuperscript{11} We have found that extensive epidural anesthesia in rabbits produces hypotension and splanchnic venodilatation.\textsuperscript{12} These changes are concurrent with ablation of sympathetic activity to the splanchnic bed, and are not explained by direct effects of local anesthetic on the vessels, altered circulating catecholamine concentrations, or by passive response to increased transmural pressure.\textsuperscript{13} Systemic local anesthetic has been shown to produce minimal circulatory changes in this model.\textsuperscript{12}

The spread of ink, which was used as an indication of bulk flow of injectate within the epidural space, slightly underestimates the extent of anesthetic effect.\textsuperscript{55} Decrease in SENA was in fact observed after two of the lumbar injections. A greater extent of anesthetic effect would act to diminish the distinction between lumbar and thoracic groups, so the observed differences in physiologic parameters may underestimate the contribution of splanchnic mechanisms.

The current study shows that epidural anesthetic effects on the veins and nerves of the splanchnic circu-

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Fig. 1. Responses in heart rate (HR), mean arterial pressure (MAP), sympathetic efferent nerve activity (SENA), and vein diameter (VD) to lidocaine injected at 0 min in the thoracic and lumbar epidural block groups. *Significant change from baseline.

Fig. 2. Responses in heart rate (HR) and mean arterial pressure (MAP) to epidural lidocaine injected at 0 min in the spontaneous ventilation and awake groups. *Significant change from baseline.
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![Diagram of thoracic and lumbar segments](image)

Fig. 3. Median segmental spread of epidural injectate for thoracic and lumbar blocks. The segmental origin of preganglionic splanchic sympathetic fibers is also shown.

... of hypotension in the various groups reflects in part the relative amount of denervated arterioles and resulting resistance changes.

In this and an earlier study, hypotension during epidural anesthesia was more dependent on the extent of blockade than on concurrence between sympathetic to increased anesthetic baroreceptor sensitivity and vascular capacitance.

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References


