Epidural Anesthesia Accelerates the Recovery of Postischemic Bowel Motility in the Rat

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Background: Intestinal ischemia is associated with derangement of gastrointestinal motility. Uncontrolled clinical observations that bupivacaine injected into the epidural space causes faster recovery of bowel motility after various abdominal operations led us to assess the hypothesis that epidural anesthesia can hasten the recovery of gastrointestinal motility in the immediate postischemic period.

Methods: Gut motility studies were performed in rats in which epidural anesthesia and intestinal ischemia could be induced without the need to provoke surgical trauma. Epidural lidocaine was compared to epidural saline in their effect on intestinal motility after a 30-min period of bowel ischemia.

Results: Total ischemia to the small bowel resulted in pronounced postischemic hypomotility as evidenced by only 0.7% of the total length of the small bowel filled with a marker meal at the end of the study period (transit index) compared with 84.4% in the control group. Lidocaine epidural anesthesia caused significantly more rapid resolution of the hypomotility (60.3% of the bowel filled with the marker meal vs. 36.9% in the controls in which saline was injected).

Conclusions: Epidural lidocaine compared to epidural saline hastens the recovery of gastrointestinal motility in rats after a 30-min period of bowel ischemia. This effect may be elicited by attenuation of sympathetic efferent inhibitory pathways or by vasodilatation caused by the sympathetic block. These results suggest that lidocaine epidural block not only alleviates pain in situations of ischemic injury to the bowel but may also hasten the recovery from postischemic paralytic ileus. (Key words: Anesthetic techniques: epidural. Anesthesiology, local. Lidocaine. Intestine: ischemia; motility.)

GASTROINTESTINAL motility is influenced by a variety of stimuli. Noxious stimulation, such as that occurring during and after abdominal trauma, laparotomy, and exploration of the intestine, is followed by reflex inhibition of gastrointestinal motility, i.e., paralytic ileus. This reflex is mainly mediated through the sympathetic nervous system.² A much stronger stimulus affecting gastrointestinal motility occurs after transient intestinal ischemia. Ischemic lesions of the small bowel may be the result of a wide range of clinical conditions associated with decrease or redistribution of blood flow, such as shock, congestive heart failure, mesenteric embolus, small bowel obstruction, cardiopulmonary bypass and hypothermia. Whereas a brief period of acute intestinal ischemia causes immediate hyperexcitability, long periods of ischemia cause prolonged inhibition of bowel motility.²,⁵

Epidural block might have a beneficial effect on postoperative gastrointestinal motility. Thoracic epidural analgesia has been shown to restore postoperative gastric and intestinal electrical activity after cholecystectomy,⁶ and lumbar epidural analgesia has been shown to reduce postoperative paralytic ileus after hysterectomy.⁷ These clinical observations are not decisive as the control groups of patients were given intraoperative and postoperative narcotics. Moreover, the effect of epidural analgesia on gastrointestinal motility was not assessed in situations of ischemic injury to the bowel. The aim of this study was to assess the effect of epidural anesthesia on gastrointestinal motility in an animal model where controlled bowel ischemia can be caused without concurrent abdominal surgery.

Materials and Methods

Preparation of Animals

All animal manipulations in this study were performed in accordance with guidelines established by the Animal Welfare Committee at this institution. All studies were performed on male Sabra rats weighing 180–220 g that were randomly assigned to the different study groups. Two preparatory procedures were performed in each rat: Insertion of an epidural catheter and placement of a nylon thread around the superior
mesenteric artery (SMA). Anesthesia for insertion of the epidural catheter was achieved by intraperitoneal injection of 30 mg/kg sodium thiopental. All other procedures were done under ether anesthesia. Animals were fasting for 18 h before each procedure with water allowed ad libitum.

Epidural Catheter. Under thiopental anesthesia the epidural space is exposed at the level of the fifth intravertebral lumbar space. A 0.61-mm (OD) polyethylene catheter (Intramedic polyethylene tubing, Clay Adams, Parsippany, NJ) is threaded cephalad to about the level of the T9 vertebra, a distance of about 30–35 mm. The proximal end of this catheter is tunneled under the skin to the posterior cervical area and sealed with modeling clay. Future epidural injections can be administered via this catheter after exposure of its end and without further surgical procedure.

Ischemia. The second procedure, done 3 days later, was the placement of a nylon thread around the SMA. A midline laparotomy incision is performed under ether anesthesia. With the bowel retracted to the left the SMA is clearly identified. A monofilament 3–0 nylon thread is passed around the SMA in order to create a loop around it and then both ends are threaded through a double lumen tube. The end of this tube is tunneled from the abdominal cavity toward the posterior cervical area with both ends of the nylon thread buried under the skin. Future pulling of both ends of this nylon thread will compress the SMA between the encircling nylon thread and the double lumen tube as long as the nylon thread is pulled and thus cause total ischemia for a controlled time period to the small bowel without the additional trauma of laparotomy and bowel manipulation. Assessment of the adequacy of this method is checked immediately before abdominal wall closure: pulling on the nylon thread should eliminate pulsations in the feeding mesenteric branch arteries and its release should cause the return of pulsations.

Motility. Motility studies were performed by placing 1 ml of a mixture of Arabic gum (gum arabic from Acacia tree, Sigma Chemical, St. Louis, MO) mixed with activated charcoal and saline into the stomach of the fasting animal via a polyethylene nasogastric tube under brief ether anesthesia. Ninety minutes later the animal is killed with ether, the abdomen opened, and ligatures made around the pylorus and ileocecal valve. The gastrointestinal tract, comprising the stomach, small intestine, and cecum, is dissected and freed from its mesentery, with its continuity retained. The intestine is then measured by laying it longitudinally. To avoid movement of intraluminal contents, the intestine was not stretched. The total length of the small bowel is thus recorded and so is the length of small bowel filled with the black meal. The black meal is easily detected through the thin wall of the rat’s small intestine. Net result of motility is expressed by the fraction of the total length of the small bowel filled with the black material (transit index).

Study Groups
See table 1.

Group A: Baseline Motility Control Group. This study was performed on the day of SMA thread procedure (3 days after the insertion of the epidural catheter). A motility study was performed with no bowel ischemia and without any material injected into the epidural catheter. Light ether anesthesia was given for 3 min to simulate the anesthesia time needed to perform the procedure for bowel ischemia. Thirty minutes later (simulating ischemia time) the marker meal was inserted into the animals stomach. At the end of 90 min, after the insertion of the marker meal, a laparotomy was done and the bowel measured on the antimesenteric side without further dissection. The site of the most distal part of the black meal in the bowel was marked with a nylon stitch in the corresponding mesentery for future remeasurement of this distance when the whole gut is dissected out. At this stage the SMA was encircled by the nylon thread for future intestinal ischemia. All the animals in this group served in study group B, thus serving as internal controls.

Group B: Baseline Motility Postischemia Group. Animals of group A were used in this group 1 week after the insertion of the nylon thread around the SMA. No material was injected into the epidural catheter as in group A, but intestinal ischemia was caused for 30 min. A motility study was started at the end of 30 min of intestinal ischemia. Ninety minutes later the bowel was harvested as previously described and the site of the nylon tie from the previous experiment (group A),

Table 1. Animal Groups According to Ischemia Initiation and the Material Injected into the Epidural Catheter

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemia</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Epidural lidocaine</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Epidural saline</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
the actual site of the most distal part of the black meal, and the total length of the bowel were recorded. The fact that this group (group B) was studied 1 week after a laparotomy whereas its control group (group A) was studied with no previous laparotomy did not introduce a bias: a pilot study performed on 20 rats showed that the bowel motility recovers completely a week after a laparotomy with no intestinal ischemia (83.9 ± 4.2 vs. 79.8 ± 4.0).

**Group C: Lidocaine Epidural Block Control Group.** This study was performed on the day of SMA thread procedure (3 days after the insertion of the epidural catheter) by injecting 0.1 ml 2% lidocaine into the epidural catheter. Successful epidural effect is confirmed by observing the freely moving rat dragging its hind limbs. Forty minutes after the epidural injection, the rats underwent light ether anesthesia to simulate the anesthesia time needed to perform the procedure for bowel ischemia. Thirty minutes later the marker meal was inserted into the animals stomach. At the end of 90 min, after the insertion of the marker meal, a laparotomy was done and the bowel measured on the antimesenteric side with the same marking procedure of the most distal site of the black meal as in group A. At this stage the SMA was encircled by the nylon thread for future intestinal ischemia. All the animals in this group served in study group D, thus serving as internal controls.

**Group D: Ischemia and Lidocaine Epidural Block Group.** Animals of group C were used in this group 1 week after the insertion of the nylon thread around the SMA. The first procedure performed was the injection of 0.1 ml 2% lidocaine into the epidural catheter. Successful epidural effect was confirmed as in group C. Forty minutes later, ischemia was initiated under light ether anesthesia. At the end of 30 min ischemia the SMA was freed from the compressing nylon thread and at the same time the motility study started by insertion of the marker meal into the animal's stomach. The various measurements described in group B were employed at the end of the motility study.

**Group E: Saline Epidural Control Group.** This study was performed on the day of SMA thread procedure (3 days after the insertion of the epidural catheter) using 0.1 ml saline. The rats underwent the same procedures employed in group C except for the usage of saline instead of lidocaine. All the animals in this group served also in study group F, thus serving as internal controls.

**Group F: Ischemia and Saline Epidural Group.** Animals of group E were used in this group 1 week after the insertion of the nylon thread around the SMA. The rats underwent the same procedures employed in group D except for the usage of saline instead of lidocaine.

**Study Structure**
Randomization of the animals for the various groups was done by preparing folded notes bearing the various groups signs (A, C, and E) and blindly selecting a note each time from a closed jar. One of the team (JS) was called to the laboratory at the completion of each motility test for bowel measurements without knowing the exact group to which that specific rat belonged. The experiments continued until there were at least ten animals in all the study groups.

**Statistical Analysis of the Results**
One-way analysis of variance (ANOVA) was used for the evaluation of the results with the post hoc Bonferroni test. Probabilities less than 0.05 were considered significant.

**Results**
Thirty-six rats were tested: 10 in groups A–B, 11 in groups C–D, and 15 in groups E–F. The differences in the number of animals among these groups are the direct consequence of the method employed for randomization and our decision to stop the study only after there were at least 10 animals in each study group. Six other rats were not included in the final study: four dragged their feet after the epidural catheter insertion, thus expressing a neurologic deficit, and two died for unknown reasons the day after the laparotomy for the insertion of the nylon thread around the SMA. The results of the motility tests performed in the various animal groups are depicted in table 2. The motility tests results are all expressed as the percentage of the total length of the animal's small bowel that is filled with the marker meal, 90 min after its introduction into the animal's stomach (transit index). Each animal was tested twice, once as a control and once in one of the three study protocols, thus enabling inherent internal control.

**Control Groups (Groups A, C, and E)**
The marker meal passed 84.4%–91.4% of the total length of the small bowel in the three animal groups.
Table 2. Motility Study Results In the Various Study Groups Expressed as the Percentage of the Total Length of the Small Bowel Filled with the Marker Meal (Transit Index)

<table>
<thead>
<tr>
<th>Group</th>
<th>Control A</th>
<th>Ischemia B</th>
<th>Control + Lidocaine C</th>
<th>Ischemia + Lidocaine D</th>
<th>Control + Saline E</th>
<th>Ischemia + Saline F</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>10</td>
<td>10</td>
<td>11</td>
<td>11</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Mean</td>
<td>84.4</td>
<td>0.7</td>
<td>91.4</td>
<td>60.3</td>
<td>90.6</td>
<td>30.9</td>
</tr>
<tr>
<td>SE</td>
<td>3.9</td>
<td>0.7</td>
<td>2.8</td>
<td>5.3</td>
<td>2.0</td>
<td>8.0</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SE.
Group A = baseline motility control group; Group B = baseline motility postischemia group; Group C = lidocaine epidural block control group; Group D = ischemia and lidocaine epidural block group; Group E = saline epidural control group; Group F = ischemia and saline epidural group.

where no intestinal ischemia was caused (groups A, C, and E) regardless of the material injected into the epidural catheter. No statistically significant difference was found in the motility study results between any two of these groups.

Ischemia Groups (Groups B, D, and F)
Total ischemia to the small bowel resulted in pronounced posts ischemic adynamic ileus in all three ischemic groups (groups B, D, and F). The most pronounced effect was seen in group B, in which intestinal ischemia was caused with no material injected into the epidural catheter: the marker meal advanced only into 0.7% of the total length of the small bowel. Posts ischemic adynamic ileus was also evident in groups D and F with motility study results of 60.3% and 30.9%, respectively. These results were significantly statistically different than the results achieved in the matching control groups (groups A and B, P < 0.001; groups C and D, P < 0.001; and groups E and F, P < 0.001).

Lidocaine epidural block (group D) caused a significantly (P < 0.001) more rapid resolution of the adynamic ileus that follows intestinal ischemia when compared to the group in which intestinal ischemia was caused with no material injected into the epidural catheter (group B) (60.3% and 0.7%, respectively, P < 0.001). This effect was also evident (P < 0.001) when the transit index was compared between the lidocaine epidural block group and the group in which saline was injected into the epidural catheter (group F), both after intestinal ischemia (60.3% and 30.9%, respectively, P < 0.001).

Discussion
The current study clearly shows the effect of epidural anesthesia on the recovery of gastrointestinal motility in the immediate postischemic period. The unique animal model used in this study, where the SMA can be totally compressed for a predetermined period without laparotomy, ascertained that the effect of bowel ischemia on gastrointestinal motility was unbiased by any effect of open abdominal surgery. The adequacy of this method was tested immediately after the insertion of the nylon thread around the SMA with elimination of pulsations in the feeding branch mesenteric arteries when the nylon thread is pulled and the return of pulsations upon its release. The technique for measurement of intestinal transit used in this study is a well-established method and has been extensively used to examine the effects of various surgical manipulations and therapeutic and toxic agents on intestinal motor function.

In the clinical setting, bupivacaine injected into the epidural space caused faster recovery of gastrointestinal motility after hysterectomy, after cholecystectomy and after colonic surgery with no effect on gastrointestinal motility in healthy volunteers. These clinical observations are not decisive as the control groups of patients were given intraoperative and postoperative narcotics. The effect of epidural bupivacaine seems to work through the sympathetic system though not through circulating catecholamines. The turnover of norepinephrine was shown to be increased in the digestive tract of the rat after surgery, but, on the other hand, removal of the adrenal medulla in rats had no significant effect on gastric emptying and on intestinal propulsion in rats subjected to laparotomy. It is assumed that during centrenuroaxis block, gastrointestinal hyperperistalsis is due to unopposed parasympathetic (vagal) activity.

The phenomenon of adynamic ileus seen after surgery is even more pronounced after intestinal ischemia. The effect of ischemic injury to the bowel on
its motility is dependent on the ischemia duration. Studies in awake dogs showed that short ischemia of less than 1 min caused immediate hyperexcitability of the segment of small bowel under study followed by an irregular spastic pattern. Longer duration of ischemic injury to the bowel causes delay in gastric emptying and slowing of the small intestinal motility, i.e., paralytic ileus.

Our study clearly shows that this effect of ischemic injury to the small bowel can be attenuated by lidocaine epidural block in accordance with previous observations in patients of the beneficial effects of bupivacaine epidural block after open abdominal surgery. Our animal model enables the separation of the ischemic insult from the surgical insult usually needed to cause the ischemia thus isolating the effect of lidocaine epidural block on the paralytic ileus caused solely by intestinal ischemia. There is no conclusive explanation for such an effect of epidural block on postischemic paralytic ileus. This effect may be elicited by attenuation of sympathetic efferent inhibitory pathways or by unopposed parasympathetic (vagal) activity as described in paralytic ileus that follows surgical trauma. Another mode of action may be through vasoconstriction caused by the sympathetic block with resultant improved perfusion in the post ischemic period. The effect elicited by saline injected into the epidural catheter on postischemic adynamic ileus, though significantly less than the effect elicited by lidocaine (P < 0.001), is even more obscure and may be caused by the pressure caused by the volume of saline injected into the epidural space. To the best of our knowledge there is no study assessing the effect of increased epidural pressure per se on gut motility. Nevertheless, the fact that postischemic adynamic ileus can be modified by epidural block is important and suggests a potential modality for attenuation of postischemic bowel effects. If this is the case, then not only lidocaine epidural block can serve to alleviate pain in the clinical situations of ischemic injury to the bowel, but it may also enhance restoration of bowel motility in the immediate posts ischemic period.

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References