Intravenous Lidocaine Speeds the Return of Bowel Function, Decreases Postoperative Pain, and Shortens Hospital Stay in Patients Undergoing Radical Retropubic Prostatectomy

Scott B. Groudine, MD*, Hugh A. G. Fisher, MD†, Ronald P. Kaufman, Jr., MD†, Manoj K. Patel, BA*, Lance J. Wilkins, MD*, Sudha A. Mehta, MPH*, and Philip D. Lumb, MBBS*

Departments of *Anesthesiology and †Urology, Albany Medical College, Albany, New York

Postoperative ileus is a concern among surgical patients. Epidural anesthesia and analgesia with local anesthetics can decrease the duration of ileus. Significant systemic absorption of local anesthesia occurs during epidural use. In this study, we examined whether many of the beneficial effects on bowel function seen with epidural lidocaine are also present when the drug is given parenterally. Forty patients undergoing radical retropubic prostatectomy were studied with one half of the patients receiving a lidocaine bolus (1.5 mg/kg) and infusion (3 mg/min, unless weight <70 kg, then 2 mg/min); the other half received a saline infusion. A blind observer recorded the patient's daily pain score, the time the patient first experienced flatulence and had the first bowel movement, and the total use of analgesics. Lidocaine-treated patients first experienced flatulence in a significantly shorter time ($P < 0.01$) than control patients. Lidocaine patients' hospital stay was also significantly shorter ($P < 0.05$); on average, they spent 1.1 fewer days in the hospital. IV lidocaine initiated before anesthesia and continued 1 h postoperatively significantly sped up the return of bowel function. Lidocaine patients were also more comfortable postoperatively. Many of the bowel function benefits attributed to epidural lidocaine are also present when the drug is administered parenterally. Additionally, the length of hospital stay was reduced in lidocaine-treated patients. **Implications:** This study prospectively examined whether IV lidocaine could affect the return of bowel function after radical prostate surgery. Lidocaine-treated patients had shorter hospital stays, less pain, and faster return of bowel function. In this population, lidocaine infusion can be a useful adjunct in anesthetic management.

(Anesth Analg 1998;86:235–9)

Ileus can be a painful and potentially expensive result of surgery, stress, or trauma. Although most often associated with intraperitoneal surgery, postoperative ileus often occurs after retroperitoneal and peripheral operations (1,2). The cost of postoperative ileus has been estimated at $750 million annually (1990 dollar unadjusted for inflation) (3). Many approaches to improve gastrointestinal function after surgery have been studied. Experimental and clinical evidence suggests that epidural anesthesia and analgesia can speed the return of normal bowel function after general anesthesia and surgery (4); however, the mechanism of this action remains unknown. A decrease in postoperative pain and opioid use, systemic absorption of local anesthetics, and blockade of sympathetic innervation of the bowel all have been suggested (4–6). The use of epidural local anesthetics can result in significant plasma levels. If systemic absorption is responsible for a significant portion of the observed salutatory effects of epidurally applied local anesthetics on bowel function, then IV delivery of the drugs should also decrease the duration of ileus.

The aim of this study was to determine whether postoperative ileus could be reduced in patients undergoing radical retropubic prostatectomy by maintaining a serum lidocaine level IV during surgery and in the immediate postoperative period. The effects of systemic lidocaine on bowel function, hospital stay, opioid use, and the patient's total hospital pain score were also investigated.

Methods

After institutional review board approval, a prospective study of 40 patients undergoing radical retropubic

Accepted for publication October 17, 1997.

Address correspondence to Scott B. Groudine, MD, Department of Anesthesiology, A-131, Albany Medical College, 47 New Scotland Ave., Albany, NY 12208. Address e-mail to Scott_Groudine@ccgateway.amc.edu.

0003-2999/98/$5.00

prostatectomy was undertaken. This procedure was chosen because only two surgeons perform the procedure at our institution, and both expressed interest in minimizing postoperative ileus in this patient population. Patients were excluded from participation in the study if they had a preexisting disorder of the gastrointestinal tract; used enemas, opioids, or anticholinergic medication chronically (7); or were ASA physical status III or more.

The study began in May 1995 and ended August 1996 (15 mo). After obtaining written, informed consent, a number from 1 to 40 was randomly drawn. Even-numbered patients received lidocaine, whereas odd-numbered patients were assigned to the control group. Immediately before induction, patients in the lidocaine group received a lidocaine bolus of 1.5 mg/kg. After tracheal intubation and positioning, a lidocaine infusion was initiated at 3 mg/min if the patient weighed ≥70 kg. The infusion rate was started at 2 mg/min for patients weighing <70 kg. After 2 h on the infusion, a steady-state lidocaine blood level was obtained. The lidocaine was continued throughout surgery and into the postanesthesia care unit (PACU). The infusion was terminated 60 min after skin closure.

Control patients received a saline infusion administered in a similar manner. The nursing staff, surgeons, and patients were all blinded. Pain scores and inquiries about first flatus and bowel movements were all made by a nurse blinded only to the patient's lidocaine status. Ketorolac (30 mg IV) was initiated for all patients in the PACU unless there was a contraindication (history of peptic ulcer disease, renal disease, or concerns about postoperative hemostasis) and continued (15 mg IV) every 6 h if needed for pain control. Morphine was used for breakthrough pain and for those patients not receiving ketorolac.

At the start of the study, patients were instructed to write down the exact time they passed their first flatus and had their first bowel movement; nurses also routinely asked each patient whether they experienced any of these bowel activities. From Postoperative Day 1 until discharge, patients were asked to score their average pain for the previous 24 h on a scale of 0–10 (0 = none; 10 = worst pain imaginable). Patients were resting when questioned. These scores were totaled for the hospital stay to give a total pain score index for each patient. At discharge, the total opioid and nonopioid analgesic use was calculated from patients' medical records.

Surgical variation was limited because both surgeons often scrubbed together and had similar operative techniques. Anesthetic management was provided by one of six anesthesiologists. All patients received nitrous oxide (50%) and isoflurane. Anesthesiologists were permitted to supplement the anesthesia with opioids when they felt it desirable. This flexibility in opioid use was necessary to encourage clinicians to enroll their patients in this study. All anesthesiologists were instructed to avoid using lidocaine on control patients. In the interest of patient safety, the anesthesiologists were not blinded and were not involved in any of the data collection or patient interviews associated with this study.

The pharmacy cost of the lidocaine infusion (2 g/500 mL) was $2.89. Fluorescence polarization immunoassay technology (TDxFLx™; Abbott Laboratories, Abbott Park, IL) was used to assay plasma lidocaine levels.

Two patients from the lidocaine group were excluded from analysis. One patient withdrew his consent for the study immediately before induction. The other patient had multiple surgical complications including prolonged leakage of urine from his surgical drains and deep vein thrombosis. These nonstudy factors resulted in a complicated and prolonged hospital course. The remaining 38 patients completed the study. All patients passed flatus before discharge.

The data was managed and analyzed using SAS (version 6.11; SAS Institute, Research Triangle Park, NC). Results are expressed as mean ± SD. Differences between the lidocaine and control group in bowel movement, time to first passage of flatus, length of hospital stay, ASA physical status, opioid use, total pain score index, and demographic data were compared using a two-tailed unpaired Student's *t*-test. Differences were considered significant if $P < 0.05$.

Results

No patient experienced identifiable adverse events related to the lidocaine infusion. Lidocaine blood levels were variable (1.3–3.7 μg/mL), but none approached a toxic level (>5 μg/mL). All patients started on the lidocaine infusion finished their full course of the drug. Complications were minimal, except for those in the one patient previously mentioned. Several patients had postoperative fevers, but only three of these required blood cultures (two control, one lidocaine-treated). All cultures were negative. There was no perioperative mortality among the 40 patients enrolled in the study.

The populations were similar with regard to ASA physical status; none were more than III (control 2.3 ± 0.6, lidocaine 2.2 ± 0.4; $P = 0.45$). The mean age of the patients was 64.4 yr (range 47–74 yr) with no significant difference between study groups.

A review of PACU records demonstrated no difference between groups in the initiation of ketorolac for postoperative pain. However, a 50% reduction in the demand for morphine was observed in the lidocaine-treated patients (Table 1). This reduced need for opioids in the PACU did not persist. Both groups required little postoperative morphine with no significant differences

in the lidocaine or control groups after discharge from the PACU. Ketorolac use was similar during hospitalization (Table 1).

Although both groups received the same amount of postoperative pain medication, patients in the lidocaine group were more comfortable. This was determined by totaling daily pain scores and comparing them between groups. This total pain score index summarizes the perioperative discomfort each patient experienced. Control patients treated with ketorolac and opioids as needed did well. Their total pain score index was 13.3 ± 7.7, and most were satisfied with their postoperative analgesia (Table 2). Lidocaine-treated patients had a two-thirds reduction in total pain score index (4.7 ± 4.0) compared with the control group. First flatus occurred approximately 33% faster in the lidocaine group (28.5. ± 13.4 h) compared with the control group (42.1 ± 16 h). This was a significant ($P < 0.01$) difference. An earlier return of bowel function was also present when the time to first bowel movement was examined. Lidocaine-treated patients had a bowel movement 61.8 ± 13.2 h after the completion of surgery. Control patients had bowel movements 73.9 ± 16.3 h after the completion of surgery. This was a significant difference ($P < 0.02$).

When time to hospital discharge was examined, the lidocaine-treated patients also fared better. Total hospitalization for lidocaine-treated patients was 4 ± 0.7 days, whereas control patients stayed 5.1 ± 2.9 days. This was of statistical significance ($P < 0.05$).

Discussion

Postoperative ileus can cause vomiting, nausea, and pain, and it adds to the expense of surgery (4,5). It is in the interest of patient care to minimize the duration of surgically induced ileus. Oral nutrition is often withheld from patients until they have demonstrated some return of bowel function, and many patients are reluctant to increase their activity when they are nauseated. Prolonged recumbency and inactivity can further prolong the duration of ileus (1). The return of normal bowel function is an important step in the recovery of most postoperative patients.

Systemic morphine and other opioids can impair colonic transport. Opioids applied to the neural axis also prolong intestinal transit time (8). The epidural administration of local anesthetics can reduce the amount of opioids needed for postoperative analgesia (4,5). Local anesthetics have a direct excitatory effect on intestinal smooth muscle (9,10), which may be the result of a blockade of inhibitory reflexes originating from the myenteric plexus (9).

Postoperative ileus is caused, in part, by the activation of several nerve reflexes. Inhibitory reflexes are activated as soon as the parietal peritoneum is entered (11). A spinal reflex originating in the gut and a peripheral reflex transmitted through the prevertebral ganglia have also been described (12).

Epidural anesthesia and analgesia used in conjunction with general anesthesia have the potential to attenuate postoperative ileus by blocking the spinal reflexes and the sympathetic innervation of bowel (2,4). This shifts the autonomic balance in favor of parasympathetics and increased motility.

A more rapid return of bowel function occurs when epidurally applied local anesthetics (specifically amides) are used intraoperatively and postoperatively, as opposed to systemic opioids (4). A few researchers failed to observe a difference, but in one of these studies, morphine was given with the epidural local (13), and in another, the epidural analgesia was continued only for the first postoperative day (7). This led to the suggestion that epidural analgesia be continued until the postoperative ileus resolves (typically two to three days after surgery) to reliably decrease ileus duration (4). Udassin et al.(14) experimentally demonstrated that epidural lidocaine (10 mg/kg) can decrease the duration of adynamic ileus in rats after ischemic injury. Control rats receiving epidural saline had prolonged ileus.

These studies suggest that epidural amide anesthetics can decrease the duration of postoperative ileus; however, systemic lidocaine can be a potent anesthetic. A plasma level of 3.2 μg/mL with 70% nitrous oxide is equal to 1.0 minimum alveolar anesthetic concentration in humans (15). This plasma level was seen in some of our patients and could explain the smaller dose of morphine required by lidocaine-treated patients in the PACU. Because systemic absorption occurs during the epidural administration of local anesthetics, the assumption that these drugs must be given epidurally to exert their effect remains untested. An epidural dose of 3 mg/kg results in a

Table 1. Analgesic Use

	Morphine (mg)		Ketorolac (mg)	
	PACU	Ward	PACU	Ward
Control	6.48 ± 5.97	7.7 ± 15.1	20.3 ± 15.6	143.3 ± 55.7
Lidocaine	3 ± 3.71	5.67 ± 8.1	20.8 ± 13.7	111.0 ± 77.3
P value	0.037	0.60	0.90	0.15

PACU = postanesthesia care unit.

Table 2. Bowel Function, Pain, and Hospital Stay

	First bowel movement (h)	First flatus (h)	Hospital stay (days)	Total pain score
Control	73.9 ± 16.3	42.1 ± 16	5.1 ± 2.18	13.25 ± 7.65
Lidocaine	61.8 ± 13.2	28.5 ± 13.4	4 ± .69	4.67 ± 3.94
P value	0.016	0.0073	0.043	0.0001

plasma lidocaine level of 1.02 ± 0.16 μg/mL (16) and demonstrates the need for appropriate control groups before an effect can be attributed to the epidural administration of an amide anesthetic.

Epidural anesthesia or analgesia does not block reflexes relayed through the prevertebral ganglia. These reflexes play an important role in postoperative ileus. Rimbäck et al. (9) demonstrated significantly faster return of bowel function in patients who received lidocaine infusions after cholecystectomy. Bowel function was assessed by propulsion of radiopaque makers, passage of flatus, and stool. Patients received a lidocaine infusion for 24 hours after surgery, and pain was treated with meperidine. Patients given lidocaine required significantly less opioids than controls and had shorter bowel transit times of the radiopaque markers. There was a trend toward faster bowel movements, but this difference was not significant. The authors concluded that the positive effects of IV lidocaine on bowel function could be due to the blockade of inhibitory sympathetic and paravertebral reflexes involved in postoperative ileus. Systemic lidocaine can significantly depress spike activity, amplitude, and conduction time in both myelinated A-δ and unmyelinated C fibers (9). Decerebrate cats experience a dose-related (lidocaine 3 μg–10 μg/mL) suppression of neuronal excitability in dorsal horn neurons from the effects of noxious thermal stimulation (17). This demonstrates the potent effects systemic lidocaine can have on the neural response to pain.

Our study differs significantly from that of Rimbäck et al. (9). We did not follow bowel function with radiopaque markers. Although first flatus and bowel movement can be voluntarily controlled by the anal sphincter and dependent on such variable as individual defecation habits, they are completely noninvasive markers of bowel recovery. Many surgeons use these landmarks in advancing diets. The passage of flatus decreases abdominal distention and improves patient comfort. The Rimbäck et al. (9) cholecystectomy population all had gallbladder dysfunction and were predominantly female. Our patients had no prior gastrointestinal disease and were exclusively male. In the interest of patient safety and clinical utility, lidocaine infusions were terminated one hour after surgery. Continuing the infusion would have required a prolonged PACU stay or transfer to a hospital bed from which the electrocardiogram could be constantly monitored. These requirements would make the use of IV lidocaine impractical because of increased expense and patient discomfort from prolonged monitoring. Our study size was larger than that of Rimbäck et al.(9), and rather than treating pain with an opioid, ketorolac was used when not contraindicated.

Ketorolac use presents a significant difference between this study and previous studies because it has antiinflammatory actions. In the rat model, ketorolac and other nonsteroidal antiinflammatory drugs can prevent ileus (18). In addition, lidocaine and the other amide anesthetics are potent antiinflammatory drugs (19). The inflammatory response has been suggested as a means of maintaining the abdominal reflexes responsible for the persistence of postoperative ileus. This can explain why the duration of postoperative ileus is not related to the duration of surgery (1). Peritoneal surgery is associated with the release of histamine, prostaglandins, and kinins (9), all of which are capable of activating afferent nerve fibers. Amide anesthetics can inhibit the migration of granulocytes (20) and their release of lysosomal enzymes (9). Like ketorolac, they are also inhibitors of prostaglandin synthesis. The antiinflammatory effect of the amides is prolonged and persists after serum levels have decreased (9). This may be why IV lidocaine exerts an effect on bowel function hours after the infusion is discontinued. By infusing lidocaine before the start of anesthetic or surgical manipulation, the full benefits of any preemptive analgesic or antiinflammatory effects are realized. A favorable interaction with ketorolac is also another possibility, because both treatment groups received ketorolac, but only those also receiving lidocaine had a significantly faster return of bowel function.

To evaluate whether IV lidocaine decreases the total pain experienced by patients undergoing retropubic radical prostatectomy, a total pain score index was created. This sum of daily pain scores clearly demonstrates that our patients treated with ketorolac did not experience severe pain and rarely needed morphine (Table 1). It also shows that patients treated with lidocaine and ketorolac experienced minimal discomfort and can have their pain controlled quite well without invasive analgesic techniques. This total pain score index can quantify the total discomfort that accompanies surgical treatments and the effectiveness of various analgesic protocols. Because these scores are additive, longer hospital stays can influence this variable. If longer stays are accompanied by a longer period of pain, then a pain score that reflects this increased discomfort is warranted. The total pain score index incorporates the duration of pain as well as the severity of pain and was developed for this study. Review of our data indicates that mean pain scores decreased steadily from Postoperative Days 1 to 3 (1.2 to 0.5 lidocaine group; 3.8 to 2.4 control group). On Postoperative Day 4, there was no significant difference in mean pain score between the lidocaine and control groups (0.9 and 0.4, respectively). This may have resulted from a disproportionate discharge of comfortable patients who received lidocaine or from the return of bowel function (less distention) to most of the control group. Differences in pain scores between groups were minimal after Postoperative Day 3. Therefore, the length of hospital stay did not significantly affect the values in the pain index. These total pain score indexes have convinced our urologists and anesthesiologists that the inherent risks (dural puncture 0.16%–1.3%, neurologic morbidity

0.01%–0.001%) (4), patient discomfort, and expense of epidural analgesia are not warranted for this procedure. The same conclusion was reached by the researchers of a comparative trial between patient-controlled analgesia and epidural hydromorphone in patients undergoing radical retropubic prostatectomy (21). We are currently examining whether this index can identify procedures in which patients will benefit from the use of more invasive analgesic techniques.

The plasma levels of lidocaine (1.3–3.7 μg/mL) were well below toxic levels (5 μg/mL) (22), which makes the need to obtain lidocaine levels for future patients questionable in this population. Lidocaine's toxicity is more pronounced in patients with congestive heart failure (23). Our inclusion criteria prevented such patients from entering the study. These low plasma levels of lidocaine may be the result of the expansion of the intravascular and extracellular spaces with crystalloid and the loss of blood and plasma during surgery.

The most impressive finding of our study is that systemic lidocaine can decrease the hospital stay. Early hospital discharge after retropubic radical prostatectomy can result in significant cost-savings. By reducing hospitalization from eight days to five days, Licht and Klein (24) showed a 32% decrease in hospital costs per patient. Earlier discharge was obtained by same-day admission, early ambulation, oral feeding, a quick change to oral pain medications, and prompt removal of surgical drains. Our urologists removed most drains on the third postoperative day. By that time, most lidocaine-treated patients had already passed flatus, had a bowel movement, ambulated, and advanced to a full diet. They were ready for discharge. Control patients were less likely to have passed flatus and had a bowel movement by the time the drains were removed. Blind surgeons felt it necessary to keep control patients in the hospital 1.1 days longer than those given lidocaine. The surgical drains of many patients undergoing retropubic radical prostatectomy are removed on the second postoperative day, making the early return of bowel function an even more important factor for early discharge.

In conclusion, in this study, we demonstrated that amide anesthetics given to attenuate postoperative ileus do not have to be administered epidurally to be beneficial. A lidocaine infusion started before induction and continued for one hour postoperatively can have an impressive effect on pain, bowel function, and hospital stay. This safe and inexpensive intervention in the operative management of patients undergoing radical retropubic prostatectomy decreases their discomfort while speeding the return of normal bowel function. This results in their earlier discharge from the hospital. Further study is warranted to examine whether similar results can be achieved in other surgical procedures, including those associated with significant opioid use or prolonged ileus.

References

1. Wilson JP. Postoperative motility of the large intestine in man. Gut 1975;16:89–92.
2. Smith J, Kelly KA, Weinshilboum RM. Pathophysiology of postoperative ileus. Arch Surg 1977;112:203–9.
3. Livingston E, Passaro E. Postoperative ileus. Dig Dis Sci 1990; 35:121–32.
4. Liu, S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia: their role in postoperative outcome. Anesthesiology 1995;82:1474–506.
5. Carpenter RL. Gastrointestinal benefits of regional anesthesia/analgesia. Reg Anesth 1996;21(Suppl):13–7.
6. Groudine S, Wilkins L. Epidural drugs also act systemically. Anesthesiology 1994;81:787.
7. Wallin G, Cassuto J, Högström S, et al. Failure of epidural anesthesia to prevent postoperative paralytic ileus. Anesthesiology 1986;65:292–7.
8. Wattwil M, Thorén T, Hennerdal S, Garvill JE. Epidural analgesia with bupivacaine reduces postoperative paralytic ileus after hysterectomy. Anesth Analg 1989;68:353–8.
9. Rimbäck G, Cassuto J, Tollesson PO. Treatment of postoperative paralytic ileus by intravenous lidocaine infusion. Anesth Analg 1990;70:414–9.
10. Biber B, Fara J. Intestinal motility increased by tetrodotoxin, lidocaine and procaine. Experientia 1973;29:551–2.
11. Summers RW, Lu CC. Approach to the patient with ileus and obstruction. In: Yamada T, ed. Textbook of gastroenterology. 2nd ed. Philadelphia: JB Lippincott, 1995:799–80.
12. Rimbäck G, Cassuto J, Faxén A, et al. Effect of intra-abdominal bupivacaine instillation on postoperative colonic motility. Gut 1986;27:170–5.
13. Hjorts NC, Neumann P, Frosig F, et al. A controlled study on the effect of epidural analgesia with local anaesthetics and morphine on morbidity after abdominal surgery. Acta Anaesthesiol Scand 1985;29:705–16.
14. Udassin R, Eimerl D, Schiffman J, Haskel Y. Epidural anesthesia accelerates the recovery of postischemic bowel motility in the rat. Anesthesiology 1994;80:832–6.
15. Himes RS Jr, DiFazio CA, Burney RG. Effects of lidocaine on the anesthetic requirements for nitrous oxide and halothane. Anesthesiology 1977;47:437–40.
16. Inagaki Y, Mashimo T, Kuzukawa A, et al. Epidural lidocaine delays arousal from isoflurane anesthesia. Anesth Analg 1994; 79:368–72.
17. Dohi S, Kitahata LM, Toyooka H, et al. An analgesic action of intravenously administered lidocaine on dorsal-horn neurons responding to noxious thermal stimulation. Anesthesiology 1979;51:123–6.
18. Cheng G, Cassissi C, Drexler PG, et al. Salsalate, morphine, and postoperative ileus. Am J Surg 1996;171:85–8.
19. Rimbäck G, Cassuto J, Wallin G, Westlander G. Inhibition of peritonitis by amide local anesthetics. Anesthesiology 1988;69: 881–6.
20. MacGregor RR, Thorner RE, Wright DM. Lidocaine inhibits granulocyte adherence and prevents granulocyte delivery to inflammatory sites. Blood 1980;56:203–9.
21. Liu S, Carpenter RL, Mulroy MF, et al. Intravenous *versus* epidural administration of hydromorphone: effects of analgesia and recovery after radical retropubic prostatectomy. Anesthesiology 1995;82:682–8.
22. Stoelting RK. Cardiac antidysrhythmic drugs. In: Stoelting RK, ed. Pharmacology and physiology in anesthetic practice. Philadelphia: JB Lippincott, 1987:327–8.
23. Calvin JE, Parrillo JE. Lidocaine and acute coronary care. Crit Care Med 1993;21:179–82.
24. Licht MR, Klein EA. Early hospital discharge after radical retropubic prostatectomy: impact on cost and complication rate. Urology 1994;44:700–4.