Randomized Control Trial

Usage of Intravenous Lidocaine Infusion with Enhanced Recovery Pathway in Patients Scheduled for Open Radical Cystectomy: A Randomized Trial

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Background: Intravenous lidocaine infusion (IVLI) reduces postoperative pain and hastens the return of bowel function.

Objectives: We aimed to compare the effects of adding lidocaine infusion to enhanced recovery pathway (ERP) on acute rehabilitation protocol.

Study Design: This study uses a double-blind, randomized design with allocation concealment in a 2-armed parallel group format among patients undergoing open radical cystectomy (RC).

Setting: The study was conducted at Assiut University Hospital, Asyut, Egypt. The study duration was March 2017 to July 2018.

Methods: After ethics committee approval, 111 patients, American Society of Anesthesiologists (ASA) physical status II-III, aged 45-65 years, scheduled for open RC with urinary diversion under an ERP, were randomly selected in a double-blind manner to receive IVLI 2 mg/minute for 4 hours or an equal volume of normal saline solution 0.9%. Postoperative pain scores, rescue analgesic consumption, times to return of bowel sounds, first flatus, first defecation, resuming of regular diet, length of hospital stay, in-hospital complications, and patient satisfaction were recorded.

Results: Patients in the lidocaine group experienced significantly lower pain scores after surgery at 6 hours ($P = 0.005$) and 12 hours ($P = 0.001$) at rest, and in the first 18 hours during mobilization ($P < 0.05$), with less paracetamol ($P = 0.04$) and meperidine ($P = 0.02$) consumption than in the control group. Between the lidocaine and the control group, mean times to return of bowel sounds (23.7 vs. 26.7 hours; $P = 0.001$), first flatus (76.5 vs. 86.5 hours; $P = 0.001$), first defecation (92.7 vs. 106.9 hours; $P = 0.001$) and resuming of regular diet (80.7 vs. 92.8 days; $P = 0.001$) were significantly shorter in the lidocaine group. Length of hospital stay, in-hospital complications, and patient satisfaction were similar in both groups.

Limitations: Limitations of this study include lack of previous research that compare the additive effects of IVLI to ERP in patients undergoing open RC. Also, the inability to measure the serum lidocaine concentration in our patients.

Conclusions: Adding IVLI to ERP improved postoperative analgesia and bowel function after open RC with urinary diversion.

Clinical trial registration: NCT03047057.

Key words: Lidocaine infusion, ileus, enhanced recovery pathway, acute rehabilitation, open radical cystectomy

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Radical cystectomy (RC) remains the gold-standard treatment for muscle invasive bladder cancer, or recurrent high-grade nonmuscle invasive bladder cancer (1). Despite the improvements in surgical technique and perioperative care, RC is an extremely morbid surgery with nearly 2% perioperative mortality, and 30%-64% morbidity at the centers of excellence, which are high for surgery with curative intent (1-3).

Postoperative ileus (POI) is a significant cause of morbidity following RC with an incidence range from 13% to 23% (2). POI has detrimental effects such as abdominal distension, nausea, vomiting, and pain, with the delay of bowel motility leading to prolonged hospital stay with increased costs (3-4). Pain relief is also important for facilitating acute rehabilitation after major abdominal surgery.

To date, there is no single drug that improves quality of life after surgery; instead, surgeons rely on a series of measures bundled together in a so called 'enhanced recovery pathway' (ERP) to minimize ileus duration and improve rehabilitation (5). ERP involves many therapeutic modalities and care approaches, such as early mobilization and nutrition, fluid restriction, prokinetic agents, minimally invasive surgery, epidural anesthesia, and analgesia (3). Intravenous (IV) lidocaine has anti-inflammatory, analgesic, and antihyperalgesic effects (6). It is a useful adjunct in ERP as when it was combined with ERP in open and laparoscopic colorectal surgeries it showed benefits in pain scores, opioid consumption, bowel function, and length of hospital stay (7).

We hypothesized that intravenous lidocaine infusion (IVLI) in the context of ERP could provide beneficial effects on acute rehabilitation in patients scheduled for open RC.

Methods

Patients

This prospective, double-blind, randomized controlled trial was approved by the Institutional Review Board of Faculty of Medicine, Assiut University (IRB no: 17300044), and was conducted in accordance with the Declaration of Helsinki after its registration at Clinical Trials.gov (NCT03047057). After providing written informed consent, 114 consecutive patients with bladder cancer were evaluated for eligibility between March 2017 and July 2018 (Fig. 1).

Patients with American Society of Anesthesiologists (ASA) physical status II-III undergoing pelvic lymph node dissection and open RC, with either an ileal conduit or an ileal orthotopic neobladder substitution for urinary diversion, were included. Exclusion criteria were known allergy to lidocaine, arrhythmia, coagulopathies, significant renal and hepatic dysfunctions, congested heart failure, inflammatory bowel disease, and chronic use of analgesics or corticosteroids.

Randomization

According to a computer-generated randomization table, patients were randomly assigned to Group I (lidocaine group) who received a continuous IVLI 2 mg/minute for 4 hours, and Group II (control group) who received a continuous IV infusion of normal saline solution 0.9% for 4 hours. Study drugs were prepared and diluted to a volume of 50 mL in an identical coded syringe. Patients, urologists, anesthesiologists, nurses, and data assessors were completely blinded to group assignment.

Preoperative and Intraoperative Care

Patient' preparations were standardized as ERP protocol. No antegrade bowel preparation was used, only patients were given 2 high enemas the evening before surgery. All patients were allowed to eat a regular diet up to the night before surgery.

During the preoperative visit, all patients were instructed on how to evaluate their pain intensity using a 10 cm visual analog scale (VAS) ranging from 0 to 10 cm, with zero signifying no pain and 10 signifying the worst imaginable pain. Also, to report their fatigue on a 10 cm VAS, with 0 cm signifying no fatigue and 10 cm signifying the worst imaginable fatigue (8).

Patients were premedicated with oral midazolam (7.5 mg) 30 minutes before induction of anesthesia. Surgery was standardized and performed with the patient in a 30° head-down position. Standard monitoring included continuous electrocardiography, pulse oximetry, invasive mean arterial pressure, central venous pressure, and tympanic temperature. An epidural catheter was inserted at the T9/T10 level, and a 0.25% bupivacaine infusion at a rate of 8 mL/hour was started until the end of the pelvic lymph node dissection, and ceased until closure of the abdominal wall.

General anesthesia was induced with IV fentanyl 1-2 μg/kg, propofol 2 mg/kg (including a single bolus of lidocaine 1.5 mg/kg), cisatracurium 0.15 mg/kg, and was maintained with isoflurane in oxygen and cisatracurium. Immediately after tracheal intubation, IV infusion of the studied solution was started and continued for

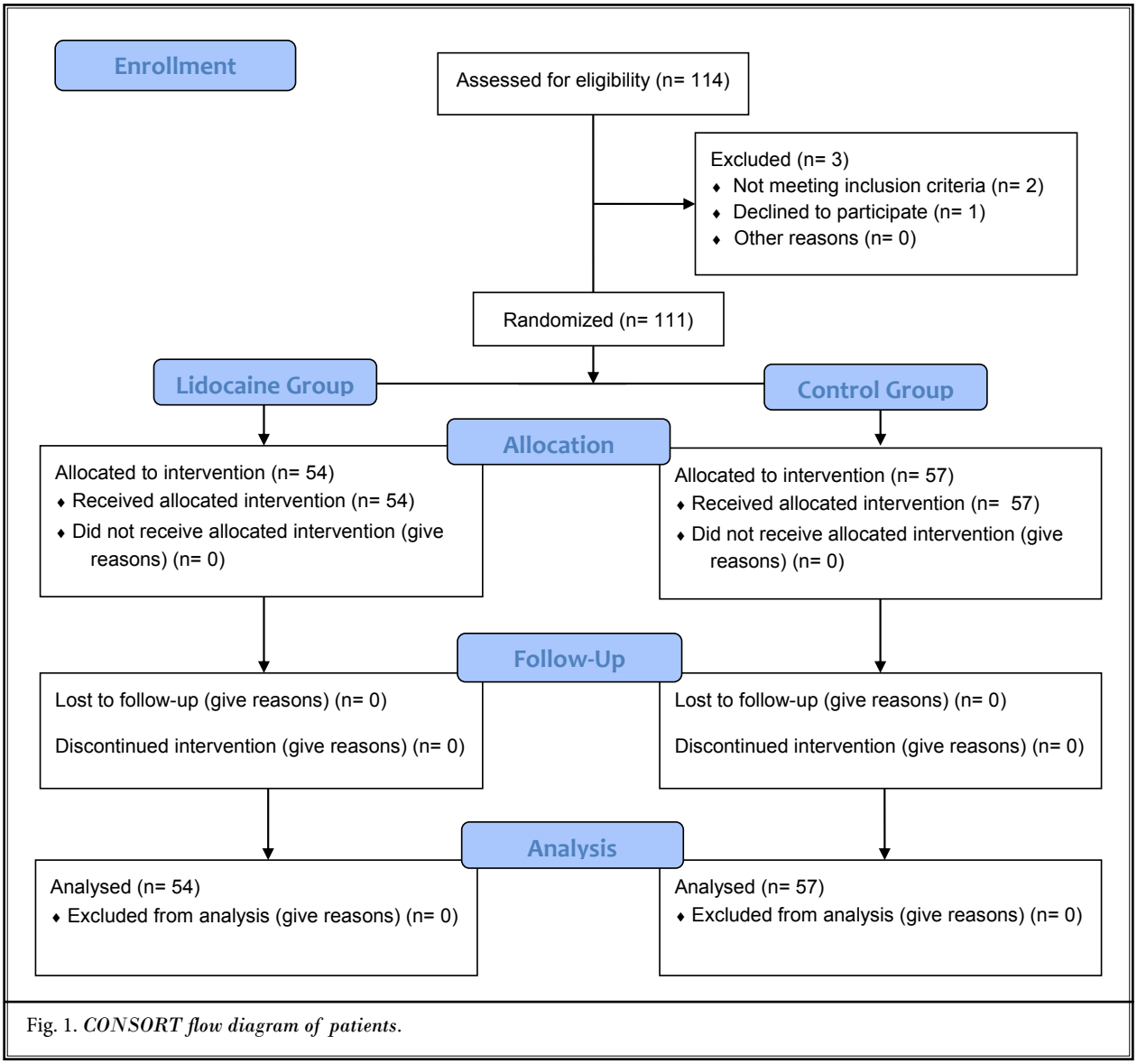

Fig. 1. *CONSORT flow diagram of patients.*

4 hours. Ventilation was mechanically controlled with a tidal volume of 8 mL/kg and a positive end-expiratory pressure of 5 mmHg. A balanced Ringer's solution was infused at the rate of 1 mL/kg/hour until the bladder was removed, followed by 3 mL/kg/hour until the end of surgery. If hypotension occurred (mean arterial pressure (MAP) < 60 mmHg) a bolus of 250 mL of balanced Ringer's solution was given, and in case of persistent hypotension this was repeated.

Blood loss of > 500 mL was replaced with an equal amount of balanced Ringer's solution. If hemoglobin values were < 8 g/dL (< 10 g/dL in coronary artery disease patients), packed erythrocyte units were transfused. Fresh frozen plasma transfusion was given if there was continuous excessive microvascular bleeding or if prothrombin time was > 1.5 times above normal (9).

Colloid solution was administrated if a MAP < 60 mmHg persisted after the previously described correction, and if severe metabolic acidosis (pH < 7.25) developed.

Postoperative Care

During closure of the abdominal wall, the epidural analgesia was reactivated with a mixture consisted of

bupivacaine 0.125% and epinephrine 2 µg/mL with an initial infusion rate of 8 mL an hour, to a maximum infusion rate of 15 mL an hour, and with additional bolus volumes of 5 mL (lockout time: 1 hour). After surgery patients were transferred to the intermediate care unit.

Pain scores were obtained at rest and during mobilization from the supine to the sitting position at 30 minutes, and 2, 6, 12, 18, 24, 48, and 72 hours postoperatively. IV paracetamol 1 g was administered as an analgesic supplement if the recorded VAS pain score was ≥ 5, and was repeated every 6 hours, if required. IV meperidine 100 mg was given as a rescue analgesic if the patient continued to have pain 30 minutes following paracetamol administration. Time to the first analgesic requirement and the total paracetamol and meperidine consumption during the first 72 hours after surgery were also recorded. Postoperative fatigue scores were also assessed at the same time points. The epidural catheter was removed on postoperative day 3, and oral pain medications were started after resumption of a regular diet. Postoperative hydration was composed of 1000 mL of balanced Ringer's solution and 500 mL of glucose 5% per day until resuming of normal diet intake (10). Nasogastric tube was not used during or after surgery unless indicated. Patients were stayed on the intermediate care unit for the first 7 postoperative days.

On postoperative day 1, active mobilization was started, patients could drink clear fluids and were encouraged to chew gum to hasten recovery of bowel function (11). Thereafter, a limited clear liquid diet was started, and patients resumed a regular diet after passage of flatus. Patients were checked hourly by auscultation for bowel sounds and were asked to note the time of first flatus and defecation and to inform the observing nurses accordingly. Nausea or vomiting were treated with antiemetic medication and recorded. Patients were evaluated for manifestation of lidocaine toxicity that included circumoral numbness, tinnitus, anxiety, headache, nausea and vomiting, seizure activity, and arrhythmias.

Body weight was measured daily. Perioperative antibiotic therapy was continued until removal of all drains and catheters. Low-molecular-weight heparin was started on the evening before surgery and maintained throughout the length of hospital stay. The moment the patient was admitted into the hospital was defined as the start of the hospitalization time (in all patients the day before surgery).

Discharge criteria from the hospital included tolerance of a regular diet, removal of all drains and catheters, and the ability to handle the urostomy bag or empty the ileal orthotopic neobladder spontaneously. On discharge, all patients were asked to rate their overall level of satisfaction with their postoperative recovery experience using a 1 to 5 scale. A score of 1 indicated very dissatisfied; 2, somewhat dissatisfied; 3, neither satisfied nor dissatisfied; 4, somewhat satisfied; and 5, completely satisfied. The length of hospital stay in days was recorded.

Statistical Analysis

Bowel function is the major objective limiting factor for hospital discharge (8). The primary outcome variable was the time to first defecation (hours) after open RC. Based on retrospective data from our institution in the same surgical population (mean time until first defecation 127.2 hours, standard deviation [SD] of 20.64 hours), a power analysis was done. For a calculated sample size of 47 patients in each group, the study was designed to have an 80% power ($\beta = 0.01$) to detect a difference of 12 hours between both groups at a 2-sided significance level of 5% ($\alpha = 0.05$) assuming an SD of 12 hours. This decrease of 12 hours was considered clinically relevant. Assuming a drop out of 20%, 57 patients per group were recruited.

The Kolmogorov-Smirnov test was applied to test the normality. The Mann-Whitney U test was used to compare continuous variables between the 2 groups. The chi-square test or Fisher exact test was used to compare categorical variables, as appropriate. A *P* value of < 0.05 was considered statistically significant.

Results

Of 114 patients, 111 fulfilled the eligibility criteria and were randomly selected and included in the final analysis (Fig. 1). There were no differences in demographic and clinical data between both groups (Table 1). Similarly, operative details and in-hospital complications were comparable between both groups (Table 2). Patients in Group I experienced significantly lower pain intensity at rest at 6 hours ($P = 0.005$) and 12 hours ($P = 0.001$), and during mobilization at 30 minutes ($P = 0.002$), 2 hours ($P = 0.005$), 6 hours ($P = 0.001$), 12 hours ($P = 0.001$) and at 18 hours ($P = 0.001$) postoperatively, compared to Group II (Fig. 2).

Time to first paracetamol administration was comparable between both groups at 6 hours postoperatively, with total paracetamol consumption in the first 72 hours postoperatively significantly lower in Group I compared to Group II [mean (SD) g; 8.7 (2.01) vs. 9.6

Table 1. *Demographic, clinical and clinico-pathological data of the patients.*

	Group I, Lidocaine group (n = 54)	Group II, Control group (n = 57)	*P*-value
Age (years)	60.5 (5.23)	59.2 (6.09)	0.337
Male/ Female, n (%)	47 (87)/ 7 (13)	49 (86)/ 8 (14)	0.869
Body weight (kg)	74.56 (3.5)	73.03 (3.5)	0.059
Mean BMI (kg/ m^2)	22.91(1.01)	23.15 (1.3)	0.277
Smoking History n (%)	40 (74.1)	44 (77.2)	0.702
ASA physical status score n (%) II III	 37 (68.5) 17 (31.5)	 38 (66.7) 19 (33.3)	0.835
Associated diseases n (%) Diabetes Hypertension COPD Cardiac	 8 (14.8) 10 (18.5) 8 (14.8) 3 (5.6)	 7 (12.3) 7 (12.3) 5 (8.8) 6 (10.5)	0.546
Preoperative Histopathology n (%) TCC SCC Adenocarcinoma	 37 (68.5) 12 (22.2) 5 (9.3)	 35 (61.4) 14 (24.6) 8 (14)	0.663
T stage n (%) T2 T3a T3b	 28 (51.9) 16 (29.6) 10 (18.5)	 19 (33.3) 25 (43.9) 13 (22.8)	0.135
Grade n (%) I II III	 10 (18.5) 13 (24.1) 31 (57.4)	 5 (8.8) 19 (33.3) 33 (57.9)	0.250
N stage n (%) N0 N1	 42 (77.8) 12 (22.2)	 35 (61.4) 22 (38.6)	0.061
Associated CIS n (%)	17 (31.5)	25 (43.9)	0.179
Neoadjuvant chemotherapy n (%)	41 (75.9)	39 (68.4)	0.378

Data are presented as mean (SD) or numbers (percentage). $P < 0.05$ was considered statistically significant. ASA: American Society of Anesthesiologists; BMI: body mass index; COPD: chronic obstructive pulmonary disease; TCC: transitional cell carcinoma; SCC: squamous cell carcinoma; T stage and N stage are pathological; and CIS: carcinoma in situ.

(2.09), respectively; $P = 0.04$]. A total of 13 (24.1%) patients in Group I and 25 (43.9%) patients in Group II required meperidine administration during the first 72 hours postoperatively ($P = 0.03$). The total dose of meperidine was significantly lower in Group I compared to Group II [mean (SD) mg; 35.2 (67.7) vs. 75.4 (98.7), respectively; $P = 0.02$].

Postoperative fatigue was significantly less in Group I than in Group II at 30 minutes, and 2, 6, and 12 hours postoperatively [$P = 0.008$, $P = 0.002$, $P = 0.004$, and $P = 0.02$; respectively] (Fig. 3).

Patients in Group I experienced significantly faster return of bowel sounds ($P = 0.001$) with shorter time to first flatus ($P = 0.001$), first defecation ($P = 0.001$), and to regular diet ($P = 0.001$) compared to Group II (Table 3).

One (1.9%) patient in Group I required nasogastric tube decompression, whereas in Group II, 4 (7%) patients required nasogastric tube decompression ($P = 0.190$) (Table 3). The mean length of hospital stay did not differ between groups ($P = 0.272$) (Table 2). No patients experienced signs or symptoms of lidocaine toxicity. Complete satisfaction with their postoperative recovery experience was noted to be higher in Group I (53.7%) compared to Group II (31.6%), but did not achieve statistical significance ($P = 0.055$) (Table 2).

Discussion

This study demonstrated that intraoperative IVLI 2 mg/minute for 4 hours added to ERP was an effective intervention that augmented postoperative analge-

Table 2. *Operative details, in-hospital complications and length of hospital stay in the 2 studied groups.*

	Group I, Lidocaine group (n = 54)	Group II, Control group (n = 57)	*P*-value
Operative time (h)	5.99 (0.5)	6.13 (0.43)	0.084
Positive lymph nodes n (%)	13 (24.1)	16 (28.1)	0.632
Type of diversion n (%) Ileal conduit Ileal orthotopic neobladder	 22 (40.7) 32 (59.3)	 22 (38.6) 35 (61.4)	0.817
Estimated blood loss (ml)	737.22 (83.14)	726.84 (113.17)	0.375
Fluid resuscitation (ml)	3794.44 (278.42)	3862.63 (211.53)	0.351
Length of hospital stay (days)	12.44 (1.66)	12.32 (2.2)	0.272
In-hospital Complications n (%) Nausea Vomiting Pneumonia Wound infection UTI DVT	 6 (11.1) 3 (5.6) 7 (13) 7 (13) 0 (0) 4 (7.4)	 8 (14) 14 (24.6) 5 (8.8) 7 (12.3) 0 (0) 5 (8.8)	0.088

Data are presented as mean (SD) or numbers (percentage). $P < 0.05$ was considered statistically significant. UTI: urinary tract infection; and DVT: deep venous thrombosis.

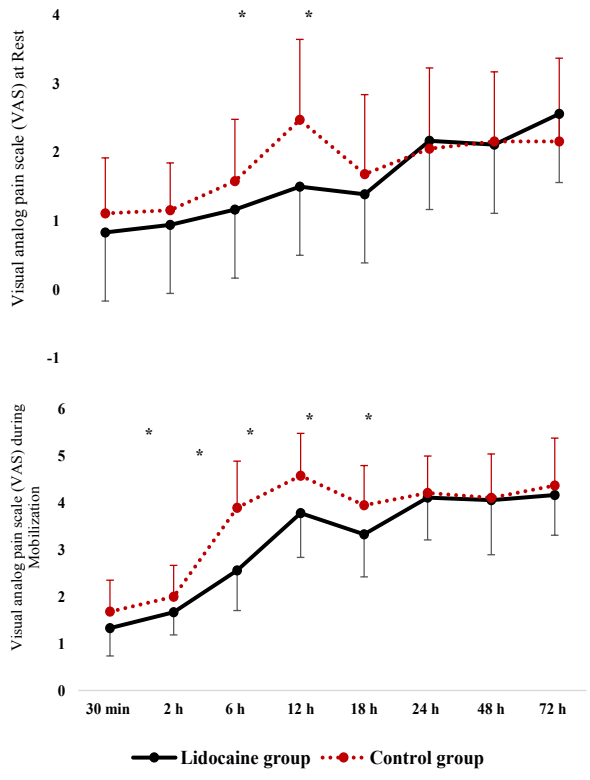

Fig. 2. *Changes in the postoperative pain scores on a 10 cm VAS, ranging from 0 to 10 cm, with zero signifying no pain and 10 signifying the worst imaginable pain both at rest and with mobilization during the first 72 hours after surgery in the 2 studied groups.* * $P < 0.05$.

sia, attenuated postoperative fatigue, enhanced the recovery of bowel function, and shortened the time to dietary intake. IVLI facilitated acute rehabilitation in patients undergoing open RC with urinary diversion with no change in length of hospital stay or in-hospital complications compared to ERP alone.

POI is one of the most common causes of morbidity following RC that leads to patient discomfort, prolonged hospital stay, and increased costs (11,12). POI is defined as "a transient stoppage of coordinated bowel motility following surgical intervention that prevents oral intake tolerance or effective transit of intestinal contents" (13). The mechanism of POI is multifactorial; it is neuronal in the acute phase and inflammatory in the late phase (6). A series of measures bundled have gathered in a so-called 'enhanced recovery pathway,' found to reduce time of care by > 30% and postoperative morbidities up to 50% (9) following RC through hastening gastrointestinal (GI) function recovery compared to traditional clinical guidelines (14).

One important modality in ERP during RC with urinary diversion is optimizing anesthesia to achieve excellent functional results and avoid failure while performing cystecto-

Table 3. *Time to return of bowel function and patient satisfaction in the 2 studied groups.*

	Group I, Lidocaine group (n = 54)	Group II, Control group (n = 57)	*P*-value
Time to return of bowel sounds (hrs)	23.7 (2.4)	26.7 (3.7)	0.001
Time to first flatus (hrs)	76.5 (15.2)	86.5 (13.9)	0.001
Time to first defecation (hrs)	92.7 (18.4)	106.9 (10.8)	0.001
Nasogastric tube use n (%)	1 (1.9)	4 (7)	0.190
Time to regular diet (hrs)	80.7 (19.3)	92.8 (13.4)	0.001
Patient satisfaction 1 = very dissatisfied 2 = somewhat dissatisfied 3 = neither satisfied nor dissatisfied 4 = somewhat satisfied 5 = completely satisfied	 0 (0) 0 (0) 5 (9.3) 20 (37) 29 (53.7)	 0 (0) 1 (1.8) 13 (22.8) 25 (43.9) 18 (31.6)	0.055

Data are presented as mean (SD) or numbers (percentage). $P < 0.05$ was considered statistically significant.

my with orthotopic bladder substitutions, reduce blood loss, and lower postoperative complications (15). These goals can be achieved mainly through the use of thoracic epidural analgesia (TEA) combined with minimal opioid administration intra- and postoperatively (16).

Although it is better to start TEA during RC with ileal orthotopic bladder substitutions immediately after anesthesia induction to spare intraoperative opioids and to reduce the surgical stress response, it is important, however, to stop the epidural infusion of local anesthetics (bupivacaine 0.25%) at the end of the pelvic lymph node dissection to avoid small bowel spasticity induced by the sympathicolysis and intact vagal activity during TEA. This avoids resection of a too long bowel segment for the ileal reservoir, often performed 60-90 minutes later (15).

Lidocaine is an amide local anesthetic that provides a simple, safe, economic, and effective strategy that affects many important clinical outcomes, such as ileus, wound-healing, analgesia, coagulation, and postoperative cognitive dysfunction (17).

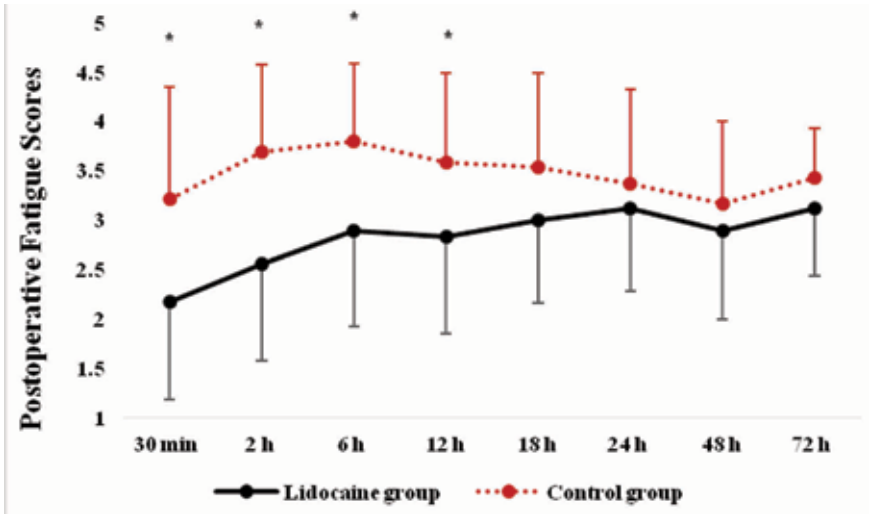

Fig. 3. *Changes in the postoperative fatigue scores on a 10 cm VAS, with 0 cm signifying no fatigue and 10 cm signifying the worst imaginable fatigue during the first 72 hours after surgery in the 2 studied groups. * $P < 0.05$.*

IVLI has been tried for many years to coax the GI system back to functioning and has recently gained renewed enthusiasm. The effects of perioperative IVLI on bowel recovery following major surgeries has been investigated using different infusion durations and dissimilar outcome measurement criteria (18-20). It is considered as a cost-effective strategy after abdominal surgery, as it improves patient rehabilitation and shortens hospital stay (21).

Elhafz et al (6), found that IVLI significantly facilitates return of bowel function after laparoscopic colorectal surgery. Herroeder et al (22), demonstrated that

IVLI (2 mg/minute) started immediately after tracheal intubation until 4 hours postoperatively had accelerated return of bowel function and shortened length of hospital stay significantly following open colorectal surgery.

In line with the former studies that used longer infusion durations across a variety of surgical populations (6,17,21,22), Grady et al (18) found that the intraoperative IVLI at 2 mg/kg/hour, with an average duration of 57 minutes, during laparoscopic gynecologic surgery accelerates the return of first flatus with no difference in time to first bowel movement compared to control group. They thought that IV lidocaine, given as a single dose or as a continuous infusion, is beneficial in the preservation of GI motility via blocking systemic inflammatory responses to surgical stress (18).

As inflammation has an important role in POI, IV local anesthetics may perform their beneficial effects on enhancing bowel recovery through targeting several steps in the inflammatory cascade that occur with surgery in a time-dependent manner (23). Perioperative lidocaine significantly attenuates the increase of complement and proinflammatory cytokines, such as IL-8 and IL-6, that have an important role in maintaining POI. Additionally, IVLI directly inhibits the sympathetic mesenteric plexus and/or reduces the opioid consumption postoperatively. However, further mechanisms of action may exist (6).

In this study, patients who received IVLI added to ERP achieved earlier return of bowel function and resumption of diet with no change in hospital stay or in-hospital complications compared to patients who received ERP alone. Several reasons might be responsible for why the hospital length of stay was not improved in the lidocaine group. First, ERP was used in both groups. Second, administration of lidocaine was limited to 4 hours only. Third, this study was powered for observing differences in mean time until first defecation, so study groups might have been simply too small to detect a difference in hospital length of stay. Finally, our studied patients were discharged after removal of all drains and catheters, as most of our patients were from far rural areas where the availability of health care for such kinds of advanced surgery are difficult to obtain.

IVLI has analgesic, antihyperalgesic, and anti-inflammatory properties (6,24). The intraoperative use of lidocaine significantly decreases postoperative pain, however, when administered postoperatively, it will not provide effective analgesia (25).

The analgesic effect of IVLI, compared to placebo or usual care, was evident at early time points (1-4 hours) and at intermediate time points (24 hours) after surgery, however, no evidence was found at later time points (48 hours). Analgesia was most obvious at early time points in patients undergoing laparoscopic and open abdominal surgery, with no evidence of effect found in those undergoing other surgeries (17).

Vigneault et al (26) have reported in their meta-analysis that at 6 hours postoperatively, IVLI decreased pain both at rest and during movement and morphine consumption. Also, it reduced time to bowel recovery and hospital stay. They concluded that abdominal surgery was strongly associated with its benefit and advised that dose and safety of IVLI should be considered before recommending its use.

In this study, IVLI reduced pain scores in the early postoperative period that was significant at 6 and 12 hours at rest and at the first 18 hours during mobilization, as well as analgesic consumption compared to the control group. The analgesic effect that extended after IVLI was stopped could be explained by the prevention of spinal or peripheral hypersensitivity, or both (8). Also, fatigue scores were significantly attenuated in the early postoperative period after IVLI discontinuation. This could be explained by the improved analgesia with reduced opioid consumption, and may be attributed to the subjective sense of heightened alertness observed in normal volunteers during local anesthetics infusion (8).

Similarly, Kaba et al (8) found that the use of IVLI in patients scheduled for laparoscopic colectomy provided significant relief of postoperative pain and fatigue, faster return of bowel function, lower opioid consumption, and hospital stay.

The analgesic effect of lidocaine could be explained that when it is used systemically, the acetylcholine levels at the cerebrospinal fluid will be increased leading to exacerbation of pain sensitivity inhibition via descending inhibitory pain pathways. Other mechanisms include its systemic anti-inflammatory activity, its connection with M3 muscarinic, glycine receptor inhibition, and endogenous opioid releasing (25).

The most appropriate dose of IV lidocaine for treating postoperative pain in a more efficient way is not yet defined. However, low doses of IV lidocaine between 1.5 to 3 mg/kg/hour (plasmatic levels < 5 μg/mL) decrease pain postoperatively with less adverse effects and without influence at nerve conduction (8,25). In this study, the lidocaine dose used was within this range and it provided better analgesia.

When lidocaine concentration increases in systemic circulation (> 5 µg/mL), signs and symptoms of its effects over central nervous and cardiovascular systems will be manifested (25). However, no local toxicity, other than a single episode of transient arrhythmia, was observed in patients who received IVLI to improve postoperative recovery after abdominal surgery (21). In our trial, none of the studied patients had experienced arrhythmia.

This study was limited first by the lack of previous research that compared the additive effects of IVLI to ERP in patients undergoing open RC, with lack of information regarding the most effective dose and duration for IVLI. We cannot determine if the improved bowel function is merely because of decreased opioid use or because of the direct anti-inflammatory effects of lidocaine. To evaluate this, a propensity matched group in terms of opioid consumption is needed that might be beyond the power of this study. Finally, there was an inability to measure the serum lidocaine concentration in our patients.

Conclusions

IVLI combined with ERP in patients undergoing open RC improved time to bowel recovery, postoperative analgesia, and fatigue, with no differences in length of hospital stay or in adverse events compared to ERP alone.

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