Original Article

Effect of preemptive intramuscular diclofenac on minimal effective-dose bupivacaine saddle block for minor perianal surgeries

ABSTRACT

Background: Preemptive analgesics are commonly used to increase analgesic efficacy and patient satisfaction. The aim of this study was to evaluate the preemptive analgesic effect of intramuscular diclofenac on minimal effective dose spinal anesthesia for perianal surgeries.

Materials and Methods: Fifty patients ASA I&II were divided randomly into two groups, control group (GC *N* = 25) and Diclofenac group (GD *N* = 25), both groups received saddle block with 5% hyperbaric bupivacaine 0.5 mL (2.5 mg). Thirty minutes before the saddle block, patients in GD received 75 mg (3 mL) diclofenac intramuscularly, whereas patients in GC received 3 mL saline intramuscularly. The differences in the time for the first analgesic request, postoperative analgesic consumption as well as, visual analog scale, were our primary outcomes.

Results: Fifty patients (25 in each group) undergoing perianal surgery completed the study successfully. The time to the first request of analgesia was significantly longer in GD 511.8 (108.07) min. compared to the GC 179.56 (49.24) min with *P* = 0.00001, as well as the total consumption of rescue analgesic (tramadol hydrochloride) was significantly less in GD 66 (23.8) mg compared to 104 (28.5) mg in the GC with *P* = 0.00001.

Conclusion: Preemptive intramuscular diclofenac sodium with minimal dose bupivacaine saddle block significantly minimized the postoperative analgesic consumption and delayed the first analgesia request after perianal surgery.

Key words: Diclofenac, preemptive analgesia, saddle block

Introduction

Effective control of postoperative pain is an issue that has been repeatedly emphasized and has received an increasing amount of attention in the past few years.[1,2] Opioids, despite their side effects, are still the main cornerstone in managing acute postoperative pain.[3] Preemptive analgesia refers to the administration of effective analgesia prior to surgical trauma. The main mechanism of preemptive analgesia is desensitization of the central nervous system and prevention of pain before its onset.[4] Non-opioid preemptive analgesics are commonly used to increase

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analgesic efficacy and patient satisfaction as well as to reduce opioid consumption and side effects. The saddle block is selective spinal anesthesia that is commonly used for perianal surgeries.[5-8]

We previously performed a prospective up-down sequential allocation study to evaluate the minimum effective dose of hyperbaric bupivacaine that is needed for inducing a satisfactory and reliable saddle block for perianal surgeries (area supplied by the most caudal spinal nerve roots.[9] Although the block produced zero motor block in the lower limbs (thus allowing early ambulation), its rapid sensory recovery resulted in an early request of analgesia and increased opioid consumption. In this prospective, randomized, double-blinded, placebo-controlled clinical trial. We hypothesized that a single dose of IM diclofenac administered before spinal anesthesia, would decrease postoperative pain, as well as delay and reduce postoperative analgesic requirement in patients undergoing minor perianal surgeries under minimal effective dose bupivacaine saddle block.

Materials and Methods

After approval from the Institutional Review Board of Standing Committee for Research Ethics on Living Creatures (SCLERC), Imam Abdurrahman Bin Faisal University on the 1st of January 2019 with IRB number (IRB-2019-01-187), registration at clinical trials.gov (NCT04849468), and obtaining informed written consent from each patient, 50 patients with ASA physical status I & II were enrolled in this prospective, controlled, randomized blinded study (25 in each group). All patients were scheduled for elective outpatient perianal surgery in the lithotomy position. Patients were excluded from the study if they have contraindications to regional anesthesia, bleeding disorders, morbid obesity, mental health problems, have a known history of allergy to amide local anesthetic drugs, on analgesic medication or psychotropic drugs, as well as if they have a language barrier, or unwilling to participate.

All patients were fasting for over 6 h. In the operating room holding area and approximately 30 min before saddle block, the concept of the "Visual Analog Scale" (VAS) and the details about the data to be collected were introduced to the patient. Using a computer-generated randomization schedule, the patients were randomly allocated into two groups; GD which received 75 mg (3 mL) IM Diclofenac in a 5-mL syringe, and GC which received 3 mL IM saline in a similar 5-mL syringe. The studied drugs were prepared immediately before injection by an anesthesiologist blinded to the study methodology and administered by a second blinded anesthesiologist.

In the operating room, an intravenous 20 gauge (G) catheter was inserted, and the patient was connected to standard monitors (ECG, noninvasive blood pressure, and pulse oximetry). Under aseptic conditions, the dural puncture was performed by staff-grade anesthesiologists, using a standard midline approach in the sitting position at the level of L3–L4 or L4–L5 intervertebral space, with a 25-G Whitacre needle with the bevel directed caudally. 2.5 mg (0.5 mL) of hyperbaric bupivacaine (Marcaine Spinal Heavy: Astra Zeneca, Lund, Sweden), which was prepared in a 1 mL tuberculin syringe, was injected. All patients remained in a sitting position for 10 min. Patients were asked whether they feel any alteration in their motor power. If not, patients were asked to position themselves without help for surgery in the lithotomy position. All patients received oxygen 5 L/min via a face mask throughout the procedure. Immediately before surgery, the sensory block level was tested by using a toothless surgical clamp that was applied gently, starting at the anal orifice and proceeding radially in different diagonal directions. Motor block was tested with the "Modified Bromage Scale" (0: no motor block, 1: able to flex the ankle and bend knees, 2: able to flex ankle, 3: full motor block). A successful block was defined as one that is sufficient to proceed with the surgery without any supplementation (intravenous analgesic, local anesthetic infiltration, or general anesthesia). Block assessment and clinical follow-up of the patients were also performed by a third blinded anesthesiologist.

The following data were recorded; patient demographic data, duration of anesthesia, duration of surgery, level of sensory and degree of motor block, immediately before surgery, at the end of the surgery, and every 30 minutes thereafter until the block has resolved. Heart rate and noninvasive blood pressure were documented at 5-minute intervals in the operating theater and the Post-Anesthesia Care Unit (PACU). In addition, the time to ambulation, time to first voiding, and time to patient discharge to home was also recorded. Postoperative pain was assessed by the "Visual Analogue Scale," where "0 signifies no pain, and 10 signifies the worst pain possible", every 30 minutes in PACU then at 4, 8, 12, and 24 h from the time of the dural puncture.

Patients with a VAS score of >4 or more were allowed to receive oral tramadol (50 mg). Patients were followed-up through a phone call to note their VAS, any possible postoperative complications (post-dural puncture headache, transient neurologic symptoms, Nausea & vomiting or backache), the time to the patient's first request for analgesia, as well as the total amount of the rescue analgesic consumption (Tramadol) over 24 h. Patient and surgeon satisfaction were reported using a four-point scale "0—

Poor, 1—Good, 2—Very good, 3–Excellent" on the first postoperative day and then 10 days later.

Statistical analysis

Assuming difference between the mean time to the first analgesic request between the GD and the GC is 90 min, and a pooled standard deviation of 85 min., the study would require a sample size of 30 patients (15 patients for each group), to achieve a power of 80% and a level of significance of 5%. However, we recruited 50 patients (25 in each group) in this study to compensate for any possible exclusion as well as to strengthen our statistical analysis.

Demographic data, duration of surgery, Time to the first analgesic request, total analgesic consumption, VAS, time to ambulation, first voiding time, and time to discharge were analyzed by using the unpaired Student's *t* test. Although the Mann–Whitney *U* test was used to compare the level of sensory block and satisfaction scores between the two groups. Gender ratio, type of surgery, and the differences in the incidence of complications were analyzed by Fisher's exact or Chi-square tests. A value of $P < 0.05$ was considered statistically significant. Analysis was performed using Statistical software version 7.0 for Windows (Statsoft).

Results

All recruited patients in both groups completed the study with a total of 25 patients in each group. All patients in both groups had a successful block and uneventfully completed their surgeries. Patient demographic and surgical data in both groups were statistically comparable [Table 1].

The time to the first request of analgesia was significantly longer in GD 511.8 (108.07) min compared to the GC 179.56 (49.24) min with $P = 0.00001$, as well as the total consumption of rescue analgesic (tramadol) was significantly less 66 (23.8) mg compared to 104 (28.5) mg in the GC with $P = 0.00001$ [Table 2].

The visual analog score was zero in both groups during PACU time and insignificantly different at 4 hr. postoperatively ($P = 0.167$). It was significantly low at 12 h and 24 h in the GD compared to the GC with $P = 0.00001$ and 0.026, respectively. However, VAS was significantly low at 8 h postoperatively in the GC compared to the GD with $P = 0.008$ [Figure 1].

The block characteristics in both groups were nearly the same, showed a restricted sensory block to a maximum of S3 as well as there was no motor block (Bromage Score = 0) and all patients were able to move and positioning themselves pre-and post-operatively [Table 3]. All patients and surgeons were satisfied with the anesthetic technique. Although the time to ambulation was comparable in both groups, the time to void as well as the time to discharge home were significantly earlier in the GD [Table 3].

Apart from three patients in each group who developed Backache, none of the patients in both groups developed PDPH, urine retention, or other relevant postoperative complications.

Table 1: Demographics and surgical data

	GC	GD	*P*
Age (ys)	39.92 (13.49)	39.28 (12.68)	0.43
Height (cm)	167.32 (9.48)	169 (9.09)	0.26
Weight (Kg)	81.32 (12)	86.32 (13.72)	0.08
Gender (male:female)	13 :12	15 :10	0.56
Duration of surgery (minutes)	31.84 (8.07)	30.84 (7.02)	0.32
Type of surgery			
Hemorrhoidectomy	8	5	0.33
Fistulectomy	10	12	0.56
Sphincterotomy	5	5	1
Fisher	3	3	1

Values are mean±standard deviation, GC, control group, GD, diclofenac group

Table 2: Time to the first request of analgesia and consumption of analgesic

	GC	GD	*P*
Time to first analgesia	179.56 (49.24)	511.8 (108.07)	0.00001
Total consumption of analgesia	104 (28.5)	66 (23.8)	0.00001

Values are mean (standard deviation), GC, control group, GD, diclofenac group.

Table 3: Block characteristics

		GC	GD	*P*
Level of sensory block	Before surgery	3.6 (0.5)	3.68 (0.47)	0.63
	After surgery	3.56 (0.5)	3.44 (0.5)	0.47
Modified Bromage Score	Before surgery	0	0	0
	After surgery	0	0	0
Maximum blocked dermatomes		3.48 (0.5)	3.32 (0.47)	
Time to ambulation		89.2 (10.58)	90.4 (10.11)	0.34
Time to void		128.4 (9.6)	116.32 (15.22)	0.0007
Time to discharge		137.48 (10.03)	128.16 (14.47)	0.01

Values are mean (standard deviation), GC, control group, GD, diclofenac group.

Discussion

Our study showed that pre-emptive analgesia using intramuscular diclofenac significantly delayed time to the first request of analgesia, and decreased consumption of

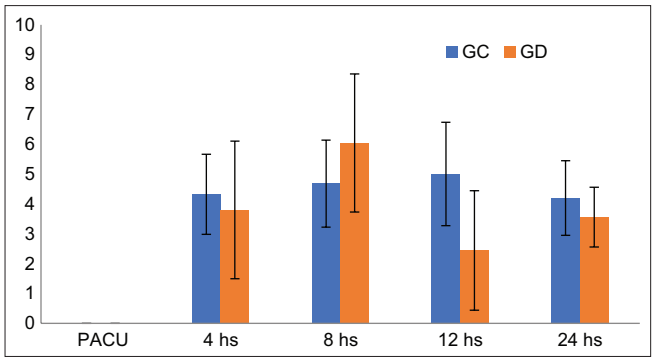

Figure 1: Visual Analogue Score. GC=Control group and GD=Diclofenac group

rescue analgesic in patients undergoing perianal surgery using minimal-dose bupivacaine saddle block.

To achieve the concept of pre-emptive analgesia, it should start before the surgical stimulus aiming at blockade of the afferent pain impulses, thus preventing acute postoperative pain as well as inhibiting central nervous system modulation, which is the leading cause for the development of chronic pain.

Despite the conflict between systemic reviews of several clinical trials regarding the benefit of pre-emptive analgesia, some randomized clinical trials supporting the beneficial effect of pre-emptive analgesia may well amount to statistically significant outcomes, especially if future studies investigating pre-emptive analgesia avoid weaknesses that have been noticed with older studies by using reasonable sample size, focusing on clinically relevant outcomes, and concentrate on specific types of surgeries as well.[9]

Our study is unique, as it is the first study to use diclofenac sodium as pre-emptive analgesia before mini-dose saddle block with a satisfactory outcome regarding duration and quality of analgesia. We designed our present study based on our previous study,[10] where we used modified Dixon's up and down method to determine the minimal effective dose of hyperbaric bupivacaine required to achieve a successful saddle block in patients undergoing peri-anal surgery. We concluded that ED_{50} of intrathecal hyperbaric bupivacaine required for reliable saddle block was 1.9 mg [95% confidence interval (CI) = 1.7–2.1 mg). The advantages of this dose were short duration, early mobility, patient and surgeon satisfaction as well as early discharge. However, the short duration of analgesia was the main disadvantage of this dose. This drawback inspired us to use a pre-emptive analgesic to overcome it in our present study.

The visual analog score was significantly low at 12 h and 24 h postoperatively in the GD compared to the GC. On the contrary, the VAS at 8 hours was significantly lower in the GC compared to the GD, which could be explained by the early request of the rescue analgesia by the majority of the patients in the GC before 8 h postoperatively (the assigned time for VAS measurement). Time to void and discharge to home was significantly earlier in the GD compared to the GC which may be explained by a better analgesia profile in the GD.

Diclofenac sodium has been used effectively for pre-emptive analgesia as shown by several investigators.[11-13] The effect of diclofenac sodium is explained by inhibition of cyclooxygenase enzyme which reduces the production of prostaglandins and thus prevents the central nervous system from being in a state of hyperexcitability known as central sensitization thereby attenuate the response of the peripheral and central nervous system to surgical trauma and pain stimuli.

We used intramuscular diclofenac as it is one of the strongest NSAI analgesics, it has a better bioavailability profile compared to the oral route, as well as it is given as a single shot and does not need pre-induction insertion of an intravenous line or necessitate time (30 min.) to be given as IV infusion (as recommended) which may disrupt the operating room schedule.

Our results are consistent with several previous studies that used pre-emptive analgesia to prolong the analgesic effect of spinal block after different type of surgeries. Usha *et al*.[14] found that pre-emptive use of gabapentin and pregabalin significantly prolonged the duration of analgesia and decreases consumption of rescue analgesia in patients undergoing gynecological surgeries under spinal anesthesia. Wang *et al*.[15] found that pre-emptive oxycodone analgesia prolonged the time to first request of analgesia and full recovery from the sensory block in patients undergoing TURP under low dose spinal anesthesia. Reddy *et al*.[16] reported a higher level of sensory block, significant prolongation in time to first analgesic request, and higher sedation scores after the use of intravenous dexmedetomidine as pre-emptive analgesia in patients undergoing orthopedic lower limb surgeries under the intrathecal block.

The design of our present study is superior to the previously mentioned studies as, it combines the advantages of both minimal dose spinal block (zero motor block with early ambulation and discharge) and the pre-emptive analgesia (increased the duration of the block, delayed the first request of rescue analgesic and decreased postoperative analgesic consumption).

Limitations

Most of the data were collected postoperatively through a phone call, whereas the patients were at home. This could be prejudiced by the patient's memory and their general mood at the time of the call. However, we tried to avoid this by giving each patient a data report sheet with a timetable to register the requested data at the proper and accurate time.

Conclusion

Intramuscular diclofenac sodium can be used safely and effectively as a pre-emptive analgesic before mini-dose saddle block, as it greatly minimizes the postoperative analgesic consumption and delays the first analgesic request after perianal surgeries. Moreover, It has no sedative or tranquilizer effect which is in favor of early discharge and day-case surgeries.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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