Original Article

Effects on heamodynamics and postoperative analgesic requirement after major abdominal surgeries: comparison between continuous epidural infusion of 0.2% ropivacaine and 0.125% bupivacaine

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ABSTRACT

Background: *Major abdominal surgeries induce neuro-humoral changes responsible for postoperative pain, various organ dysfunctions and prolong hospitalization. Inadequate pain therapy prolongs the hospital stay and increases the mortality rates. Epidural analgesia confers excellent pain relief leading to a substantial reduction in the surgical stress response. Type 2 diabetic patients have multiple comorbidities with cardiovascular complication and they are more vulnerable to pain. The purpose of this study was to compare the effect of ropivacaine and bupivacaine with fentanyl on haemodynamic and postoperative analgesic requirement of type 2 diabetic patients for major abdominal surgeries.*

Methods: *This prospective, double blind, randomized study were conducted in sixty patients who were going to be operated for major abdominal surgeries from 1st January 2022 to 30th June 2022 at the department of Anaesthesiology and Surgical ICU, BIRDEM General Hospital, Shahbagh, Dhaka, Bangladesh. The study population was randomly divided into group R & group B with 30 patients in each group. Every patient received an epidural block in the sitting position at the T_{8-9} or T_{9-10} level via 18 G Touhy needle. Each patient in group R received 0. 2% ropivacaine with 2 µgm. fentanyl / ml solution through epidural catheter @ 6 - 14 ml / hr. and group B received 0.125% bupivacaine with 2 µgm. fentanyl / ml solution through epidural catheter@ 6 - 14 ml / hr.*

Results: *Peroperative mean systolic blood pressure, mean diastolic blood pressure, mean arterial blood pressure and heart rate were more stable in group R but statistically not significant ($p>0.05$) and in post operative period group R patients had significantly lower mean visual analogue scale (VAS) score than group B which was statistically significant ($p<0.05$) but additional analgesic requirement were slightly higher in group B which was not statistically significant ($p>0.05$).*

Conclusion*: The results of our study suggest that epidural analgesia using ropivacaine 0.2% infusion is more effective than bupivacaine when used for postoperative pain relief and ropivacaine can be used as a safe alternative to bupivacaine for major abdominal surgeries.*

Key words: *bupivacaine, epidural, major abdominal surgery, ropivacaine, type 2 diabetes mellitus.*

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INTRODUCTION

Postoperative pain is one of the most common issues following major abdominal operation. Insufficient pain therapy prolongs the hospital stay and raises the mortality rates.[1] Poorly controlled pain after surgeries is strongly associated with development of chronic pain.[2] The type of surgery plays an important role in severity of postoperative pain. Age, sex, psychological factors or pharmacological factors also play an important role for postoperative pain.[3]

Effective control of postoperative pain blunts autonomic, somatic and endocrine responses and results in early recovery, mobilization and discharge from hospital. The current concept for postoperative pain management is multimodal approach. Continuous epidural infusion of a low concentration of local anaesthetic, alone or in combination with opioids, provides sustained profound analgesia with minimal sedation after major surgical procedures.[4,5] Postoperative epidural infusion of bupivacaine is more effective than parenteral opioids, especially during mobilization and may reduce either postoperative morbidity or length of hospital stay.[6-10]

The pain therapy after abdominal and thoracic surgeries is adequately successful by using continuous epidural infusion.[11] Epidural bupivacaine has been used extensively for providing adequate postoperative pain relief in patients undergoing major abdominal surgeries. Now a day a new long-acting local anaesthetic drug ropivacaine has increasingly replaced bupivacaine for the said purpose because of its similar analgesic properties, lesser motor blockade, greater selectivity for sensory blockade and cardiac stability.[12,13]

Ropivacaine causes reversible inhibition of sodium ion influx and thereby blocks impulse conduction in nerve fibres.[14] This action is potentiated by dose-dependent inhibition of potassium channels.[15] Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres; therefore, it has selective action on the pain-transmitting A ä and C nerves rather than Aâ fibres, which are involved in motor function. As the ropivacaine is less lipophilic than bupivacaine and that, together with its stereo selective properties[16] contributes to ropivacaine having a significantly higher threshold for cardiotoxicity and central nervous system (CNS) toxicity than bupivacaine in animals and healthy volunteers.[17] The lower lipophilicity of ropivacaine versus bupivacaine correlated with the lesser cardio-depressant effects of both ropivacaine isomers than of the bupivacaine isomers in animal studies.[16]

Diabetes mellitus specially type 2 is the most common endocrine abnormality encountered in surgical patients and is associated with increased perioperative morbidity and mortality mainly due to the cardiovascular and renal complication. Surgery in the presence of general anaesthesia produces a diabetogenic response. Surgical stress leads to reproducible physiological, metabolic and hormonal responses, characterized by on altered carbohydrate metabolism, a net loss of protein and an increased lipolysis. They are due to an increased secretion of catecholamines, adrenocrtichotrophic hormone (ACTH), cortisol and cytokines.[18] Cortisol prolongs and amplifies the hyperglycaemic effects of catecholamines by stimulating gluconeogenesis, and by increasing insulin resistance.[19] The increase in blood glucose in diabetic patients during the first hours of a stressful event is closely related to an increase in catecholamines. So, for diabetic patients, it is a great concern during major abdominal operation to control perioperative stress response and adequate pain management with less side effects local anesthetic agent. Ropivacaine is the pure S (-) - enantiomer of racemic bupivacaine. R(+) and S(-) enantiomers of local anaesthetics have been demonstrated to have different affinity for different ion channels of sodium, potassium and calcium; this results in a significant reduction in CNS and cardiac toxicity (cardiotoxicity) of the S(-) enantiomer as compared with the R(+)enantiomer.[20] So, ropivacaine could be a better alternative of bupivacaine for type 2 diabetic patient for the management of perioperative stress response and analgesia. Our goal in this study was to compare the ropivacaine-fentanyl solution with bupivacaine-fentanyl solution in type 2 diabetic patients to determine the perioperative haemodynamic response and analgesic requirement by recording visual Analogue scale (VAS) score, noninvasive blood pressure and continuous ECG monitoring.

METHODS

This randomized double-blind study was conducted from 1st January 2022 to 30th June 2022 at the department of Anaesthesiology and Surgical ICU, BIRDEM General Hospital, Shahbagh, Dhaka, Bangladesh. After

Institutional Review Board (IRB) (No. BIRDEM/IRB/2021/266) approval and informed written consent, a total of 60 adult patients with type 2 diabetes mellitus with ASA physical status II and III scheduled for various elective major abdominal surgeries under combined anaesthesia (general plus epidural) were consecutively enrolled in this study. They were divided into two groups 30 in each group randomly allocated by envelop method where Group R (n=30) received 0.2% ropivacaine with 2 µgm. fentanyl / ml solution through epidural catheter @ 6 - 14 ml / hr and Group B (n=30) received 0.125% bupivacaine with 2 µgm. fentanyl / ml solution through epidural catheter@ 6 - 14 ml / hr. The study solutions for infusion were prepared by a Diploma in Anaesthesia (DA) 2nd year student who was not involved in the clinical care of the patient. Both patient and anaesthesiologist caring for recording parameters were blinded to the group of study solution. All patients were reassured and the anaesthetic procedure was explained on the day before the operation. Intravenous access was established in all patients in the operating room with base line arterial blood pressure (non-invasively) and heart rate obtained. Every patient received an epidural block in the sitting position at the T8-9 or T9-10 level via 18 G Touhy needle. After epidural insertion every patient received taste dose of 3 ml 2% lignocaine with adrenaline (1:1000 dilution). After confirming every patient received a bolus dose of 7 ml of 0.2% ropivacaine for group R and 0.125% bupivacaine for group B, each patient received general anaesthesia with induction dose of inj.Fentanyl 2 microgram/kg, inj. Propofol 2 mg/kg and muscle relaxant inj.Atracurium 0.5 mg/kg. After induction, general anaesthesia was maintained by 60% N_2O and 40% O_2 and continuous infusion of propofol @ 4 mg/kg/hr – 6 mg/kg/hr. An incremental dose of muscle relaxant inj. Atracurium 1/4th of initial dose was given every 20 minutes interval. Each patient in group R received 0.2% ropivacaine with 2 µgm. fentanyl / ml solution through epidural catheter @ 6 - 14 ml / hr. and group B received 0.125% bupivacaine with 2 µgm. fentanyl / ml solution through epidural catheter@ 6- 14 ml / hr just after induction of general anaesthesia. The infusion dose was adjusted by targeting the mean arterial blood pressure about 60 – 90 mm Hg throughout the peroperative and post operative period.

Monitoring of heart rates (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MABP) were recorded peroperatively 15 minute after infusion (t1), 30 minute after infusion (t2), 45 minute after infusion (t3) 60 minute after infusion (t4) 90 minute after infusion (t5), 120 minute after infusion (t6), 150 minute after infusion (t7), 180 minute after infusion (t8), 210 minute after infusion (t9) and 240 minute after infusion (t10). In post-operative ward patients were asked to mark their pain level based on 0-10 cm visual analogue scale (VAS) score as soon as patient fully responded to verbal command and recovered from full cognitive ability. VAS scores were recorded at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour at post-operative ward after end of surgery. Total analgesia consumed in the first 24 hours was recorded. In postoperative period inj. tramadol hydrochloride 100 mg IV was used as a rescue analgesic according to patient requirement. Duration of surgery and duration of anesthesia were also recorded.

Data processing

Data were collected using a pretested observational checklist. Data collectors were one Diploma in Anaesthesia (DA) 2nd year student and one DA 1st year student and they were supervised by principal investigator. The data were reviewed from completed structured data retrieval form to ensure completeness and quality of data. After data quality was assured, forms were collected and assigned consecutive number (code) for ease of data entry. The data was entered using the Epi-Info version 7.0 and clean-up has been made to check accuracy, consistency and errors identified were corrected and finally transported to SPSS V 20 for analysis.

Shapiro Wilk test with p value <0.05 for non-normally distributed data and histogram with bell-shaped were used to test for normal distributions of data while homogeneity of variance were assessed using Levene's test for equality of variance. Numeric data were described in terms of mean ± SD for symmetric data like age, HR and median (inter-quartile range) for asymmetric numeric data like 24 hour VAS score and total analgesia consumption. A comparison of numerical variables between the study groups was done using the Student's t test for independent samples with parametric distribution and Mann-Whitney test for non-parametric distribution. For comparing categorical data, Chi-square

test was performed. P values less than 0.05 were considered statistically significant.

RESULTS

Total patients were 60, among them 42 were male and 18 were female. ASA categorization (II, III) of group R were 20/10 and of group B were 22/8 patients. Demographic data for each group was similar (Table I). in 40 patients epidural catheter were inserted at the level of T8/9 out of which 18 patients were group R and 22 two patients were group B. In 20 patients, epidural catheter were inserted at the level of T9/10 out of which 12 patients were in group R and 8 patients were in group B.

According to the operative procedure, 6 patients (10%) underwent Whipple's procedure, 18 patients (30%) underwent triple bypass, 15 (25%) patients underwent biliary reconstruction, 12 patients (20%) underwent anterior resection, 6 patients (10%) underwent right hemicolectomy and 3 patients (5%) underwent left hemicolectomy (Table II). The mean duration of surgery for Whipple's procedure 4.10 hour, for triple bypass 3.30 hour, for biliary reconstruction 3.20 hour, for anterior resection 3.40 hour, for right hemicolectomy 2.50 hour and for left hemicolectomy 2.10 hour (Table II). The mean duration of anaesthesia for Whipple's procedure 4.20 hour, for triple bypass 3.40 hour, for biliary reconstruction 3.25 hour, for anterior resection 3.50 hour, for right hemicolectomy 2.55 hour and for left hemicolectomy 2.20 hour (Table II).

Peroperative mean HR (Table III), mean SBP (Figure 1), mean DBP (Figure 2) and MABP (Figure 3) were low in ropivacaine group than bupivacaine group but statistically not significant (P > 0.05).

The mean values of postoperative visual analogue scale (VAS) pain scores were lower in the ropivacaine group in comparison to the bupivacaine group, which was statistically significant at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour ($p<0.05$) (Figure 4). Additional rescue analgesic inj. Tramadol hydrochloride 100 mg IV were needed for fourteen patients in group B where as eight patients were needed in group R. No cases of cardiac depression or central nervous system toxicity occurred by local anaesthetic.

Table I. Demographic variables of study subjects

Variables	Group-R (n=30)	Group-B (n=30)	p value
Age (years)	45.8 ± 7.5	49.5 ± 8.7	0.066^{ns} *
Sex (M/F)	22/8	20/10	0.74^{ns} **
Weight (kg)	62.30±8.44	63.67±7.13	0.54^{ns} *
ASA (II/III)	20/10	22/8	0.26^{ns} **

All values were presented as mean± SD or in frequencies. Data were analyzed using unpaired * student t-test & ** Chi-square test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

Table II. Distribution of the patients by type and duration of operation (N=60)

Types of operation	Frequency	Duration of surgery (hours) Mean±SD	Duration of anaesthesia (hours) Mean±SD
Whipple's procedure	6 (10%)	4.10±1.12	4.20±1.10
Triple bypass	18(30%)	3.30±0.85	3.40±0.82
Biliary reconstruction	15(25%)	3.20±0.75	3.25±0.72
Anterior resection	12(20%)	3.40±0.65	3.50±0.62
Right hemicolectomy	6(10%)	2.50±0.63	2.55±0.61
Left hemicolectomy	3(5%)	2.10±0.23	2.20±0.21
Total	60(100%)	3.10±0.70	3.18±0.54

All values were presented as mean± SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant

Table III. Comparison of mean heart rate peroperative period of the study respondents (N=60)

Time	Group-R (n=30) Mean±SD	Group-B (n=30) Mean±SD	p value
t1	78.6±5.4	80.2±2.3	0.09^{ns}
t2	70.6±5.2	72.3±6.2	0.09^{ns}
t3	70.4±6.1	73.0±3.8	0.23^{ns}
t4	69.1±4.5	71.5±4.2	0.52^{ns}
t5	68.6±4.2	69.5±2.6	0.18^{ns}
t6	68.5±6.2	70.1±4.5	0.65^{ns}
t7	68.2±7.2	69.5±4.1	0.50^{ns}
t8	67.8±7.7	68.9±5.0	0.18^{ns}
t9	67.5±5.0	69.7±4.3	0.55^{ns}
t10	67.4±5.0	69.2±5.2	0.81^{ns}

All values were presented as mean± SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant, t1-10 = different data recording time)

The mean heart rate at different time in peroperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05).

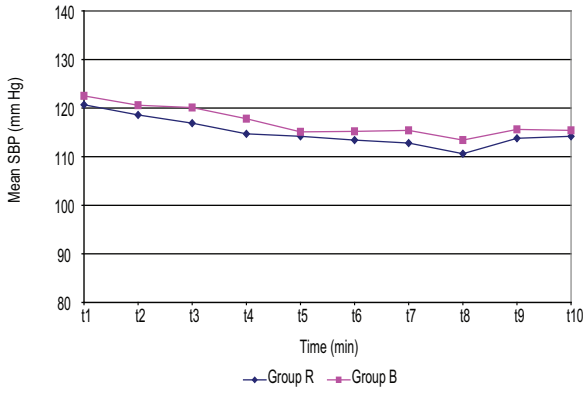

Figure 1. Line diagram showing mean systolic blood pressure (SBP) in two groups

The mean systolic blood pressure at different time in peroperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05).

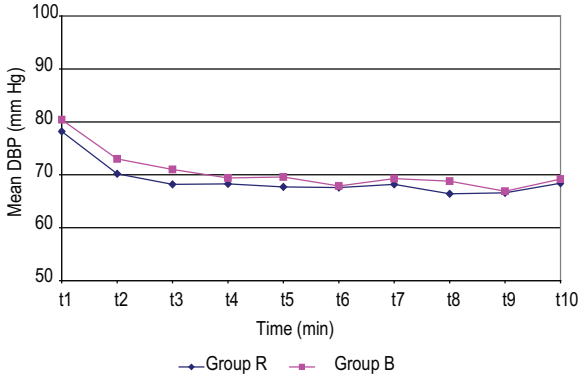

Figure 2. Line diagram showing mean diastolic blood pressure (DBP) in two groups

The mean diastolic blood pressure at different time in peroperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05).

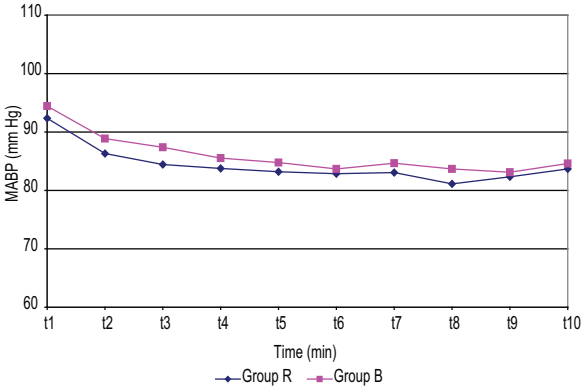

Figure 3. Line diagram showing peroperative mean arterial blood pressure (MABP) in two groups

The mean arterial blood pressure at different time in peroperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05).

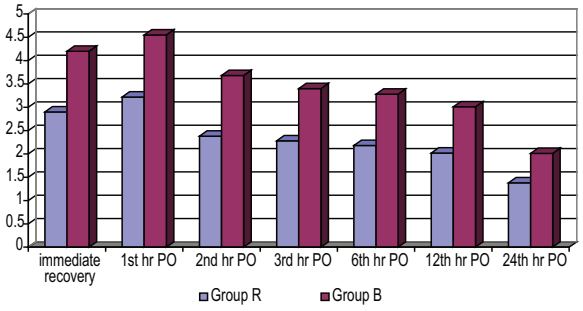

Figure 4. Bar diagram showing postoperative VAS score in two groups

The mean VAS scores at postoperative period between two groups. Statistical significant were observed in between groups ($p < 0.05$). P value < 0.001 was considered highly significant. Mann-Whitney test.

DISCUSSION

For effective postoperative epidural analgesia, adding opioid to local anaesthetic causes synergistic action in substantia gelatinosa at the dorsal horn of the spinal cord, [21] enhances duration and intensity of analgesia and also reduces LA dose and related side effects such as sympathetic and motor blockade.[22]

Epidural analgesia is considered as the gold standard analgesic technique for major abdominal surgeries. This strategy has the potential to provide complete analgesia and it is particularly effective at optimizing functional pain relief, thus improving patient satisfaction and postoperative outcome. The postoperative surgical stress response could contribute to various organ dysfunctions in susceptible individuals, thus leading to a difficult and prolonged recovery and rehabilitation.[23] There is a common consensus that a reduction in the stress response is followed by a reduced postoperative major morbidity and improved surgical outcome.[24, 25]

It has been postulated that pain relief represents an effective method to reduce surgical stress response, since afferent neural stimuli and activation of autonomic nervous system together with other reflexes by pain serve as a major release mechanism of the endocrine and metabolic responses.[23] Thus, one of the beneficial effects of epidural analgesia results from obtunding the postoperative stress response by provision of optimal analgesia. Many reported randomized studies with different analgesia regimens have been combined in meta-analysis; further more often there is no distinction between thoracic and lumber epidural blockade or various techniques of administration, facts that limit the interpretation of these findings.[26, 27] The use of well-documented physiological advantages of epidural analgesia in such a postoperative care program leads to decrease of morbidity across major abdominal procedures and significantly improves the quality of postoperative recovery.[28, 29]

In our study we observed that hemodynamic parameters mean HR, systolic BP, diastolic BP, mean MAP were more decrease in ropivacaine group compared to bupivacaine group but was not statistically significant ($p<0.05$). Berti et al. reported similar observations in patients undergoing major abdominal surgeries while comparing a ropivacaine 0.2 % versus bupivacaine 0.125 % in combination with fentanyl 2 µg/ml.[30]

The present study also showed that the mean VAS score at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour postoperative ward were lower in ropivacaine group compared to bupivacaine group ($p<0.05$) and the total analgesic consumption were also lower in ropivacaine group in compared to bupivacaine group which were statistically significant ($p = <0.001$). Jagtap et al. reported similar findings when comparing ropivacaine-fentanyl versus bupivacaine-fentanyl for intrathecal use in lower limb surgeries.[31] Our results are similar to those of Berti et al., as they also reported higher supplemental analgesic consumption in patients receiving combination of 0.125 % bupivacaine and 2 µg/ml fentanyl as compared to those who received 0.2 % ropivacaine.[32] Similarly, Kanai A et al. also reported least VAS scores in patients receiving 0.2% ropivacaine with 2.2µg/ml fentanyl in their study.[33]

Conclusion

We conclude that ropivacaine offers more haemodynamic stability with significantly superior postoperative analgesia through epidural infusion with reduced rescue analgesic dose consumption. Hence it can be recommended as a safer choice of epidural local anaesthetic for postoperative analgesia following major abdominal surgeries for type 2 diabetic patient.

Limitations

Our study had few limitations. A larger sample size, assessment of degree of ambulation and a longer period of assessment of upto 48 hours would have helped us delineate further advantages of ropivacaine fentanyl epidural infusions for postoperative pain relief.

Authors' contribution: All authors paneled the research, collected & analyzed darta, read and approved the final manuscript for submission.

Conflicts of interest: Nothing to declare.

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