Efficacy of port-site infiltration with ropivacaine alone versus ropivacaine with fentanyl for postoperative analgesia in patients undergoing laparoscopic procedures

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Abstract

Background and aims: Wound infiltration as a pre-emptive measure to relieve post-operative pain is a common practice following laparoscopic procedures. The addition of adjuvants like opioids to local anesthetics can facilitate the prolongation of postoperative analgesia. Our primary aim was to compare the analgesic efficacy of peri-portal infiltration of Ropivacaine alone versus Ropivacaine with Fentanyl in patients undergoing laparoscopic operations.

Methods: The study was conducted on 80 ASA physical status I and II patients, aged 18 to 65 years, undergoing surgical procedures under general anesthesia. Group R was infiltrated with Ropivacaine (0.5%) (18ml+2ml saline) while in Group RF, Ropivacaine(18ml) with Fentanyl 2ml (100µg)] was infiltrated around ports, before wound closure. At the end of the surgery, one of our study drug solutions was infiltrated, to which the patient as well as the assessor were blinded. Postoperative pain was assessed by the VAS (visual analog scale) score. Injection Tramadol 100mg was given as a rescue analgesic if the VAS score was ≥ 3. Student's t-test and Fischer's exact test were applied for continuous and categorical variables; Kruskal Wallis and Mann Whitney U test for nonparametric data. The entire statistical analysis was done using STATA 13[STATA CORP. TEXAS, USA] software.

Results: The mean duration of analgesia was significantly longer in group RF, with a requirement of fewer doses of rescue analgesics, compared to group R.

Conclusion: The addition of Fentanyl to Ropivacaine for periportal infiltration was found to be superior to Ropivacaine alone in providing effective postoperative analgesia as well as reducing the requirement of rescue analgesics.

Keywords: Ropivacaine, Fentanyl, Post-operative analgesia, Port site infiltration, VAS (Visual Analogue Scale), Laparoscopic procedures.

Introduction

Laparoscopic surgeries though less invasive than open surgeries, are responsible for considerable post-operative discomfort in many patients, leading to increased length of stay[1]. Severe pain following laparoscopy defeats the very purpose of minimally invasive surgery. Therefore, it is imperative to adopt strategies to minimize post-operative pain[2].

The surgical wound is a major source of post-operative pain that necessitates local anesthetic injection at the site[3]. Wound infiltration with local anesthetic is an important part of multimodal analgesia and has been recently incorporated into enhanced recovery programs. It blocks pain transmission from nociceptive afferents directly from the wound surface and also decreases local inflammation following

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injury[4,5,6]. Although single-dose local anesthetic infiltration is effective but has a short duration of action[7,8].

Bupivacaine and Ropivacaine are the most commonly used local anesthetics for wound infiltration in present-day practice. Ropivacaine is a long-acting local anesthetic drug belonging to the amino amide group. Being less lipophilic than Bupivacaine it has decreased potential for the central nervous system and cardiac toxicity[9]. For this reason, it is being widely used for postoperative analgesia.

The addition of adjuvants to local anesthetics like opioids, vasoconstrictors, and α2 agonists can facilitate the prolongation of postoperative analgesia. Several studies have evaluated the role of fentanyl as an adjuvant to local anesthetics in neuraxial and peripheral nerve blocks as well as in local infiltration in open surgical procedures[10,11]. However, there is limited evidence regarding the effectiveness of adjuvant use for port site infiltration in laparoscopic surgery, when early patient discharge is planned. Fentanyl is an effective adjuvant with local anesthetics and enhances the quality and duration of analgesia. It selectively binds to μ-receptors in the central nervous system (CNS) mimicking the effect of endogenous opiates. Recent research has shown that opioid agonists have peripheral action as well[12].

Therefore, this prospective double-blind randomized study was an attempt to evaluate the efficacy of fentanyl as an adjuvant with Ropivacaine for port-site infiltration, in laparoscopic operations, as a part of the multimodal analgesic regimen[13].

Method:

This randomized double-blind study was conducted on 80 patients of ASA physical status I and II, aged 18-65 years, undergoing laparoscopic surgeries. Patients with known drug allergies to study drugs, history of seizures, chronic pain syndromes, and placement of drain during surgery or conversion to open procedure were excluded from the study. After obtaining approval from the ethical committee, pre-operative informed consent for participation was obtained from each patient. The Visual Analogue Scale (VAS) for the description of post-operative pain was also explained to all patients.

All patients were given tablet Alprazolam 0.25mg orally, the night before surgery and advised to remain nil orally for fluids and solids, at least 6 hours before surgery.

On arrival in the operation theatre, each patient's baseline heart rate, non-invasive blood pressure (NIBP), and oxygen saturation were recorded and noted. Subcutaneous 0.5ml local anesthetic was given as a test dose to check local anesthetic sensitivity.

No pre-emptive analgesics were administered. All patients were premedicated with Midazolam 0.03mg/kg, Ondansetron 0.08mg/kg and Glycopyrrolate 0.004mg/kg intravenously. General anesthesia was induced with Thiopentone 3-5mg/kg, Fentanyl 2μ/kg, and Atracurium 0.5mg/kg. For intraoperative analgesia, Fentanyl 1 μ/kg was repeated hourly. Anesthesia was maintained with Sevoflurane and air in an oxygen mixture (1:1) and infusion of Atracurium at 0.3 mg/kg/hr. Pneumoperitoneum was established using a Verres needle, and also, two or three trocars (5 and 10mm) were used.

All operations were performed by surgeons experienced in laparoscopy and carried out under general anesthesia performed by the same team.

Patients were randomly allocated by computer-generated random number tables to one of two groups comprising forty patients each. Eighty opaque sealed envelopes containing the code numbers for group R and group RF were prepared and were opened just before infiltration. The patient as well as the assessor were blinded to the study drug solution. The study drug solution was infiltrated subcutaneously, deep muscularly as well as in and around the incision line.

Group R: received local infiltration with 0.5% Ropivacaine 18ml + 2ml normal saline for all ports.

Group RF: received local infiltration with 0.5% Ropivacaine 18 ml + 2ml Fentanyl (100μg) for all ports.

Sample size with justification

The sample size was calculated on the basis of a previous study by Bhandari G et al[22], which evaluated the analgesic effect of two different doses of Fentanyl in combination with Bupivacaine for surgical site infiltration in modified radical mastoidectomy, considering mean change in VAS score to be 0.80 with a pooled standard deviation (SD) of 0.60. Assuming 50% difference between the two groups, the sample size was calculated at 80% power and 5% alpha error, using the following formula:

$$N = \frac{2 \times (Z_{1-\alpha/2} + Z_{1-\beta})^2 \times SD^2}{(d-\delta)^2}$$

$$N = \frac{2 \times (1.96+0.84)^2 \times (0.60)^2}{(0.80-0.40)^2}$$

$$N = 35.25$$

Where N = Required sample size in each group

$Z_{1-\alpha/2}$ = 1.96 at α = 0.05

$Z_{1-\beta}$ = 0.84 at β = 0.1

SD = Pooled standard deviation from the previous study

d = Real difference between the groups

δ =Clinically acceptable margin of error

Considering dropouts due to either conversion to open procedure, patient refusal or peri-operative adverse event, a sample size of forty was taken in each group.

Results:

The Mean duration of analgesia in the patients' given Ropivacaine was 325.88±84.76 min i.e. approximately 5.43 hours while in those given Ropivacaine with Fentanyl, it was 544.63±88.19 min i.e. approximately 9.07 hours. As evident, the difference between the two groups was highly significant with a p value<0.0001.

Mean doses of rescue analgesia in the groups R and RF. The number of doses rescues analgesic administered was significantly higher in Group R than in Group RF (p value<0.05) patients in the R group received 3 rescue analgesics (87%) whereas, in the RF group, the maximum number of patients received 1 dose of rescue analgesia (62.5%). The difference in the total doses of rescue analgesia between the groups was highly statistically significant. (p-value<0.05)

The Mean VAS score in the patients receiving Ropivacaine was gradually increasing from 0 hrs and reached a peak around 4 hrs which was statistically significantly higher than the VAS score (p value<0.05) in the patients receiving Ropivacaine with Fentanyl. The rescue analgesia was given to the patients at this point after which the VAS score gradually decreased. In the patients receiving Ropivacaine with Fentanyl, the peak of VAS score was observed at around 8 hrs which was again statistically significantly higher than those receiving only Ropivacaine (p value<0.05). This might be due to the rescue analgesic effect in the Ropivacaine group. At this point in time, the patients were given the rescue analgesia in Ropivacaine with Fentanyl group leading to a decrease in VAS score.

Sedation score was observed in both the groups postoperatively between 0 to 30 min. However, the sedation score in Ropivacaine with fentanyl was statistically significantly higher than that in the plain Ropivacaine group

Heart Rate (HR) In the R group, it was seen that the HR was gradually increasing till the peak reached 4 hrs which was significantly higher (p-value <0.05) than that in the RF group at this point of time. In the RF group, the peak was observed at 8 hrs and it was significantly higher (p value <0.05) than that in the R group. The surge in the HR was following the increased intensity of the pain felt by the patients in both groups

Discussion

Wound infiltration is a simple method of providing postoperative analgesia that can be easily administered by the surgeon or assistant just before incision or wound closure[7] improving postoperative analgesia, it results in lower opioid consumption and faster patient recovery. The addition of fentanyl to local anesthetic enhances the duration and quality of the block[14].

We compared the analgesic efficacy of peri-portal infiltration of Ropivacaine alone versus Ropivacaine with Fentanyl in patients undergoing Laparoscopic operations, in terms of postoperative analgesia and requirement of rescue analgesics. Post-extubation sedation scores of patients, as well as hemodynamic parameters, were observed in both groups[15,16,17,18].

In our study mean VAS score[19,20] in patients receiving Ropivacaine alone peaked around 4 hours, while it was 8 hours in patients receiving Ropivacaine with fentanyl (p-value <0.05). Shahi KS et al[21] conducted a study on port site infiltration of Bupivacaine in combination with Fentanyl (50 and 100µg) in laparoscopic cholecystectomy. Patients receiving Bupivacaine with 100µg of Fentanyl did not require any rescue analgesic, which was statistically significant at 4 and 6 hours when patients in other groups complained of pain with a higher VAS score. It was comparable to our findings.

Bhandari G et al[22] conducted a similar study with Bupivacaine and Fentanyl in two different doses (50µg and 100µg) for wound infiltration in modified radical mastoidectomy. VAS scores remained low and no patient in either group required rescue analgesia. However, VAS scores were significantly lower in the second group. Naithani U et al[23] studied the efficacy of wound infiltration using Bupivacaine versus Ropivacaine using Fentanyl (25µg) for postoperative analgesia in abdominal surgeries under spinal anesthesia. All patients in their study received Diclofenac 75mg 12 hourly. The highest VAS score in the group receiving Bupivacaine with Fentanyl was achieved at 6 hours as in our study.

Variation in Heart Rate (HR) was directly proportional to the pain felt by the patients in the individual groups, maximum at 4hrs and 8hrs for Ropivacaine and Ropivacaine with Fentanyl respectively. Chander R et al[24] observed the highest HR at 6hrs in the Bupivacaine group while it was highest at 12 hours

with Bupivacaine and Fentanyl when patients felt maximum pain following abdominal surgery, comparable to our findings. In patients undergoing cesarean section, Bhardwaj S et al[25] observed a gradual postoperative decline in HR with Ropivacaine and Ropivacaine with Dexmedetomidine infiltration, but the latter showed a greater decrease in HR.

In our study, patients in both groups experienced mild sedation postoperatively between 0 to 30 min (evaluated by Ramsay sedation score[26]) Sedation in Ropivacaine with fentanyl group was significantly higher than in the plain Ropivacaine group in the post-operative period for the initial 2 hours. Bhandari et al did not observe sedation in any of their patients receiving fentanyl (100 µg) infiltration.

Drugs used for wound infiltration should have good efficacy, long duration, and lower systemic toxicity. The addition of adjuvants to LA improves the quality and duration of LA and reduces the supplemental dose requirement of analgesics. Ropivacaine being less cardiac and neurotoxic than Bupivacaine is preferred when large volumes are needed. Opioids were initially thought to have only a central action, but recent research have shown that opioid agonists have peripheral action as well. The peripheral action is mediated through λ as well as κ receptors located on primary afferent veins[17].

Fentanyl administration may be associated with sedation, nausea, vomiting, and bradycardia. However, no significant hemodynamic effects were observed in our study. None of the patients in either group developed hypotension or bradycardia. The lower HR in Group RF could be either due to hemodynamic effects of fentanyl or might indicate better pain control in this group. Mild Sedation was observed in Group RF for the first 2 hours postoperatively.

Owing to decreased tramadol consumption, none of the patients had nausea and vomiting. Patients in Group RF were more satisfied than those in Group R, indicating superior analgesic efficacy of wound infiltration with a combination of Ropivacaine and Fentanyl.

The limitation of the study includes the possibility of confounding results with varying degrees of surgical instrumentation in different laparoscopic procedures.

Conclusion

The addition of Fentanyl to Ropivacaine was found to be superior to Ropivacaine alone in providing effective postoperative analgesia and minimizing the requirement for rescue analgesics. The combination also provided stable hemodynamics with a minimal surge in blood pressure and heart rate.

Based on our findings, port-site infiltration with Ropivacaine and Fentanyl can be recommended for routine use, as a component of a multimodal analgesia regimen in laparoscopic procedures. However, larger randomized controlled trials are needed to authenticate the results.

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