

Comparison of Clonidine versus Fentanyl as an Adjuvant to Intrathecal Ropivacaine for Intraoperative Efficacy and Post Operative Analgesia in Infraumbilical Surgeries

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Abstract: *Background:* Ropivacaine is a newer local anesthetic, proven to have a better safety margin than bupivacaine and lignocaine. While maintaining this advantage and improving the intraoperative quality of anesthesia, the use of analgesic adjuvants has been proven to be valuable. *Aim & objective:* Comparison of clonidine versus fentanyl as an adjuvant to intrathecal ropivacaine for intraoperative efficacy and post operative analgesia in infraumbilical surgeries. *Settings and Designs:* Randomized double-blind control trial. *Methodology:* Seventy patients were randomly divided in two groups. Ropivacaine-Clonidine group (RC) received 60 mcg of clonidine with 15 mg of 0.5% isobaric ropivacaine, Ropivacaine Fentanyl group (RF) received 25 mcg of fentanyl with 15 mg of 0.5% isobaric ropivacaine intrathecally. The onset and duration of sensory-motor block were recorded. The total analgesia time, sedation score, hemodynamic parameters, and side-effects were noted. *Result:* The duration of sensory block in RC (316 ± 21.9), RF (227 ± 26.3), and motor block in RC (247 ± 28.4), RF (199.3 ± 20.2). In clonidine group, there was significant prolongation of sensory block ($P < 0.001$), motor block ($P < 0.001$) and the total analgesia time ($P < 0.001$). Hypotension and bradycardia occurred in 8.6% and 11.4% respectively in patients of clonidine group, where as pruritis was experienced by 11.4% patients in fentanyl group. *Conclusion:* Ropivacaine when combined with clonidine or fentanyl provided adequate subarachnoid block for infraumbilical surgeries, where in clonidine has advantage over fentanyl as it increased the duration of subarachnoid block and prolonged the postoperative analgesia.

1. Introduction

Ropivacaine has been proved and accepted as a safer option compared with bupivacaine and lignocaine due to the cardiotoxic effects of the former and neurotoxic effects of the latter.[1,2] Its efficacy in use for ambulatory surgery is justified since it has early motor and sensory recovery. Several studies have examined the effects of intrathecal ropivacaine in both laboring women and patients undergoing minor surgery.[3,4] Very few studies have evaluated its use in anesthesia for major limb surgery.[5] While maintaining the advantage of intrathecal ropivacaine and improving the perioperative quality of anesthesia and analgesia, various adjuvants have been used. Intrathecal opioids are synergistic with local anesthetics and intensify the sensory block without increasing the sympathetic block.[6,7] However, catastrophic delayed respiratory depression with opioids have prompted further research to develop non opioid analgesics. Clonidine is a partial agonist of the α_2 adrenoceptor and acts as an analgesic and sedative. Administered intrathecally along with local anesthetics, it helps improve the quality of the block and postoperative analgesia.[8] We conducted this study to evaluate the intraoperative efficacy of fentanyl and clonidine as adjuvants to intrathecal ropivacaine and postoperative analgesia for infraumbilical surgeries .

Aim & objective

We conducted this study in 70 patients of ASA grade 1& 2 to evaluate the efficacy of fentanyl and clonidine as adjuvants to intrathecal ropivacaine for intraoperative quality of anesthesia and postoperative analgesia in infraumbilical surgeries.

2. Procedure and Methodology

After obtaining approval from the hospital ethics committee and written informed consent from the patients, a prospective randomized double-blind study was carried out on 70 patients of American Society of Anesthesiologists physical status I and II. Patients of either sex, between 18 and 60 years of age undergoing infraumbilical surgeries were included in the study. Patients having contraindications to spinal anesthesia, a resting heart rate of less than 60/min, allergy to amide local anesthetic, a significant history of substance abuse and women of child bearing potential were excluded. Visual analogue score (VAS) for pain was explained to the patients preoperatively. It is a 10-point scale in which "0" indicates no pain and "10" indicates worst imaginable pain.[9]

The patients were randomly allocated into two groups of 35 patients each by using the random table.

Group RF: 15 mg of 0.5% isobaric ropivacaine with 25 mcg fentanyl.

Group RC: 15 mg of 0.5% isobaric ropivacaine with 60 mcg of clonidine.

The volume of the drug was kept constant at 3.5 mL by adding saline wherever necessary.

On arrival in the operation theatre, after confirming adequate starvation, patient's heart rate, blood pressure (BP), oxygen saturation (SpO₂), and electrocardiogram (ECG) were monitored. Intravenous access was established and 500 mL of Ringer Lactate infused. After ensuring sterile conditions, spinal anesthesia was performed by accessing the subarachnoid space with 25 G Quincke spinal needle via the L4-5 or L3-4 intervertebral space in the sitting position. After ensuring free flow of cerebrospinal fluid, patients

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received one of the two study drugs. The drug combinations were prepared by the first anesthesiologist. However, various observations were made by the second anesthesiologist who was blinded of the drug administered.

Throughout the study pulse, BP, respiratory rate, ECG, and SpO₂ were monitored. A decrease of more than 25% from the baseline in the systolic blood pressure (SBP) was considered hypotension and inj. ephedrine, 6 mg, intravenous (IV) was administered in incremental doses. A decrease in the heart rate below 50 beats/min was considered bradycardia and inj. atropine, 0.6 mg, IV was administered. The level of sensory block and the grade of motor block were evaluated at 2,4,6,8 10, and 15 min and thereafter at 15 min interval over 2h. VAS and sedation score were monitored every 15 min. The sensory block level was evaluated with the pin prick test and the motor block level was determined according to the Bromage scale:

Bromage scale

- Grade I: Free movement of legs and feet.
- Grade II: Just able to flex knees with free movement of feet.
- Grade III: Unable to flex knees but with free movement of feet.
- Grade IV: Unable to move legs or feet.

During the tracking of the sensory block in patients, a maximum sensory block level, time to achieve maximum sensory block and the time for sensory block to regress to L1 dermatome were monitored. While tracking the motor block, time to achieve maximum degree of motor block and its regression to Bromage I was noted.

The level of sedation was assessed using sedation score described by Chermik and Gilling[10] as follows:

- Grade 0: Wide awake.
- Grade 1: Calm and comfortable, responding to verbal commands.
- Grade 2: Sleeping but arousable.
- Grade 3: Deep sleep, not arousable.

In the postoperative period, the time of first analgesic demand was noted and inj. diclofenac, 75 mg, was administered. Patients were observed for any discomfort, nausea, vomiting, shivering, pruritus, bradycardia, and any other side-effects. All patients were observed in the post anesthesia recovery room and later in the ward. Severe pruritus and nausea/vomiting were treated with inj. chlorpheniramine maleate, 10 mg and inj. ondansetron, 4 mg, respectively.

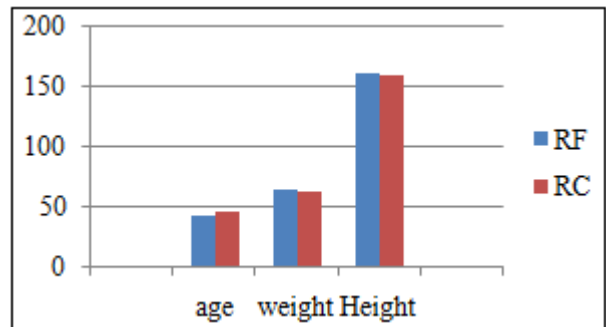
3. Results

The demographic data in both the groups were not comparable in terms of age, gender, weight, height, and duration of surgery [Table 1].

Table 1: Demographic data

| Variable | Fentanyl (RF) | Clonidine (RC) |
|---------------------------|---------------|----------------|
| No. of patients | 35 | 35 |
| Age (years) | 34.2±8.1 | 33.2±7.9 |
| Weight (kg) | 58.6±9.7 | 58.7±8.8 |
| Height (cm) | 168.5±10.3 | 166.5±10.5 |
| Sex (M:F) | 19:16 | 16:19 |
| Duration of surgery (min) | 73.3±9.5 | 73.9±9.7 |

Values are in mean ± standard deviation P > 0.05-Not significant. RC: Ropivacaine-clonidine group; RF: Ropivacaine Fentanyl group



The duration of sensory block in RC group (316 ± 21.9) and RF group (227 ± 26.3), and motor block in RC group (247 ± 28.4), RF group (199.3 ± 20.2). In clonidine group, there was significant prolongation of sensory block (P < 0.001), motor block (P < 0.01) and the total analgesia time (P < 0.001). Hypotension and bradycardia occurred in 8.6% and 11.4% respectively in patients of clonidine group, whereas pruritus was experienced by 11.4% patients in fentanyl group.

The time required for sensory onset taken as T6 level was faster in the fentanyl group (7.1 ± 2.1 min) as compared with the clonidine group (7.7 ± 2.3 min) but not significant P > 0.05. Time taken for sensory regression to L1 dermatome was more with clonidine group (316.0 ± 21.9 min) than fentanyl group (227.9 ± 26.3 min) which was highly significant, P < 0.001.

Duration of motor block with regression to grade 1 Bromage scale was significantly more with the clonidine group (247 ± 28.4 min) than the fentanyl group (199.3 ± 20.2 min), P < 0.01. Total analgesia time too was significantly longer in the clonidine group (358.9 ± 28.7 min) as against fentanyl group (231.1 ± 33.9 min), P < 0.001. Time for rescue analgesia was, therefore, significantly prolonged in the clonidine group as compared to the fentanyl group

Table 2: Spinal block characteristics

| Variables | Fentanyl (RF) | Clonidine (RC) | P value |
|--------------------------------------|---------------|----------------|---------|
| Time to reach T6 sensory level (min) | 7.1±2.1 | 7.7±2.3 | >0.05 |
| Time to sensory regression L1(min) | n 227.9±26.3 | 316±21.9 | <0.001 |
| Time to motor regression (Grade I) | 199.3±20.2 | 247±28.4 | <0.001 |
| Total analgesia time (min) | 231.1±33.9 | 358.9±28.7 | <0.001 |

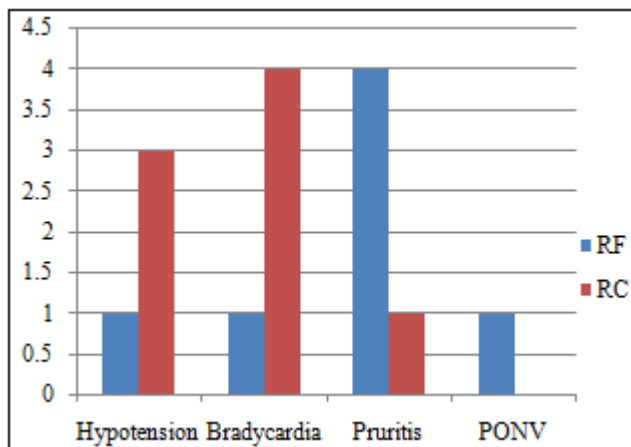
Values are in mean ± standard deviation P > 0.05 Not significant, P < 0.05 significant, P < 0.01 Highly significant, P < 0.001 Very highly significant. RC: Ropivacaine-clonidine group; RF: Ropivacaine Fentanyl group

Three patient (8.6%) in the clonidine group had hypotension (drop >25% SBP) as compared with one patient (2.8%) in the fentanyl group and responded to inj. ephedrine, 6 mg along with IV fluids.

In the clonidine group four patients had bradycardia requiring inj. atropine 0.6mg. Nausea/vomiting was experienced by one patient each in the fentanyl group. Pruritus was present in four patients (11.4%) in the fentanyl group [Table 3]. They responded to inj. ondansetron, 4 mg, and inj. chlorpheniramine maleate 10 mg, respectively

Table 3: Side effects

| Variables | Fentanyl (RF) | Clonidine (RC) |
|-----------------|---------------|----------------|
| Hypotension | 1 | 3 |
| Bradycardia | 1 | 4 |
| Pruritus | 4 | 1 |
| Nausea/vomiting | 1 | 0 |

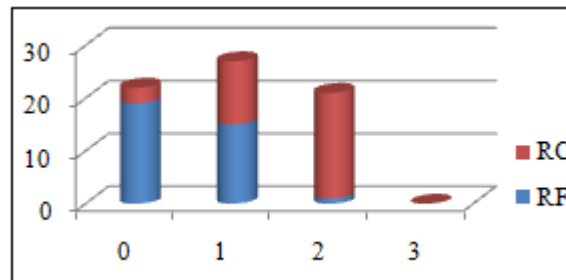


RC: Ropivacaine-clonidine group; RF: Ropivacaine Fentanyl group

In the fentanyl group, 15 patients (43%) had a sedation score of 1-2 as compared with 28 patients (80%) in the clonidine group who were calm and sleeping comfortably [Table 4]. None of the patients in either group had respiratory depression.

Table 4: Sedation score

| Sedation score | Fentanyl (RF) | Clonidine (RC) |
|----------------|---------------|----------------|
| 0 | 19 | 3 |
| 1 | 15 | 12 |
| 2 | 1 | 20 |
| 3 | 0 | 0 |



The chi-square statistic is 29.1602. The p-value is < 0.00001. The result is significant.

Degree of sedation was statistically significant among the two groups. Fentanyl group has 19 patients of score 0, 15 patient of score 1 and 1 patient of score 2. Whereas clonidine group has 3 patients of score 0, 12 patients of score 2 and 20 patients of score 2.

4. Discussion

In the present study, intrathecal ropivacaine (15 mg) with adjuvants, fentanyl (25 mcg), and clonidine (60 mcg) provided satisfactory anesthesia for infraumbilical surgeries. The duration of anesthesia for patients who received clonidine as adjuvant with ropivacaine in the spinal block experienced a prolonged sensory anesthesia, dense and a longer duration of motor block and a significantly prolonged postoperative analgesia as compared with the ropivacaine-fentanyl group.

Ropivacaine has been proved to be a well-tolerated regional anesthetic. For intrathecal use, its efficacy as compared with bupivacaine is in the ratio of 3:2, that is, 15 mg ropivacaine provided similar motor and hemodynamic effects but less potent anesthesia than 10 mg bupivacaine.[11]

The quest for providing long duration anesthesia of optimum quality while maintaining the advantage of ropivacaine furthered the research of using analgesic adjuvants with intrathecal ropivacaine.

A study by Boztug et al.,[12] evaluated the effects of low dose intrathecal ropivacaine with and without fentanyl for arthroscopic knee surgery. They concluded that although 25 mcg of fentanyl added to 8 mg ropivacaine provided shorter sensory and motor blockade than 10 mg Ropivacaine alone, small doses of ropivacaine and fentanyl can be safely used for arthroscopic knee surgery, thus reiterating the safety of intrathecal ropivacaine with adjuvant for ambulatory surgeries.

Our endeavor was to evaluate the efficacy of ropivacaine with adjuvant for infraumbilical surgeries. A study conducted by Yegin et al.,[13] evaluated the effect of intrathecal fentanyl 25 mcg added to 18 mg of ropivacaine for trans-urethral resection of prostate and found significant improvement in the duration and quality of anesthesia without causing substantial increase in frequency of major side effects. This is comparable to our study with the fentanyl group, where the subarachnoid features were satisfactorily met for the infraumbilical surgeries.

Intrathecal clonidine, an alpha-2-agonist, provides effective relief of pain. Several studies have shown that a combination of clonidine with a local anesthetic may improve the quality of subarachnoid block and prolong the postoperative analgesia.[14,15]

In our study, we have compared 60 mcg clonidine and 25 mcg fentanyl with 0.5% isobaric ropivacaine (15 mg) intrathecally. Sensory and motor blockade were significantly prolonged with clonidine group as compared with fentanyl group. The time for demand for first rescue analgesia was also prolonged with clonidine group. Similar results have been observed in other studies.

De Kock et al.,[16] evaluated the association of small dose of intrathecal ropivacaine (8 mg) with different doses of intrathecal clonidine (15, 45, 75 mcg) in four groups, for ambulatory surgery. Sagiroglu et al., [8] used 15 mcg and 30 mcg clonidine as adjuvant in 1% ropivacaine (12 mg). They found significant prolongation of sensory and motor block with higher dose of clonidine in their respective group.

McNamee et al.,[5] studied the efficacy of two concentrations of intrathecal ropivacaine, 2.5 mL of 0.75% (18.75 mg) and 1% (25 mg), without adjuvants, in patients undergoing total hip arthroplasty. The duration of sensory and motor blockade was prolonged in the group that received 25 mg of ropivacaine. Intraoperative hypotension requiring treatment with inj. ephedrine occurred in 24% of patients in both the groups. This could be because of higher concentration of ropivacaine used. In the present study, we reduced the dose of local anesthetic and supplemented with analgesic adjuvants. The incidence of hypotension and bradycardia observed was 8.6% with the clonidine group and 2.8% in the fentanyl group. De Kock et al., and Sagiroglu et al., reported a statistically significant reduction in mean BP in which higher doses of clonidine was added to ropivacaine.[8,16]

Intraoperative pruritus is a disturbing side effect of fentanyl. Patra et al.,[17] reported an incidence of 46%, whereas Khanna et al.,[18] reported in 20% cases. In our study, we observed pruritus in four patients (11.4%) in the fentanyl group.

Our aim of providing good-quality anesthesia and prolonged postoperative analgesia for infraumbilical surgeries was satisfactorily met by using adjuvants, fentanyl (25 mcg), and clonidine (60 mcg) with 15 mg ropivacaine intrathecally. Clonidine prolonged the subarachnoid block and the postoperative analgesia compared with fentanyl. The hemodynamic parameters need to be closely monitored when adjuvants are used and more caution exercised with clonidine usage. Further research is desirable to calibrate the various dosage combinations of ropivacaine and clonidine for optimum response.

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