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COMPARISON OF INTRAPERITONEAL INSTILLATION OF ROPIVACAINE (0.2%) WITH FENTANYL VERSUS ROPIVACAINE (0.2%) WITH DEXMEDETOMIDINE FOR POSTOPERATIVE ANALGESIA AFTER LAPAROSCOPIC GYNAECOLOGIC SURGERIES: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND CLINICAL STUDY



Anaesthesiology

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ABSTRACT

Background- Intraperitoneal Instillation of Local Anaesthetic in combination with Fentanyl or Dexmedetomidine has been shown to improve postoperative analgesia after laparoscopic surgery. Intraperitoneal route blocks visceral afferent signals and modifies visceral nociception. **Aims & Objectives** - Primary objective was to compare Duration of Analgesia using Ropivacaine with Fentanyl versus Ropivacaine with Dexmedetomidine using Visual Analogue Scale. Secondary objectives were to compare number of Rescue analgesia required in 24 hours, Haemodynamic parameters and any side effects. **Materials and Methods-** Total 60 Patients, ASA Grade I and II, posted for Elective Laparoscopic Gynaecologic surgery were Randomly divided into two groups. Patients of RF Group received 32 ml (30 ml 0.2% Ropivacaine + 1 ug/kg Fentanyl diluted in 2 ml Normal saline) and Patients of RD group received 32 ml (30 ml 0.2% Ropivacaine + 1 ug/kg Dexmedetomidine diluted in 2 ml Normal saline). At the end of surgery, 16 ml solution was instilled on inferior aspect of diaphragm (8 ml on each side) and remaining 16 ml was instilled on operative site via 5 mm side port. The visual analog scale, hemodynamic Variables and Side Effects were compared. The Data Analysis was carried out using Unpaired Student's t-Test and Chi-square test using Medcalc Software. **Results-** Demographic Data and hemodynamic parameters are comparable. Duration of Postoperative Analgesia was prolonged in RD Group as compared to RF Group (p=0.0006). Number of Rescue Analgesia required in 24 hours was less in Group RD as Compared to Group RF (p < 0.0001). **Conclusion-** Intraperitoneal Instillation of Ropivacaine- Dexmedetomidine provided better and prolonged Analgesia as compared to Ropivacaine- Fentanyl.

KEYWORDS

Intraperitoneal Instillation, Ropivacaine 0.2%, Fentanyl, Dexmedetomidine

INTRODUCTION

Laparoscopic procedures involve insufflations of the abdomen by using a gas. pain after laparoscopic surgery is complex in nature having three different components; e.g., Parietal, visceral, and shoulder tip pain⁽¹⁾.

Effective pain control encourages early ambulation, reduced the risk of deep vein thrombosis and pulmonary emboli, decreases the risk of pulmonary complications and decreases incidence of tachycardia⁽²⁾.

To avoid post-laparoscopy pain; multimodal analgesic techniques have been used in practice. These include parenteral use of nonsteroidal anti-inflammatory drugs, opioids, alpha-2 receptor agonists, local infiltration with local anaesthetics, epidural and intrathecal opioids, and local anaesthetics as well as intraperitoneal routes⁽³⁾.

In this modern era of surgery, intraperitoneal instillation of local anaesthetic agents has become important method to control postoperative pain, nausea and vomiting⁽⁴⁾.

Intraperitoneal administration of local anaesthetic agents provides antinociception by affecting nerve membrane-associated protein and by inhibiting the release and action of prostaglandins which stimulate nociceptors and cause inflammation⁽⁵⁾.

Along with Local anaesthetic, Fentanyl, Tramadol Dexmedetomidine and Magnesium sulfate were used safely^(5,7,8,9). These adjuvants improve quality of analgesia.

Intraperitoneal instillation of 0.2 % Ropivacaine provides effective analgesia. Fentanyl is an opioid which safely and effectively used intraperitoneally for postoperative analgesia in patients undergoing laparoscopic surgeries. Dexmedetomidine is an Alpha-2 adrenergic

receptor agonist. In addition, intraperitoneal local anaesthetics in combination with Dexmedetomidine has shown to improve postoperative pain after laparoscopic gynaecologic Surgeries.

So, We conducted this study to evaluate the analgesic efficacy of intraperitoneal Ropivacaine with Fentanyl and Ropivacaine with Dexmedetomidine after laparoscopic gynaecologic surgeries.

Primary Objectives

To compare the analgesic effect of Ropivacaine (0.2%) With Fentanyl (1ug/kg) versus Ropivacaine (0.2%) with Dexmedetomidine(1ug/kg) for postoperative analgesia after laparoscopic gynaecologic surgeries by measuring duration of post operative pain relief using Visual Analogue Scale (VAS) score.

Secondary Objectives

To compare the number of rescue analgesics required in first 24 hours and to monitor hemodynamic parameters and any side effects.

METHODOLOGY

This Prospective, Randomized, Double-blind clinical study was carried out after getting permission from institutional ethical committee for human research -PG research (IECHR-PGR) From January 2022 up to October 2022. (Approval date – 11th JAN 2022). CTRI NUMBER: CTRI/2022/03/041354.

Patients posted for elective laparoscopic surgeries in gynaecology, ASA physical status I and II and age from 18 to 65 years were included in the study.

Patients who refused to give consent, having history of allergy to study drug, cardiovascular and respiratory disease, chronic pain syndrome of neurological diseases, on beta blocking agents and who require peritoneal drain after surgery were excluded.

Sample size was calculated using parameter Duration of Analgesia

with mean difference of 33.4 with mean 89.3±13.2(group RF) and 122.7±24.5(group RD), at 95 % confidence and 80% power that came 6 in each group, using Open Epi software. (B.lakshmi Praveena et al,2019, Anaesthesia, Essays and Researches) So, to further authenticate the study, we took 30 Patients in each group. The patients were randomly allocated into two groups of 30 each by opaque sealed envelope method.

Grouping Of Patients:

Group RF: (N=30) Patients were received intraperitoneal instillation of Ropivacaine (30ml of 0.2%) plus Fentanyl (1 ug/kg diluted in 2 ml normal saline).

Group RD: (N=30) Patients were received intraperitoneal instillation of Ropivacaine (30ml of 0.2%) plus Dexmedetomidine (1 ug/kg diluted in 2 ml normal saline)

Total Volume taken was 32 ml in both Groups.

Day before surgery, preoperative checkup done, all patients were educated about the visual analogue scale pain score and Informed written consent was obtained.

On the day of surgery, nil by mouth status was confirmed.

On arrival to operating room, 18 gauge intravenous catheter was inserted. Multipara monitor was attached. Baseline pulse rate, blood pressure, Spo2 were recorded.

Premedication: Inj. Glycopyrrolate 5 mcg/kg IV, Inj. Tramadol 1 mg/kg IV and Inj. Ondansetron 4mg IV given.

Preoxygenation was done for 3 minutes. Induction of general anaesthesia was accomplished with inj. xylocard 1.5mg/kg, inj. Propofol 2 mg/kg iv, iv and inj. Succinylcholine 2 mg/kg iv to facilitate endotracheal intubation. Maintenance of anaesthesia was done with Sevoflurane, O2: N2O(50%:50%) and Vecuronium bromide 0.1 mg/kg iv bolus dose followed by 0.02 mg/kg incremental dose as and when required. Nasogastric tube of appropriate size was inserted. Mechanical Ventilation was adjusted to maintain Etco2 between 35-40 mmHg. Intraabdominal pressure was maintained between 12 -14 mmHg. Patients were placed in 15 – 20-degree Trendelenburg position.

At the end of surgery, after peritoneal wash and suctioning, patients Of RF group were received 32 ml of Ropivacaine plus Fentanyl, intraperitoneally.

Patients of RD group were received 32 ml Ropivacaine Plus Dexmedetomidine instilled intraperitoneally.

In all patients, total of 16 ml solution was instilled on inferior aspect of diaphragm (8 ml on each side) and remaining 16 ml on operative site via the 5 mm side port.

After that CO2 was removed from intraperitoneal cavity and skin incisions were sutured after local infiltration with 0.25% bupivacaine 2 ml in each port incision in both groups.

Neuromuscular block was reversed with Inj. Neostigmine 50 mcg/kg IV and Inj. Glycopyrrolate 10 mcg/kg IV and patient was extubated after fulfillment of criteria for extubation. Patients were shifted to recovery room, they were monitored for any complications, duration of postoperative analgesia was assessed using VAS at regular intervals up to 24 hours postoperatively.

IV paracetamol 1 gm was given as rescue analgesic when VAS ≥4 or on demand up to maximum dose of 4 gm in 24 hours. Time to first analgesic requirement after completion of surgery, total analgesic requirement in the first 24 hours postoperatively and occurrence of adverse events in the postoperative period was recorded.

Qualitative data was analyzed by Chi-square test. Quantitative data was presented as mean±standard deviation (SD) and they were analyzed by student's "t" test using medcalc software (Version 12.5.0.)

RESULTS

The Demographic data in our study were comparable to each other with respect to age, weight, ASA physical status and duration of

surgery.(Table-1)

Different types of gynaecologic surgeries Like Laparoscopic ovarian cyst removal, Laparoscopic myomectomy, DHL with PCOD drilling Laparoscopic hysterectomy were included in the study. which were comparable in both the groups. Intraoperative and postoperative patients were hemodynamically stable and no statistically significant different between both groups.

VAS was higher in group RF as compared to group RD at 30 min, 60 min, 90 min, 2 hours, 4 hours, 6 hours, 8 hours, 12 hours, 18 hours and 24 hours. P value <0.05 which was statistically significant.(Table-2)

Time to first requirement of rescue analgesia was 8 ±3.8 hours in group RF as compared to 11 ±4 hours in group RD(p=0.0006) which was statistically highly significant.(Graph-1)

Total rescue analgesia required in 24 hours was less in group RF (3 ±0.74) as compared to group RD (2.1 ±0.8) which was statistically highly significant(p<0.0001).(Graph-2)

In group RF, 6 (20%) patients had nausea, whereas in group RD 5 (16.66%) patients had nausea. Which was statistically not significant(p>0.05). 4 (13.33%) patients in group RF had vomiting whereas 3 (10%) patients in group RD had vomiting which was statistically not significant (p>0.05).

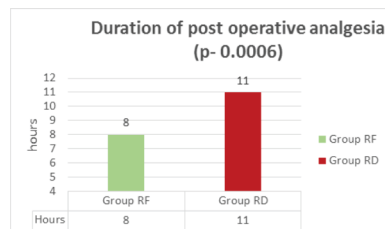
We found no incidence of shoulder pain and other postoperative complications in both groups.

Table1: Demographic Data

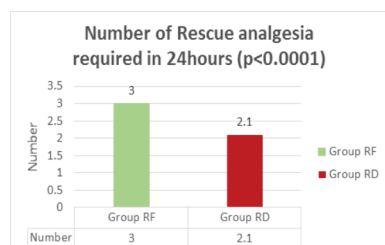
Demographic Data	Group RF (N-30)	Group RD (N-30)	P value
Age (years)	31.33 ± 4.85	30.36 ± 5.52	0.4744
Weight(kg)	59.93 ± 6.59	59.23 ± 9.63	0.7438
ASA Grade (III)	(12 \ 18)	(14 \ 16)	
Duration of surgery (minutes)	78.50±7.78	78.33±7.58	0.9320

Table 2: Assessment Of Visual Analogue Score(VAS)

Time	Group RF (n – 30)	Group RD (n – 30)	P value
30 min	1 ± 0.9468	0.2333 ± 0.4301	0.0002
60 min	1.1 ± 0.9948	0.3666 ± 0.7648	0.0022
90 min	1.9 ± 1.4	0.63 ± 0.89	0.0001
2 hours	2.4 ± 0.9684	0.63 ± 0.88	0.0001
4 hours	2.7666 ± 0.7738	0.66 ± 1.1547	0.0001
6 hours	3.3666 ± 1.5862	1.73 ± 1.2802	0.0001
8 hours	3.6 ± 1.2757	2.73 ± 0.9802	0.004
12 hours	4.4 ± 1.8864	3.66 ± 0.71	0.05
18 hours	4.7333 ± 1.4840	3.93 ± 1.3373	0.03
24 hours	6 ± 0.8709	4.9666 ± 1.4967	0.0018



Graph : 1 Time To Requirement Of First Rescue Analgesia



Graph : 2 Number Of Analgesic Doses Required In 24 Hours

DISCUSSION

Laparoscopic procedures have revolutionized gynaecologic surgeries

and have almost replaced traditional open surgeries. Because of gas insufflation and raised intraperitoneal pressure during laparoscopic surgeries, there is peritoneal inflammation and neuronal rupture with linear relationship between abdominal compliance and resultant severity of postoperative pain⁽⁶⁾

The concept of Intraperitoneal local anaesthetics (IPLA) has been used to reduce shoulder tip pain, overall pain, nausea and vomiting, and hospital stay⁽⁴⁾.

We choose intraperitoneal route in our study because it blocks visceral afferent signals and modifies visceral nociception. Hodgson PS et al, suggested that local anaesthetic agents when given intraperitoneally acts by affecting nerve membrane associated proteins and inhibits release and action of prostaglandins and other agents that sensitize or stimulate the nociceptors and contribute to inflammation⁽⁵⁾. Absorption from large peritoneal surface may be the mechanism of analgesia⁽⁶⁾.

Ropivacaine, new long-acting amide local anesthetic that is formulated as pure S-enantiomer, is chemically related to Bupivacaine, but it has been shown to be less toxic to cardiac and central nervous systems and Ropivacaine is safest local anaesthetic than Bupivacaine⁽⁷⁾.

Ropivacaine possesses anti-inflammatory activity that may further reduce pain when administered locally⁽⁸⁾. Many studies have used Ropivacaine as local anaesthetics for intraperitoneal instillation for postoperative analgesia in laparoscopic surgeries^(2,9,10,11,12,13,14).

Fentanyl is opioid which safely and effectively used for postoperative analgesia as an adjuvant to local anaesthetic in intraperitoneal instillation^(9,15).

Dexmedetomidine has been used for intraperitoneal instillation in various study successfully^(2,9,10,12,16). Antinociceptive effect of Dexmedetomidine is seen at the dorsal root neuron level, where it blocks release of substance P in the nociceptive pathway, through action on inhibitory G protein, which increases the conductance through potassium channel⁽⁹⁾.

We choose 0.2% concentration of Ropivacaine 30 ml + 1 ug/kg Fentanyl or 1 ug/kg Dexmedetomidine diluted in 2 ml Normal Saline (total 32 ml).

B.Lakshmi praveena et al used 0.2% Ropivacaine 30 ml + 1 ug/kg Fentanyl or Dexmedetomidine diluted in 2 ml Normal Saline (total 32 ml) and Sunil chiruvella et al, also used (0.2%) concentration of Ropivacaine 30 ml + 2 ml Normal Saline (total 32 ml)⁽⁹⁾.

Kumari A et al and Meena RK et al, used 0.5% Ropivacaine 18 ml + 2 ml normal saline for intraperitoneal instillation, so they used high concentration with low volume than our study^(13,14).

In this study, low concentration of Ropivacaine with higher volume of Drug was instilled.

In our study, VAS was higher in group RF as compared to group RD at 30 min, 60 min, 90 min, 2 hours, 4 hours, 6 hours, 8 hours, 12 hours, 18 hours, and 24 hours time intervals. (P value <0.05).

B. Lakshmi praveena et al, observed in their study that VAS was higher in group RF (intraperitoneal instillation of Ropivacaine with Fentanyl) as compared to group RD (intraperitoneal instillation of Ropivacaine with Dexmedetomidine) at 30 minutes, at 60 minutes, at 4 hours, at 8 hours, at 12 hours, at 16 hours and at 24 hours and this difference was statistically significant⁽⁹⁾.

Ranjita acharya et al, observed in their study that VAS score was higher in GROUP R (intraperitoneal instillation of Ropivacaine) as compared to group RD (intraperitoneal instillation of Ropivacaine with Dexmedetomidine) at 24 hours (p-value- 0.001). VAS score at different time intervals was significantly lower after second postoperative hours⁽¹⁰⁾.

In our study, time to first requirement of rescue analgesia was 8 ± 3.8 hours in group RF as compared to 11 ± 4 hours in group RD (p=0.0006) which was statistically highly significant.

Ranjita acharya et al, noticed that the time interval for requirement of

first rescue analgesia after laparoscopic gynaecologic surgery was lesser in Ropivacaine group (242.5 ± 19.84 minutes) as compared to Ropivacaine with Dexmedetomidine group (487.7 ± 40.96 minutes), which was statistically significant⁽¹⁰⁾.

B. Lakshmi praveena et al, noticed that time interval for the requirement of first rescue analgesia was lesser in Ropivacaine with Fentanyl group (89.3 ± 13.2 minutes) as compared to Ropivacaine with Dexmedetomidine group (122.7 ± 24.5 minutes)⁽⁹⁾. Our results are in consonance with the above-mentioned study. Intraperitoneal instillation of Ropivacaine with Dexmedetomidine provides longer pain free period than Ropivacaine with Fentanyl. But time to requirement of first rescue analgesia was longer in our study than above mentioned study, as they have used this instillation in laparoscopic cholecystectomy, which is a complex surgery, so pain is different than other laparoscopic surgeries⁽¹⁷⁾.

In our study, total number of rescue analgesia required in 24 hours was less in group RF (3 ± 0.74) as compared to group RD (2.1 ± 0.8) in our study (p < 0.0001).

B. Lakshmi praveena et al, noticed that total analgesic consumption of Diclofenac in 24 hours was 135.7 ± 75.1 mg in Ropivacaine with Fentanyl group and 95.3 ± 15.6 mg in Ropivacaine with Dexmedetomidine group had which was statistically significant⁽⁹⁾.

Sunil Chiruvella et al, also observed that total analgesic consumption in 24 hours was less in RD group, as compared to R group. They used Diclofenac as rescue analgesia in their study. R group had 175 ± 75 mg and RD group had 95 ± 15 mg of Diclofenac consumption in 24 hours which was statistically significant⁽²⁾.

Shoulder pain is a common and frequent complication after laparoscopic gynaecologic surgeries. It occurs due to diaphragmatic stretching with phrenic nerve neuropraxia. We found no incidence of shoulder pain in both groups. The postoperative period was uneventful in all the patients in both the groups.

Limitations Of Study

We evaluated pain by VAS score as interpreted by patients, so it becomes subjective and might vary from patient to patient with their understanding and pain tolerance.

CONCLUSION

From our study, We can conclude that Intraperitoneal instillation of Ropivacaine (0.2%) with Fentanyl (1ug/kg) and Ropivacaine (0.2%) with Dexmedetomidine both provided safe and effective postoperative analgesia after laparoscopic gynaecologic surgeries.

Intraperitoneal Instillation of Ropivacaine- Dexmedetomidine provided better and prolonged postoperative Analgesia as compared to Ropivacaine- Fentanyl after laparoscopic gynaecologic surgeries.

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Conflicts Of Interest: None

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