International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Pathak N et al. Int J Reprod Contracept Obstet Gynecol. 2018 Apr;7(4):1561-1566
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20181356

Original Research Article

A clinical comparative study of ropivacaine versus ropivacaine with fentanyl by continuous epidural infusion for post-operative analgesia and ambulation in patients undergoing major gynecological surgery

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Received: 06 February 2018
Accepted: 07 March 2018

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ABSTRACT

Background: To compare the effect of continuous epidural infusion of ropivacaine versus ropivacaine-fentanyl for post-operative analgesia and ambulation in patients undergoing major gynaecological surgeries.
Methods: A total of 60 patients of age 20 to 50 yrs of body mass index (BMI) within normal range (18.5to24.9 kg/m^2) posted for major gynecological surgeries were divided into two equal groups (Group R and RF) in a prospective, randomized, double-blind fashion. In Group RF (n=30) 0.1% Ropivacaine with 2µg/ml Fentanyl and in Group R (n =30) 0.1% ropivacaine were used. General anaesthesia was given to all patients. Continuous epidural infusion using elastomeric pump was started at '0' post-operative hours at 6ml/hour. Post -operative pain (Visual Analogue Scale Score), ambulation (James Modified Bromage Scale) and side effects were noted at 0, 2, 4, 6, 12, 18, 24, 36 and 48hrs.
Results: The differences in VAS Score of subjects of both the groups were statistically significant($p<0.05$) at 18 hrs, 24hrs, 36hrs and 48 hrs and the differences in Modified Bromage Scale of subjects of the groups were statistically similar at most of the time intervals. Also, the side effects were statistically similar between the groups.
Conclusions: Author concluded that ropivacaine-fentanyl is better than ropivacaine alone by continuous epidural infusion for post-operative analgesia in major gynecological surgeries with no statistically significant side effects, effect on ambulation being similar in both the groups.

Keywords: Ambulation, Epidural anesthesia, Fentanyl, Gynaecology, Ropivacaine, Visual analogue pain scale

INTRODUCTION

A revolution in the management of acute postoperative pain has occurred during the past 3 decades. To reduce morbidity, effective pain control is required in the post-operative patients.[1,2] Depending on the extent of surgery, immunity of the patient becomes low leading to increased complications in post-operative period. Adequate analgesia in post-operative patients reduces stress hormone levels and improves immunity.[3-5]

Gynaecological surgeries are done by abdominal approach, so continuous epidural analgesia can provide post-operative pain relief in adult patient. Author decided to conduct the study for assessing the effectiveness of adding fentanyl to ropivacaine in patient undergoing gynaecological surgery.

Decreasing the local anaesthetic concentration can reduce motor blockade leading to ease of ambulation in post-operative period. In comparison to bupivacaine,

ropivacaine is known to have lesser cardiotoxicity and motor blockade, with similar pain relief at equivalent analgesic doses.[6-10]

Fentanyl is a synthetic opioid with a short duration of action and rapid onset. It is full agonist on opioid receptor. Epidural fentanyl has been widely used as analgesic adjuvant. Its main site of action is the substantia gelatinosa. It blocks fibres carrying nociceptive impulses both pre and post synaptically.[11]

Therefore, author performed a randomized, control, prospective study to evaluate the effect of continuous epidural infusion of ropivacaine versus ropivacaine-fentanyl for pain relief and ambulation in patients who underwent gynaecological surgeries.

METHODS

After getting permission from the Institutional Ethical Committee study was conducted in patients posted for gynecological surgery. A written and informed consent was taken. All the patients scheduled for major gynecological procedures were visited a day prior to surgery. A thorough pre-anaesthetic checkup was done including the detailed history and physical examination. Specific questions were asked related to previous exposure of any surgery under general anaesthesia. All routine investigations as per local institutional protocol were advised. Fasting for solids for 6-8 hours and 2 hours for clear fluids were ordered. No anxiolytics were advised during preop visit.

On the basis of pilot study, VAS score at 48 hours in Group R was 3.3±1.1 and in Group RF was 2.7±0.4. Taking these values as reference, the minimum required sample size with 80% power of study and 5% level of significance is 30 patients in each study group. So total sample size taken is 60 (30 patients per group).

A total of 76 patients were assessed for eligibility, 4 did not meet inclusion criteria, 3 declined to participate and 2 patients were excluded because of altered investigations. Out of left 67 patients, 7 were lost to follow up. A total of 60 patients of age 20-50 years, American Society of Anesthesiologists physical status I and II of normal Body Mass Index (18.5-24.9kg/m^2) undergoing major gynecological procedures were included in the study.

Exclusion criteria were patient refusal for the procedure, any contraindication to epidural anaesthesia, patient with diseased/ deformed spine/ backache, patient with diabetes, hypertension, coagulation abnormalities or any other severe systemic illness.

Using sealed envelope method for randomization, 60 patients were equally and randomly allocated into two groups- (Group R and RF) in a double-blind fashion (Figure 1). To reduce the observer bias, study drug preparation and data collection was done by an anesthesiologist not involved in present study.

- Group R - (n =30) 0.1% Ropivacaine (Total volume = 275 ml)
- Group RF - (n=30) 0.1% Ropivacaine with 2µg/ml fentanyl (Total volume = 275 ml)

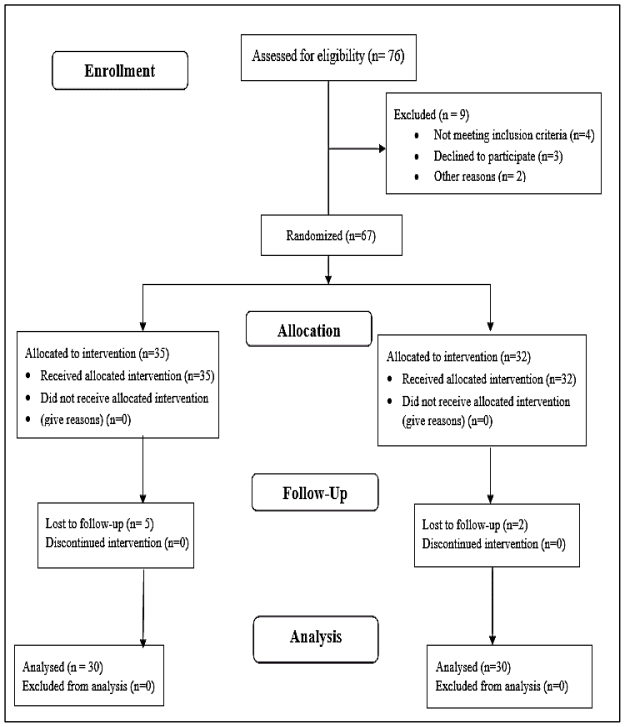

Figure 1: Consort flow diagram.

On the day of surgery patient was nursed in operation theaters and procedure was explained thoroughly to the individual. Standard routine monitoring using 5 lead Electrocardiogram (ECG), Pulse-Oximetry (Spo2), and noninvasive blood pressure (NIBP) was applied. 20G intravenous peripheral line was taken in non-dominant arm and ringer lactate infusion was started.

All patients received lumbar epidural anaesthesia in sitting position with legs extended on the OT table. The 18G (Brand Portex) Tuohy's Epidural needle with 20 G Epidural Catheter was used in all patients. loss of resistance using LOR Syringe was defined as identification of lumbar epidural space. Epidural catheter was inserted up to 4cm in epidural space. 3mL of 2% lidocaine with 1:200,000 epinephrine was given through the catheter to check for intrathecal/intravascular placement. Intrathecal placement was ruled out by absence of tingling and numbness in lower limbs within 4 mins of administering drug. Intravascular placement was ruled out by absence of increase in heart rate >20% of baseline within 4 mins of administration of drug. General anaesthesia was induced with *i.v.* injections of propofol 2mg/kg and succinyl choline 1.5mg/kg and tracheal intubation was performed. Anaesthesia was maintained

with N2O:O2 (67:33) ventilation and isoflurane (0.5-1%). Adequate skeletal muscle relaxation was maintained with loading dose of vecuronium (0.06mg/kg) followed by intermittent *i.v.* boluses of 0.01mg/kg as and when required.

Residual neuromuscular block was antagonized with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg and patient were extubated at the end of surgery.

No drug was given through epidural intra-operatively. Drugs were given in respective groups through an elastomeric continuous epidural infusion pump of capacity 275ml which is a light weight, non-electric pump, easily carried around by the patient, not interfering with patient's ambulation.

After extubation patients were assessed using Modified Aldrete Score. The infusion was started at '0' post-operative hours at a rate of 6ml/hour. After this the patients were assessed for Post -operative pain (VAS Score; 0 = no pain to 10 = worst pain imaginable), Ambulation (James Modified Bromage Scale; 0 = no motor block, 1 = unable to raise extended leg but able to move knee and foot, 2 = unable to raise extended leg or knee but able to move foot, 3 = complete motor block of lower limb) and hemodynamic parameters (HR, SBP, DBP, SpO2), for 48 hours at various time intervals (0,2,6,12,18,24,36,48hrs), pain and ambulation being primary outcomes. Also, side effects, requirement of rescue analgesia and anti-emetics were noted. Side effects were secondary outcomes. Author have used following definitions for side effects-

Respiratory depression (Respiratory Rate <10/min and SpO2 <92%), vomiting (expulsion of undigested food through the mouth), Nausea (sensation of being about to vomit), Pruritis (sensation of itching (most commonly involves face when opioids are given through spinal/epidural route) and Delayed GI Motility (absence of return of bowel sound(as auscultated with stethoscope)/passage of flatus (as told by patient) >48 hrs-detected by investigator-author).

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD. The statistical formulae used were mean, standard deviation, chi-square test and student t test. Level of significance: (p >0.05- Not significant, p <0.05-Significant, p <0.01-Highly significant, p <0.001- Very highly significant).

RESULTS

Demographic variables like weight (P=0.363), age wise distribution (p=0.8624) of subjects and baseline hemodynamic variables of both the groups were statistically similar and were statistically insignificant, as depicted in Table 1.

Table 1: Demographic and baseline characteristics of two groups.

Hemodynamic variables	Group R (n=30)		Group RF (n=30)		Statistical significance	
	Mean	SD	Mean	SD	't' value	'p' value
Heart rate (per min)	80.3	14.7	85	16.7	1.158	0.251
Systolic BP (mm Hg)	129.9	8.1	131.9	6.3	1.123	0.266
Diastolic BP (mm Hg)	81.3	6.2	82.9	5.2	1.022	0.311
SpO2	99.8	0.6	100	0	1.989	0.051
RR	15.1	1.3	14.9	1.3	0.485	0.629
Body weight (kgs)	56.25	6.73	53.77	8.88	0.917	0.363
Mean age	37.28	10.06	39.18	11.41		0.8624*

* =Chi-square test, P<0.05 significant

Table 2: Comparison of VAS at different time intervals between the groups.

Time interval	Group R			Group RF			Statistical significance	
	No.	Mean	SD	No.	Mean	SD	't' value	'p' value
0 hrs	30	8.5	1.1	30	8.1	1.3	1.107	0.273
2 hrs	30	7.4	1.1	30	7.1	1.4	0.835	0.407
4 hrs	30	6.7	1.2	30	6.5	1.1	0.801	0.426
6 hrs	30	5.8	0.9	30	5.9	1.6	0.405	0.687
12 hrs	30	5.1	1.1	30	4.6	1.5	1.369	0.176
18 hrs	30	5.4	1.3	30	4.2	1.3	3.526	0.0008
24 hrs	30	4.5	1.1	30	3.7	1.1	4.159	0.0001
36 hrs	30	3.5	1.4	30	2.6	0.9	2.773	0.0074
48 hrs	30	3.4	1.8	30	2.7	0.5	3.292	0.0016

The differences in VAS Score of subjects of both the groups were statistically significant at 18 hrs (P=0.0008), 24hrs (P=0.0001), 36hrs (P=0.0074) and 48 hrs (P=0.0016) as shown in Table 2.

The difference in Modified-Bromage scale of subjects of both the group was statistically insignificant at all the intervals except at 2 hours (P=0.0092) as shown in Table 3.

Table 3: Comparison of Modified-Bromage scale at different time intervals between the groups.

time interval	Group R			Group RF			Statistical significance	
	No.	Mean	SD	No.	Mean	SD	't' value	'p' value
0 hrs	30	1.2	1.6	30	0.9	0.3	0.992	0.325
2 hrs	30	0.3	0.4	30	0.7	0.5	2.693	0.0092
4 hrs	30	0.2	0.4	30	0.2	0.4	0.602	0.549
6 hrs	30	0.2	0.4	30	0.1	0.3	1.077	0.286
12 hrs	30	0.2	0.4	30	0.1	0.3	1.077	0.286
18 hrs	30	0.1	0.3	30	0.1	0.3	0.460	0.647
24 hrs	30	0	0	30	0.1	0.3	1.795	0.077
36 hrs	30	0	0	30	0.1	0.3	1.795	0.077
48 hrs	30	0	0	30	0.1	0.3	1.795	0.077

Table 4: Side effects in study population.

Side effects	Group R		Group RF		Statistical significance	
	No.	%	No.	%	χ^2	'p' value
Vomiting	2	6.7	7	23.3	3.268	0.070
Respiratory depression	0	0	0	0	-	-
Delayed GI motility	0	0	3	13.3	3.158	0.076
Pruritis	0	0	0	0	-	-

Side effects was studied between the two groups and is shown in Table 4. Vomiting was found to be in higher proportion of subjects from Group RF as compared to Group R but this difference was statistically similar (p=0.070). Delayed GI Motility (absence of passing of flatus >48 hrs) was found to be in higher proportion of subjects from Group RF as compared to Group R but this difference was statistically similar (p=0.076). Respiratory depression and pruritis were seen in none of the patients in either of the groups.

DISCUSSION

Anesthesiologist's are specialized clinicians who treat pain by adopting various techniques and drugs. Pain, if not treated may result into various physiological changes, including rise in heart rate, blood pressure, restricted physical activity.

Author decided to use Ropivacaine in our study because it has a wider margin of safety, less motor blockade, less cardiovascular or neurological toxicity in comparison to local anaesthetics used earlier.

Epidural opioid produce pain relief with less degree of motor/ sympathetic blockade. Epidural opioids when given, because of their lipophilicity have the propensity to go to the intrathecal space.[12-15] Administration of local anaesthetics and opioids together by epidural route, results in decrease in dose of both the drugs, and therefore there is decrease in systemic side effects such as hypotension, pruritis, nausea and vomiting, respiratory depression.[16-18]

Author conducted our study in major gynaecological surgeries so as to maintain uniformity in intensity and quality of post-operative pain in all the patients. Since we have used lumbar epidural because of ease of the technique we had to use lower abdominal surgeries. The surgeries included were total abdominal hysterectomies, exploratory laparotomies which ended finding ovarian cysts/ adnexal mass and myomectomy.

On analysis of the demographic profile the age and weight were comparable in the groups. The difference in VAS Score of subjects was statistically significant at 18 hrs, 24hrs, 36hrs and 48hrs which shows better degree of post-operative analgesia in RF group after 18 hrs. The difference in modified bromage scale of subjects of both the groups was statistically non-significant at all the above intervals except at 2 hrs which shows similar degree of ambulation in both the groups.

Vomiting was found to be in higher proportion of subjects from Group RF (7/30 patients) as compared to Group R (2/30 patients) but this difference was statistically similar (p=0.07). The difference may be attributed to systemic absorption of the opioid (fentanyl)

when used in epidural infusion. All these patients had Rescue anti emetic (Inj. Ondansetron 4mg *i.v.* stat) was given which prevented any further episodes of vomiting in all the patients. Delayed GI Motility (absence of passing of flatus >48 hrs) was found to be in higher proportion of subjects from Group RF (3/30 patients) as compared to Group R (no patient) but this difference was statistically similar (p=0.076). We can attribute this difference to either manipulation of bowel during surgery, any pre-existing gastro intestinal disease or usage of any sympathomimetic drugs or opioids. Respiratory depression and pruritis were seen in none of the patients in either of the groups.

The results are consistent with the study conducted by Lee et al who conducted a randomised double-blind comparative study in 210 patients.[19] They used epidural infusions at the rate of 7ml/hour for patients who underwent lower extremity/ lower abdominal surgery. 210 patients were divided into two equal groups in which 105 patients received 0.1% ropivacaine and other 105 patients received 0.1% ropivacaine plus 1µg/mL fentanyl. They measured Pain score and side effects at 0, 0.5, 1, 3, 6, 12, and 24 hours. Patient profiles were statistically similar between the groups. Pain relief scores were not different in the two groups in the first hour of starting the drugs.

However, in the ropivacaine/fentanyl group pain relief was better after the first hour and this difference lasted till the end of the infusion. The adverse events (hypotension, nausea, vomiting, pruritus, paraesthesia, urinary retention and motor block) were similar between the two groups during 24 hours of assessment. Therefore, they concluded that the addition of fentanyl 1µg/mL to ropivacaine improves the quality of pain relief.

Altienzar MC et al conducted a randomised study for patients in labour and found that 0.1% ropivacaine with fentanyl 2microg/mL via epidural was adequate for analgesia in first stage of labour.[20] The quality of pain relief was similar to that obtained using 0.2% ropivacaine with fentanyl 2microg/mL and there was no difference in motor or sensory block.

The limitations of our study are small sample size, lack of continuous monitoring of hemodynamic parameters and that it was limited to female population and we could not assess the effect of drugs on male population.

CONCLUSION

Author can conclude that ropivacaine with fentanyl is better than ropivacaine alone when given through continuous epidural infusion in major gynaecological surgeries in context of better quality of post-operative analgesia as measured by VAS Score with no significant side effects, effect on ambulation being similar in both the groups as measured by Modified-Bromage Scale.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Pathak N, Tiwari T, Singh S, Manik YK, Dhama VK, Dahiya S. A clinical comparative study of ropivacaine versus ropivacaine with fentanyl by continuous epidural infusion for post-operative analgesia and ambulation in patients undergoing major gynecological surgery. Int J Reprod Contracept Obstet Gynecol 2018;7:1561-6.