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CLINICAL EFFICACY OF ISOBARIC ROPIVACAINE ALONE AND WITH FENTANYL IN SPINAL ANAESTHESIA FOR VAGINAL HYSTERECTOMY: A PROSPECTIVE, RANDOMIZED, COMPARATIVE STUDY

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ABSTRACT

BACKGROUND: Aim of this study was to assess the clinical efficacy of 4 ml of 0.75% ropivacaine alone and with 25mcg fentanyl in spinal anaesthesia for vaginal hysterectomy regarding sensory and motor block characteristics, success rate, haemodynamic profile and complications. **METHODS:** Present study was conducted in a randomized double blind fashion on 60 patients, 30 in each group of ASA physical status I-II posted for vaginal hysterectomy. All patients under study were randomly divided into two groups of 30 patients in each group using sealed envelope technique. **GROUP R:** Patients received 4 ml 0.75% Isobaric Ropivacaine hydrochloride [Ropin (neon labs)] **GROUP RF:** Patients received 4ml 0.75% Isobaric Ropivacaine [Ropin (neon labs)] with 25µg Fentanyl hydrochloride [Fenstud] We evaluated whether addition of fentanyl to intrathecal ropivacaine could make a significant effect on onset and duration of analgesia, sensory and motor block.

RESULTS

- Isobaric Ropivacaine [4 ml 0.75% (30 mg)] alone and with fentanyl (25mcg) in spinal anaesthesia produced effective sensory-motor blockade of sufficient duration with stable hemodynamic profile to accomplish vaginal hysterectomy.
- Addition of fentanyl offered the advantage of accelerating the sensory onset and prolonging the duration of analgesia and sensory block, without affecting sympathetic or motor block characteristics.

CONCLUSIONS: Owing to early recovery in motor functions and lesser cardio-neuro toxicity, ropivacaine seems to be a good option for spinal anaesthesia.

KEYWORDS: Isobaric Ropivacaine, Fentanyl, Spinal Anaesthesia, Vaginal Hysterectomy.

INTRODUCTION

Prolapse of the uterus and/or vaginal walls is a common condition with up to 11% of women requiring surgery during their lifetime.[1] Vaginal hysterectomy is a procedure in which the uterus is surgically removed through the vagina. The operation is performed in a hospital setting and can be performed under general or spinal anaesthesia (with or without sedation). spinal anaesthesia is a convenient, early and effective method of anaesthesia for variety of surgical procedures, especially for lower abdominal and lower limb surgeries. The subarachnoid block has got inherent advantages like intense motor and sensory blockade, good relaxation, reliability, avoid side effects of multiple drugs used in general anaesthesia, no postoperative respiratory depression, nausea, vomiting, drowsiness etc.

Many intrathecal anaesthetic agents have been used to produce acceptable level of anaesthesia. Among them, lignocaine and bupivacaine were most widely used. But use of lignocaine is now declined because of shorter duration of block and association with transient neurological symptoms. Bupivacaine is still the most commonly used intrathecal agent, but when inadvertently injected systemically, it causes cardio – neuro toxicity, cardiovascular collapse and even death. Ropivacaine, a levo isomer of bupivacaine shares many physicochemical properties with it and has shown a better safety profile over bupivacaine due to the reduced central nervous system and cardiac toxicity.[2,3] Ropivacaine has low lipid solubility; hence, it blocks nerve fibers involved in pain transmission to a greater degree than those controlling motor functions.

Ropivacaine can provide adequate surgical anaesthesia without compromising early ambulation and discharge. Local anaesthetic when used alone is associated with short duration of action. Thus early analgesic intervention is needed in postoperative period. Various adjuvants have been used intrathecally to improve the quality and duration of the spinal anaesthesia along with better postoperative analgesia like epinephrine, neostigmine, midazolam, ketamine, opioids and, α-2 receptor agonists (clonidine, dexmedetomidine).[4,5] Opioid analogues have been used as additives in spinal anaesthesia to accelerate the onset, prolong the duration of block and to improve the quality of perioperative analgesia by acting on opioid receptors. Intrathecal opioids selectively decrease nociceptive afferent input from A-delta and C-fibers without affecting dorsal root axons or somatosensory evoked potentials. Fentanyl (a lipophilic opioid) has a rapid onset and short duration of action following intrathecal administration. The co-administration of opioids reduces the total dose of local anaesthetics requirement for anaesthesia and significantly prolongs the duration of complete and effective analgesia without prolonging the duration of motor block. It prolongs the duration of postoperative analgesia and reduces analgesic requirement in early postoperative period following spinal block.[6]

Ropivacaine has successfully been used in spinal anaesthesia for cesarean section,[7] urological surgeries,[8] lower limb orthopedic surgeries,[9] however, its use in vaginal hysterctomy is not much investigated. This study was planned to assess the clinical efficacy of 4 ml of 0.75% ropivacaine alone and with 25mcg fentanyl in spinal anaesthesia for vaginal hysterectomy regarding sensory and motor block characteristics, success rate, haemodynamic profile and complications. Our ultimate objective is to find out if isobaric ropivacaine would produce effective spinal anaesthesia for vaginal hysterectomy; being less cardiotoxic it could become a better alternative to bupivacaine. We also evaluated whether addition of fentanyl to intrathecal ropivacaine could make a significant effect on onset and duration of analgesia, sensory and motor block.

MATERIAL AND METHODS

After approval from the institutional ethical committee, this prospective, randomized, double blind, comparative study was conducted in Department of Anaesthesia at Panna Dhai Mahila Chikitsalya, R.N.T. Medical College, Udaipur (Raj.) and informed consent was taken from each patient for participation in the study. Present study was conducted on 60 patients, 30 in each group of ASA physical status I-II posted for vaginal hysterectomy. The patients having age between 40-80 year, weight 30-80 kg and height >140cm, were included. Exclusion criterias were patient refusal, any contraindication to regional anaesthesia ,history of significant coexisting diseases like ischemic heart disease, hypertension, heart blocks, impaired renal functions, rheumatoid arthritis, severe liver disease and morbid obesity etc., presence of malnourished patient, anemia, fused spine, coagulation disorder, diabetes, psychiatric illness, thyroid disease, patient on any medication for systemic disease and allergy to amide local anaesthetics and opioids.

This study was conducted in a randomized double blind fashion. All patients under study were randomly divided into two groups of 30 patients in each group using sealed envelope technique.

Group R: Patients received 4 ml 0.75% Isobaric Ropivacaine hydrochloride [Ropin (neon labs)]

Group RF: Patients received 4ml 0.75% Isobaric Ropivacaine [Ropin (neon labs)] with 25µg Fentanyl hydrochloride [Fenstud]

Before the commencement of anaesthesia, patient was explained about the methods of sensory and motor block assessments. All patients were kept fasting overnight. After arrival in the preanaesthetic room, intravenous access with 20G i.v cannula was established and an infusion of Ringer lactate was commenced to preload the patient with 10 ml/kg before spinal anaesthesia. Injection midazolam 1 mg I.V. and Injection ondansetron 4 mg I.V. was given as pre-anaesthetic medication. Standard monitoring was used throughout the operation with the help of a multiparamonitor having noninvasive blood pressure (NIBP), electrocardiograpy (ECG) and pulse oximetry (SpO2). Baseline blood pressure, heart rate and SpO2 were recorded. Throughout the procedure the patient was oxygenated with oxygen at 5L/min through ventimask. Blood, colloid, crystalloid was administered as per need.

Patients were placed in lateral position and after taking full aseptic precautions, lumbar puncture was performed in L3/L4 or L4/L5 inter space in midline, using quincke spinal needle of 25G. Correct needle placement was identified by free flowing cerebro- spinal fluid (CSF) and the drug was injected as per group allocation. After the injection of the drug, the spinal needle was removed, sterile dressing was applied and the patient was placed supine. The time of end of intrathecal injection was taken as “time 0” for further data recording.

- Motor block was assessed using the modified Bromage scale as

(0= no motor block)
(1=inability to raise extended legs)
(2=inability to flex knees)
(3=inability to flex ankle joints)

- The motor block was also assessed at 3 min. after SAB then at every 2 min. till 15 min.or maximum bromage score was achieved..Maximum motor block (Bromage score) and onset time of motor block (time to reach maximum Bromage score) was recorded.
- Surgery was allowed to commence in spinal anaesthesia on achieving T10 sensory level and Bromage score of 2 or 3. In 15 min. after SAB if

sensory level is below T10 but there is adequate sensory block on the operative site (perineum) on pinching with artery forcep, along with bromage score 2 or 3,then also surgery was allowed to commence in spinal anaesthesia with an aim of achieving supplementing analgesia at anytime if needed. If it was not achieved till 30 min of SAB it was considered as 'failed case' and general anaesthesia was given to accomplish surgery, and the case was excluded from further data analysis.

- If surgery started in spinal anaesthesia after achieving above criteria but the patient complained of intraoperative pain, anaesthetic supplementation in the form of fentanyl 2mcg/kg / ketamine 1mg/kg / propofol infusion (50-100mcg/kg/min) were given as per need and case was considered as 'partially successful'. If pain persisted case was converted to general anaesthesia and declared as a 'failed' case.
- If surgery was completed in spinal anaesthesia without supplementation of analgesia the case was declared as "completely successful case".
- Clinical efficacy (success rate) was graded as.

➢ Completely successful - if no supplementation given)
➢ Partially successful - if fentanyl/ ketamine/ propofol were given
➢ Failure - if converted to general anaesthesia

- Success rate in each group was defined as number of cases in whom surgery could be completed without supplementation analgesia.
- Vital parameters like SBP (systolic blood pressure), DBP (diastolic blood pressure), HR (heart rate), SpO_2 were recorded 5min before intrathecal injection (baseline) and at every 5min after SAB till 15 minutes then every 15 minutes till completion of surgery.
- The incidence of pruritus, nausea, vomiting were recorded.
- In postoperative phase, sensory and motor block were assessed at every 30 minutes, till sensory recovery upto S1 (lateral side of foot) dermatome achieved and Bromage score returned to zero. Time to regression to S1 (Duration of sensory block) and Time to return of Bromage score 0 (Duration of motor block) in minutes were noted.Time of first complaint of pain in postoperative period were recorded and considered as 'duration of analgesia' and Inj. Tramadol 100mg i.v. was given as rescue analgesia. Any postoperative complaints like nausea, vomiting, headache, pruritus or others were recorded, and treated accordingly

STATISTICAL ANALYSIS

The data were entered and analyzed by using MS Excel and Epi info-6. Quantitative data were represented as arithmetic mean, standard deviation and analyzed by using student –t test or ANOVA as per need. Qualitative data were presented as number (proportion or percentage) and analyzed by Chi square test. P value <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Both groups were statistically comparable regarding mean age, weight of patients and duration of surgery(60-90 min).

Table 1: Sensory Onset.

Sensory onset	Group R	Group RF	P value
Time to T_{10} (min).			
Mean±SD Range	4.25±1.33 (3-7)	3.33±0.75 (3-7)	0.003
Time to peak sensory level (min).			
Mean±SD Range	12.33±1.60 (9-15)	7.46±0.86 (7-9)	0.001

Table 1 shows that time to reach T_{10} sensory level was significantly shorter in group RF (3.33±0.75min) as compared to group R (4.25±1.33 min) (p = 0.003). Time to reach peak sensory level was also significantly shorter in group RF (7.46±0.86 min) as compared to group R (12.33±1.60 min) (p = 0.001). It implicates that addition of fentanyl to isobaric Ropivacaine resulted in significant shortening in sensory onset time.

Table 2: Peak Sensory Level.

	Peak sensory level	Group R (n=30)	Group RF (n=30)	P value
Patients distribution according to peak sensory level n(%)	T_4	24 (80%)	24 (80%)	
	T_6	4(13.3%)	6(20%)	
	T_8	2(6.67%)	0(0%)	
Mean±SD		$T_{4.53±1.16}$	$T_{4.4±0.81}$	0.06
Range		T_4-T_8	T_4-T_6	
Median		T_4	T_4	

Peak sensory level ranged from T_4 to T_8 in Group R and T_4 to T_6 in Group RF, however median value of peak sensory level was the same T_4 in both groups. Most of the patients in Group R and Group RF had peak sensory level of T_4 (n=24, 80%). Mean peak sensory level was comparable in Group RF ($T_{4.4±0.81}$) and Group R ($T_{4.53±1.16}$) (P = 0.06) (Table 2). It implicates that peak sensory level was little higher when fentanyl was added to Ropivacaine, though it could not reach statistical significance, p=0.06.

Table 3: Comparison of duration of sensory block.

Time (min)	Group R	Group RF	P value
Sensory regression to S_1			
Mean±SD	303.33±34.64	331.16±7.95	<0.001
Range	(240-340)	(315-350)	

Table 3 shows that time to sensory block regression to S_1 is significantly longer in group RF (331.16±7.95 min) as compared to group R(303.33±34.64 min) (P<0.001). This implicates that addition of fentanyl to Ropivacaine results in significant prolongation of duration of sensory block.

Table 4: Duration of analgesia (Time to first rescue analgesic)

Time for first rescue analgesia(min)	Group R	Group RF	P value
Mean±SD	239.16±20.51	271.0±34.17	<0.01
Range	(230-270)	(220-330)	

Table 4 shows that duration of analgesia as defined by time of requirement of first rescue analgesic dose is significantly longer in group RF (271.0±34.17 min) as compared to group R (239.16±20.51 min) (p = 0.007). This implicates that addition of fentanyl to Ropivacaine results in significant prolongation in duration of analgesia.

Table 5. Motor block characteristics

Time (min)	Group R	Group RF	P value
Mean Bromage score	3	3	
Time to B_3 (Bromage score 3)			
Mean±SD	6.6±1.22	5.26±1.01	0.31
(Range)	(5-9)	(5-9)	
Time to regression to B_0 (Bromage score 0)			
Mean±SD	280.5±16.62	289.83±19.40	0.40
(Range)	(260-305)	(260-310)	

All patients in both groups had Bromage score of 3 signifying complete motor block. Time to reach Bromage score of 3 (motor onset) is comparable in group RF (5.26±1.01 min) and group R (6.6±1.22min) (P = 0.31).Time to regression to bromage 0 (duration of motor block) was also stastistically comparable in Group RF (289.83±19.40 min) and Group R (280.5±16.62 min), (P = 0.40). It implicates that addition of fentanyl to Ropiavacaine do not make any difference in motor block characterstics. There was no significant difference in motor onset time , maximum motor block and duration of motor block, in Group R and Group RF.(p>0.05).

Mean heart rate, mean systolic and diastolic blood pressures after SAB are statistically comparable in both the groups at all time intervals intraoperatively (P > 0.05).

Respiratory parameters

SpO_2 remained 98% to 100% throughout the surgery in all patients at all time intervals. None of the patients has respiration rate <12/min or SpO_2 <92% on air during the study showing that incidence of respiratory depression or hypoxia was nil in both groups.

During the study period only adverse effect observed was single episode of hypotension and bradycardia that occurred in 2 patients in Group R (6.67%) and 1 patient in group RF (3.33%) in intraoperative period. These were successfully treated with single dose of mephentermine 6 mg and inj. Atropine (0.4 mg) respectively. Incidence of hypotension and bradycardia was minimal and comparable in two groups (P= 1.00). No other adverse effect was observed in study. None of the patient complained about pain, in both groups, surgeon also did not complain about relaxation or operative condition in any case. Thus incidence of complaints by patient and surgeon was 0%. Supplemental analgesia was not required in any of the patient in two groups hence supplementation rate was 0% in the study. Surgery of vaginal hysterectomy was completed in all patients (n=30,100%) of both groups in spinal anaesthesia without supplementation.Thus incidence of 'completely successful' cases was 100% in both group. Incidence of partial success or failure was 0% in both group.

DISCUSSION

Spinal anaesthesia is a preferred technique for gynaecological surgeries and bupivacaine is still the most commonly used local anaesthetic agent. Ropivacaine is levo-isomer of bupivacaine which is less toxic than bupivacaine. Our study clearly demonstrates that addition of fentanyl to Ropivacaine results in significant shortening of onset time of sensory block. It is a well known fact that opioids act synergistically to intrathecal opioids and potentiate the block. Opioids work in

intrathecal space by agonist interaction with opioid mu receptors in dorsal gray horn of spinal cord which modulates the function of afferent pain fibres.[10] Another contributing factor was change in baricity of Ropivacaine solution by adding Fentanyl ,therefore intrathecal solution became little hypobaric in Group RF as compared to Group R and resulted in faster onset of sensory block in Group RF in present study. Opioids such as fentanyl are hypobaric and when added to a local anaesthetic will render the subsequent mixture even more hypobaric. Parlow et al[11] stated that the addition of opioids to isobaric local anaesthetic alters the density of the resulting solutions, as well as the direction and extent of spread in a spinal model.

Results of present study clearly show that addition of fentanyl to Ropivacaine lead to significant shortening of sensory onset time, because fentanyl has synergestic effect with local anaesthetic and addition of fentanyl also makes the intrathecal solution hypobaric facilitating its cephalic spread.

SENSORY BLOCK DURATION

Fentanyl acts on μ receptor in the spinal cord and exerts its action by opening K+ channels and reducing Ca++ influx resulting in inhibition of transmitter release.[12] This is the reason that patients in whom fentanyl was given along with ropivacaine in spinal anaesthesia had significantly longer duration of the sensory block as compared to patients receiving ropivacaine alone.

MOTOR BLOCK CHARACTERSTICS

The results of our study demonstrated that addition of fentanyl to ropivacaine in spinal anaesthesia accelerated the sensory onset but has no effect on motor onset time. The synergistic interaction between spinal opioids and local anesthetics is characterized by enhanced somatic analgesia without effect on the degree or level of the local anaesthetic induced sympathetic or motor blockade.[13,14]

MOTOR BLOCK DURATION In our study time to return to Bromage 0 was 280.5± 16.62 min in Group R and 289.83±19.40 min in Group RF, which was Stastistically comparable (P=0.40).

In our study there was no significant difference in motor block duration in group R Sheikh et al[15] reported that time to complete regression of motor block was 170.0±19.7min in bupivacaine (10mg) group as compare to 170.0±13.9 min in bupivacaine (10mg) plus fentanyl (12.5mcg) group in caesarean section which was statistically comparable. Khanna et al[16] reported that time to complete regression of motor block was 160.9±5.5 min in bupivacaine (12.5mg) group as compare to 163.75±2.9 min in bupivacaine (12.5mg) plus fentanyl (25 mcg) group in geriatric patients undergoing hip replacement or DHS, there was no significant difference in motor block duration. It implicates that addition of fentanyl to intrathecal local anaesthetic has no effect on motor block characteristics (onset, extent, duration) because Intrathecal opioids enhance sensory block without potentiating motor and sympathetic block.

Comparison of sensory and motor block duration within groups

Ropivacaine is a long acting, enantiomerically pure (s-enantiomer) amide local anaesthetic, with a low lipid solubility which blocks nerve fibers involved in pain transmission (Aδ and c fiber) to a greater degree than those controlling motor function (Aβ) fibers.[17] This was the reason that motor block duration was shorter as compared to sensory block duration in various studies[8,18,19] using ropivacaine in spinal anaesthesia including ours. Thus use of isobaric ropivacaine in spinal anaesthesia imparts the benefits of early mobilisation and voiding owing to shorter motor block duration.

DURATION OF ANALGESIA

Significantly better postoperative analgesia in terms of prolonged duration, reduced pain scores, reduction in analgesic consumption has also been reported while using intrathecal fentanyl as an adjuvant to levobupivacaine[20] and bupivacaine.[15] Intrathecal opioids enhance sensory block without affecting motor and sympathetic block. Among them fentanyl has rapid onset of action, bind strongly to plasma protein and potentiates the afferent sensory blockade.[13,14]

SUPPLEMENTAL ANALGESIA /CLINICAL EFFICACY

In our study vaginal hysterectomy was accomplished in spinal anaesthesia using ropivacaine alone or with fentanyl in all cases without need of any supplementation. Hence success rate was 100% in both Group R and RF. It was because peak sensory level was around T4 and Bromage score was 3 in both Groups. Even one case in Group R was converted to abdominal hysterectomy but surgery was conveniently carried out in spinal anaesthesia without supplementation. Previous studies have also shown that ropivacaine in spinal anaesthesia alone and with fentanyl produced effective sensory motor block of sufficient duration to accomplish various surgeries without need of supplemental analgesia. The studies were as follows: Gupta et al in TURP[21] and infraumbilical surgeries.[18]

HEMODYNAMIC PARAMETERS

In our study, HR, SBP, DBP, and SpO_2 showed no significant change from baseline during intraoperative period in both groups. Both two groups were statistically comparable regarding vital parameters like heart rate, systolic blood pressure, diastolic blood pressure and SpO2 during intra-operative period ($p > 0.05$).

This showed that isobaric Ropivacaine alone and with fentanyl in spinal anaesthesia produces effective sensory motor blockade without affecting hemodynamic variables significantly.

SIDE EFFECTS

Hypotension and Bradycardia

In present study, only observed side effects were hypotension and bradycardia after spinal anaesthesia which too were minimal. Single episode of hypotension and bradycardia that occured in 2 patients (6.67%) in Group R and 1 patient (3.33%) in Group RF which was successfully managed with single dose of 6 mg of mephentermine i.v and 0.4 mg of atropine i.v. There were no significant difference regarding side effects between two groups ($p > 0.05$).

CONCLUSION

We conclude that

- Isobaric Ropivacaine [4 ml 0.75% (30 mg)] alone and with fentanyl (25mcg) in spinal anaesthesia produced effective sensory-motor blockade of sufficient duration with stable hemodynamic profile to accomplish vaginal hysterectomy.
- Addition of fentanyl offered the advantage of accelerating the sensory onset and prolonging the duration of analgesia and sensory block, without affecting sympathetic or motor block characteristics.
- Owing to early recovery in motor functions and lesser cardio-neuro toxicity, ropivacaine seems to be a good option for spinal anaesthesia.

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