

Isobaric Ropivacaine (0.75%) With Or Without Nalbuphine for Spinal Anaesthesia in Endoscopic Urological Surgery: A Prospective, Randomized, Controlled, Double Blind Study

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Abstract

Aims and Objective: Spinal anesthesia is a safe and reliable technique for urological surgery, providing excellent analgesia and muscle relaxation. Ropivacaine is a long-acting anesthetic drug with a greater margin of safety compared to bupivacaine. Nalbuphine is a mixed agonist-antagonist opioid that provides analgesia and sedation without significant side effects. The aim of this study was to evaluate the effect of intrathecal nalbuphine on sensory and motor block characteristics, prolongation of postoperative analgesia and side effects when used as an adjuvant with isobaric 0.75% ropivacaine in spinal anesthesia.

Materials and Method: This prospective, randomized, controlled, double-blind study included 60 patients undergoing elective endoscopic urological surgery under spinal anesthesia. Patients were randomly allocated into two groups: Group I received isobaric ropivacaine (0.75%) 2.5 ml with normal saline 1 ml, while Group II received isobaric ropivacaine (0.75%) 2.5 ml with nalbuphine (0.8mg). Sensory and motor block characteristics, postoperative analgesia, and side effects were assessed.

Results: The mean onset time of sensory block in group II was found to be significantly less than in group I, ($p = 0.006$). The mean onset time of motor block and time to complete motor block was significantly earlier in Group II as compared to Group I ($p=0.0277$ and $p=0.046$ respectively). The time to first rescue analgesic was significantly longer in Group II ($p=0.0054$), and the number of doses required in 24 hours was significantly lower in Group II ($p=0.0018$).

Conclusion: The addition of nalbuphine to isobaric ropivacaine (0.75%) for spinal anesthesia in endoscopic urological surgery improves sensory and motor block characteristics, prolongs postoperative analgesia, and reduces the requirement for rescue analgesics.

Keywords: Endoscopic urological surgery. Nalbuphine, Ropivacaine, Spinal anesthesia.

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Introduction

Spinal anesthesia (SA) is preferred technique for urological surgery as compared with general anesthesia (GA) because it allows early detection of symptoms of over hydration, transurethral resection of prostate (TURP)

syndrome, bladder perforation and also provide postoperative analgesia. [1,2] Various local anesthetics (LA) has been used for spinal anesthesia since their introduction. i.e., lignocaine, bupivacaine, levobupivacaine, ropivacaine. A good

choice of anesthetic is the one which produces rapid and smooth onset of action, an effective surgical response, postoperative analgesia, early recovery, and no or minimal side effects. [3,4] Bupivacaine is commonly and widely used local anesthetic drug which provides less incidences of transient radicular pain and hence is the drug of choice for ambulatory spinal anesthesia [5]. However, for day care surgeries and short surgical procedures, a prolonged motor block is not desirable, hence ropivacaine is a good choice of anesthetic for short and ambulatory procedures under spinal anesthesia thus leading to early recovery of motor function, decreases incidence of DVT and short hospitalization. [6,7]

Ropivacaine is a long-acting anesthetic drug which belongs to the pipercoloxylidides group and has a propyl group on the piperidine nitrogen atom compared to bupivacaine which has a butyl group. Ropivacaine which is a pure S (-) enantiomer developed for reducing potential CNS and cardiac toxicity whereas bupivacaine is a racemate mixture. [6]

It has greater margin of safety, low lipid solubility and higher capacity to block sensory nerve fibers than motor nerve fibers which is usually desirable in day care /ambulatory surgery unlike bupivacaine which cause profound motor blockade but sometimes less intense anesthetic blockade result in requirement of supplemental analgesia to perform surgery and hence to improve the block quality and to prolong the effect of spinal blockade as well as to augment postoperative analgesia with minimal side effects, various intrathecal adjuvants like opioids (i.e., morphine, fentanyl, nalbuphine) and others like clonidine, dexmedetomidine, neostigmine, epinephrine have been used. [3-5]

Nalbuphine is a mixed agonist-antagonist. It produces analgesia and sedation without μ side effects (nausea, vomiting, pruritis, constipation, respiratory depression, and tolerance/dependance). It has a short duration of action, a consistent lipid solubility and rapid clearance compared with other opioids. [7]

Administration of nalbuphine with ropivacaine provide synergistic effect thus enhance the quality and duration of block and prolongs the time of postoperative analgesia with minimal side effects. [8] Therefore this study was planned to evaluate the effect of intrathecal nalbuphine on sensory and motor block characteristics, prolongation of postoperative analgesia and side effects when used as an adjuvant with isobaric 0.75% ropivacaine in patients undergoing elective endoscopic urological surgery under spinal anesthesia.

Material and Methods

This prospective, randomized, double-blinded,

controlled trial was conducted after obtaining approval from the Institutional Research Ethical Committee [GMCH/IRRC/PG20/2021/5603(85)] and written informed consent.

A total of sixty patients of ASA grade I-III, aged eighteen to sixty years, of either gender undergoing elective urological surgery under spinal anesthesia were included in the study. (Fig 1)

Patients were excluded from the study if they refused, had a history of hypersensitivity to the study drug, had local infection at the site of the block, coagulopathy, spinal deformity, or complete block failure.

Patients were randomly allocated into two groups of thirty patients each using a computer-generated random number table. Each group received study drugs as follows: Group I received isobaric ropivacaine (0.75%) 2.5ml with 0.9% normal saline 1ml, while Group II received isobaric ropivacaine (0.75%) 2.5ml with nalbuphine 0.8mg diluted in 0.9% normal saline 1ml. The anesthesiologist who prepared the study drug was not part of the study, and the patients and anesthesiologist were blinded to group assignment and study drugs.

All patients underwent pre-anesthetic checkups and were explained the spinal anesthesia procedure in detail during the pre-anesthetic visit. Patients fasted for 8 hours and were preloaded with Ringer's lactate solution before spinal anesthesia was administered with the study drug.

Under all aseptic precautions spinal anesthesia was given with study drug as per group allocation in sitting position at the level of L3-L4, or L4-L5 interspace using a 25G Quincke's spinal needle after free flow of cerebrospinal fluid. After spinal anesthesia patients were placed in supine position.

Sensory block assessment was done by loss of pinprick sensation, and motor block characteristics were assessed using the Modified Bromage score. Sedation was assessed using the Ramsay sedation scale. Hemodynamic monitoring was done.

If patient complained of pain during surgery, inj. fentanyl 50 μ g intravenously was administered (partial failure). If patients still complained of pain, the patients were administered general anesthesia (complete failure). Patients with partial failure were included in study but patients with complete failure were considered as dropout.

Hypotension, bradycardia, nausea, vomiting, and other side effects were managed accordingly. Data were recorded including demographic data, sensory block characteristics, motor block characteristics, requirement of analgesics, incidence of hypotension and bradycardia, time to first rescue analgesic, total number and doses of analgesic drug postoperatively, side effects, Ramsay Sedation

Score, and Patient Satisfaction Score. Patients were assessed after 24 hours for postoperative analgesia and asked about patient satisfaction score.

Results

Table 1 shows no significant difference between the two groups regarding demographic data as mean values of age, weight, height, sex, ASA grade, duration of surgery ($p > 0.05$).

Table 2 shows the sensory and motor block characteristics following spinal anaesthesia. The mean onset time of sensory block in group II was found to be significantly less than in group I, ($p = 0.006$.) The mean time to reach maximum height of sensory block in group II was significantly earlier than in group I ($p = 0.03$), whereas two segment regression time was significantly earlier in group I (127 ± 24.52) as compared to group II (149 ± 31.00) $p = 0.003$. The mean onset time of motor block and time to complete motor block was significantly earlier in Group II as compared to Group I ($p = 0.0277$ and $p = 0.046$ respectively). Similarly, the duration of motor block was highly significantly more in Group II (188 ± 35.44) as compared to Group I (114 ± 27.74); $p = 0.0001$.

Table 3 shows the number of patients and maximum height of sensory block. In group I 18 patients achieved maximum level of T6 as compared to 15 patients in group II. Three patients in group I achieved only T10 level. Two patients in group II reached up to T4 level.

Table 4 shows comparison of Bromage score between both the groups. Ten patients of Group I achieved only Bromage score 1 while maximum

patients (21) of Group II have Bromage score 2 and 7 patients achieved Bromage score 3 which was statistically significant. ($p = 0.0252$).

Comparison of complete success of block and requirement of supplement analgesia in both the group showed that 29(96.66%) patients in group II had complete successful block while just 1 (3.33%) patient had partial block while in group I 27(90%) patients had successful block and 3 (10%) patients had partial block.

Requirement of supplementation of fentanyl and total doses was more in group I (3 patients in group I required supplement $5 \pm 15.26 \mu\text{g}$ fentanyl vs 1 patient required fentanyl $1.67 \pm 9.12 \mu\text{g}$ in group II).

Table 5 shows the time of first requirement of rescue analgesia (hours) which was found to be significantly prolonged in Group II as compared to Group I, $p = 0.0054$. The number of doses required in 24 hours was significantly more in Group I vs Group II, $p = 0.0018$.

Figure 2 Shows the Incidence of hypotension was more in Group I but statistically non-significant. Incidence of nausea and vomiting was more in Group II but found to be non-significant ($p = 0.4167$).

Ramsay sedation score in both the groups at different time intervals which was found to be non-significant; $p > 0.05$. Satisfaction score by the patients between the two groups after 24 h which was excellent in 12 patients (40%) in group II and 10 patients (33.33%) in group I, which was found to be statistically non-significant ($p = 0.450$).

Table 1: Comparison of demographic data in both groups (Mean \pm SD)

Patient profile	Group I (n=30)	Group II(n=30)	P value
Age (years)	48.47 \pm 12.22	48.83 \pm 13.92	0.9156
Sex M/F	25(83.33%)/5(16.6%)	27(90%)/3(10%)	0.45
Weight (Kg)	65.7 \pm 7.91	67.93 \pm 6.362	0.2338
Height(cm)	163.4 \pm 6.67	164.83 \pm 4.857	0.34
ASA I/II/III	12/16/2	14/15/1	0.77
Duration of surgery (min)	42.8 \pm 13.81	40.83 \pm 13.524	0.5788

Table 2: Comparison of sensory and motor block characteristics in both groups (Mean \pm SD)

Characteristics	Group I(n=30)	Group II (n=30)	P value
Onset of sensory block (min) T10 dermatome	8.13 \pm 1.73	6.73 \pm 2.06	0.006*
Maximum sensory block height (thoracic dermatome) – Median	T6	T6	0.1206
Ti Time to reach maximum sensory block (min)	13.07 \pm 3.18	11.53 \pm 2.08	0.03*
Two segment regression time (min)	127 \pm 24.52	149 \pm 31.00	0.003*
Onset of motor block (min) Bromage grade 1	5.53 \pm 1.94	4.33 \pm 2.17	0.0277*
Time to complete motor block(min) Bromage grade 3	15.3 \pm 9.69	11.4 \pm 4.07	0.046*
Duration of motor block(min)	114 \pm 27.74	188 \pm 35.44	0.0001**

$p > 0.05$ = Non significant, $p < 0.05$ = significant (denoted by *)

Table 3: Comparison of number of patients and maximum level of sensory block between both the groups

Thoracic dermatome Level	Group I(n=30)	Group II(n=30)	P value
T10	3 (10%)	0	-
T9	2(6.6%)	2(6.6%)	1
T8	2(6.6%)	5(16.66)	0.227
T7	4(13.33%)	3(10%)	0.688
T6	18(60%)	15(50%)	0.436
T5	1(3.3%)	3(10%)	0.300
T4	0	2(6.6%)	-

p>0.05= Non significant, p<0.05 =significant (denoted by *)

Table 4: Comparison of Bromage score among both the group

Bromage score	Group I(n=30)	Group II(n=30)	P value
0	0	0	0.0252*
1	10(33.33%)	2(6.66%)	
2	17(56.66%)	21(70%)	
3	3(10%)	7(23.33%)	

p<0.05 =significant (denoted by *)

Table 5: Comparison of post-operative requirement of rescue analgesia in both groups (Mean ±SD)

Variable	Group I(n=30)	Group II(n=30)	P value
Time to first rescue analgesia(hours)	6.93±2.95	10.06±5.15	0.0054*
Number of doses (in 24 h)	1.76±0.56	1.30±0.53	0.0018**
Total dose (mg) in 24 h	176.67 ±56.83	130±53.49	0.0018**

p<0.05 = significant (denoted by *), p≤0.001=highly significant (denoted by **)

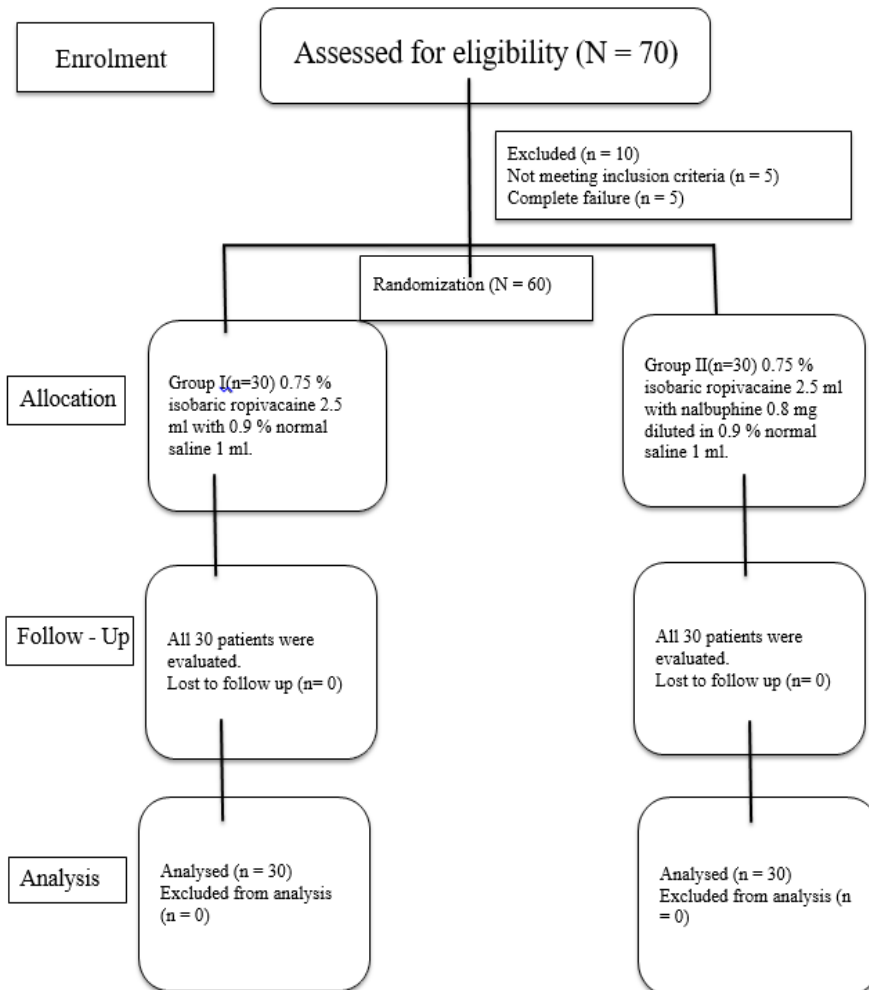


Figure 1: Consort Flow Diagram showing allocation of patients at different stages of study

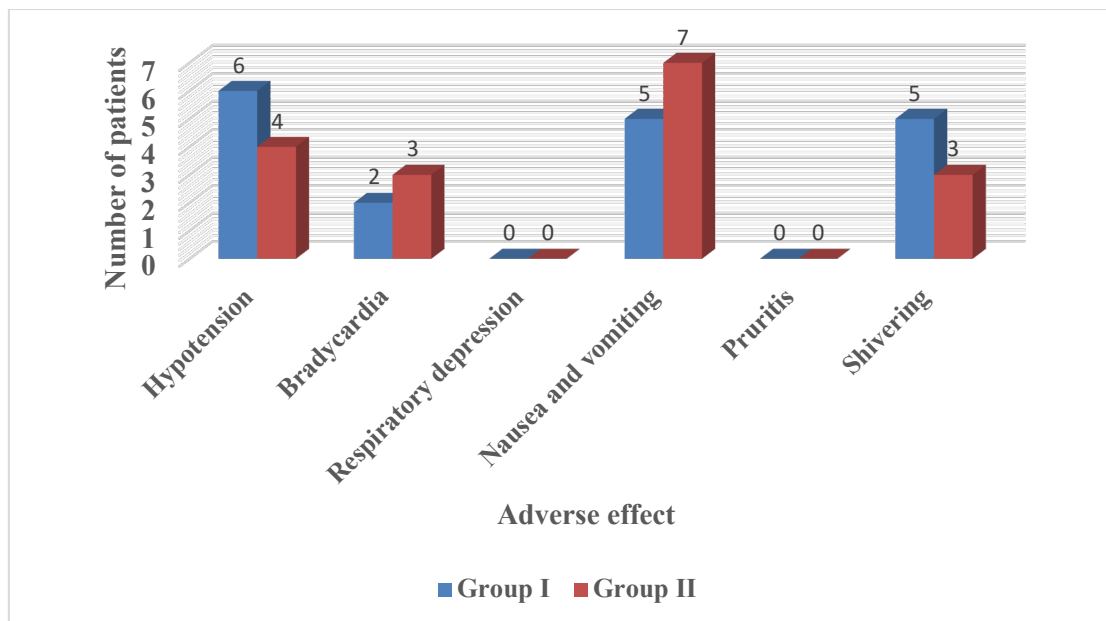


Figure 2: Graphical representation of comparison of intraoperative and postoperative adverse effects

Discussion

The most commonly used anesthetic technique for endoscopic urological surgeries is spinal anaesthesia (SA). Urological surgeries mostly completed in less than sixty min, therefore early recovery and discharge is desirable. In this study ropivacaine was used because it is a newer amide local anaesthetic and may be a good choice for ambulatory anaesthesia compared to bupivacaine. Ropivacaine has no effect on the spinal cord blood flow and doesn't induce neurotoxic effects after intrathecal administration in dogs and rabbits. [9,10]

Hemodynamic effects can also be minimized by using isobaric ropivacaine 0.75% a pure S(-) enantiomer which has reduced lipophilicity and decreased potential for central and cardiovascular toxicity when compared to other local anesthetics. [11]

Various studies have found that intrathecal injection of isobaric ropivacaine produced a sensory block of variable extent due to inadequate distribution of block, so adjuvant are added to improve the quality of sensory and motor characteristics of block. Hyperbaric ropivacaine produces more predictable and reliable sensory and motor block, with faster onset than a plain solution.[12] Since commercial preparations of hyperbaric ropivacaine was not available at the time of this study therefore plain ropivacaine was used in this study.

Opioid when added to local anesthetic, these two types of drugs eliminate pain by acting at two different sites. [13] Nalbuphine produces agonist activity at the κ -opioid receptor and an antagonist activity at the μ -opioid receptor, and hence it can

produce analgesia without the unwanted side effects of the μ -agonist opioid.

Demographic data regarding age, sex, weight, height, ASA grade, and duration of surgery were found to be comparable in both groups in this study which were similar to other studies. [14-22]

The onset of sensory block (T-10 dermatome) was significantly faster in Group II (nalbuphine with 0.75% isobaric ropivacaine) (6.73 ± 2.06 min) than in Group I (8.13 ± 1.73), ($p = 0.006$). The mean time to reach maximum height of sensory block was significantly earlier in Group II (11.53 ± 2.08) than in Group I (13.07 ± 3.18) $p = 0.03$, whereas two segment regression time was significantly earlier in Group I (127 ± 24.52) as compared to Group II (149 ± 31.00) $p = 0.003$.

Maximum patients achieved T6 level in Group I (60%) and in Group II (50%). Three patients in Group I achieved only T10 level. Two patients in Group II reached up to T4 level. Borah TJ et al [22] studied effect of three different doses of nalbuphine (0.4mg, 0.8 mg, 1.6 mg) as an adjuvant with plain ropivacaine (0.75%) in elective lower limb surgeries and found that the onset time of sensory block was faster in 0.8 mg and 1.6 mg nalbuphine as compared to 0.75% plain ropivacaine. However, it was not statistically significant ($p > 0.05$). The two- segment regression time was found to significantly higher in nalbuphine groups as compared to plain ropivacaine group ($p = 0.013$) which was similar to our present study.

Mukherjee A et al [23] in their prospective randomized study used 0.2,0.4,0.8 mg nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine 12.5 mg for elective lower limb orthopedic surgeries and found that onset of sensory block was comparable

in nalbuphine groups and without nalbuphine (hyperbaric bupivacaine) groups but two segment regression time of sensory blockade was prolonged progressively in nalbuphine groups with higher dose (0.4,0.8 mg).

Similarly, Jyothi B et al [20] found that onset of sensory block was comparable in nalbuphine groups and without nalbuphine (hyperbaric bupivacaine) groups but two segment regression time of sensory blockade was prolonged in nalbuphine groups as compared to bupivacaine group.

The mean onset of motor block (Bromage scale 1) was significantly earlier in Group II (4.33 ± 2.17 min) as compared to Group I (5.53 ± 1.94 min); $p = 0.0277$. Similarly, the time to complete motor block (Bromage scale 3) was also found significantly earlier in Group II (11.4 ± 4.07 vs 15.3 ± 9.69 min); $p = 0.046$. The duration of motor block was significantly higher in Group II, $p = 0.0001$. Borah TJ et al [22] found motor block onset was comparable in all groups but duration of motor block were found to be significantly prolonged with higher doses of nalbuphine ($p < 0.05$) while Mukherjee A et al [23] found that both onset and duration of motor block was comparable in all groups. ($p = 0.369$ and 0.592 respectively).

Partial failed spinal block was found in three patients of ropivacaine group while one patient of nalbuphine group had partial failed spinal who were given fentanyl $50 \mu\text{g}$ as supplement analgesia intraoperatively (total dose $150 \mu\text{g}$ in ropivacaine and $50 \mu\text{g}$ in nalbuphine group). Naithani U et al [16] conducted a randomized double-blind study to evaluate the dose dependent effect of intrathecal dexmedetomidine ($3 \mu\text{g}$ and $5 \mu\text{g}$) on isobaric ropivacaine 0.5% in abdominal hysterectomy under spinal anesthesia and found total failure rate to be 10 % ($5 \mu\text{g}$ group) and 12.5 % ($3 \mu\text{g}$ group).

Various other studies found total failure rate between 10% to 16 % and lesser failure rate was seen with higher dose of ropivacaine as compared to lower doses. The different incidence of failed spinal might be due to different dose of isobaric ropivacaine, different type of adjuvant, different methods to evaluate sensory and motor block in different surgeries. [18,19] The VAS score immediately and 2 h postoperatively were comparable in both groups which might be due to effect of intrathecally used local anesthetic drugs. However, after 4 h VAS score was found to be significantly more in group I as compared to group II upto 24 h ($p < 0.05$).

The time to first requirement of rescue analgesia was found to be significantly higher in group II (10.06 ± 5.15 h) as compared to group I (6.93 ± 2.95

h); $p = 0.0054$. The total number of doses and total consumption of rescue analgesia (tramadol 100 mg) in 24 h was significantly more in group I as compared to group II; $p = 0.0018$ in this study.

Similar to our study Jyothi B et al [20] found patients who received bupivacaine with nalbuphine had significantly longer duration for first request of analgesia when compared with patients who received bupivacaine alone. Tiwari AK et al [21], found less VAS in groups receiving nalbuphine at 90,120 and 150 min after induction as an adjuvant to 0.5 % hyperbaric bupivacaine as compared to patients who did not receive nalbuphine.

Borah TJ et al [22] did not found any significant difference in VAS score (3.16 ± 0.55 , 3.08 ± 0.81 and 3.28 ± 0.73 at 210 min) between nalbuphine group and without nalbuphine group. Similarly, Mukherjee A et al [23] found that although VAS scores were comparable, the duration of analgesia was prolonged in all groups receiving nalbuphine with mean of 278.5 ± 6.04 min in patients receiving 0.8mg nalbuphine as compared to mean duration of 237 ± 5.64 min in 0.4 mg nalbuphine. ($p = 0.000$).

Sedation score was recorded intra and postoperatively in patients in which complete block was achieved. Patients in group I and group II had Ramsay sedation score between two and three which was found to be not significant; $p > 0.05$ and none of the patients had score more than three in both the groups. Jain N et al [24], compared two adjuvants with bupivacaine (group F- received fentanyl $20 \mu\text{g}$ +0.5% bupivacaine vs group N 0.4 mg nalbuphine +0.5% bupivacaine) they found significantly higher sedation score in fentanyl group at 30 and 60 minutes; $p < 0.05$ while no significant difference at 90 and 120 min between the two groups.

Bindra et al [25], compared nalbuphine 0.8 mg with bupivacaine in group I and fentanyl ($20 \mu\text{g}$) with bupivacaine in group II and 0.5% bupivacaine alone in group III, they found that RSS was significantly higher in group II as compared to group I and III at 30- and 60-min $p < 0.05$ and no significant difference were found at 90 and 120 min among all three groups. These studies shows that fentanyl when used intrathecally with bupivacaine has more sedation as compared to nalbuphine and bupivacaine alone upto 60 min but did not have any significant difference after 60 min.

The incidence of hypotension and bradycardia were not significantly different in both the groups ($p = 0.48$ and 0.4167 respectively). Mukherjee et al [23] found higher incidence of adverse effect with 0.8 mg nalbuphine which was contradictory to our results and this might be due to use of hyperbaric bupivacaine, different demographic profile and different type of surgery.

In this study, none of patient had respiratory depression. Since respiratory depression is predominantly μ receptor-mediated and nalbuphine is a μ receptor antagonist, respiratory depression effect is expected to be attenuated by nalbuphine. Increasing the dosage from 0.8 to 2.4 mg did not cause any respiratory complications which was also found in studies done by Culebras et al, Jyothi B et al and Tiwari et al. [17,20,21] Nalbuphine, antagonize morphine-induced side effects apart from its potent analgesic property. Hence, it might be a good choice, especially if the patient has history of μ side effects.

Borah et al [22], found all four groups (0.4, 0.8, 1.6 mg nalbuphine and plain ropivacaine) were statistically comparable in terms of adverse effects although the 1.6 mg group had slightly higher incidence of adverse effects.

Garg K et al [26] compared fentanyl 25 μ g vs nalbuphine 0.8 mg intrathecally with 0.5 % hyperbaric bupivacaine in patients undergoing urological procedures. They found that the onset of sensory and motor block was comparable in both groups but nalbuphine group had significantly higher duration of sensory and motor block. The requirement of rescue analgesia was significantly higher in fentanyl group. They also found that intraoperative and postoperative hemodynamic were comparable while incidence of pruritis and shivering was significantly higher in fentanyl group. Similarly, various other studies found that intrathecal nalbuphine prolongs the postoperative analgesia and could be used as an alternative to other opioids like fentanyl, morphine. [27,28].

Conclusion

To conclude, present study demonstrates that the addition of nalbuphine to isobaric ropivacaine (0.75%) for spinal anesthesia in endoscopic urological surgery significantly improves sensory and motor block characteristics, prolongs postoperative analgesia, and reduces the requirement for rescue analgesics.

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