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ORIGINAL RESEARCH

Effects of intraperitoneal instillation of Dexmedetomidine versus Fentanyl as adjuvants to Ropivacaine for postoperative pain management after Laparoscopic Cholecystectomy: A Comparative randomized control study

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Abstract

Background: Laparoscopic cholecystectomy has revolutionized the gall bladder surgery as a day care procedure but for post-operative pain. This study compared the efficacy of Dexmedetomidine (1 μg/kg) and Fentanyl (1 μg/kg) as intraperitoneal adjuvant to 0.375% ropivacaine (40ml) given perioperatively for post-operative pain management in patients undergoing laparoscopic cholecystectomy surgeries under general anaesthesia.

Materials & Methods: A total of 110 patients fulfilling the eligibility criteria were enrolled in the study and were randomized either to receive combination of ropivacaine with fentanyl (Group RF; n=55; mean age 39.02 years; 94.5% females) or combination of ropivacaine with Dexmedetomidine (Group RD; n=55; mean age 38.75 years; 90.9% females) respectively. Post-operative vital parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation) were noted. Sedation scores were measured using Ramsay Sedation Score. All the patients were followed up till 24 hours at every 2 hourly interval for pain (measured using Numeric Rating Scale), dose and amount of rescue analgesia (Diclofenac). Adverse effects, if any were noted.

Results: Average NRS scores over 24 hours were significantly lower in RF as compared to RD group. Amount of rescue analgesia, number of patients requiring rescue analgesia and number of dosages of rescue analgesia required were significantly higher in RD as compared to that in the RF group. Post-operative sedation scores were significantly higher in RD as compared to that in RF group. No adverse effect was noted in RF group whereas in RD group, there was 1 (1.8%) patient each experiencing fever and headache as the adverse effect.

Conclusion: Findings of the study showed that though both the combinations were safe to use, however, combination of fentanyl with ropivacaine provided far better analgesic effect without causing much sedation as compared to combination of dexmedetomidine with ropivacaine.

Keywords: Laparoscopic cholecystectomy, postoperative pain, analgesia, ropivacaine, fentanyl, dexmedetomidine

Introduction

Cholecystectomy, i.e., removal of gall bladder is one of the most commonly performed surgical procedures. Though, a number of gall bladder diseases are indications for this, however, cholelithiasis (gall stone disease) is the commonest indication for this. Over the years, frequency of cholelithiasis cases is increasing rapidly, resulting in an increased number of cholecystectomy procedures throughout the world. Laparoscopy's acceptance as a hallmark surgical approach is largely due to its benefits: smaller incisions, minimal intraoperative blood loss, reduced postoperative pain, faster recovery, shorter hospital stays, and improved cosmetic results.[1]

Laparoscopic cholecystectomy is performed using regional blocks, preferably brachial plexus block that

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are administered using local anesthetic at the block location. Brachial plexus block is a suitable alternative or a valuable addition to general anaesthesia for patient undergoing upper extremity surgery.[2] It has a long history, existing to date, providing surgical anesthesia and rehabilitating analgesia, as well as also it has demonstrated to be a useful, safe and sure technique suitable for almost all the age groups. Over the last few years, with increasing popularity of regional anesthesia over general anesthesia, use of such regional block techniques has increased substantially. These techniques not only are safer as compared to the general anesthesia, having fewer side effects, early block achievement and longer block duration but also result in an increased patient satisfaction apart from reducing the hospital stay substantially.[3]

Bupivacaine has been the most widely used long-acting local anaesthetic for several decades. Ropivacaine is a long-acting amide local anesthetic with a potentially improved safety profile when contrasted to bupivacaine. Intraperitoneal injections of local anaesthetic have been proposed to minimize postoperative pain after laparoscopic surgeries. Adjuvants are often added to local anaesthetics for nerve blocks to prolong its anaesthetic effects.[4] Alpha 2 agonists such as clonidine or dexmedetomidine and opioids like fentanyl combined with Bupivacaine has shown to increase the duration of anaesthesia significantly. While fentanyl, an opioid, has been shown to be highly effective, however, its systemic use is often criticized, side effects (>10% patients) include persistent or recurrent depression of ventilation, diarrhea, nausea, constipation, dry mouth, somnolence, confusion, asthenia (weakness) and sweating. Hence, a number of alternatives for opioids have been discovered and being used for systemic as well as local administration.[5]The present study was conducted to assess effects of intraperitoneal instillation of Dexmedetomidine versus Fentanyl as adjuvants to Ropivacaine for postoperative pain management after laparoscopic cholecystectomy.

Materials & Methods

The study was carried out on 110 patients scheduled to undergo laparoscopic cholecystectomy in Department of Anesthesiology, Hind Institute of Medical Sciences (HIMS), Ataria, Sitapur. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups. Group RF (n=55) - To receive 40ml of 0.375% Ropivacaine +2ml fentanyl (1µ gm. /kg) = 42 ml. Group RD (n=55) - To receive 40ml of 0.375% Ropivacaine+2ml Dexmedetomidine (1µgm/kg)=42ml. Baseline blood pressure (BP) and heart rate (HR), respiratory rate (RR), Oxygen saturation (SpO2) were checked before conducting the procedure. BaselineHeart rate (HR), SpO2, ECG, non-invasive blood pressure (NIBP) was monitored continuously during the procedure. General anesthesia was given under all aseptic precautions. Postoperatively NRS score was measured at every 2 hours till 24 hours.Total duration of rescue analgesia, complications and sedation was graded using the Modified Ramsay Sedation Scale etc. Results thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Comparison of baseline vital parameters between two groups

Parameter	Group RF (n=55)		Group RD (n=55)		Statistical significance	
	Mean	SD	Mean	SD	't'	'p'
Heart rate(bpm)	81.02	9.30	83.47	8.30	-1.460	0.147
SBP(mmHg)	120.53	9.36	120.75	9.51	-0.121	0.904
DBP(mmHg)	76.18	9.95	79.15	7.50	-1.764	0.081
MAP(mmHg)	90.75	10.31	91.96	8.02	-0.692	0.491
SpO2(%)	100	0	100	0	-	-

Table I shows that at baseline mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and SpO2 were 81.02±9.30 bpm, 120.53±9.36 mmHg, 76.18±9.95 mmHg, 90.75±10.31mmHg and 100% respectively in Group RF and 83.47±8.30 bpm, 120.75±9.51 mmHg, 79.15±7.50 mmHg, 91.96±8.02 mmHg and 100% respectively in Group RD. Statistically, there was no significant difference between two groups for any of these parameters (p>0.05).

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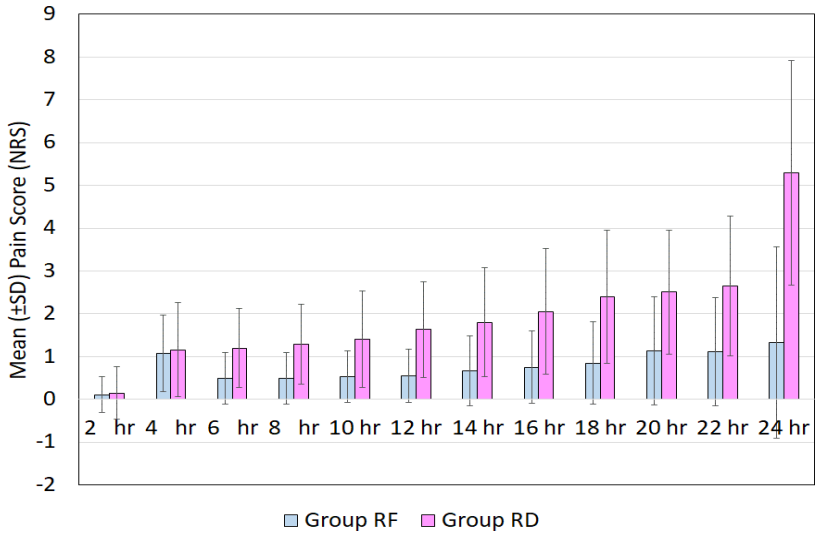

Graph I Between group comparison of pain score (NRS) at different time intervals

Assessment of post-operative pain was done at 2 hourly intervals till 24 hours. Pain scores of group RD were higher as compared to group RF at all the periods of observation. Difference in pain scores of two groups were not found to be statistically significant initially (at 2 hours and 4 hrs). At 6 hours and thereafter till 24 hours, pain scores of group RD were significantly higher as compared to group RF.

Table: II Between group comparison for Ramsay sedation score (Highest)

Sedation score	Group RF (n=55)		Group RD (n=55)		Statistical significance	
	No.	%	No.	%	χ^2	'p'
RSS1	44	80.0	2	3.6	65.910	<0.001
RSS2	11	20.0	53	96.4		

Table II shows that majority of patients of RD group had Ramsey sedation score 2 (96.4) rest of the patients had score 1 while majority of patients in RF group had Ramsey sedation score 1 (80.0%), rest 20% had score 2. Proportion of cases with higher score was significantly higher in RD as compared to that in Group RF ($p<0.001$).

Table; III Between group comparison of time to first rescue analgesic and total dosages of rescue analgesic required

Parameter	Group RF (n=55)		Group RD (n=55)		Statistical significance	
	Mean	SD	Mean	SD	't'	'p'
Time to first rescue analgesia (hrs)	23.78	0.99	21.06	3.98	4.932	<0.001
Dosages of rescue analgesia	No.	%	No.	%	χ^2	'p'
Nil	42	76.4	14	25.5	36.097	<0.001
One	12	21.8	17	30.9		
Two	1	1.8	16	29.1		
Three	0	0.0	6	10.9		
Four	0	0.0	2	3.6		

Table III shows that time to first rescue analgesia was significantly longer in group RF (23.78±0.99 hours) as compared to that in group RD (21.06±3.98 hours) ($p<0.001$).Rescue analgesia was not required in 42 (76.4%) of group RF and 14 (25.5%) of group RD patients. There were 24 (43.6%) patients in RD group who required more than one doses of rescue analgesia as compared to only 1 (1.8%) patient of group RF. Statistically, there was a significant difference between the two groups for need of rescue analgesia ($p<0.001$).

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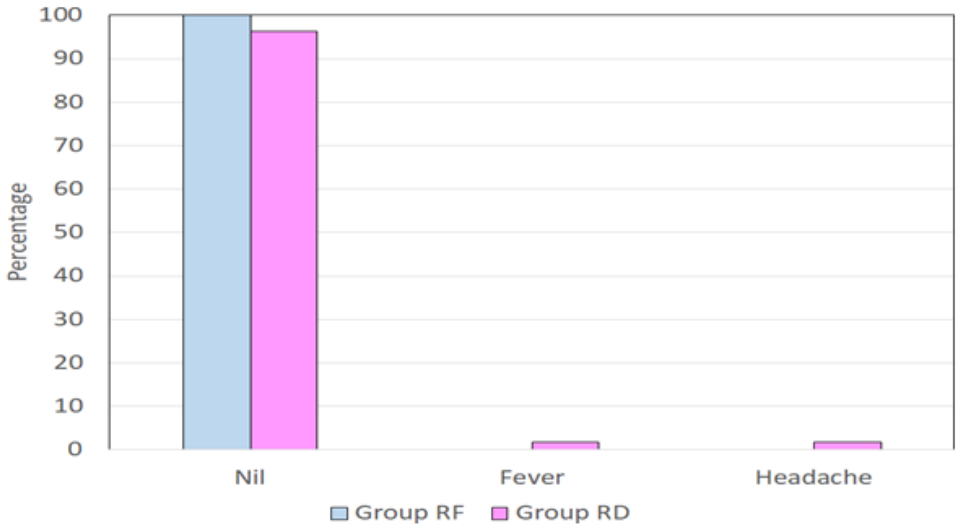

Graph: II Between group comparison for adverse effects

No adverse effect was noted in group RF. In group RD, there was 1 (1.8%) case each presenting with fever and headache respectively. Statistically, the two groups were comparable for headache profile (p>0.05).

Discussion

Cholecystectomy is one of the most frequently performed surgical procedures worldwide. The development of minimally invasive techniques, such as laparoscopic cholecystectomy, has enabled it to become a potential day care procedure. However, one significant barrier to this is post-operative pain, which is a critical factor in determining overall patient satisfaction. Therefore, targeted strategies are needed to reduce post-operative pain and enhance the patient's overall experience.[6]

Pre-emptive analgesia is an effective strategy to manage post-operative pain before it begins. Various drugs and analgesic agents have been proposed for this purpose, administered through different routes, primarily oral and intravenous. These include Oral etoricoxib, oral diazepam, intravenous ibuprofen, intraperitoneal bupivacaine, intravenous diclofenac in combination with ketamine. However, none have gained widespread clinical acceptance for routine use. In the recent years, perioperative intraperitoneal infiltration of local anesthetics in combination with other drugs has emerged as a useful safe and effective strategy with minimal adverse effects.[7] A number of combinations for this purpose have been proposed. While bupivacaine and ropivacaine are some of the most common principal drugs used for this purpose, their combination with adjuvant use of opioids like fentanyl, morphine and tramadol has been shown to increase their efficacy. In the recent years some new drugs like dexmedetomidine have also been proposed to have a promising response in this direction. However, there are not many studies comparing their performance under different environments.[8] Hence, the present study was carried out to compare the efficacy of Dexmedetomidine (1 µg/kg) and Fentanyl (1 µg/kg) as intraperitoneal adjuvant to 0.375% ropivacaine (40ml) given perioperatively for post-operative pain management in patients undergoing laparoscopic cholecystectomy surgeries under general anesthesia.

For this purpose, a total of 110 patients fulfilling the eligibility criteria were enrolled in the study and were randomized either to receive combination of ropivacaine with fentanyl (Group RF; n=55;mean age 39.02 years; 94.5% females) or combination of ropivacaine with Dexmedetomidine (Group RD; n=55; mean age 38.75 years; 90.9% females).

With respect to mean age and sex of patients, it was reflective of early middle age female dominance. As most of the cases underwent laparoscopic cholecystectomy with gall stone disease as indication, the dominance of early middle- aged females can be well justified.[9] However, there are some workers who described the mean age of patients lower than ours and with a dominance of male. Praveena et al[10] in their study reported the mean age as 37.2 and 36.1 years and proportion of males as 70% and 72.5% respectively.

In the present study we found both the drugs to have a comparable and stable hemodynamic profile. Intraperitoneal infiltrations are generally known to have no adverse impact on hemodynamics. In other studies too, hemodynamics has not been reported to be affected and both the trial drugs in combination with ropivacaine or bupivacaine have been found to be comparable.[11,12,13] However, there are some studies that have reported intraoperative heart rate and blood pressure to be lower in RD as compared to RF group. But it must be understood that intraoperative hemodynamics cannot be attributed to these drug combinations as these drugs are generally administered at the end of procedure, immediately before the skin closure.

In the present study, we observed that average NRS scores over 24 hours were significantly lower in RF as compared to RD group. We also observed that amount of rescue analgesia, numberof patients requiring

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rescue analgesia and number of dosages of rescue analgesia required were significantly higher in RD as compared to that in the RF group. Thus, in effect, ropivacaine with fentanyl outperformed ropivacaine with dexmedetomidine with respect to post-operative pain management.

Most of the exiting evidence in literature is not in agreement with our findings. Workers like Praveena et al[10], Modir et al[11], Thomas et al[14] and Soni et al[13] found post-operative pain scores to be higher in RF as compared to that in RD group, significantly longer time to rescue analgesia and significantly lower amount/dose of rescue analgesia in RD as compared to RF group in different dose combinations. Incidentally, none of the studies found such categorical differences in pain scores, duration of analgesia and dosages of analgesia as seen in the present study. Even combination of fentanyl and dexmedetomidine to bupivacaine instead of ropivacaine have at the most shown the two drugs to be comparable with respect to their post-operative pain management efficacy.[11] As such, there is no prior study supporting the trend of outcomes seen in the present study.

In the present study, we found RD group to have higher sedation scores as compared to RF group. This is in agreement with the observation of Gupta et al[12] who also observed a similar trend.No adverse effect was noted in RF group whereas in RD group, there was 1 (1.8%) patient each experiencing fever and headache as the adverse effect. As such most of the other studies also did not report any major adverse effect. However, some studies have reported them to be significantly higher in RF as compared to that in the RD group.

Conclusion

Findings of the study showed that though both the combinations were safe to use, however, combination of fentanyl with ropivacaine provided far better analgesic effect without causing much sedation as compared to combination of dexmedetomidine with ropivacaine.

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