Assessment of intraperitoneal instillation of levobupivacaine plus Dexmedetomidine versus ropivacaine plus Dexmedetomidine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy: A comparative study

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Abstract
Background: The present study was undertaken for assessing and comparing the efficacy of intraperitoneal instillation of Levobupivacaine plus Dexmedetomidine and Ropivacaine plus Dexmedetomidine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

Materials & methods: 40 patients were randomly divided into two groups of 20 each using sealed envelopes. Group A: Patients were given levobupivacaine plus Dexmedetomidine, and Group B: patients were given ropivacaine plus dexmedetomidine. Proforma was made and complete demographic and clinical profile of all the patients was recorded. Postoperatively the patients were assessed for pain utilizing visual analogue scale (VAS). Mean time to first analgesic requirement was recorded. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

Results: In the present study, mean age of the subjects of Group A and group B was 42.8 years and 45.3 years respectively. There were 12 males and 8 females in group A and 11 males and 9 females in group B. Mean VAS score among the subjects of group A at baseline, 1 hour, 6 hours and 12 hours was 1.4, 2.7, 3.1 and 1.8 respectively. While comparing the VAS at different time intervals, non-significant results were obtained. Mean time to first analgesic requirement among the patients of group A and group B was 315.8 minutes and 267.4 minutes respectively. Significant results were obtained while comparing the mean time to first analgesic requirement among the subjects of the two study groups.

Conclusion: Analgesia provided by Levobupivacaine plus Dexmedetomidine is significantly better than Ropivacaine plus Dexmedetomidine in terms of first analgesic requirement.

Keywords: Levobupivacaine, Intraperitoneal, Ropivacaine

Introduction
Laparoscopic cholecystectomy technique essentially has replaced the open technique for routine cholecystectomies since the early 1990s. At this time, laparoscopic cholecystectomy is indicated for the treatment of cholecystitis (acute/chronic), symptomatic cholelithiasis, biliary dyskinesia, acalculous cholecystitis, gallstone pancreatitis, and gallbladder masses/polyps. These indications are the same for an open cholecystectomy. The advantages of laparoscopic procedures over open procedures are as follows: Lesser hemorrhage; better cosmetic results; lesser postoperative pain; and shorter recovery time, leading to shorter hospital stay and less expenditure [1,2].

Regional anesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anesthetic. Bupivacaine, the widely used local anesthetic in regional anesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (−) isomer and dextrobupivacaine, R (+) isomer. Severe central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anesthesia have been linked to the R (+) isomer of bupivacaine. The levorotatory isomers were shown to have a safer pharmacological profile with less cardiac and neurotoxic adverse effects. The decreased toxicity of levobupivacaine is attributed to its
Faster protein binding rate. The pure S (−) enantiomers of bupivacaine, i.e., ropivacaine and levobupivacaine were thus introduced into the clinical anesthesia practice. Levobupivacaine has been recently introduced into Indian market and is being widely used in various health set-ups. Such an increased usage mandates documentation of evidence based literature with regards to risk and safety concerns as well as clinical issues related to levobupivacaine [3–5]. Hence; under the light of above mentioned data, the present study was undertaken for assessing and comparing the efficacy of Intraperitoneal Instillation of Levobupivacaine plus Dexmedetomidine and Ropivacaine plus Dexmedetomidine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

Materials & methods

It was prospective, randomized, double blind study comprising of 40 patients of American Society of Anesthesiologists (ASA) grade I and II of age group 18 - 65 years of either sex, admitted and scheduled to undergo laparoscopic cholecystectomy surgery under general anesthesia. All patients were randomly divided into two groups of 20 each using sealed envelopes. Group A: Patients were given 40ml of 0.125% levobupivacaine plus dexmedetomidine 1mcg/kg Group B: Patients were given 40ml of 0.2% ropivacaine plus dexmedetomidine 1mcg/kg

A Proforma was made and complete demographic and clinical profile of all the patients was recorded. Postoperatively the patients were assessed for pain utilizing visual analogue scale (VAS). Mean time to first analgesic requirement was recorded. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

Results

In the present study, mean age of the subjects of Group A and group B was 42.8 years and 45.3 years respectively. There were 12 males and 8 females in group A and 11 males and 9 females in group B. Mean VAS score among the subjects of group A at baseline, 1 hour, 6 hours and 12 hours was 1.3, 2.3, 2.5 and 1.9 respectively. Mean VAS score among the subjects of group B at baseline, 1 hour, 6 hours was 1.4, 2.7, 3.1 and 1.8 respectively.

While comparing the VAS at different time intervals, non significant results were obtained. Mean time to first analgesic requirement among the patients of group A and group B was 315.8 minutes and 267.4 minutes respectively. Significant results were obtained while comparing the mean time to first analgesic requirement among the subjects of the two study groups.

Discussion

Cholelithiasis or gallstones are hardened deposits of digestive fluid that can form in your gallbladder. The gallbladder is a small organ located just beneath the liver. The gallbladder holds a digestive fluid known as bile that is released into your small intestine. In the United States, 6% of men and 9% of women have gallstones, most of which are asymptomatic. In patients with asymptomatic gallstones discovered incidentally, the likelihood of developing symptoms or complications is 1% to 2% per year. Asymptomatic gallbladder stones found in a normal gallbladder and normal biliary tree do not need treatment unless they develop symptoms. However, approximately 20% of these asymptomatic gallstones will develop symptoms over 15 years of follow-up. Ropivacaine is the pure S (−) enantiomer of ropivacaine, and is a long-acting amide local anaesthetic agent, eliciting nerve block via reversible inhibition of sodium ion influx in nerve fibres.

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves; and small nerves are blocked more easily than larger ones [6–9]. Hence; under the light of above mentioned data, the present study was undertaken for assessing and comparing the efficacy of Intraperitoneal Instillation of Levobupivacaine plus Dexmedetomidine and Ropivacaine plus Dexmedetomidine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

In the present study, mean age of the subjects of Group A and group B was 42.8 years and 45.3 years respectively. There were 12 males and 8 females in group A and 11 males and 9 females in group B. Mean VAS score among the subjects of group A at baseline, 1 hour, 6 hours and 12 hours was 1.3, 2.3, 2.5 and 1.9 respectively. Mean VAS score among the subjects of group B at baseline, 1 hour, 6 hours and 12 hours was 1.4, 2.7, 3.1 and 1.8 respectively. Rapolu S et al compared antinociceptive effects of intraperitoneal instillation of bupivacaine plain and bupivacaine with dexmedetomidine in patients undergoing laparoscopic cholecystectomy. Study was conducted on 100 adult patients of ASA physical status 1 and 2 in the age group of 18 years to 60 years, posted for elective laparoscopic cholecystectomy under general anaesthesia. Patients were randomly divided on an alternate basis into two groups of 50 each. Group B: (n=50) patients received Intraperitoneal bupivacaine 50 ml 0.25% + 5 ml normal saline. Group DB: (n=50) Intraperitoneal bupivacaine 50 ml 0.25% + dexmedetomidine 1 μg/kg with normal saline 5 ml. (14%) patients of group B and 2 (4%) patients of groups B+D had postoperative shoulder pain. They concluded that Intraperitoneal instillation of dexmedetomidine with bupivacaine prolongs the duration of postoperative analgesia as compared to that with bupivacaine alone [10].

In the present study, while comparing the VAS at different time intervals, non-significant results were obtained. Mean time to first analgesic requirement among the patients of group A and group B was 315.8 minutes and 267.4 minutes respectively. Significant results were obtained while comparing the mean time to first analgesic requirement among the subjects of the two study groups. Acharya R et al conducted randomized, prospective, controlled study to compare the analgesic efficacy of intraperitoneal ropivacaine plain and ropivacaine plus dexmedetomidine for

| Time (hours) | Group A | Group B | p-value |
|-------------|---------|---------|--------|
| 0           | 1.3     | 1.4     | 0.46   |
| 1           | 2.3     | 2.7     | 0.16   |
| 6           | 2.5     | 3.1     | 0.11   |
| 12          | 1.9     | 1.8     | 0.46   |

Table 1: Comparison of VAS

| Time (minute) | Group 1 | Group 2 | p-value |
|---------------|---------|---------|--------|
| Mean          | 315.8   | 267.4   | 0.0011 (S) |

Table 2: Time to First Analgesic Requirement
postoperative analgesia after total laparoscopy hysterectomy. The patients were allocated into the following two groups: The patients in ropivacaine group (R group) (N = 40) were given 38 ml of 0.2% ropivacaine plus 2 ml of normal saline (NS) and the patients in ropivacaine plus dexmedetomidine group (RD group) (N = 40) were given 38 ml of 0.2% ropivacaine combined with 0.5 µg/kg dexmedetomidine (diluted in 2 ml NS) through trocars. It was concluded that the antinociceptive effects of the IP instillation of ropivacaine in combination with dexmedetomidine are superior to ropivacaine alone in laparoscopic hysterectomy case [11]. Abd El-Hamid AM et al evaluated the effect of intraperitoneal levobupivacaine plain and levobupivacaine plus sufentanil for postoperative analgesia after Laparoscopic cholecystectomy. Ninety patients were divided into three groups. Group C (n=29) received 50 ml of intraperitoneal normal saline, group L (n=31) received 50 ml of intraperitoneal levobupivacaine 0.25%, and group LS (n=30) received 50 ml of intraperitoneal levobupivacaine 0.25% plus 20 µg sufentanil. They concluded that intraperitoneal instillation of levobupivacaine with sufentanil reduces not only the intensity of postoperative pain but also the total rescue analgesic dose consumption [12].

Conclusion
Analgesia provided by Levobupivacaine plus Dexmedetomidine is significantly better than Ropivacaine plus Dexmedetomidine in terms of first analgesic requirement.

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