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Evaluation of Effect of Intraperitoneal Dexmedetomidine versus Fentanyl as Adjuvant of Bupivacaine Infiltration for Pain Relief after Laparoscopic Cholecystectomy

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ABSTRACT

Background:*Postoperative pain management is an important factor for good surgical outcomes. Acute pain gives a warning for potential tissue damage. Trauma, post-operative pain, muscle spasm are examples of acute pain. Management of it aims to reduce or eliminate pain with minimal side effects. The effective relief of pain is of the utmost importance to anyone who is undergoing surgery.* ***Objectives:*** *The aim of the study was to evaluate and compare the effect of adjuvants Dexmedetomidine and Fentanylwith 0.25% Bupivacaine infiltration intraperitoneally for laparoscopic cholecystectomy in terms of pain severity.* ***Methods:****The sample was selected by random sampling in two groups distributed as- group A (patients received wound infiltration of total 50ml of 0.25% Bupivacaine with 1µg/kg Fentanyl intraperitoneally) and group B (patients received wound infiltration of total 50ml of 0.25% Bupivacaine with 1µg/kg Dexmedetomidine intraperitoneally). A detailed pre-anaesthetic evaluation including history, thorough clinical examination and all relevant investigations, were done for all the patients. All patients were introduced preoperatively with the visual analogue scale (VAS) for the measurement of pain. A change of BP, pulse, pain status and any complications were evaluated and compared. All the information were recorded in the data collection sheet. All collected information was checked very carefully to identify the error in the data.****Results:****The sample was selected by random sampling in two groups distributed as- group A (patients received wound infiltration of total 50ml of 0.25% Bupivacaine with 1µg/kg Fentanyl intraperitoneally) and group B (patients received wound infiltration of total 50ml of 0.25% Bupivacaine with 1µg/kg Dexmedetomidine intraperitoneally). A detailed pre-anaesthetic evaluation including history, thorough clinical examination and all relevant investigations, were done for all the patients.* ***Conclusion:****Postoperative pain management has always been a part of the anaesthesiologist's role in the most immediate postoperative period and the development of acute postoperative pain services has extended this interest beyond the post-anaesthesia care unit.*

Keywords:*Trauma, Muscle spasm, Laparoscopy, Abdominal distension, Gallbladder.*

I. INTRODUCTION

The perception of pain is one of the universal experiences of mankind. Pain is explained from physical, social, emotional, psychological aspects. In the past centuries, there are great expansion in understanding and explanation of the nervous system. With this knowledge, parallel improvement of explanation of pain also occurred. [1] Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". [2]

Surgical interventions have achieved advancements, precision and excellence in recent years. From surgeon's knife to robotic surgery, people want it perfect. According to the American Society of Anesthesiologists' practice guidelines for acute pain management in the perioperative setting, acute post-

operative pain is defined as "pain present in a patient after performing surgical procedure". [3] New metrics are being assessed for the improvement of surgical quality performance. Post-operative pain is one of those metrics which is related to surgical outcome. [4] In the last 20 years technology has changed surgical care. Now it is evolving rapidly following the introduction and expansion of minimally invasive surgery. Laparoscopic Cholecystectomy (lap chole) is a popular example of the evolution of surgeries. Despite these remarkable improvements, inadequate pain management after surgery is making it substandard.

Individuals vary markedly in the intensity of their pain in response to the identical procedure, injury or noxious stimuli. This variation has made the treatment of post-operative pain more complicated. Good postoperative pain control is an important part of adequate postoperative care. [5] Effective and appropriate postoperative pain management aims to facilitate rapid recovery and return to full function, reduce morbidity, allows early discharge and affects the quality of life of patients. Collaboration of different categories of health care providers are needed for this. Pain after laparoscopic cholecystectomy is an outcome of tissue injury, abdominal distension, local trauma, secondary to gallbladder removal, chemical irritation of the peritoneum and the pneumoperitoneum. Though it should be less painful procedure, many patients suffer from pain in form of somatic pain, visceral pain and shoulder pain after laparoscopic cholecystectomy. [6]

Different anaesthetic techniques are also introduced to overcome postoperative pain. Wound infiltration can be an option to reduce pain in laparoscopic cholecystectomy. It is a technique of analgesia efficient in different surgical settings. Thus, it appears that wound infiltration may give some advantage for postoperative recovery after laparoscopic cholecystectomy. Bupivacaine is a long-acting local anaesthetic that can have an effect on producing analgesia. Subcutaneous infiltration with bupivacaine has fewer side effects. [7] Many adjuvants are used with Bupivacaine for this purpose. Alpha 2 -adrenergic agonists show analgesic and sedative properties when used as an adjuvant to regional anaesthesia. [8]

Dexmedetomidine is a selective α2 -adrenoreceptor agonist; it has an α2 /α1 selectivity ratio which is eight to 10 times higher than that of clonidine. [9] The antinociceptive effects of Dexmedetomidine occur at the dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway and through action on inhibitory G protein, which increases the conductance through potassium channels. [10] On the other hand, Fentanyl is a μ opioid receptor agonist. A dose of 100 microgram of Fentanyl can produce equivalent analgesia of 10mg of Morphine. It is widely used for its rapid onset, short acting time, dose dependent analgesic action, high cardiovascular stability and minimal histamine release. [11] On this backdrop, this randomized, double-blind, controlled study was undertaken to evaluate and compare the effect of Dexmedetomidine and Fentanyl with pre-emptive intraperitoneal 0.25% Bupivacaine infiltration for laparoscopic cholecystectomy in terms of post-operative pain.

II. METHODOLOGY

This Randomized controlled trial study was carried out in the Department ofAnesthesia, Analgesia and Intensive Care Medicine of Bangladesh Medical College Hospital, during January July 2020 to June 2021.A total of 45 patients were participated in the study. The patients with ASA grade I & II planned for elective Laparoscopic cholecystectomy under general anaesthesia were included according to selection criteria. A total of 58 patients were enrolled for the study. Exclusion criteria were hypersensitivity to test drugs, past history of spine surgery, patients with known to have renal, liver or heart disease, morbidly obese and history of alcohol abuse. After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation. Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24).

III. RESULTS

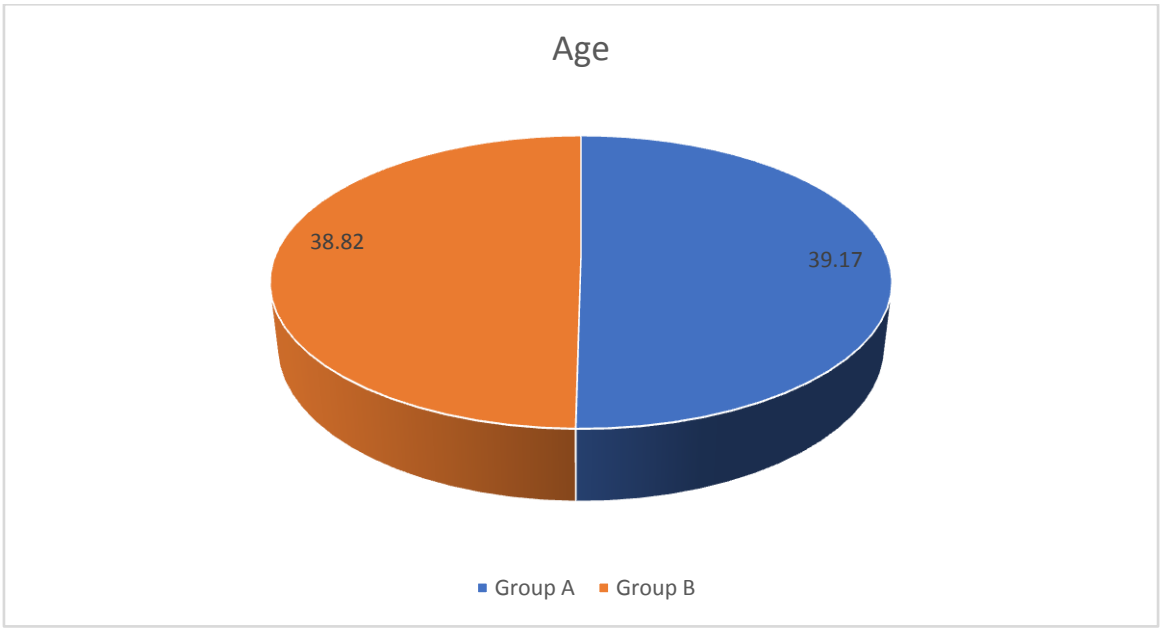

Figure-1: Age distribution of the study population

Fig-1 shows the age distribution of the study population, it was observed that (39.17%) patients were belonged to group A and (38.82%) in group B. And P value was >0.005.

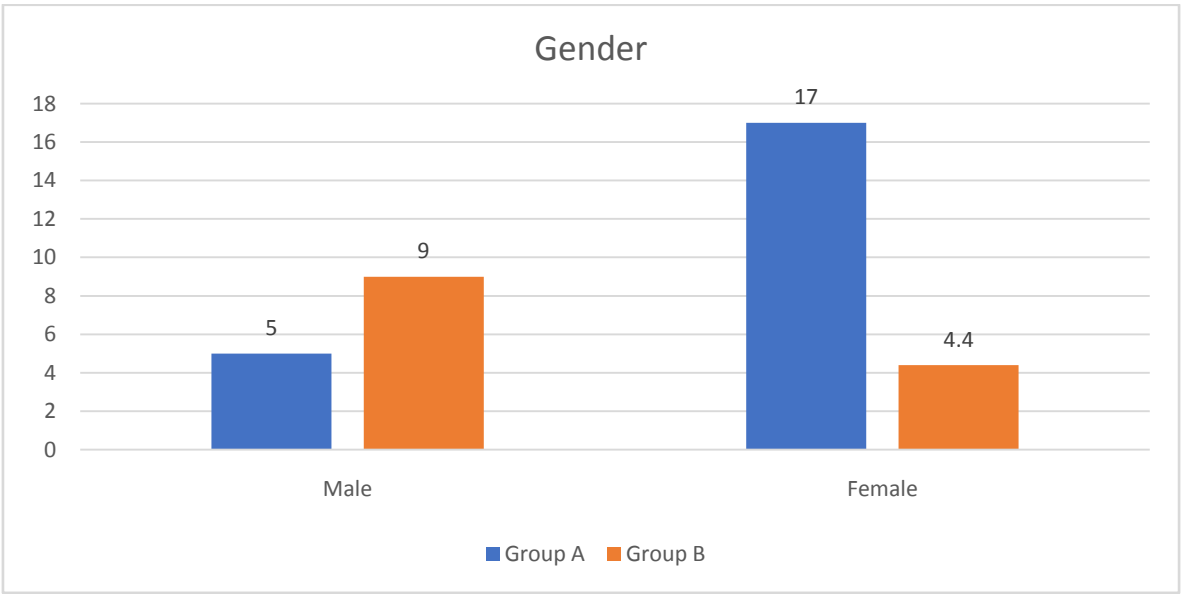

Figure-2: Sex distribution of the study population

Fig-2 shows the shows sex distribution of the study population, it was observed that majority 17% patients were female in group A and 5% in group B. And 4.4% patients were male in group B and 9% in group B.

Table-1: Demographic characteristics of the enrolled patients at baseline

Variables		Group A	Group B	P value
Systolic Blood pressure	Mean±SD	109.94±4.61	108.25±3.29	>0.05
Diastolic blood pressure	Mean±SD	69.45±2.83	68.33±3.06	>0.05
Respiratory rate	Mean±SD	15.37±0.31	15.26±0.24	>0.05

Table1 shows the characteristics of the enrolled patients at baseline, it was observed that the Mean±SD of Systolic Blood Pressure was 109.94±4.61 in Group A and 108.25±3.29 in Group B.
And according to the Mean±SD of Diastolic blood pressure, 69.45±2.83 was in Group A and 68.33±3.06 was in Group B. And Respiratory rate was 15.37±0.31 in Group A and 15.26±0.24 in Group B.

Table-2: Comparison of post-operative pain intensity up to 12th post-operative hour between Group A and Group B

Post-operative hour	Group A	Group B	P value
After two hours	78.22 ± 17.06	61.91 ± 11.24	<0.001
After four hours	51.78 ± 14.03	39.99 ± 16.42	<0.001
After six hours	36.91 ± 13.83	25.54 ± 12.99	<0.001
After eight hours	27.78 ± 14.35	24.27 ± 13.82	>0.05
After ten hours	25.48 ± 16.06	19.73 ± 14.05	>0.05
After twelve hours	17.61 ± 17.70	17.50 ± 14.52	>0.05

Table 2 shows the Comparison of post-operative pain intensity up to 12th post-operative hour between Group A and Group B. According to post-operative hour it was observed that, the After 2 hours 78.22 ± 17.06 was in group A and 61.91 ± 11.24 was in group B. After 6 hours 36.91 ± 13.83 was in group A and 25.54 ± 12.99 was in group B. And After 10 hours 25.48 ± 16.06 was in group A and 19.73 ± 14.05 was in group B

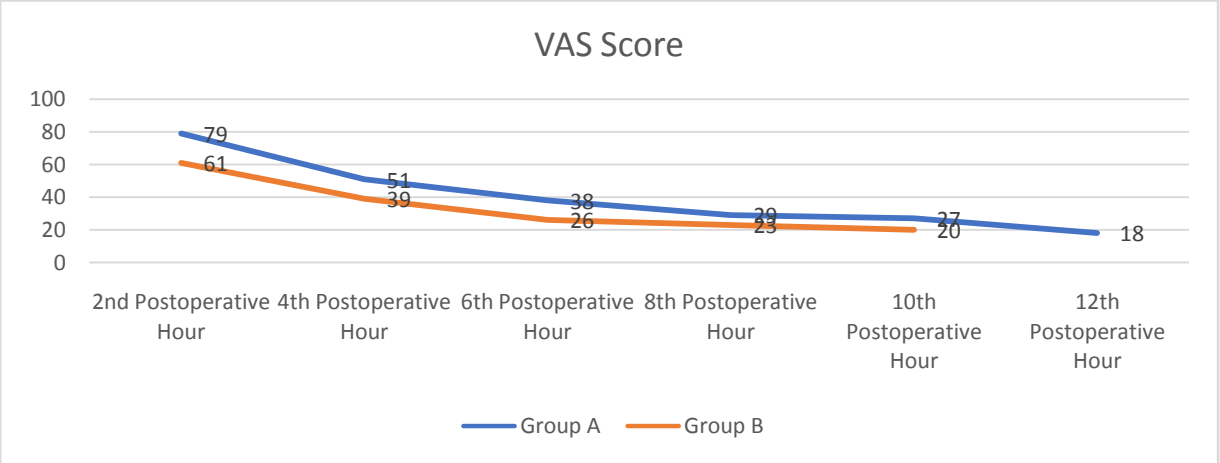

Figure-3: Comparison of post-operative pain up to 12th postoperative hour between Group A and Group B

Fig-3showing decreasing VAS sore over time up to 12th post-operative hour in both Group A and Group B.
Here, blue line denotes post-operative pain intensity in VAS score in Group A and orange line denotes Group B.

Table-3: Comparison of total morphine consumption (mg/ml) between Group A and Group B

Total morphine consumption (mg/ml)	Group A	Group B	P value
	8.63 ± 1.48	7.27 ± 0.98	<0.001

Table 3 shows the Comparison of total morphine consumption (mg/ml) between Group A and Group B. According to total morphine consumption (mg/ml) it was observed that, 8.63 ± 1.48 was in group A and 7.27 ± 0.98 was in group B. And P value was >0.001.

IV. DISCUSSION

One of the primary objectives of this study was to evaluate the effect of wound infiltration on post-operative pain. At post-operative period, patient was assessed six times at two hours interval. Gradual reduction of pain score, assessed with Visual Analogue Scale, was experienced by patients of both arm for 12 post-operative hours after laparoscopic cholecystectomy.

After two hours of procedure, mean ± SD of postoperative pain intensity Group A was 78.22 ± 17.06. In Group B it was 61.91 ± 11.24. The difference between VAS score was statistically significant. Painintensity was highest at this assessment both in group A and B. The reason of this increased pain score was may be the movement from recovery room to post-operative room. After four hours of operation, mean ± SD of VAS score in Group A and Group B was 51.78 ± 14.03 and 39.99 ± 16.42 respectively. Mean ± SD of postoperative pain intensity in Group A was 36.91 ± 13.83 after six hours. In the Group B this score was 25.54 ± 12.99. Difference of pain scores between these two assessments were statistically significant. At last, three assessments with pain score, after eight, ten and twelve hours of surgical procedure, pain score reduced. After eight hours of operation, mean postoperative pain intensity was 27.78 ± 14.35 Group A. Group B is 24.27 ± 13.82. The difference between Group A and Group B is not statistically significant. After ten hours, mean postoperative pain intensity in VAS score showed by Group A was 25.48 ± 16.06. On the other hand, in Group B the mean score was 19.73 ± 14.05. The difference was not statistically significant. In Group A, mean VAS score of postoperative pain intensity after 12 hour of surgical procedure was 17.61 ± 17.70. In Group B this score was 17.50 ± 14.52. The difference between both arms was not statistically significant.

But after six hours of performing procedure, pain score assessed with VAS significant. Park et al found similar kind of result in use of Bupivacaine with adjuvant Dexmedetomidine and Fentanyl in paediatricorthopaedic surgery. They found the use of dexmedetomidine as an adjuvant had a significantly greater analgesic and local anesthetic-sparing effect, compared to fentanyl. Van ray et al (1992) in a studyconducted over 50 patients compare the effect of 0.25% bupivacaine with 0.9% normal saline. [32] Thisstudy showed that wound infiltration with 0.25% bupivacaine is not effective in decreasing postoperative analgesic requirements. Wright (2003) in his study, infiltrated wound with 0.5% bupivacaine at the end of appendicectomy in children. [33] Post operative pain was significantly less ($p < 0.03$) in the group of taking wound infiltration. Loizides et al (2014) in his review article over seventeen trial of 1095 patients showed that, at wound infiltration group, post-operative pain at four to eight hours and at nine to twenty-four hours was reduced compared to no active intervention. [34] On a visual analogue scale of 0 to 10 cm, mean reduction of pain was about 1 cm at four to eight hours and 0.4 cm at nine to 24 hours at infiltration group. Volume of local anesthetics needed for reducing postoperative pain is an important factor. Conflicting results were shown study conducted by Khosravi et al. (2020). They suggested that bupivacaine with dexmedetomidine is effective only in 1st post-operative hour, but at 3rd and 6th hour patients with Fentanyl experienced less pain. [35] Different variation of pain scores at each assessment time was observed. There are individual differences in pain perception with identical procedure. But several other patient or technical factors may have also affected pain score in this study. Patients who suffered from chronic pain may had reported pain which was unrelated to surgical procedure. Patients who had previous history of surgery and narcotic consumption may had an increased tolerance to analgesic and reported more pain. In some patient's epigastric and umbilical ports had to make widened to facilitated removal of gallbladder. This widening may had resulted in increased pain score. Graphical representation also depicts that difference between both arms were reducing with time. After 6-hour pain score between two groups are almost close.

Decreased intensity of post-operative pain has benefits over reduced analgesic requirements. In this study total morphine consumption was significantly lower in Group B (7.27 mg/ml) compared with Group A (8.63 mg/ml). Difference of morphine consumption was between two groups was decreasing with time. Morphine consumption between Group A and Group B was significantly different at first six hours ($p<0.01$). But at last, six hours this difference was not significant ($p>0.05$). So, with decreasing pain score morphine consumption also decreased significantly at first six hours. This is consistent with the findings ofElkahim et al. who found significant difference in total morphine requirements betweendexmetedomidineand fentanyl. [36] Honoura *et al.* concluded in their study that addition of dexmedetomidine to bupivacaine and fentanyl has improved intraoperative condition and quality of postoperative analgesia. [37]

So, this study demonstrates potential ability of Dexmetedomidine as adjuvant of bupivacaine infiltration intraperitoneally to decrease pain score and analgesic requirement over use of Fentanyl as adjuvant.

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

V. CONCLUSION

Wound infiltration with bupivacaine with adjuvant had significantly reduced post-operative pain score for six hours in this study. Total morphine consumption also significantly decreased. However, using adjuvant

with Bupivacaine has improved post-operative pain condition significantly. Dexmedetomidine is more effective than fentanyl in terms of reducing post-operative pain and analgesic consumption. On the other hand Fentanyl is more cost effective. So, more study is needed on this regard.

VI. RECOMMENDATION

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for future use and emphasize points to ensure better management and adherence.

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