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A clinical study of post-operative analgesia with intravenous paracetamol versus dexmedetomidine in patients undergoing laparoscopic cholecystectomy

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Abstract

Pain management, stable hemodynamics and early post-operative recovery are the new challenges in ambulatory surgeries. The literature rates post-operative pain in laproscopic cholecystectomy as mild to severe pain. Our objective is to assess the post-operative analgesia with intravenous paracetamol versus dexmedetomidine in patients undergoing laproscopic cholecystectomy.

Methods: After ethical committee clearance, 60 patients were randomly allocated into two groups after informed consent. Patients between 18-50 years, ASA 1or 2 were included and those on opioids, any anti-inflammatory drugs, and hypersensitivity to study drugs were excluded. Group D received intravenous dexmedetomidine 1µg/kg as bolus over 10 min followed by dexmedetomidine infusion at 0.25ml/kg/h (0.25ml = 0.5µg). Group P received 1 g intravenous paracetamol in 100ml solution of normal saline over 10 min followed by infusion of 0.25ml/kg/h of normal saline.

Results: Demographic parameters were comparable between the groups. Time for first rescue analgesia, and total doses of analgesia in 24 h in group D was 225.33±29.12 and 2.73±0.64 and in group P was 143.33±28.96 and 4.23±0.77 respectively with p value 0.001 which was statistically significant.

Conclusion: Dexmedetomidine loading dose 1µg/kg and maintenance dose 0.5µg/kg is a good anesthetic adjuvant for general anesthesia to reduce post-operative requirement of analgesia in laparoscopic surgeries.

Keywords: General anesthesia, dexmedetomidine, paracetamol, visual analogue scale, postoperative analgesia

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Introduction

Laparoscopic cholecystectomy (LC) is normally associated with minimal pain compared to an open Cholecystectomy. However, Postoperative pain is still the main complaint in LC leading to prolonged hospital stay. Moderate abdominal and shoulder pain is experienced by 36-63% of patients in 24-48 hours after LC and up to 13% of patients experience severe pain [1]. General anesthesia with inhalational agents with adjuvant intravenous agents provides better sedation, analgesia and hypnosis [2]. Drugs with these effects including benzodiazepines and opioids are already established in the literature [2-4]. Opioids remain one of the main options for postoperative pain relief after LC and are widely used. However, Opioids have side effects such as nausea and vomiting, sedation, respiratory depression, urinary retention and paralytic ileus, which may outweigh the benefits of analgesia, especially after abdominal surgery. It has been recommended to use opioids after abdominal surgery only when non-opioid drugs provide insufficient analgesia [5].
Intravenous (IV) Paracetamol is the most commonly used drug as an injectable type of acetaminophen. It is a popular antipyretic and analgesic with little anti-inflammatory action. New intravenous agents like alpha2 adrenergic agonist produce sedation, anxiolysis and analgesia [6, 7]. Dexmedetomidine is a potent alpha2 adrenoreceptor agonist having sedative, analgesic and sympatholytic properties [8]. It binds to transmembrane G protein binding receptors in the brain and spinal cord with a dose dependent alpha 2 selectivity.

Stimulation of alpha 2 adrenoreceptor subtypes results in:
1. **Alpha 2A:** Mediates sedative and antinociceptive actions.
2. **Alpha 2B:** Causes vaso constrictive cardiovascular effect.
3. **Alpha 2C:** Modulates dopaminergic neurotransmission, hypothermia and a variety of behavioral responses.

In this background, this study is aimed to evaluate and compare IV paracetamol with IV dexmedetomidine administered preoperatively in laparoscopic cholecystectomy to evaluate postoperative narcotic requirement.

Methodology

Source of data

After obtaining ethical clearance 60 patients who satisfied the inclusion criteria undergoing elective laparoscopic cholecystectomy surgeries under general anesthesia during the period of study were included in the study.

Type of study

A prospective, randomized, double blinded study.

Inclusion criteria

1. Patients aged between 18 to 50 years of age.
2. ASA grade I and II patient.

Exclusion criteria

1. Patient refusal.
2. Patients taking non-steroidal anti-inflammatory drugs, opioids.

3. Patients with hypersensitivity to paracetamol and dexmedetomidine.

Sample size

As per previous published study duration of analgesia of 79.25 minutes and standard deviation of 50.85 minutes, keeping the power at 80% and confidence interval at 95%, to detect a minimum of 30% difference in the duration of analgesia between two groups, a sample of 26 will be required in each group. We have included 30 patients in each group to compensate for any possible dropouts.

Method of collection of data

Patients satisfying the inclusion criteria were selected during the study period from the operation register on a daily basis. After obtaining a written informed consent, sixty patients were recruited for this study. They were allocated into two groups of 30 each. Preoperatively, the patients were made familiar of their role in the study and the use of 10 cm VAS with end point to be labeled as 0 = no pain and 10 = excruciating worst possible pain.
On receiving patient in operating room, the patient monitoring included electrocardiogram (ECG), noninvasive blood pressure (NIBP), heart rate (HR), oxygen saturation (SPO_2). The baseline HR, NIBP, SpO_2 scores were recorded.
Computer based randomization was done and allocation concealment was done by sealed envelope method. An anesthesiologist not involved in the management of the case opened a sealed envelope randomly and loaded drugs as per the drugs in the envelope:

D group:
1) Dexmedetomidine 1µg/kg in 100 ml normal saline and connected to an infusion pump.
2) Dexmedetomidine 2µg/ml in 50 ml normal saline and connected to a syringe pump.

P group:
1) Paracetamol 1g in 100 ml normal saline and connected to an infusion pump.
2) Normal saline in a 50 ml syringe and connected to a syringe pump.

Visual analogue scale

Pain was assessed using a standard 10 cm Visual Analogue Scale (VAS) by an independent anesthesiologist.
A VAS consists of a line, often 10 cm long, with verbal anchors at either end. In the numerical scale, 0 corresponds to no pain and 10 designate the worst possible pain. The patient places a mark at a point on the line corresponding to the patient rating of pain intensity. Patients were asked to choose a point on the line that represents the intensity of their current state.

Results

Table 1: Comparison of duration of surgery in two groups studied

Variables	Group D	Group P
Duration of Surgery (Min)	91.17±19.33	96.67±30.15

Duration of surgery was similar between the groups with p value of 0.40.
VAS scores in immediate postoperative period. 10 patients in group P had pain scores of 3 and needed rescue analgesic within first 30 min postoperatively compared to group D were

none of the patients needed additional analgesics. Tramadol 1.5mg/kg was given for rescue analgesia. The mean value of VAS was more in Group P (paracetamol) compared to Group D (dexmedetomidine) at 1 h postoperatively, Except VAS score at 15 min after surgery, in dexmedetomidine group was higher but was never >3 and no additional analgesics were needed.

Table 2: Pain Scores-Visual Analogue Scales

Vas	Group D	Group P	P Value
Postoperative At 15 Min	1.33±0.76	1.17±0.95	0.456
Postoperative At 30 Min	1.43±0.68	2.17±0.79	<0.001**
Postoperative At 45 Min	1.77±0.63	2.93±0.83	<0.001**
Postoperative At 60 Min	1.87±0.63	2.43±0.77	0.003**
Postoperative At 2 H	2.33±0.48	2.43±0.97	0.615
Postoperative At 4 H	2.5±0.63	3.53±1.22	<0.001**
Postoperative At 12 H	2.8±0.48	3.53±1.01	<0.001**
Postoperative At 24 H	2.87±0.35	3.5±0.78	<0.001**

First Rescue analgesia was given when the patients had VAS of 3 or higher. It is the duration from the test drug given, to the time the patients had VAS of 3 or higher and rescue analgesia inj. Tramadol was given.

Table 3: Time for first rescue analgesia

Variables	Group D	Group P	
Time For First Rescue(Min)	225.33±29.12	143.33±28.96	<0.001**

Time for first rescue analgesia, showed p value 0.001 which was statistically significant.

Table 4: No. doses of analgesia patients obtained in 24 h post- operative period

Variables	Group D	Group P	
No. of Doses of Analgesia In 24 H	2.73±0.64	4.23±0.77	<0.001**

Discussion

In this study, the hypothesis that post-operative analgesia with intravenous dexmedetomidine was better than paracetamol was evaluated. There are studies which have shown the role of dexmedetomidine both loading and maintenance dose showing effective post-operative analgesia and reduced analgesic requirement in the post-operative period in comparison with placebo. This study is done to compare these effects with paracetamol.

Dexmedetomidine is a more selective α2-agonist, has a shorter duration of action than clonidine. It suppresses nociceptive neurotransmission, terminating propagation of pain signals leading to analgesia. Its sympatholytic effect causes hypotension and bradycardia, an effect judiciously used to attenuate the stress response of surgery. Other useful effects include decreased salivation, increased glomerular filtration, decreased intraocular pressure and decreased shivering threshold.

Jasbir Kaur *et al*. [9] had concluded that Dexmedetomidine is an excellent drug as it decreased the magnitude of hemodynamic stress response to tracheal intubation, surgery and extubation. In our study there was significant reduction in heart rate in dexmedetomidine group in intraoperative & postoperative period in the initial 1 h but later they were not significant. The present study is in line with an earlier study of Hye Won Shin [10] who highlighted using preanesthetic dexmedetomidine 1μg/kg showed that there was no difference in MAP between the groups, but heart rate of dexmedetomidine group was lower compared to the control

group.
Studies like Bijoy Kumar Panda *et al*. [11] showed that in dexmedetomidine group there was 40% reduction in diclofenac requirement compared to clonidine group. The average fentanyl dose was reduced by 33% and 44% in clonidine and dexmedetomidine group respectively compared to control group. Varshali *et al*. [12] in her study demonstrated that the intraoperative requirement of fentanyl in dexmedetomidine decreased from 100 $\pm$ 10µg to 60 $\pm$ 10µg. Our study also shows analgesic action of dexmedetomidine. The time for first rescue analgesia was increased by 82 min compared with paracetamol.

Conclusion

We conclude that dexmedetomidine loading dose 1µg/kg and maintenance dose 0.5µg/kg is a good anesthetic adjuvant for general anesthesia which reduces post-operative requirement of analgesia in laparoscopic surgeries.

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