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Research Paper

Efficacy of preemptive intravenous paracetamol in laparoscopic cholecystectomy surgery: A hospital based study

Medical Science

KEYWORDS : Cholecystectomy, Postoperative and Pain.

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ABSTRACT

Preemptive analgesia could be defined as analgesia that prevents the development of pathological pain. With this concept, referred to as preventive analgesia, it is believed that through application of an analgesic medicine or technique, pain will either subside or be prevented prior to the painful stimulus. This study evaluate the efficacy of intraoperative intravenous paracetamol plus tramadol for early postoperative pain relief after laparoscopic cholecystectomy. These findings suggest that, the early post-operative analgesic effect of 1 g of paracetamol in patients undergoing cholecystectomy. Because of providing decreased opioid consumption with lower side effects, paracetamol can be safely used in post-operative pain management.

Introduction:

Pain is an unavoidable part of the human experience. However, there is no way to objectively measure an individual's pain. It is a subjective experience, informed by each individual's particular physical, psycho-logical, historical, social and cultural experiences and circumstances. Preemptive analgesia could be defined as analgesia that prevents the development of pathological pain. [1] With this concept, referred to as preventive analgesia, it is believed that through application of an analgesic medicine or technique, pain will either subside or be prevented prior to the painful stimulus.[2,3,4] Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[5] Postoperative pain, which is a form of acute pain caused by noxious stimulation due to injury. It is typically associated with neuroendocrine stress response that is proportional to pain intensity.[6] It differs from other types of pain in that it is usually, but by no means always, transitory with progressive improvement over a relatively short time course. Four physiological processes are involved: transduction, transmission, modulation and perception.[5] Systemic response to different organ system includes cardiovascular, respiratory, gastrointestinal, urinary endocrine, hematological and immune system.[5]

Some of the concerns about the side effects of analgesics, such as nausea and respiratory depression, leads to implementation of inadequate doses of pain relievers and and also leads to unnecessary patient complaints.[6]

Paracetamol is a centrally acting drug, which inhibits prostaglandin synthesis and cyclooxygenase (COX) of nervous system. Paths based on spinal serotonergic mechanism of action of other central mechanisms may be involved in the acting mechanism of paracetamol.[7,8] In clinical practice, paracetamol does not cause the side effects that seems typically with other nonsteroid antiinflamatory drugs (NSAID), which are thought to occur due to inhibition of peripheral COX-1 (gastric toxicity, antiplatelet activity).[7] The results of controlled clinical trials, the recommended therapeutic doses, is safe and well tolerated, supports that it has high safety profile similar as placebo. Paracetamol is considered to be a safe drug, and it does not have such as gastrointestinal problems or central side effects according to other NSAI drugs and opioids.[9]

Preemptive pain control is an issue dealt with in recent years. Here, regional or systemic analgesics are applied before the start of the surgical procedure, thus by preventing central sensitization of pain pathways it is intended to reduce the amount of analgesic and analgesic requirements.[10] By taking action of antinociceptive before the administration of nociceptive stimulus, ability to reduce the requirement of and amount of analgesia demonstrated experimentally. However, data from several clinical studies have shown differences and not support it at all times. Also, there are some people who indicates that analgesia is better in this method on the other hand some other those who have advanced that there is no difference.[11]This study has been designed to explain the effect of preemptive iv paracetamol reduces the dose of postoperative opioid and nausea and vomiting.

Material and Methods:

The present study was conducted in the Mahatma Gandhi Medical College & Hospital, Jaipur during the period from January 2011 to November2011. The 30 patients aged between 20-60 years were admitted for elective laparoscopic cholecystectomy surgery under general anaesthesia were classified as an American Society of Anaesthesiologists(ASA) physical status I and II as per inclusion & exclusion criteria. The patients were randomly divided into 2 equal groups. In Group-A(cases) received the combination of intravenous 1 g paracetamol, plus 0.75 mg/kg tramadol and Group-B(controls) received an equal volume of intravenous normal saline before surgery. On arrival of the patients in the operation theatre intravenous line was inserted. Before intravenous Induction by thiopental 3-5/mg/kg body weight all patients were preoxygenated with 100% oxygen for 2 minutes after receiving a pre-induction dose of fentanyl 1µg/kg body weight. Endotracheal intubation was facilitated by succinylcholine 1.5mg/kg body weight, Vecuronium 0.1 mg/kg body weight was given for muscle relaxation and anaesthesia was maintained with a combination of oxygen 33%, N2O 66% and halothane 0.5-1%. Ventilation was controlled to maintain ETCO2 between 35 to 40 mmHg. Intraoperative proper hydration was maintained with normal saline or Hartman's solution. Tracheal extubation was performed after reversal of neuromuscular blocking agent by neostigmine 0.04-0.05 mg/kg b.w and atropine 0.02 mg/kg b.w. After completion of operation all patients were taken to postoperative ward and nursed for 24 hours. Both groups received opioid (Pethedine) through patient control analgesia (PCA) in postoperative ward and postoperative pain assessed by means of Visual Analogue scale (VAS). Total opioid dose measured in both groups and Post operative complications like nausea and vomiting were recorded at 1, 6, 12, 18 and 24 hours.

Data was collected in a prescribed form and analyzed by using SPSS (Statistical Package for Social Sciences). The test statistics used to analyze the data were Student's t-Test, Fisher's Exact Test and repeated measure ANOVA. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant. The summarized data were presented in the form tables.

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Results and Discussion:

There were no significant differences between the groups with regard to demographic variables (age, gender, weight and height) and surgery time (Table-1). Out of 30 patients, 15 treated by iv paracetamol 1 gm 60 min before surgery considered as case and another 15 treated by an equal volume of intravenous normal saline before surgery as control. All the clinical variables were followed up at 1, 6, 12, 18 and 24 hours of intervals following intervention. The findings of the study derived from data analysis are presented below:

Table 1: Comparison of Demographic properties and operation duration:

Parameters		Group A (n=15)	Group B (n=15)
Gender	Male	8	9
	female	7	6
Age (Yrs)		42.8±9.9	41.5±7.8
Weitht (Kg)		72.8±10.1	70.5±8.1
Height (cm)		168.5±6.5	165.3±7.0
ASA	I	10	12
	II	5	3
Operation duration	<60	68.3±10.6	54.8±9.9
	>60		

Table 2: comparison of pain score

Pain score	Group A (n=15)	Group B (n=15)
01 hrs	4.7 ± 0.3	4.4 ± 0.3
06 hrs	2.9 ± 0.2	2.7 ± 0.3
12 hrs	1.8 ± 0.2	1.7 ± 0.2
18 hrs	1.1 ± 0.2	1.0 ± 0.1
24 hrs	0.7 ± 0.3	0.8 ± 0.5

Statistically Significant (P<0.05)

Table 3: First analgesic requirement time and post-operative analgesic requirements:

variables	Group A (n=15)	Group B (n=15)
First analgesic reguirement time (min)	143.0±102.8	90.9±63.1
Analgesic consumption (tramadol mg)	56.0±86.5	100.0±84.8
Number of patients requiring supplemental analgesic in first 6 h (n)	6/15	8/15
Number of patients requiring supplemental analgesic in 6-12 h (n)	2/15	4/15
Number of patients requiring supplemental analgesic in 12-24 h (n)	0/15	0/15
Number of patients requiring supplemental analgesic (n)	8/15	12/15

Table 4: Incidence of side effects (%)

parameters	Group A (n=15)	Group B (n=15)
Nausea	4(26.66)	5(33.33)
Vomiting	3(20)	4(26.66)
Allergic reaction	-	-
Hypotension	-	1(6.66)
Urinary retention	-	-

This study demonstrates that preemptive iv paracetamol produces significant opioid sparing effects compared to placebo in post-operative patients following cholecystectomies. It decreased 24 h total opioid consumption and increases the time to first analgesic use, thus its analgesic effect was not enough as a sole agent.

Preemptive analgesia means that an analgesic intervention is started before the noxious stimulus arises in order to block peripheral and central nociception. [3,12,13] NSAIDs when given before tissue damage (preemptive) may play an important role in peroperative pain management by reducing the inflammatory response in the periphery and thereby decreasing sensitization of the peripheral nociceptors.[3,14,15] Many trials have been able to demonstrate preemptive effect of NSAIDs on the reduction of postoperative pain in laparoscopic cholecystectomy.[16] In our study, pain was less intense in patients who received preemptive paracetamol than those who did not receive the same throughout the whole period of observation (from 1st hour to 24th hour following operation).

Fijalkowska *et al.*[17] investigated the effectiveness of iv paracetamol to 92 patients scheduled for laparotomy or laparoscopy. Laparoscopy group, 16.3% of patients, the need for additional morphine, while the laparotomy group, 71.4% patients had additional morphine requirement. In conclusion, they reported that paracetamol reduces the need for opioid analgesics but in major surgeries a multimodal approach must be needed. Guner *et al.*[18] study that compared paracetamol and tramadol, they reported paracetamol and tramadol reduce opioid requirements after major abdominal surgeries, but alone could not provide adequate analgesia, therefore in major surgeries a multimodal approach have to be needed.

Also in our study in group B, we identified additional analgesic requirement in 54% patients while in group A, we identified additional analgesic requirement in 40% patients. We have identified that the implementation of preemptive iv paracetamol reduce the need for additional analgesics significantly. Also paracetamol reduces opioid requirements, we think that in major surgeries a multimodal analgesic approach would be more comfortable.

Toygar *et al.*[19] reported that application of paracetamol 1 g iv preoperatively and intraoperatively and every 6 h for 24 h for continued infusions of 1 g in patients scheduled for lumbar discectomy surgery may provide a better post-operative analgesia according to in the control group, will extend the time of the post-operative first morphine request, and reduce post-operative use of total morphine. Also, there is no preemptive analgesic effect of preoperative paracetamol application, but further studies may be required on the subject stated.

In our study, it is identified that the use of preemptive iv paracetamol reduce opioid requirements, prolong the duration to first need of analgesia and provide a significant reduction in post-operative pain scores.

In studies, it is showed that paracetamol did not make gastric irritation, erosion or bleeding whereas very rarely trombocytopenia, leukopenia, neutropenia, simple skin rash or hypersensitivity reactions from urticaria to anaphylactic shock have been reported.[20] Also in our study, these kinds of side-effects have not been encountered, patients who have peptic ulcus and have risk of bleeding have not been included in our study because of the current risk of thrombocytopenia.

The most frequent side effects are nausea and vomiting. However, the type of surgery, anesthetics, hypotension and the supplemental agents used should all be considered.[21] In our placebo controlled study, surgery type and general anesthesia applied was standard and there was no difference between the groups in peroperative hemodynamic values. Visceral and pelvic pains are frequent causes of post-operative nausea and vomiting. Studies reported the improvement of nausea after treatment of pain.[22-24]

Dejonckheere *et al.*[25] reported an increased incidence of nausea with tramadol compared to propacetamol. In our study, the incidence of nausea was 34% in Group B and 27% in Group A, and the incidence of vomiting was 26% and 20%, respectively. One patients in Group B, had hypotension, whereas none of the patients in Group A had hypotension. The reason for high incidence of nausea and vomiting in Group B and Group A may be due to higher consumption of opioids in the post-operative period, hypotension and pain.

Conclusion:

These findings suggest that, the early postoperative analgesic effect of 1 g of paracetamol in patients undergoing cholecystectomy. Because of providing decreased opioid consumption with lower side effects, paracetamol can be safely used in post-operative pain management.

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