

# The Analgesic Efficacy of Paracetamol Versus Ketorolac in Day-case Gynaecological Laparoscopic Procedure: A Comparative Study

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## Abstract

**Background:** Gynaecological laparoscopy is a commonly performed procedure. Providing anesthesia for this can present a challenge, particularly in the day surgery population. Poor analgesia, nausea and vomiting can cause distress to the patient and increased cost for the health system, because of overnight admission. In this review we discuss anesthetic and analgesic techniques for day case gynaecological laparoscopy.

**Objectives:** Our study is undertaken to compare the efficacy of intravenous paracetamol versus ketorolac for post operative analgesia after gynaecological day case laparoscopic procedures.

**Method:** Sixty (60) female patients 20 – 40 years of age, of ASA I/II were randomized into two equal groups of 30 patients each. Patients of group A received intravenous paracetamol 1gm and group B received intravenous ketorolac 30mg just after induction of general anesthesia. Postoperative pain was evaluated by standard 10cm linear visual analogue scale (VAS) at different time intervals. When VAS was more than 3 rescue analgesic 50mg tramadol intravenously stat was given.

**Results:** In group A that was paracetamol group and group B that was ketorolac group the visual analogue scale (VAS) almost similar but total analgesic consumption in ketorolac group were slightly higher than paracetamol group. In paracetamol group 4 patients and in ketorolac group 6 patients required rescue analgesic dose.

**Conclusion:** Our results indicate that IV paracetamol has better analgesic potency than IV ketorolac for postoperative analgesia after day case gynaecological laparoscopic procedure.

**Keywords:** Intravenous paracetamol, intravenous ketorolac, day case gynaecological laparoscopic procedures, post operative analgesia.

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## Introduction:

Laparoscopy was first performed about a century ago, but came into more routine practice around 50 years ago.<sup>1</sup> This was initially confined to gynaecological diagnostic procedures and sterilization. The rapid advances that have occurred in surgical procedures date from developments by general surgeons. Gynaecological laparoscopic surgery has

developed recently, and is used for ovarian surgery, laparoscopically-assisted vaginal hysterectomy (LAVH), and LAVH with radical hysterectomy. For diagnostic surgery, there is a clear reduction in operative trauma with laparoscopy compared to laparotomy. Other benefits of laparoscopic surgery include reduced hospital stay, as also improving cosmetic results and patient satisfaction.

This review will focus on day-case laparoscopy. It is essential that the analgesia provided is sufficient for the patient to mobilize by the evening of surgery and control the pain which may persist for several days after the operation. The pattern of pain may change over this period, with pain in different sites becoming more or less prominent.<sup>2</sup> Anesthetic and surgical techniques must therefore take into consideration pain that occurs outside the direct observation of the medical team. Steps must also be taken to minimize side effects such as nausea, vomiting, and dizziness. A suggested target for overnight admission due to pain or nausea is  $\leq 1\%$ .<sup>3</sup>

In laparoscopic procedure pain is associated with incisions for the operative ports. Lower abdominal pain may depend on the extent of intraperitoneal manipulation during diagnostic laparoscopy. Upper abdominal, shoulder tip, and postural high back pain after laparoscopy are likely to be caused by gas retained in the peritoneal cavity. Carbon dioxide is usually used to expand the abdomen to allow surgical visualization. Although it is a soluble gas in comparison to oxygen and nitrogen. It can take up to two days to be absorbed from the peritoneal cavity. Pain from the residual gas is of delayed onset and may present once the patient has gone home. Hohlrieder et al found that the worst pain after gynaecological laparoscopic surgery was felt in the shoulder in 1% of the patients, two hours after surgery, but in 70% of the patients 24 hours after surgery.<sup>4</sup> Stanley et al found that the pain attributed to intraperitoneal gas was as frequent as abdominal wall pain at 24 hours, but declined markedly by 48 hours, along with a corresponding reduction in the retained gas shown on x-ray.<sup>5</sup>

Paracetamol is one of the most widely used drugs for the treatment of fever and pain. It is used perioperatively in oral, rectal, and parenteral formulations. It is still not confirmed whether it acts peripherally and/or centrally and it acts on which analgesic pathway. Because of its efficacy, safety, lack of clinically significant drug interactions, and lack of the adverse effects associated with other analgesics, intravenous paracetamol is an important component of a multimodal analgesic treatment plan.<sup>6</sup>

Nonsteroidal anti-inflammatory (NSAIDs) drugs act by inhibiting the cyclooxygenase enzymes, and by decreasing the peripheral and central prostaglandin production. They not only reduce

the inflammation that occurs due to tissue injury and decrease prostaglandin production but also attenuate the response of the peripheral and central components of the nervous system to noxious stimuli, leading to lesser peripheral and central sensitization. These properties seem to make NSAIDs ideal drugs to use in a preemptive fashion.<sup>7</sup> Ketorolac acts by inhibiting both cyclooxygenase and lipoxygenase enzyme hence prevents synthesis of both prostaglandin and leukotrienes, and may enhance endogenous opioids release. Because of these properties of ketorolac is more potent than any other NSAIDs.

Pain after laparoscopy is treated optimally with local anesthetic, paracetamol, NSAIDs, and opioids if required.<sup>8</sup> This study was performed to compare the efficacy and safety of use of IV paracetamol, and IV ketorolac for management of postoperative pain after gynaecological laparoscopic procedure in day case surgery.

#### **Methods:**

This randomized single-blind study was conducted from January to July 2015 at the department of Anesthesia & Surgical ICU of BIRDEM General Hospital, Shahbagh, Dhaka, Bangladesh. After approval from hospital ethics committee and getting informed written consent to participants in the study, 60 patients aged 15-40 years, ASA physical status I & II for elective day case gynaecological diagnostic laparoscopy and laparoscopic ovarian cystectomy were recruited. They were divided into two groups randomly by envelop method where Group A received IV paracetamol and group B received IV ketorolac. Intravenous access established in all patients in the operating room with base line arterial blood pressure (non-invasively) and heart rate obtained. Each patient was received General anaesthesia with induction dose of inj.Fentanyl 2microgram/kg, inj. Propofol 2mg/kg and muscle relaxant inj.Atracurium 0.5mg/kg. After induction, general anaesthesia maintained by 60% N<sub>2</sub>O and 40% O<sub>2</sub> and continuous infusion of Propofol @ 5mg/kg/hr. After induction group A received intravenous paracetamol 1gm and group B received intravenous ketorolac 30mg slowly.

Patients refusal, emergency surgery, ASA physical status III or more, patients with morbid obesity, allergy to tested drugs or having Coagulopathy were excluded.

### Data processing and analysis:

Statistical analysis was done using software SPSS (Statistical Package for Social Science), version 15. Demographic & haemodynamic data were analysed using unpaired student t-test or chi-square( $X^2$ ). Statistically significance was set at p-value < 0.05.

### Results:

Sixty patients who underwent day case gynaecological laparoscopic procedure (diagnostic laparoscopy, ovarian cystectomy etc) were enrolled in the study. Diagnostic laparoscopy were in group A 21 and in group B 20, total 41 out of 60 cases and ovarian cystectomy were in group A 9 cases and group B 10 cases, total 19 out of 60 cases. Demographic data for each group was similar (Table I). Postoperative satisfaction with the intravenous paracetamol and intravenous ketorolac analgesia was similar with median scores of 73 (IV Paracetamol) and 71 (IV ketorolac) (VAS;

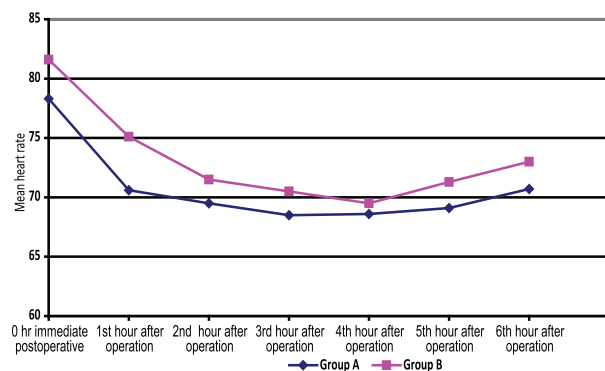
100mm= extremely satisfied) in the first 6 hour after operation. There was no significant difference between groups for heart rate (Figure 1), systolic blood pressure (Figure 2), diastolic blood pressure (Figure-3) and postoperative analgesic requirements (Figure 4). Total drug consumption of group A that is paracetamol group was 30gram and for group B that is ketorolac group was 900mg. When VAS score was more than three rescue doses of 50 mg IV tramadol was given in both group. In group A three patients and group B four patients were required single dose rescue analgesic. Patients demand for rescue dose for group A on an average 3<sup>rd</sup> hrs and for group B 4<sup>th</sup> hrs (Table I) after operation.

ASA categorization (I, II) of group A was 20/10 and of group B was 22/08 patients. Our postoperative repeated visits for assessment of pain by VAS and provide increased patient satisfaction.

**Table-I. Demographic variables**

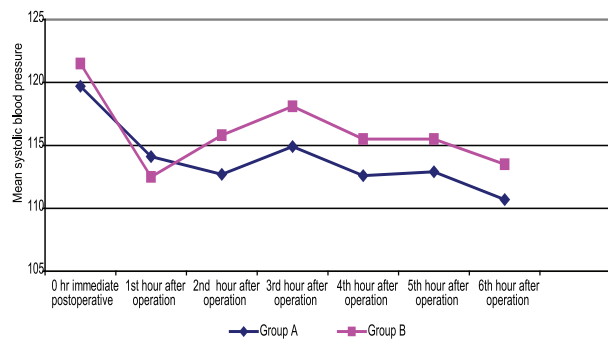
Variable	Group-A Paracetamol (n=30)	Group-B Ketorolac (n=30)	p value
Age (years)	34.40±11.12	36.20±12.55	0.56 <sup>ns</sup>
Weight (kgs)	57.67±8.13	56.30±9.44	0.55 <sup>ns</sup>
Type of operation	21/9	20/10	0.78 <sup>ns</sup>
First analgesic demand (hours)	3.03±9.44	4.07±8.13	0.63 <sup>ns</sup>

All values were presented as mean±SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value < 0.05. (NS=not significant).



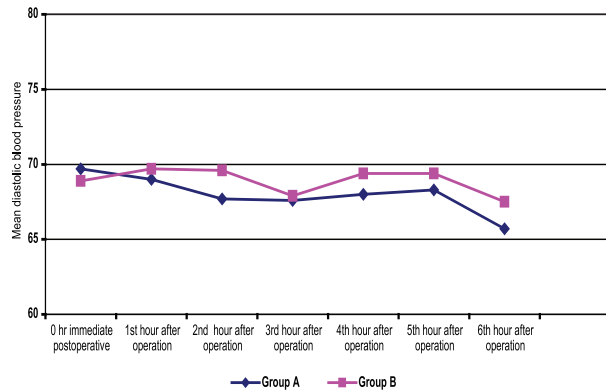
**Fig.-1: Line diagram showing postoperative heart rate in two groups**

The mean heart rate at different time in postoperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05)



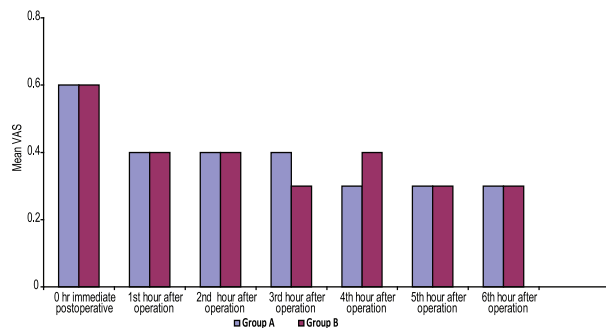
**Fig.-2: Line diagram showing postoperative mean systolic blood pressure in two groups**

The mean systolic blood pressure at different time in postoperative period compared between two groups. No statistical significant were observed in between groups (p > 0.05)



**Fig-3:** Line diagram showing postoperative mean diastolic blood pressure in two groups

The mean diastolic blood pressure at different time in postoperative period compared between two groups. No statistical significant were observed in between groups ( $p > 0.05$ )



**Fig-4:** Diagram showing VAS score in two groups

The mean VAS at postoperative period compared between two groups. No statistical significant were observed in between groups ( $p > 0.05$ )

## Discussion

Pain is the most frequent complaint leading to delayed discharge after laparoscopic procedure. Poor pain control during the perioperative period leads to complications in both long and short-term periods. Among these complications, atelectasis, pneumonia, deep vein thrombosis, pulmonary embolism, psychological trauma etc. can be severe. With a good analgesic treatment plan, the anxiety, morbidity, cost and length of hospital stay in the postoperative period are decreased.

Pathophysiology of postoperative pain is multifactorial, and predominantly of inflammatory

in nature from skin incision and tissue damage. Inflammatory cytokines, interleukins and prostaglandins produced from the arachidonic acid pathway induce a neuroinflammatory soup, which sensitizes peripheral A $\delta$  and C fibres. Ischaemia from retraction of tissue, as well as disrupted blood supplies, contributes to pain significantly, characterized by low tissue pH and high lactate levels at the site of incision.<sup>9,10</sup> The overall pain after laparoscopic procedures is a conglomerate of three different components: incision pain (somatic pain), visceral pain (deep intra-abdominal pain), and shoulder pain (referred to visceral pain).

The objective of our study was the comparison of I.V paracetamol and I.V ketorolac for postoperative analgesia after laparoscopic gynaecological day case surgery.

Paracetamol (acetaminophen), a non- opioid centrally acting analgesic, is widely prescribed. Of the non-opioid analgesics, paracetamol is perhaps the safest and most cost effective non-opioid analgesic when it is administered in analgesic dosages.

Paracetamol solution is a unit dose form, ready for infusion. It was introduced in 2002. A ready to use formulation of intravenous paracetamol does not require reconstitution and is not associated with contact dermatitis or pain on injection. The availability of intravenous paracetamol preparation may aid accurate administration of drug to patients at higher risk of dose related hepatic toxicity, including neonates.<sup>11</sup>

I.V administration of paracetamol has already demonstrated its analgesic efficacy in patients with postoperative pain following gynecologic surgery<sup>12,13</sup>, retinal surgery<sup>14</sup>, dental surgery<sup>15,16</sup>, hand surgery<sup>17</sup>, spinal fusion surgery<sup>18</sup> and orthopedic surgery.<sup>19,20</sup>

Postoperative pain was determined by the VAS for up to six-hour intervals: immediate postoperative period, 01 hour, 2 hours, 3 hours, 4 hours, 5 hours and six hours after the extubation, and if the Visual Analog Scale (VAS) was more than 3, rescue dose was administered.

Varrassi et al<sup>21</sup> compared the analgesic efficiency and tolerability of proparacetamol and ketorolac after gynecologic surgery. In this study they demonstrate that the relative morphine

requirement of the proparacetamol group was similar to that of the ketorolac group. This suggests that proparacetamol is effective in the management of postoperative pain when combined with an opioid analgesic. Side effects were all similar.

Landwehr et al<sup>22</sup> compared iv paracetamol and metamizol for postoperative analgesia after retinal surgery. They found that iv paracetamol and metamizol had similar analgesic effects on control group.

Another study that compared morphine and proparacetamol after dental surgery made by Aken et al<sup>23</sup>.found that there was no difference between morphine paracetamol. Adverse effects were significantly larger in the morphine group.

Rawal et al.<sup>24</sup> Compared oral metamizol, oral tramadol and IV paracetamol for the postoperative analgesia at home after ambulatory hand surgery. This study showed that tramadol provided the most effective analgesia as compared with the other group. But in this study, side effects were higher in tramadol group.

Gin et al<sup>25</sup> Compared intramuscular ketorolac and pethidine for analgesia after laparoscopic cholecystectomy. They showed that there were no differences between the two agents.

The analgesic drugs in this study have different mechanisms of effect. Acetaminophen has analgesic and antipyretic effects similar to aspirin, but neither the side nor the mechanism of the analgesic effects of acetaminophen has been clearly defined.<sup>26</sup>

It is generally thought to be mediated peripherally.<sup>27</sup> Through evidence suggests a direct action within the central nervous system.<sup>28</sup> Pethidine is a centrally acting analgesic with a weak affinity for  $\mu$ -opioid receptors. It has modifies pain transmission by inhibiting neuronal nor adrenaline and serotonin uptake, as well as stimulating the release of serotonin.<sup>29</sup>

In a study by Brodner and colleagues on patients undergoing mild to moderate surgery with general anesthesia, it was concluded that Paracetamol and other nonopioid analgesics have a similar effect. Postoperative pain was reduced with non-narcotic medication in comparison to placebo with no effects

on pain control. Furthermore, in our study, the effects of Paracetamol were significant in the pain control.

This study revealed that there was no significant difference in behavioral pain score between patients treated with paracetamol and those treated with ketorolac at post operative period.

This study shown that intravenous paracetamol appeared as effective as ketorolac in the management of mild to moderate pain patients undergoing laparoscopic day case procedure.

In conclusion, our study was the first study conducted in Bangladesh population. It demonstrated the usefulness of intravenous paracetamol for the postoperative pain management after laparoscopic gynaecological day case procedure.

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