

# Comparing the Analgesic Effects of IV Paracetamol Plus Ketorolac and IV Fentanyl for Pain Control after Thyroidectomy

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## ABSTRACT

**Objective:** To determine the analgesic effects of intravenous paracetamol plus ketorolac and intravenous fentanyl for pain control after Thyroidectomy.

**Study Design:** A Randomized Control Trail study.

**Place and Duration of Study:** This study was conducted at the Department of Anesthesiology, Nishtar Hospital Multan, January 2017 to December 2017.

**Materials and Methods:** Total 128 patients was included in our study. All patients were divided in two equal groups, group P and Group F, with 64 patients in each group. Group P patients received IV paracetamol plus ketorolac where as Group F patients were managed by IV fentanyl for postoperative pain. Visual Analog Scale on 0-10 was used for assessment of pain and whole procedure was explained to the patients. Pain scores were interpreted as 0=no pain, 1-4=mild pain, 5-7=moderate pain and 8-10=severe pain. Data regarding age, VAS score and side effects was analyzed by using SPSS version 23. Mean and standard deviation was calculated for numerical variables, while frequency and percentage was calculated for qualitative variables. Statistical analysis was carried out using computer software SPSS version 23. T test was applied for quantitative data and Chi square test for qualitative data. P value less than or equal to 0.05 was taken as significant.

**Results:** In group-P, 55(85.94%) patients experienced mild pain, 6(9.37%) patient experienced moderate pain and 3(4.69%) patients suffered severe pain. In group-F, 57(89.06%) patients experienced mild pain and 7(10.94%) patients experienced moderate pain. The difference in efficacy of drugs in both the groups was not statistically significant (p=0.211).

**Conclusion:** There was no significant difference found between intravenous paracetamol plus ketorolac and fentanyl in terms of pain control.

**Key Words:** Paracetamol, Ketorolac, Fentanyl, Thyroidectomy

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## INTRODUCTION

Post operative management requires particular attention after surgical procedures and interventions. With recent advances it has been now possible to understand the physiology of pain and complications it can create, along with its management.

Narcotics especially short acting narcotics are in wide use in intra as well as postoperative pain management in multiple procedures <sup>1</sup>. Fentanyl belongs to the opioid class of analgesics and it is synthetic opioid, with rapid onset of action and high lipid solubility <sup>2</sup>. Its onset takes two minutes and it provides analgesic effect from thirty to sixty minutes <sup>3</sup>.

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As far as the side effects of fentanyl are concerned, pruritus, respiratory depression, thoracic and skeletal muscle rigidity are the common side effects <sup>4</sup>. It has also been associated with delayed discharge from hospital postoperative. Fentanyl has its pharmacological effect directly on central nervous system. Clinically it is analgesic as well as sedative in action. It decreases pain perception and increases tolerance of the patient for pain; where as feeling of pain still might exist as such <sup>5</sup>. Mood alteration, euphoria, drowsiness and dysphoria are other effects of this opioid drug. It depresses respiration and depresses cough reflex and also results in pupil constriction.

In contrast to fentanyl, paracetamol is a non opioid drug used for pain relief <sup>6</sup>. It has proved to be effective and quite safe drug in management of mild to moderate pains. Different routes are used for administration of paracetamol i.e. oral, rectal and intravenous. Intravenous paracetamol has been popularly recognized in literature during recent times, as a potent analgesic. It readily crosses blood brain barrier, maintaining high concentrations in cerebrospinal fluid and acts as anti-

nociceptive via central nervous system. Paracetamol was first introduced in 2002 as an intravenous drug<sup>7</sup>. Its onset takes five to ten minutes and its peak effect is obtained within an hour and it provides analgesia for four to six hours<sup>8</sup>. Although it has no side effects of respiratory depression, circulatory depression and sedative effect but it is only effective in mild or moderate pain. Paracetamol is an excellent option when immediate venous injection is required for mild to moderate pain relief or fever. It is also proved to be safe in terms of side effects as compared to NSAIDS and opioids. Moreover it is also useful when only venous injection is possible for mild to moderate pain and fever especially postoperatively. Paracetamol has similar analgesic effects to NSAIDS. Among NSAIDS Ketorolac is an effective analgesic for efficient control of mild to moderate pain. But literature has shown that its long term use can cause local hemorrhage, GI bleed and renal insufficiency.

Rationale of our study is to conduct this trial so that postoperative pain management after thyroidectomy can be improved. Even though multiple studies have discussed the role of opioids and other analgesics in pain control, in this study we are comparing two specific drugs i.e. paracetamol and fentanyl when given intravenously. Very little data was found regarding comparison of these two drugs that is why it requires to be studied further.

## MATERIALS AND METHODS

This randomized control trial was conducted in department of Anesthesiology, Nishtar Hospital Multan from January 2017 to December 2017. Ethical was obtained from Department Ethics Committee. Total no. of 128 patients was included in our study. Sample size was calculated using the reference study by Muhammad Ali Asghar et al<sup>9</sup>. Sample size was calculated using non probability sampling technique. All patients were divided in two equal groups, group P and Group F, with 64 patients in each group. Group P patients received IV paracetamol plus ketorolac where as Group F patients were managed by IV fentanyl for postoperative pain. All the patients were selected for elective surgery for thyroid disease. Inclusion criteria was patient presenting for thyroidectomy because of thyroid enlargement, either hyperthyroid or euthyroid in outdoor patient department of Nishtar Hospital Multan. Patient with previous addiction, psychiatric illness, severe renal impairment or hepatic disease, allergy to paracetamol or opioids and BMI of equal to or greater than 30 were excluded from the study.

Thyroidectomy was performed by a surgeon with at least five year experience and researcher collected data from patients by himself. General anesthesia provided perioperatively was same in both groups. Midazolam and fentanyl was injected as premedication and

propofol and atracurium were used for induction of anesthesia.

Fifteen minutes before the completion of the procedure an injection of fentanyl was injected intravenously and in the end muscle relaxation was reversed by the use of neostigmine and atropine. Postoperatively IV paracetamol plus Ketorolac 15mg/kg was injected in group P and IV fentanyl 2μg/kg was injected in Group F patients. Visual Analog Scale on 0-10 was used for assessment of pain and whole procedure was explained to the patients. Pain scores were interpreted as 0=no pain, 1-4=mild pain, 5-7=moderate pain and 8-10=severe pain.

If any patient complained of pain of VAS >4, meperidine was injected. It was used as an adjunctive therapy in case patient demanded or until VAS becomes 4 or less than 4. Total no. of doses was calculated along with total dose given to each patient. Data regarding side effects of analgesia was also collected for postoperative nausea, vomiting, respiratory rate, pruritus and urinary retention. All data was collected through a predesigned Performa. Mean and standard deviation was calculated for numerical variables, while frequency and percentage was calculated for qualitative variables. Statistical analysis was carried out using computer software SPSS version 23. T test was applied for quantitative data and Chi square test for qualitative data. P value less than or equal to 0.05 was taken as significant.

## RESULTS

Total of 128 patients were divided into two equal groups. Means of age, weight and height were 27.90±3.72 years, 65.17±6.21 kg and 157.86±6.16 cm in Group-P and 26.73±3.74 years, 26.73±3.74 kg and 159.97±6.17 cm in Group-F, respectively. There was no statistically significant difference. Both the groups consisted of 36 (56.25%) patients of ASA-I and 28 (43.75%) patients of ASA-II class, each. (Table-1)

**Table No.1: Demographic and Anesthetic Data**

Variable	Group-P (n=64)	Group-F (n=64)	p-value
Age (Years)	27.90±3.72	26.73±3.74	0.957
Weight (Kg)	65.17±6.21	26.73±3.74	0.951
Height (cm)	157.86±6.16	159.97±6.17	0.836
ASA I (%)	36 (56.25)	36 (56.25)	0.571
ASA II (%)	28 (43.75)	28 (43.75)	

Data are presented as Mean ± Standard Deviation and Number (percentage); ASA=American Society of Anesthesiologists.

In group-P, 55(85.94%) patient's experienced mild pain, 6(9.37%) patient's experienced moderate pain and 3(4.69%) patients suffered severe pain. In group-F, 57(89.06%) patients experienced mild pain and 7(10.94%) patients experienced moderate pain. The difference in efficacy of drugs in both the groups was not statistically significant ( $p=0.211$ ). (Table-2)

In group-P, out of 64 patients, 6 (9.37%) experienced nausea, 3(4.69%) experienced vomiting, and 2 (3.12%) experienced respiratory depression. In group-F, out of 64 patients, 9 (14.06%) experienced nausea, 8 (12.5%) experienced vomiting, 8 (12.5%) experienced respiratory depression, and 3 (4.69%) experienced muscular rigidity. The difference was statistically significant ( $p=0.013$ ). (Table-3)

**Table No.2: Comparison of Pain Relief in Both Groups**

Severity of Pain	Group-P (n=64)	Group-F (n=64)	p-value
Mild	55 (85.94)	57 (89.06)	0.211
Moderate	6 (9.37)	7 (10.94)	
Severe	3 (4.69)	0 (0)	

Data are presented as number (percentage);  $p=0.211$ , not significant statistically.

**Table No.3: Side Effects**

Side Effect	Group-P (n=64)	Group-F (n=64)	p-value
Nausea	6 (9.37)	9 (14.06)	0.013
Vomiting	3 (4.69)	8 (12.5)	
Respiratory Depression	2 (3.12)	8 (12.5)	
Muscular Rigidity	0 (0)	3 (4.69)	

Data are presented as number and percentage, N (%);  $p=0.013$ , statistically significant

## DISCUSSION

Pain management has reached new advances in recent time, especially postoperative pain management. It is due to the fact that poor pain management during perioperative periods results in severe long term as well as short term complications. These complications include anxiety, morbidity, postoperative hospital stay and expenses. With provision of good analgesia, these tiresome complications can be totally avoided or at least reduced.

Short acting opioids are in common use for pain control in postoperative period after multiple surgical procedures of short durations. It is because of the fact that these drugs provide good analgesia <sup>10, 11</sup>. Despite the fact that these drugs are very effective in controlling pain, but resource variability in developing countries like ours force the care providers to look for alternate safe modalities for pain control. In practice we commonly face the challenge of unavailability and

shortage of short acting narcotics which restrict the anesthesiologists to use alternatives. Fentanyl even though is an opioid analgesic it has lesser side effects like, respiratory depression, bradycardia and hypotension, etc as compared to the other drugs in this group <sup>12</sup>.

Intravenous paracetamol is theoretically more acceptable and has a greater predictability as compared to the oral and rectal routes of administration. It readily crosses blood brain barriers and shows its analgesic effects within few minutes up till 4 hours after which its effects starts to wear off. The reason why it is preferred in most surgical procedure is that, it has no effects on mental status, respiratory rate, renal function, gastrointestinal mucosa and bleeding <sup>13</sup>. Our study aimed at finding the efficacy of IV paracetamol plus Ketorolac and fentanyl in pain management after thyroidectomy.

A comparison of IV paracetamol and placebo was carried out by Sinatra et al <sup>14</sup> after orthopedic surgery. In that study it was found that intravenous paracetamol given over the period of 24 hours for pain ranging from moderate to severe, provided very effective and rapid analgesia and that paracetamol was well tolerated by the patients. In another study IV paracetamol was compared with oral ibuprofen for postoperative pain in patients undergoing cesarean section. In this study these two drugs were used in addition to morphine and results proved that IV paracetamol had better efficacy as compared to the oral ibuprofen <sup>15</sup>. A study conducted by Tsang et al <sup>16</sup> compared opioid sparing effect of IV paracetamol in preoperative hip fracture patients. Results showed significant opioid sparing effect of IV paracetamol and also provided satisfying results in terms of pain control.

In a comparative study of IV paracetamol and IV morphine in pain management of acute limb trauma patients showed that even though paracetamol and morphine were equal in reduction of pain and requirement of rescue medication yet paracetamol had significantly lower incidence of side effects as compared to the morphine. There was no significant variation between the two groups in terms of patient satisfaction and pain relief <sup>17</sup>.

In another study 84 patients undergoing knee arthroscopy were studied for mild to moderate pain management by using IV morphine and IV paracetamol just before awakening from general anesthesia. Like our study no significant difference was found in the efficacy of the two groups and it was found that morphine was associated with greater number of side effects as compared to the IV paracetamol <sup>18</sup>. Similar results were found in multiple other studies where IV paracetamol was compared to IV fentanyl and other IV opioids in postoperative pain management <sup>19</sup>.

## CONCLUSION

There was no significant difference found between intravenous paracetamol plus ketorolac and fentanyl in terms of pain control, but less side effects in term of nausea, vomiting, respiratory depression and muscle rigidity was group paracetamol plus ketorolac as compared to fentanyl group.

### Author's Contribution:

Concept & Design of Study:	Munir Ahmad
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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