

A Comparative Study Between Intravenous Ketorolac and Intravenous Paracetamol to Alleviate Post-Intubation Sore Throat

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ABSTRACT

Background: Context: Complains of pain in throat have been recorded in patients subjected to intubation of the trachea to such an extent as requiring analgesic interventions. In the modern multi-modal analgesia approach, non-opioid and NSAID group of drugs are in vogue to provide perioperative analgesia. Ketorolac and Paracetamol are two such drugs employed to treat surgical pain. **Aim:** To study and compare the effectivity of Ketorolac and Paracetamol in decreasing throat pain following endotracheal intubation. Settings and design: Prospective randomised parallel assigned single blind control study. **Methods:** Conducted on 120 consenting adult patients who required endotracheal intubation for surgery. They were divided into 3 groups of 40 patients each - C, K and P. Group K patients were premedicated with IV Inj. Ketorolac and Group P patients with IV Inj. Paracetamol 10 minutes before induction of anaesthesia. Group C patients were the Control group. All patients were administered standard identical general anaesthetics. After recovery from anaesthesia, the incidences and severity of pain in throat was assessed and graded. The observations were tabulated and statistically analysed. Statistical analysis used: OpenEpi online software. **Results:** Both Ketorolac and Paracetamol decreased incidences and severity of throat pain. Ketorolac premedication provided better results than Paracetamol. **Conclusion:** Intravenous Ketorolac and Paracetamol both lessen sore throat caused by tracheal intubation.

Keywords: Ketorolac, Paracetamol, Post operative Sore throat.

Key messages: Premedication with intravenous Ketorolac or Paracetamol, alleviates post-operative sore throat.

INTRODUCTION

Every medical intervention, while helping the patient to recover, leaves behind some unforeseen, undesirable tell-tale after-effects. Endotracheal intubation is the most relied method used to secure airway in anaesthetised patients and trauma victims. Patients nursed in Intensive Care Units require prolonged intubation for respiratory support. Complains of sore throat, hoarse voice and cough have been documented in these patients two to six hours following tracheal extubation.^[1-3] The incidences being reported as 14% by McHardy and Chung to 80% by some other observers.^[4-9] Postoperative sore throat has also been cited as a cause of delayed discharge, longer hospital stays. It has

been described as the eighth most undesirable postoperative experience of patients by Macario et al.^[3,7]

To alleviate this unpleasant sequelae, apart from minimal airway handling, intubation only after complete relaxation of vocal cords with endotracheal tubes that are smaller in size and have high-volume-low-pressure cuffs; or intubating with spiral-embedded or micro-cuffed tubes have been employed. So also pharmacological interventions like applying jellies of Lignocaine/Cinchocaine, K-Y jelly or Betamethasone gel on the surface of the endotracheal tube before intubation; gargling with warm saline, or solutions of Lignocaine, Ketamine, Benzidamine hydrochloride, Azulene sulfonate or Aspirin before intubation or after extubation; sucking lozenges of local anaesthetic (Amethocaine); and inhaling Fluticasone or steam or Beclomethasone, etc have been prescribed to provide relieve from this disagreeable irritating sensation. But all these have shown mixed results.^[2,10-13] Search is still on for a better remedial procedure.

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Paracetamol and Ketorolac are two non-opioid analgesic agents that have now gained wide acceptance for postsurgical pain relief.^[14-18] Keeping in mind that pain (soreness) in throat was the complaint received from the suffering patients, the aim of this study was to evaluate and compare the efficacy of 'Ketorolac' and 'Paracetamol' in preventing Post-Operative Sore Throat (POST) when administered intravenously as a premedicant in patients requiring endotracheal intubation for surgery.

MATERIALS AND METHODS

This was a prospective parallel assigned single blind random study. Our primary goal was to observe for incidences of sorethroat and assess their severity. The secondary aim was to check the effect on duration of postsurgical analgesia and also to note any untoward side effects. Permission from the ethics committee of our institution was taken. Patients were explained about the nature of the study. Their written consent was obtained. Between the years 2014 and 2016, One hundred and twenty patients posted for elective surgery under general anaesthesia needing endotracheal intubation were randomly selected and divided into three groups of forty each. Both male and female patients between the ages eighteen to sixty years, having average body built and belonging to ASA grades I and II were enrolled in this study. Following patients were excluded from this study:

- Patients refusing to be part of the study,
- Patients having respiratory tract infection, Bronchial asthma, Acid peptic disease, hepatic, renal or cardiac disorders,
- History of allergy to NSAID group of drugs,
- Patients anticipated to pose difficulty in intubation.

Twelve sealed opaque envelopes, four of which contained cards labeled K, four with cards labeled P and rest four having cards labeled C inside were prepared, mixed and kept inside a box. After selection of the patients, an investigator who was not part of drug administration nor data collection or analysis randomly picked and opened one of these envelopes and assigned the patients accordingly to one of the three groups named K, P or C. Each group consisted of forty subjects. The study drugs were administered by the OT pharmacist, being not involved in the data collection and analysis. As the Inj.Paracetamol infusion is supplied in hundred ml infusion bottles, hence it was only possible to have a single blind study. Here the patient was blinded to the study drug being administered.

Group K - received Inj.Ketorolac(30mg) I.V. ten minutes before induction of anaesthesia.

Group P - received Inj.Paracetamol(1gm) I.V. ten minutes before induction of anaesthesia.

Group C - were studied as the control group and received neither Inj.Ketorolac nor Inj.Paracetamol. All the patients were administered IV Inj.Glycopyrrolate(0.2mg), Inj. Midazolam (0.05 mg/kg), Inj.Pentazocin (0.5mg/kg), Inj. Ranitidine (50mg). Anaesthesia was induced with intravenous Inj.Propofol(2mg/kg). Trachea was intubated with appropriate size oro-tracheal tubes under direct laryngoscopic vision, facilitated by intravenous Inj. Vecuronium bromide(0.1mg/kg). Cuff of the tube was inflated with air. After confirmation of appropriate placement, the tube was fixed. Anaesthesia was maintained with Nitrous Oxide : Oxygen (60:40), Isoflurane(0.4%) and intermittent incremental doses of intravenous Inj.Vecuronium with controlled ventilation. At the end of surgery, all anaesthetics were withdrawn. Residual neuromuscular paralysis was reversed with Inj. Neostigmine (0.05mg/kg) and Inj. Glycopyrrolate (0.1mg/kg). We used high-volume-low- pressure single-use type Portex endotracheal tubes. The tubes were not lubricated. No local anaesthetic was applied over the endotracheal tubes or on laryngo-tracheal mucosa. Pressure inside the cuff was maintained between 20 – 25 cm H₂O. Heart Rate, Non-invasive Blood Pressure, ECG and SpO₂ were continuously monitored.

The incidence and severity of 'sore throat' in the post-operative period (POST) were recorded and graded at 0, 2, 4 & 24 hours following recovery from anaesthesia by using the following Verbal Rating Scale:

Grade 0 = No Pain

Grade I = Mild/Slight Pain

Grade II = Moderate Pain

Grade III = Severe Pain

Grade IV = Very Severe Pain.

Patients requiring more than 2 attempts at intubation were excluded from this study. Following recovery from anaesthesia, Inj.Diclofenac(75mg) was administered IM as rescue analgesic when the patients complained of pain or VAS of pain was more than 3.

RESULTS

Observations

The following parameters were observed:-

1. Incidences and severity of Postoperative sore throat,
2. Perioperative haemodynamic changes,
3. Duration of postoperative analgesia,
4. Side-effects if any.

The data obtained was tabulated. Statistical analysis for significance was done applying OpenEpi software. Qualitative analysis was done using Chi square test. ANOVA test was done for quantitative analysis of the data. P<0.01 was considered to be significant.

The incidences and severity of sore throat were studied as the primary outcomes of this investigation and duration of postoperative analgesia as the secondary outcome. The following are the data obtained in this study:-

Table 1: Comparison Of Demographic Variables (Mean ± SD)

Parameters	Group - C (N=40)	Group - K (N=40)	Group - P (N=40)	P-Value
AGE (In Years)	38.10 ± 7.87	36.7 ± 8.64	37.95 ± 9.38	0.553
BODY WEIGHT (In Kg)	52.60 ± 11.90	54.85 ± 8.54	57.15 ± 5.69	0.085
Male / Female	24 / 16	26 / 14	22 / 18	0.0659
Asa Grade (I/II)	32 / 8	28 / 12	30 / 10	0.586
Mean duration of surgery (in minutes)	121.25 ± 24.57	137.75 ± 25.67	124.75 ± 29.53	0.016

The demographic data observed among 3 groups were comparable without any significant statistical difference.

Table 2: Incidences Of Postoperative Sore Throat (Chi Square Test using 3x2 table)

Time Of Observation	Group - C	Group - K	Group - P	P-Value

Table 3: Severity Of Postoperative Sore Throat.

Grade of Severity	0 Hour			2 Hour			6 Hour			24 Hour		
	C	K	P	C	K	P	C	K	P	C	K	P
Grade 0	0	0	0	0	0	0	0	0	0	0	0	0
Grade I(Mild)	10	8	9	12	5	7	8	1	4	3	1	3
Grade II (Moderate)	13	2	6	5	3	3	5	1	2	4	0	1
Grade III (Severe)	2	0	0	3	0	0	2	0	0	1	0	0
Grade IV (Very Severe)	0	0	0	0	0	0	0	0	0	0	0	0
Total	25	10	15	20	8	10	15	2	6	8	1	4

Group C:

- Out of 40 patients, 62.5% developed POST at 0 hour. Of these 40% had mild, 52% moderate and 8% experienced severe degree of sore throat at the end of the surgery.
- After 2 hours, 50% patients had POST, of which 60% were mild, 25% moderate and 15% severe in nature.
- After 6 hours, 37.5% of patients developed POST, of which 53.3% were of mild, 33.3% moderate and 13.3% of severe degree.
- After 24 hours, out of 40 studied patients, 20% had POST. Of these, 37.5% had mild, 50% moderate and 12.5% severe sore throat.
- Gradual decrease in percentage of POST in control group was due to administration of rescue analgesia (Inj. Diclofenac 75 mg) when patients complained of pain.

	(N=40)	(N=40)	(N=40)	
0 HOUR	25 (62.5 %)	10 (25.0 %)	15 (37.5%)	0.002
2 HOUR	20 (50.0 %)	8 (20.0 %)	10 (25.0%)	0.008
6 HOUR	15 (37.5 %)	2 (5.0 %)	6 (15.0%)	0.0007
24 HOURS	8 (20.0 %)	1 (2.5 %)	4 (10.0%)	0.041

- P<0.01- was considered to be significant
- In Group-K and Group-P incidences of POST at 0 hr, 2 hr, 6 hr were significantly less in comparison to control group.
- In Group-C, at the end of surgery(0 hr), out of 40 patients, 62.5% complained sore
- Thro at in comparison to 25% in Group-K and 37.5% in Group-P.
- At 2hr, 50% patients complained sore throat in Group-C, 20% in Group-K, 25% in Group-P.
- At 6hr, in Group-C incidence of POST was 37.5%; 5% in Group-K and 15% in Group-P.
- At 24hr, in Group-C 20% had POST in comparison to 2.5% in Group-K and 10% in Group-P.
- In this study we observed that, IV Inj. Ketorolac and Inj. Paracetamol significantly decreased the incidence of POST by the end of 0hr, 2hr and 6hr in comparison to control group.

In Ketorolac Group (K):

- At 0 hour, only 25% of studied patients suffered from POST; of which 80% were mild, 20% moderate, while no patient complained of severe pain.
- At the end of 2 hours, out of the 20% patients who developed POST, 62.5% were mild, 37.5% moderate in nature and none had severe form.
- After 6 hours, only 5% had POST, of which 50% had mild and 50% had moderate form.
- At 24 hours, only 1 patient (2.5%) had POST, and it was mild in nature.
- None of the patients of Group-K developed severe form of POST & a smaller number of patients complained of sore throat in comparison to control group.

In Paracetamol Group (P):

- From 40 patients studied, 37.5% developed POST at the end of surgery; of which 60% were mild and 40% of moderate severity while none suffered of severe type.
- After 2 hours, 25% patients complained of POST, of which 70% were of mild degree and 30% moderate, while no patient developed severe form.
- At 6 hours, of the 15% patients who developed POST, 66.6% suffered of mild and 33.3% from moderate sore throat.
- When examined after 24 hours, only 10% patients suffered from POST. Of these, 75% were mild and 25% were of moderate severity.
- Incidence and severity of POST was also less in Group-P in comparison to control group.

Table 4: Total Duration Of Postoperative Analgesia (Mean ± SD)

Time for requirement of Rescue analgesia (in Hours)	Group C (n=40)	Group K (n=40)	Group P (n=40)
	2.95 ± 0.83	6.85 ± 1.63	5.67 ± 1.57

By using ANOVA test, the P-value calculated was 0.0001 (Highly Significant) Time for requirement of rescue analgesia in Group-K and Group-P was later in comparison to control group. Duration of analgesia was more in Group-K in comparison to Group-P. Thus, decrease in postoperative analgesic demand was an added advantage of Ketorolac and Paracetamol premedication.

Table 5: Perioperative Cardiovascular Variables (Mean ± SD)

CVS Parameters	Group C (n=40)	Group K (n=40)	Group P (n=40)	P-value
Pulse Rate (in Minutes)	88.15 ± 5.40	85.70 ± 9.03	89.05 ± 5.07	0.075
Systolic Blood Pressure (mmHg)	123.40 ± 7.11	120.70 ± 7.98	121.00 ± 7.15	0.113
Diastolic Blood Pressure (mmHg)	78.30 ± 7.26	78.10 ± 6.20	75.40 ± 5.98	0.088

P-value was calculated by using ANOVA test. No statistically significant difference was observed in the cardiovascular parameters among the three groups.

Table 6: Incidences Of Side Effects Of Studied Drugs

	Group C (n=40)	Group K (n=40)	Group P (n=40)
Nausea	0	2	0
Vomiting	0	0	0
Others	0	0	0

Two (2) patients In Group-K complained of nausea. No other side effects were observed in all the three groups in this study.

DISCUSSION

In the year 2012 Maria Jaensson et al analysed the factors responsible for female patients developing sore throat following endotracheal intubation.^[1] They observed that age above 60 years, use of larger sized endotracheal tubes, application of throat packs were significant contributors to development of pain in throat. Incidentally, their analysis also showed that, intracuff pressure less than 20cm water was associated with development of postoperative hoarseness of voice. J Saleem and S Athar in an article published in Critical Care in 2008 reported that incidences of POST occurred more with PVC than Armoured endotracheal tubes.^[19] Trauma to the laryngo-pharyngeal mucosa and submucosal structures caused by the endotracheal tubes and other aids to intubation have been attributed as factors for development of POST.^{4,20} McHardy and Chung have reported that laryngoscopy and endotracheal intubation injures the laryngeal and tracheal mucosa leading to oedema and haematoma of the vocal cords. They have also reported formations of ulcers and granulomas of the cord structures in patients subjected to tracheal intubation.^[4] Trauma, ulcers, granulomas – all produce tissue inflammation of which pain is a predominant presenting feature. NSAID group of drugs are gaining grounds in the modern trend of multimodal approach to peri-operative pain management. Ketorolac tromethamine is said to be very effective in reducing postsurgical tissue inflammation and pain.^[21-23] On the other hand, intravenous Paracetamol, is also being increasingly employed as a pre-emptive analgesic agent for effective management of acute surgical pain.^[14-16] So we analysed the effectiveness of these two drugs in diminishing the symptoms of POST. This study was conducted on surgical procedures lasting in average 1.5 hours to 2.5 hours. We noted significantly less incidences of sore throat in patients premedicated with IV Ketorolac and Paracetamol in comparison to control group of patients at 0 hour, 2 hours and 6 hours following tracheal extubation. After 24 hours, though comparatively more number of patients still suffered from POST, but it was statistically not significant. Upon analyzing the severity of throat pain, we noticed that in patients who had received Ketorolac and Paracetamol, the pain was mostly mild in nature at all points of times. Some patients did suffer from moderate pain in these two groups, but they were observed to be comparatively less. None of the patients given Ketorolac or Paracetamol suffered from either severe or very severe degree of POST. While in the control group, although soreness was of mild

degree in greater number of cases at different times of observations; we marked that, in this group, comparatively more patients suffered from moderate pain immediately after extubation. Though none of the patients in control group had very severe POST, however, significant percentage of patients described the pain as severe type. The gradual decrease in incidents and severity of POST that happened in control group in later periods of time can be explained as due to the effect of rescue analgesic Inj.Diclofenac.

In comparison to the control group, the duration of postoperative analgesia was greatly increased in patients who had received Ketorolac or Paracetamol, the p-value being highly significant. Ketorolac provided longer postsurgical pain control in comparison to Paracetamol.

Ketorolac and Paracetamol premedication did not produce any significant effect on the cardiovascular system in our study. While two(2) patients in the Ketorolac group complained of nausea, we did not observe any other notable side effects of the studied drugs in our current series of patients.

In two independent studies of prevention of POST where a control group was compared with IV Ketorolac and the other compared a control group with IV Paracetamol, it had been observed that in patients premedicated with either of these compounds, there was decrease in incidences and severity of POST and patients had prolonged duration of postoperative analgesia.^[24,25]

CONCLUSION

- Premedication with Inj.Ketorolac or Inj.Paracetamol decreases the incidences, intensity and severity of sore throat following tracheal intubation as well as decreases the demand for postoperative analgesia.
- Intravenous Inj. Ketorolac gives better results when compared to intravenous Inj.Paracetamol. This might be due to its anti-inflammatory effect.

Limitations

1. Small sample size.
2. Effect of throat pack not studied.
3. Effect on patients on prolonged intubation needs to be observed.

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