e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 1274-1284

Original Research Article

A Randomised Control Trail Comparing the Efficacy of Pre-Emptive Peri Tonsillar Infiltration of Ropivacaine with Dexmeditomedine and Ropivacaine with Ketamine in Children Coming for Elective Adenotonsillectomy: A Prospective Study

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Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 26-04-2024
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Conflict of interest: Nil

Abstract:

Tonsillectomy is one of the most common surgical procedures in otolaryngology. The most common complication of surgery is acute pain, delayed oral intake, delayed haemorrhage, dehydration, prolonged hospital stays.

Methods: 90 ASA I and ASA II patients, between 4-13years, were randomly divided into three groups(n=30). Group R received 0.75% ropivacaine 0.2ml/kg total 5ml, 2.5ml on each side, Group RK received 0.75% ropivacaine 0.2ml/kg with ketamine 1mg/kg (total 5ml), Group RD received 0.75% ropivacaine 0.2ml/kg with dexmedetomidine 1mcg/kg (total 5ml). We have observed parameters like MOPS score (modified objective pain scale), time of rescue analgesia, total analgesic consumption in first 24 hours, time of first oral intake and adverse effects like sedation, respiratory depression, bradycardia, nausea, vomiting, shivering, delayed haemorrhage.

Results: Better MOPS score in Group RK when compared to Group RD, Group R. Time of first oral intake was (348.17+27.05), (398.33+51.83) and (433+41.49) respectively which was statistically highly significant(P=0.000). Total consumption of analgesics in 24 hours was 113.25+31.96, 56+26.34 and 66.03+25 respectively in Group R, RK and RD which was statistically highly significant(P=0.000).

Conclusion: Pre-emptive peritonsillar infiltration of ropivacaine along with adjuvants for post tonsillectomy pain is a safer choice of analgesia.

Keywords: Tonsillectomy, Peritonsillar Infiltration, Ropivacaine, Dexmedetomidine, Ketamine.

Introduction

Tonsillectomy is one of the most common procedures in paediatric otolaryngology. Children have high incidence of post-operative pain which can lead to laryngospasm, odynophagia, airway obstruction, sedation, nausea, and vomiting [1][2][3]. It is essential to treat post-operative pain effectively, various combinations of analgesics have been tried, among them NSAIDS, opioids, ketamine, as well as peritonsillar infiltration of local anaesthetics with opioid, ketamine and alpha 2 agonists [4][5][6][7].

The local anaesthetics were used either by topical application or by tonsillar fossa infiltration, either before or after the surgery to reduce the post tonsillectomy pain and many times the surgeons use local anaesthetics along with epinephrine to reduce the tonsillectomy bleeding and to block nociceptive transmission after tissue damage [8].

Most used local anaesthetic was lignocaine with adrenaline pre operatively in the peri tonsillar area. Since lignocaine is short acting anaesthetic, will not be sufficient to reduce the post-operative pain, hence long acting ropivacaine with additives will prolong the post-operative analgesia and reduce the morbidity [9].

Ropivacaine is long-acting amide group of local anaesthetic. It is an S (-) enantiomer of bupivacaine. The mechanism of action of ropivacaine is like other amide group of local anaesthetics. Decreased lipophilicity of ropivacaine associated with decreased potential for CNS and CVS toxicity when compared to bupivacaine, which makes it superior to bupivacaine. Its protein binding capacity results in long duration of action for 6-8hours [10][11]. Ketamine is an NMDA receptor antagonist; it prevents central sensitisation

of pain and consecutively reduce post-operative pain. Using sub anaesthetic dose of ketamine pre-emptively as an analgesic adjuvant to local anaesthetics will have very good post-operative analgesia with less opioid consumption post operatively [12].

Dexmedetomidine is highly selective alpha 2 adrenergic agonist, which produces dose dependent sedation, anxiolysis and analgesia by acting on spinal and supra spinal areas without respiratory depression [13][14].

Dexmedetomidine is being used off label as an adjuvant agent in paediatric patient for sedation and analgesia in critical care, MRI suit, and endoscopy units. It decreases the opioid usage intra and post operatively and prevents the emergence delirium and post anaesthesia shivering.

Methodology:

After obtaining ethical committee clearance 6-13 years of age group children, of ASA I and II who were posted for elective adenotonsillectomy under general anaesthesia were randomly divided into 3 groups:

1. **Group R** received peritonsillar infiltration of ropivacaine 0.75% (0.2ml/kg) constituted into 5ml (2.5ml on each tonsil)
2. **Group RK** received peritonsillar infiltration of ropivacaine 0.75% (0.2ml/kg) plus ketamine (1mg/kg) constituted into 5ml (2.5ml on each tonsil)
3. **Group RD** received peritonsillar infiltration of ropivacaine 0.75% (0.2ml/kg) plus dexmedetomidine (1mcg/kg) constituted into 5ml (2.5ml on each tonsil).

Study drug was given after induction before incision. Patients were given Inj. Propofol 2.5mg/kg body weight and Inj. Vecuronium 0.1mg/kg body weight. Premedicated with Inj. Midazolam 0.02mg/kg plus Inj. Fentanyl 2mcg/kg plus Inj. Dexamethasone 100mcg/kg and Inj. Ondansetron 100mcg/kg. The following parameters were recorded, time of infiltration, duration of surgery, time of first oral intake, time of first demand for rescue analgesia and total analgesic consumption in 24 hours, the pain was assessed by using modified objective pain scale score (MOPS).

Inclusion Criteria:

1. All ASA grade I and grade II patients between 6-13 years age group.

Exclusion Criteria:

1. All ASA grade III and IV patients
2. Diabetes and congenital heart disease
3. Obesity (BMI 30kg/m^2) and sleep disorders
4. Drug allergy
5. Allergic bronchitis
6. Haemoglobinopathies

Results:

Demographic Data:

Table 1: Age distribution of patients

Age cat		Group			
	Group R	**Group RK**	**Group RD**	**Total**	**p value**
1 to 5	2 (6.67%)	2(6.67%)	3(10%)	7 (7.78%)	0.469
6 to 10	14 (46.67%)	20(66.67%)	14(46.67%)	48 (53.33%)	Chi square
11 to 13	14 (46.67%)	8(26.67%)	13(43.33%)	35 (38.89%)	
Total	30 (100%)	30(100%)	30(100%)	90 (100%)	

Table 1 shows age distribution among three groups. 1- 5 years were 7.78%, 6 to 10 years were 53.33% and 11 to 13 years were 38.89%. the difference for the mean age among the three groups were statistically not significant. (p=0.469)

Table 2: Comparison of mean age group in years in the three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Age in years	9.73 ±2.45	9 ±2.61	9.2 ±2.73	.531

Table 2 shows the mean age in years distribution of the three groups. The mean age in years of Group R is 9.37± 2.45, Group RK is 9± 2.61 and Group RD is 9.2±2.73. there was no statistically significant difference between the groups.

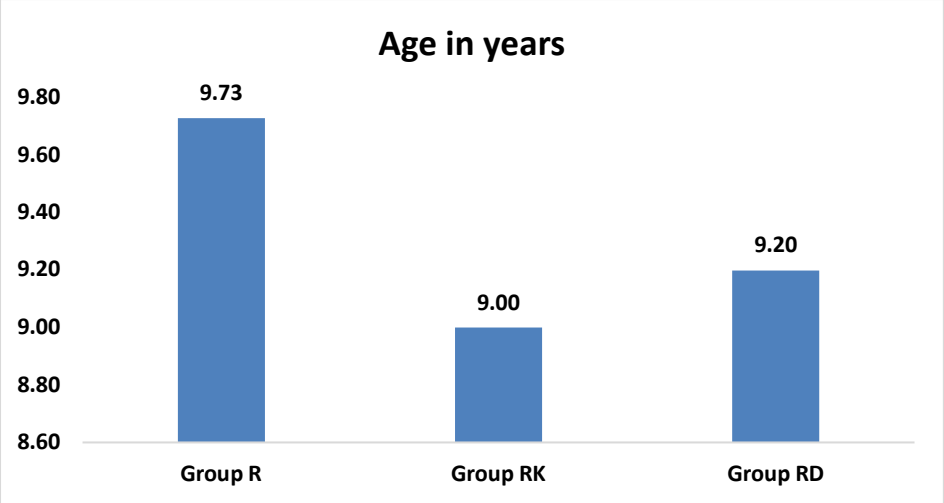

Figure 1: Comparison of mean age group in years in three groups

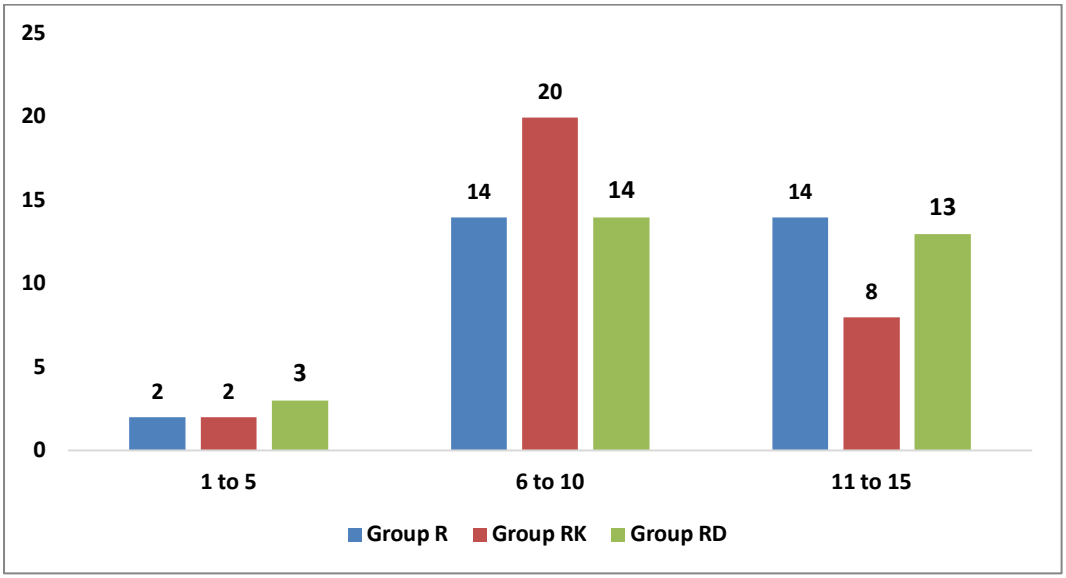

Figure 2: Graphical representation of age distribution

Table 3: distribution of sex among the three groups

Sex	Group				
	Group R	**Group RK**	**Group RD**	**Total**	**p value**
Female	17 (56.67%)	17(56.67%)	11(36.67%)	45 (50%)	0.202
Male	13 (43.33%)	13(43.33%)	19(63.33%)	45 (50%)	Chi square
Total	30 (100%)	30(100%)	30(100%)	90 (100%)	

Table 3 shows sex distribution among the three groups, which were statistically not significant. (p=0.202)

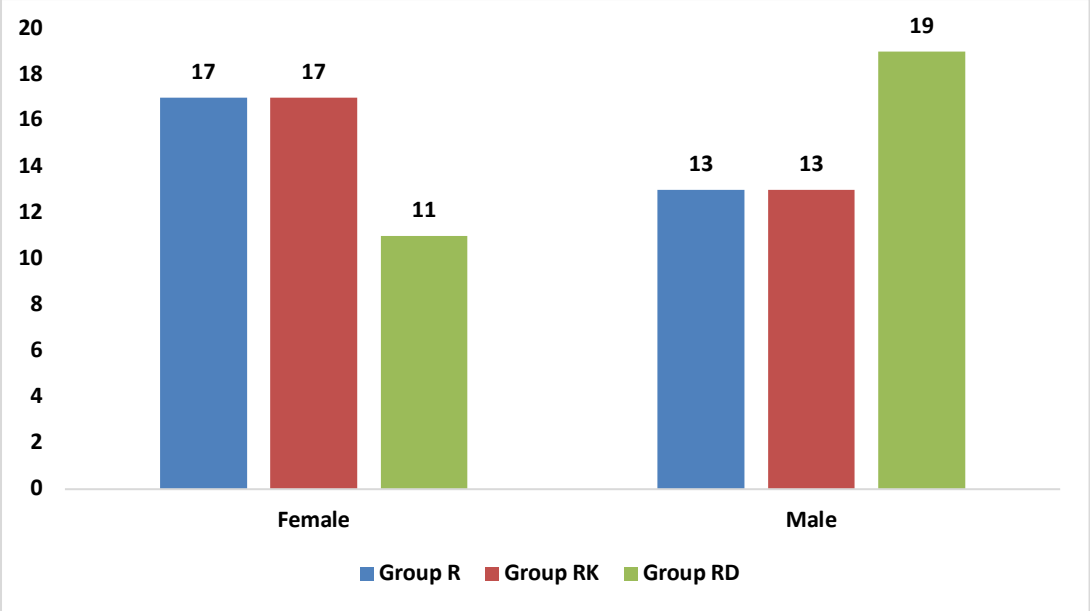

Figure 3: Graphical representation of sex distribution among the three groups

Table 4: Comparison of the mean weight among the three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Weight in kgs	27.7 ±6.35	25.13 ±7.26	23.27 ±7.29	.052

Table 4 shows the mean body weight distribution in three groups. The mean body weight in Group R is 27.70±6.35, Group RK is 25.13± 7.26 and Group RD is 23.27± 7.29. There was statistically no significant difference in the mean body weight distribution among the three groups. (p=0.052).

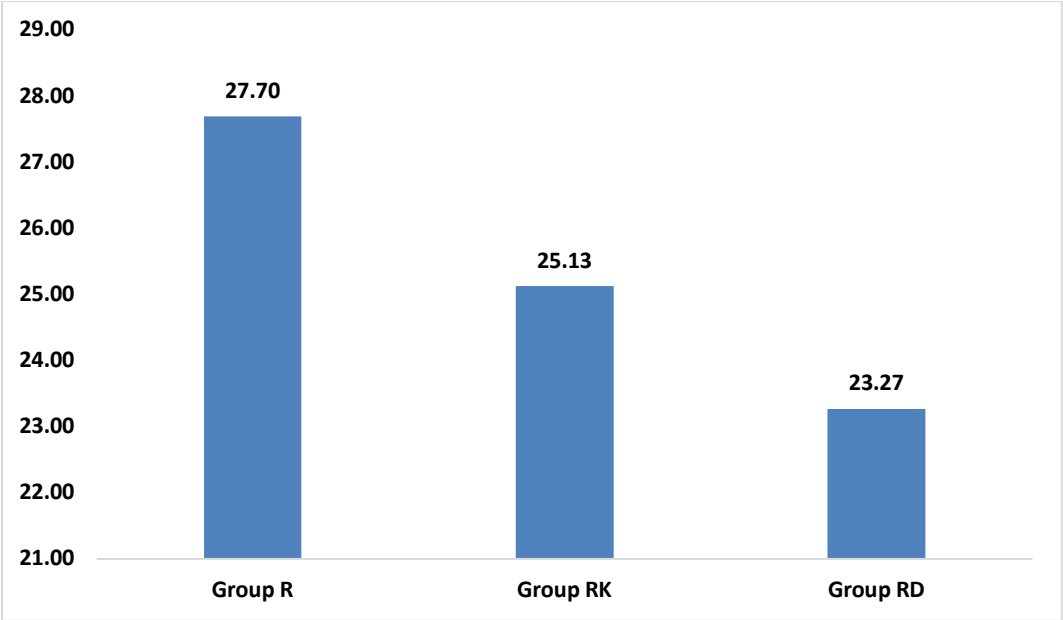

Figure 4: Graphical representation of mean weight among the three groups

Table 5: Comparison of the mean duration of surgery among three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Duration of surgery(mins)	63.8 ±12.95	62.9 ±11.23	60.9 ±11.4	.628

Table 5 shows the distribution of mean duration of surgery among the three groups. The mean duration of surgery in Group R is 63.8±12.95, Group RK is 62.90 ± 11.23 and Group RD is 60.90 ± 11.4. There was no statistically significant difference between the mean duration of surgery in the three groups. (p=0.628)

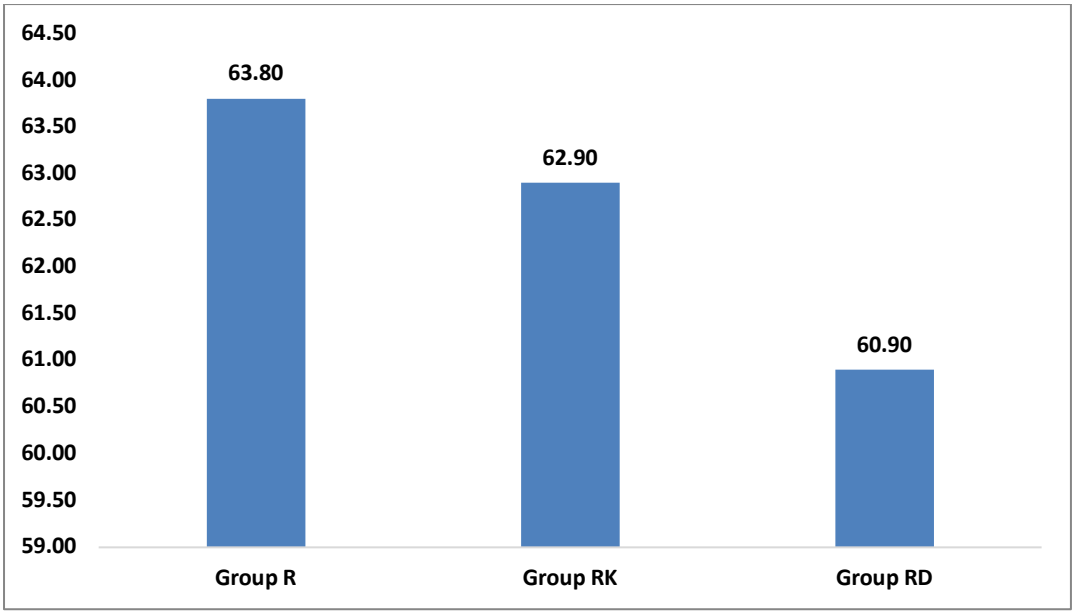

Figure 5: Graphical representation of the mean duration of surgery in three groups

Table 6: Comparison of mean duration of the time of first oral intake in the three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Time of first oral intake	433 ±41.49	348.17 ±27.05	398.33 ±51.83	**.000**

Table 6 shows the mean duration of time of first oral intake in the three groups. The mean duration of time of first oral intake in Group R is 433± 41.49, Group RK is 348.17± 27.05 and Group RD is 398.33± 51.83. There is statistically significant difference in the mean duration of time of first oral intake between the three groups. (p=0.000) Group RK earlier intake when compared to Group RD and Group R. (Group RK< Group RD< Group R).

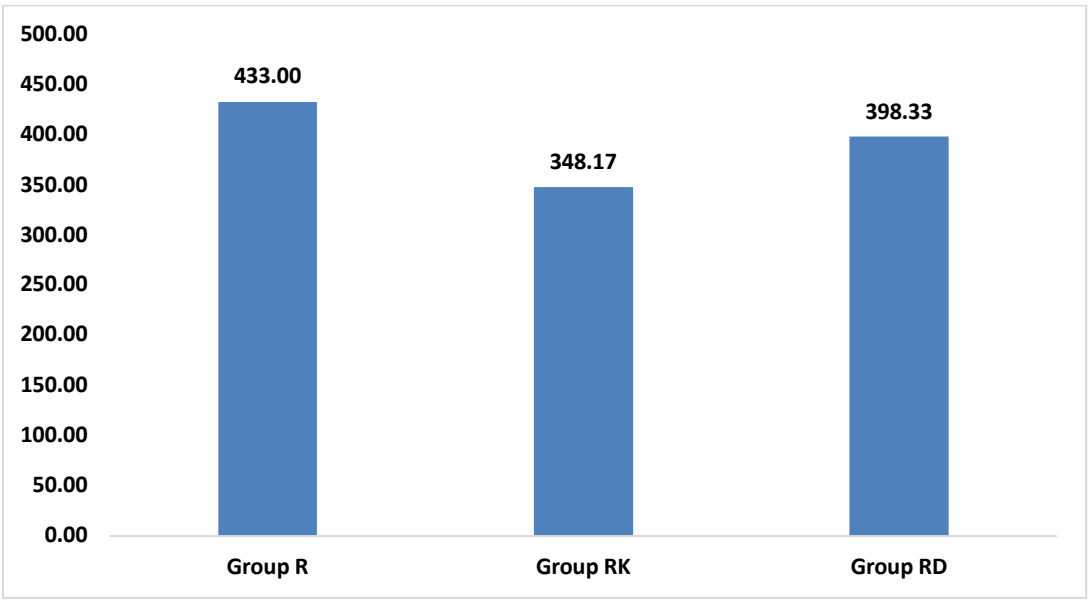

Figure 6: Graphical representation of mean duration of the time of first oral intake in the three groups

Table 7: Comparison of the mean duration of the time for first rescue analgesia

Group	Group R	Group RK	Group RD	p value (ANOVA)
Time of demand for analgesia overall	401.33 ±51.58	509 ±29.75	450.93 ±40.07	**.000**

Table 7 shows the mean duration of the time for first rescue analgesia. The mean duration of time for first rescue analgesia in Group R is 401.33±51.38, Group RK is 509± 29.75 and Group RD is 450± 40.07. There is highly statistically significant difference in the time for first rescue analgesia between the three groups.

(p=0.000). The mean duration of first rescue analgesia was prolonged in Group RK when compared to Group RD and Group R. (Group RK> Group RD > Group R).

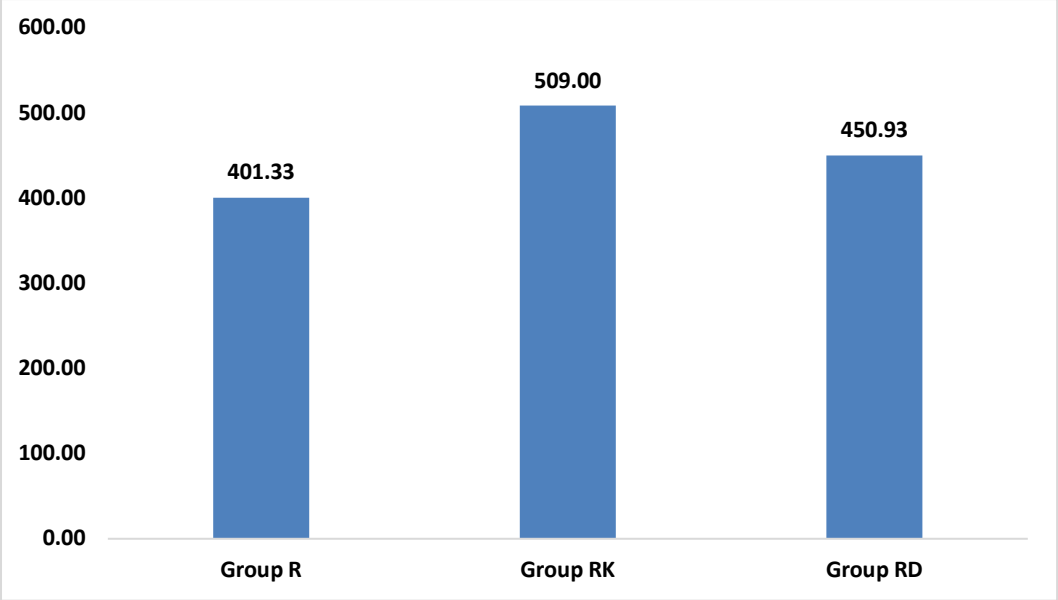

Figure 7: Graphical representation of the mean duration of the time for first rescue analgesia

Table 8: Comparison of mean of total analgesic consumption in 24 hours among the three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Total analgesic used in 24hrs	113.25 ±31.96	56 ±26.34	66.03 ±25	**.000**

Table 8 shows the mean of total analgesic consumption in 24 hours in the three groups. The mean of total analgesic consumed in 24 hours in Group R is 113.25± 31.96, Group RK is 56± 26.34 and Group RD is 66.03± 25. There is highly statistically significant difference in the mean of total analgesic consumed in 24 hours between the three groups. (p=0.000). Children belonging to Group R consumed highest dose of Injection Diclofenac when compared to Group RK and Group RD. (Group R> Group RD > Group RK).

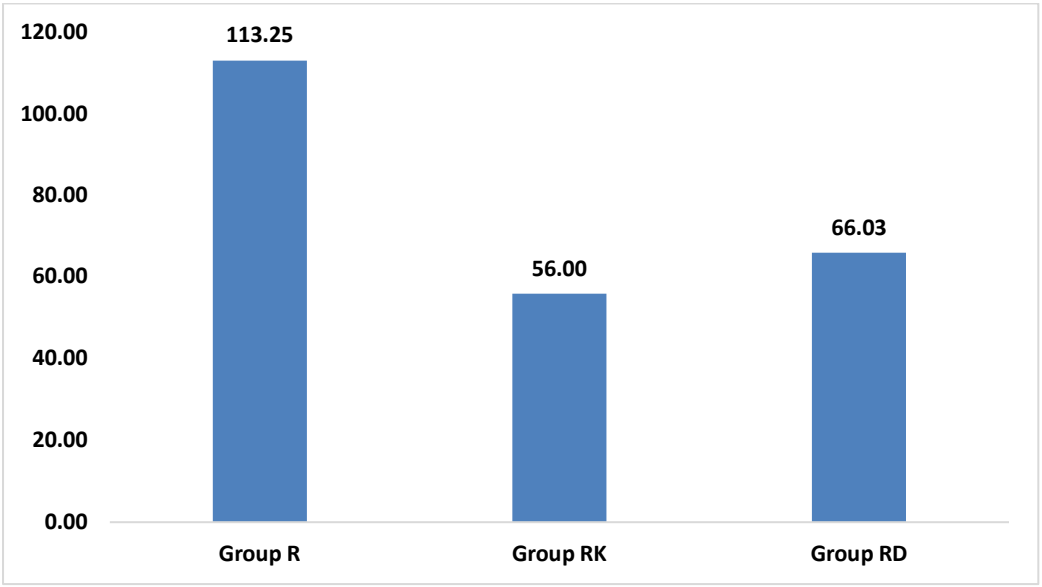

Figure 8: Graphical representation of the mean of total analgesic consumed in 24 hours among three groups

Table 9: Comparison of the mean of family satisfaction score between three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
Family satisfaction score	1.03 ±0.41	1.9 ±0.31	1.7 ±0.47	**.000**

Table 9, shows the mean of family satisfaction score between the three groups. The mean family satisfaction score of Group R is 1.03± 0.41, Group RK is 1.90± 0.31 and Group RD is 1.70± 0.47. There is highly statistically significant difference among the groups for the mean family satisfaction score. (p=0.000). Family satisfaction score was best with Group RK when compared to Group RD and Group R. (Group RK better than Group RD, which was better than Group R).

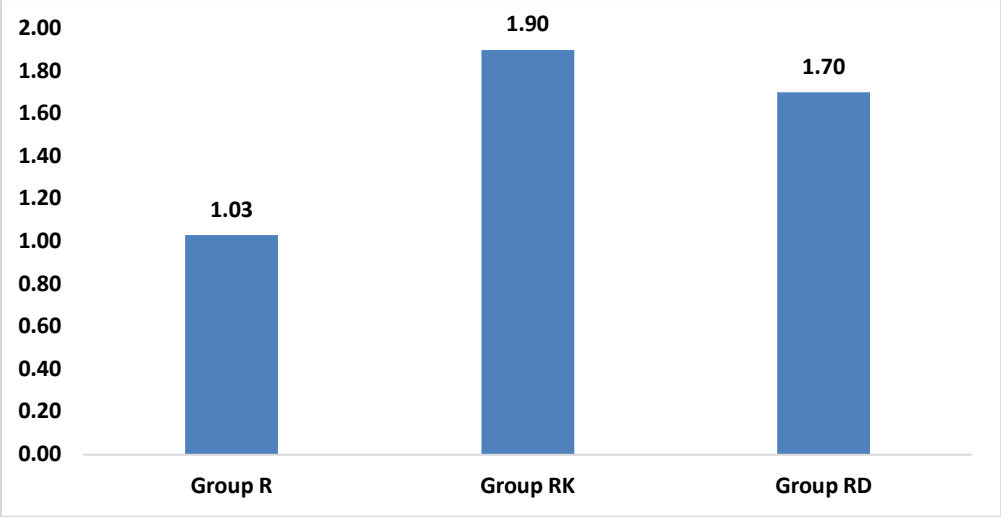

Figure 9: Graphical representation of the mean of family satisfaction score between three groups

Table 10: Modified Objective Pain Scale score at different intervals among three groups

Group	Group R	Group RK	Group RD	p value (ANOVA)
MOPS/1st Hr	2.83 ±0.7	1.73 ±0.64	1.93 ±0.64	**.000**
MOPS/2nd Hr	2.67 ±0.55	1.63 ±0.56	2.17 ±0.38	**.000**
MOPS/4th Hr	2.87 ±0.82	1.73 ±0.52	2.37 ±0.56	**.000**
MOPS/6th Hr	4.4 ±1.13	2.47 ±0.86	3.43 ±1.07	**.000**
MOPS/8th Hr	3.77 ±1.04	4.4 ±1.28	4.73 ±0.87	**.003**
MOPS/12th Hr	2.83 ±0.75	3.3 ±0.75	2.87 ±0.73	**.029**
MOPS/16th Hr	3.1 ±1.18	2.4 ±0.5	2.7 ±0.92	**.014**
MOPS/20th Hr	3.8 ±1.37	2.27 ±0.98	2.7 ±1.06	**.000**
MOPS/24th Hr	2.27 ±0.78	1.8 ±0.61	2.13 ±0.51	**.019**

Table 10 shows Modified Objective Pain Scale (MOPS) scores among three groups at different intervals. MOPS score includes parameters like crying, movements, agitation, posture and verbal. MOPS score of >5 out of 10 considered as a significant score for analgesic supplementation. The mean MOPS score in Group R was highest at the earliest interval (6^{th} hour) when compared to Group RK and RD. In Group RK and RD, highest OPS score was recorded at 8^{th} hour interval. Hence, analgesic consumption in Group R was more when compared to other two groups. The mean MOPS score was statistically highly significant at 1^{st}, 2^{nd}, 4^{th}, 6^{th} and 20^{th} hour interval among the three groups. (p=0.000). The mean MOPS was statistically significant at 8^{th}, 12^{th}, 16^{th} and 24^{th} hour interval among the three groups. (p=0.003, 0.029, 0.014 and 0.019 respectively).

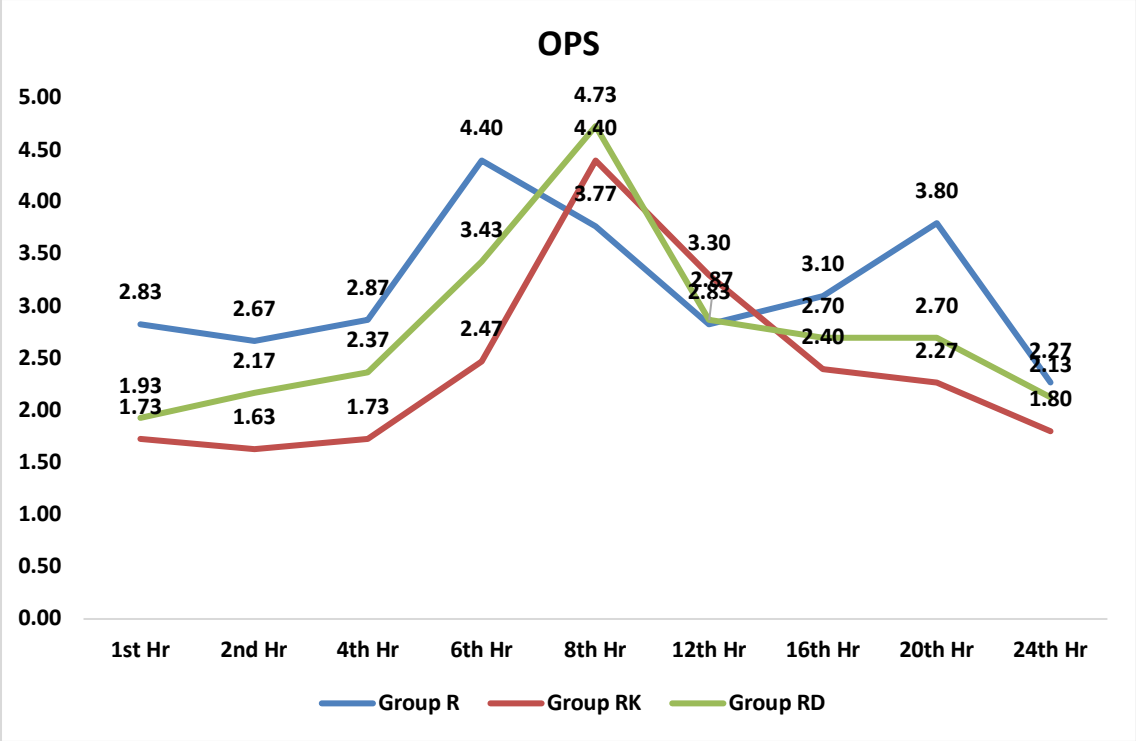

Figure 10: Graphical representation of Modified Objective Pain Scale score at different intervals among the three groups

Table 11: Dependent Variable (Post-hoc Bonferroni) among the three groups

Dependent Variable (Post hoc-Bonferroni)	Group 1	Group 2	p value
Age in years	Group R	Group RK	.834
	Group R	Group RD	1.000
	Group RK	Group RD	1.000
Weight in kgs	Group R	Group RK	.473
	Group R	Group RD	**.048**
	Group RK	Group RD	.909
Duration of surgery(mins)	Group R	Group RK	1.000
	Group R	Group RD	1.000
	Group RK	Group RD	1.000
Time of first oral intake	Group R	Group RK	**.000**
	Group R	Group RD	**.005**
	Group RK	Group RD	**.000**
Time for rescue analgesia	Group R	Group RK	**.000**
	Group R	Group RD	**.000**
	Group RK	Group RD	**.000**
Total analgesic used in 24hrs	Group R	Group RK	**.000**
	Group R	Group RD	**.000**
	Group RK	Group RD	.503
Family satisfaction score	Group R	Group RK	**.000**
	Group R	Group RD	**.000**
	Group RK	Group RD	.169
MOPS/1st Hr	Group R	Group RK	**.000**
	Group R	Group RD	**.000**
	Group RK	Group RD	.731
MOPS/2nd Hr	Group R	Group RK	**.000**
	Group R	Group RD	**.001**
	Group RK	Group RD	**.000**
MOPS/4th Hr	Group R	Group RK	**.000**
	Group R	Group RD	**.011**

	Group RK	Group RD	**.001**
MOPS/6th Hr	Group R	Group RK	**.000**
	Group R	Group RD	**.001**
	Group RK	Group RD	**.001**
MOPS/8th Hr	Group R	Group RK	.075
	Group R	Group RD	**.002**
	Group RK	Group RD	.698
MOPS/12th Hr	Group R	Group RK	.051
	Group R	Group RD	1.000
	Group RK	Group RD	.079
MOPS/16th Hr	Group R	Group RK	**.011**
	Group R	Group RD	.278
	Group RK	Group RD	.617
MOPS/20th Hr	Group R	Group RK	**.000**
	Group R	Group RD	**.001**
	Group RK	Group RD	.444
MOPS/24th Hr	Group R	Group RK	**.019**
	Group R	Group RD	1.000
	Group RK	Group RD	.145

A Bonferroni test is perhaps the simplest post-hoc analysis which includes series of t-test performed on each pair of groups. The number of groups quickly grows the number of comparisons, which inflates the type 1 error rates. The demographic variables like age, sex, weight, and duration of surgery among the three groups were not statistically significant. Whereas the primary objective variables like time of first oral intake, time for rescue analgesia, total analgesic consumption in 24 hours, family satisfaction score and MOPS score were statistically highly significant among Group RK and RD when compared to Group R. Though the two variables like time of first oral intake and time for first rescue analgesia were statistically highly significant among the three groups.

Table 12: Criteria of modified objectives pain score (MOPS)

Criteria	Finding	Points
Crying	none consolable not consolable	0 1 2
Movement	none restless thrashing	0 1 2
Agitation	asleep/calm mild hysterical	0 1 2
Posture	normal flexed holds injury site	0 1 2
Verbal	asleep/no complaint complains/cannot localize complains/can localize	0 1 2

MOPS score of >5 out of 10 considered as a significant score for analgesic supplementation.

Discussion

Tonsillectomy is one of the most common procedures in paediatric otolaryngology. Post tonsillectomy pain caused by inflammation, nerve irritation and pharyngeal muscle spasm and they have high incidence of post-operative pain, which can be accompanied by laryngospasm, odynophagia, airway obstruction, post-operative nausea and vomiting. Traditionally pain was treated with opioids and NSAIDS**,** however these agents are associated with respiratory depression, post op nausea, vomiting and post op bleeding respectively. Inadequate treatment of post tonsillectomy pain causes reduced oral intake, prolonged hospital stays and significant dehydration. Hence present study is to compare efficacy and duration of post-operative analgesia and time of oral intake by using pre-emptive peritonsillar infiltration of ropivacaine along with dexmedetomidine and ketamine [1],[2],[3],[4],[5],[6], [7],[11],[15].

There are different methods of achieving analgesia by using local anaesthetics which could be pre incisional as pre-emptive analgesia or post tonsillectomy peri tonsillar infiltration. Various local anaesthetics like lignocaine, bupivacaine, ropivacaine have been studied, among all local anaesthetics ropivacaine is superior agent with a less motor block and prolonged sensory block. Adding alpha 2 agonist like dexmedetomidine and ketamine to ropivacaine enhances the efficacy and duration of analgesia.[18][19]. Demographic data of present study like age, sex, weight and duration of surgery were comparable among the three groups, which was statistically not significant (P>0.05).

Pain scale used to assess the pain was modified objective pain scale score (MOPS), which includes crying, movements, agitation, posture and verbal. MOPS score of more than 5 out of 15 was considered as significant score for analgesic supplementation. The MOPS score was significantly high in Group R at 1st, 2nd, 4th, 6th, and 20th hour when compared to Group RK and Group RD (P=0.000), this can be comparable with Mohammed Ibrahim et al and Manal S Farmawy et al study.

The mean duration of time for 1st rescue analgesia in Group R is 401.33+51.38, Group RK is 509+29.75 and Group RD is 450+40.07, which is highly statistically significant between three groups. The first rescue analgesia was prolonged in Group RK when compared to Group RD and Group R (P=0.000). This can be comparable with Manal S Farmawy et al and Vida Ayatollhi et al.

The total analgesic consumption in first 24 hours was significantly high (P=0.000) in Group R children when compared to Group RK and Group RD, which can be comparable with Manal S Farmawy et al study.

The time of first oral intake was earlier in Group RK (348.17+27.05) when compared to Group RD (398.33+51.83) and Group R (433+41.49) which was statistically highly significant. We have not noticed single side effects in any of our patients.

Conclusion

Pre-emptive peritonsillar infiltration of Injection Ropivacaine along with adjuvants like ketamine and dexmedetomidine provides effective post-operative analgesia with early oral intake without any adverse effects, which leads to good family and patient satisfaction. Hence pre-emptive peritonsillar infiltration is a better alternative to conventional mode of analgesics.

References

1. M.B. Ugur et al. Effects of intramuscular and peritonsillar injection of tramadol before tonsillectomy: a double blind randomized, placebo-controlled clinical trial Int. J. Pediatr. Otorhinolaryngol. 2008.
2. O.N. Aydin et al.Pain prevention with intraoperative ketamine in outpatient children undergoing tonsillectomy or tonsillectomy and adenotomy. J. Clin. Anesth. 2007; 71: 735-9.
3. K.S. Ugur et al. The comparison of preincisional peritonsillar infiltration of ketamine and tramadol for postoperative pain relief on children following adenotonsillectomy Int. J. Pediatr. Otorhinolaryngol. 2013.
4. J.E. Beyer et al.Discordance between self-report and behavioral pain measures in 3–7 year old children following surgery J. Pain Symptom Manag. 1990.
5. J.A. Sterne et al.Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis J. Clin. Epidemiol. 2001.
6. T. Engelhardt et al. Tramadol for pain relief in children undergoing tonsillectomy: a comparison with morphine Paediatr. Anaesth. 2003.
7. Z. Ozer et al. Efficacy of tramadol versus meperidine for pain relief and safe recovery after adenotonsillectomy Eur. J. Anaesth. 2003.
8. Grainger J, Saravanappa N. Local anaesthetic for post-tonsillectomy pain: a systematic review and meta-analysis. Clinical Otolaryngology. 2008 Oct; 33(5):411-9.
9. Gupta AK, Gupta S, Meena DS, Sharma U. Post-tonsillectomy pain: different modes of pain relief. Indian Journal of Otolaryngology and Head and neck surgery. 2002 Apr 1; 54(2):136.
10. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian journal of anaesthesia. 2011 Mar; 55(2): 104.
11. Sood AS, Pal P, Gill GS. Peritonsillar Ropivacaine Infiltration in Paediatric Tonsillectomy: A Randomised Control Trial. Iranian Journal of Otorhinolaryngology. 2020 Jul; 32(111):207.
12. Cho HK, Kim KW, Jeong YM, Lee HS, Lee YJ, Hwang SH. Efficacy of ketamine in improving pain after tonsillectomy in children: meta-analysis. PloS one. 2014 Jun 30; 9(6): e101259.
13. Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia. 1999 Feb; 54(2):146-65.
14. Maze M, Scarfini C, Cavaliere F. New agents for sedation in the intensive care unit. Critical care clinics. 2001 Oct 1; 17(4):881-98.
15. El Sonbaty MI, Abo el Dahab H, Mostafa A. Preemptive peritonsillar ketamine infiltration:

postoperative analgesic efficacy versus meperidine. Middle East journal of anaesthesiology. 2011 Feb 1; 21(1):43-51.
16. Farmawy MS, Rashad MM. Preemptive analgesia by peritonsillar ketamine versus ropivacaine for post-tonsillectomy pain in children. Egyptian Journal of Anaesthesia. 2014 Jan 1; 30(1):1-5.
17. Ayatollahi V, Behdad S, Hatami M, Moshtaghiun H, Baghianimoghadam B. Comparison of peritonsillar infiltration effects of ketamine and tramadol on post tonsillectomy pain: a double blinded randomized lacebocontrolled clinical trial. Croatian medical journal. 2012 Apr 15; 53(2): 155-61.
18. 18. Dexmedetomidine Added to Ropivacaine Extends the Duration of Interscalene Brachial Plexus Blocks for Elective Shoulder Surgery When Compared with Ropivacaine Alone: A Single-Center, Prospective, Triple-Blind, Randomized Controlled Trial G. Fritsch T. Danninger+5 authors C. Brummett Medicine Regional anesthesia and pain medicine. 2013.
19. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study. D. Marhofer S. Kettner P. Marhofer S. Pils Maria Weber M. Zeitlinger Medicine. British Journal of Anaesthesia. 2013.