Section: Anaesthesiology

Original Research Article

EFFICACY OF PREMEDICATION WITH ORAL PARACETAMOL, DICLOFENAC SODIUM AND THEIR COMBINATION FOR ANALGESIA IN ADULTS UNDERGOING OTOLARYNGOLOGIC SURGERY

Mary Margaret B[1], Kshma Kilpadi[2], Sunil Achinthalu[1], M. Manjuladevi[2], Sarika Sudhir Naik[3]

[1]*Assistant Professor, Department of Anaesthesiology, St. peter's medical college, Hosur, Tamil Nadu, India*
[2]*Professor, Department of Anaesthesiology, St. John's medical college, Bangalore, Karnataka, India*
[3]*Professor and Head, Department of Anaesthesiology, St. peter's medical college, Hosur, Tamil Nadu, India*

Received *: 03/07/2024*
Received in revised form *: 23/08/2024*
Accepted *: 07/09/2024*

Corresponding Author:
Dr. Sunil Achinthalu,
Assistant Professor, Department of Anaesthesiology, St. Peter's medical college, Hosur, Tamil Nadu, India
Email: achinthalusunil@gmail.com

DOI:10.70034/ijmedph.2024.3.117

Source of Support: Nil
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2024; 14 (3); 651-657

ABSTRACT

Background: Achieving effective pain control during the postoperative period continues to be a clinically significant issue in facilitating the recovery process. The aim of this prospective randomized double blind placebo controlled study was to evaluate the analgesic efficacy of oral paracetamol and diclofenac sodium sustained-release when administered alone or in combination before elective Otolaryngologic surgery in adults.

Materials and Methods: This study include 80 adult patients aged 15-65yrs, they were randomized into four groups as follows n= 20 in Group I, placebo [Vit. C 500mg per oral (PO)]; n=20 in Group II, [Paracetamol 1000mg PO]; n=20 in Group III [Diclofenac sodium sustained release 100mg PO] and n=20 in Group IV, [paracetamol 1000mg and diclofenac sodium sustained-release 100mg PO]. The drug was administered 45min before elective otolaryngologic surgery. All patients received standard anaesthetic technique. During the postoperative period, pain was assessed using visual analogue scale (VAS), requirement of rescue analgesia and side effects.

Results: There was significant reduction of postoperative pain in group II, group III and group IV compared to group I and there was no statistically significant difference found between group II, group III and group IV in reducing postoperative pain. There was comparable reduction of postoperative pain between group II and group III with no statistical significance.

The time of first rescue analgesia administration was significantly shorter in group I (p =0.004) compared to the other groups, and the total dose of rescue analgesia was statistically significant between the study groups with (p = 0.013), the total dose being maximum in group I.

The need for rescue analgesia was reduced to 50% in group IV compared to 15%, 25% and 30% in group I, group II and group III respectively, but no statistical significance found with p=0.1. With respect to side effects, nausea, vomiting and sedation, there was no significant difference between the groups.

Conclusion: We conclude that oral premedication with paracetamol 1000mg and diclofenac sodium sustained-release 100mg and their combination provides effective analgesia in the postoperative period after otolaryngologic surgery. The combination provides better opioid sparing effect than either drug given alone. Hence, paracetamol and diclofenac sodium sustained-release (NSAIDs) can be used safely as an alternative to opioids in reducing postoperative pain after otolaryngologic surgery.

Keywords: Analgesia; Visual Analogue Scale; Rescue Analgesia; Opioid; Non-opioid;

INTRODUCTION

Achieving effective pain control during the postoperative period continues to be a clinically significant issue in facilitating the recovery process. For this, effective analgesia is an essential part of postoperative management. The current armamentarium of analgesic drugs and techniques for the management of postoperative pain continues to grow at a rapid rate. However, effective treatment for acute postsurgical pain still poses unique challenges for practitioners.[1,2] The expanding patient population requires a perioperative analgesic regimen that is highly effective, has minimal side effects, is intrinsically safe, and can be easily managed in the community.[3] Therefore major goal in the management of postoperative pain is to minimize the dose of medication and lessen the side effects while providing adequate analgesia. This goal is best accomplished with multimodal and pre-emptive analgesia.[2]

Adequacy of postoperative pain control is one of the most important factors in determining when a patient can be safely discharged from a surgical facility and has a major influence on the patient's ability to resume their normal activities of daily living. Hence, effective postoperative pain relief leads to earlier mobilization, shortened hospital stay, reduced hospital cost and increased patient satisfaction.[4]

Perioperative analgesia has traditionally been provided by opioid analgesics; however, extensive use of opioids is associated with an array of peri-operative side effects, such as respiratory depression, drowsiness, sedation, postoperative nausea vomiting (PONV), pruritis, urinary retention, ileus, and constipation which can delay hospital discharge.[1,5] Intraoperative use of large bolus doses or continuous infusions of potent opioid analgesics such as remifentanil may actually increase postoperative pain as a result of their rapid elimination or the development of acute tolerance.[6] In addition partial opioid agonists (e.g., tramadol) are also associated with increased side effects(e.g., nausea, vomiting, ileus) and patient dissatisfaction compared with both opioid and non-opioid analgesics.[7-9] Therefore, anaesthesiologists and surgeons are increasingly turning to non-opioid analgesic techniques as adjuvants for managing pain during the perioperative period to minimize the adverse effects of opioid analgesics.[2] Hence, the search is on for regimes of non-opioid analgesia with less adverse effects and patients satisfaction in patients undergoing otolaryngologic surgery. This study is an effort in that direction.

Aims and Objectives

- To study the pre-emptive analgesic efficacy of oral paracetamol, diclofenac sodium and a combination of these drugs in adult patients undergoing otolaryngologic surgery.
- To study the opioid sparing effect of oral paracetamol and diclofenac sodium and a combination of these drugs in the perioperative period.

MATERIAL AND METHODS

Study design: This is a randomized double-blind placebo-controlled study. After obtaining institutional ethical committee approval, written informed consent, this study was conducted on patients posted for elective otolaryngologic surgery under general anaesthesia at St. John's Medical College and Hospital, Bangalore, during the period October 2010 to October 2011.

Eighty patients randomly allocated to four groups. Each group had 20 patients; these patients were in the age group of 15 - 65 years, of either sex and belonged to ASA I and II. The drugs used were Tab. Paracetamol and Diclofenac sodium sustained release, for the analgesic and opioid sparing effect.

Group I: Placebo VitC 500mg peroral(PO).

Group II: Paracetamol 1000mg PO.

Group III: Diclofenac sodium sustained-release 100mg PO.

Group IV: Paracetamol 1000mg and Diclofenac sodium sustained-release100mg PO.

Inclusion criteria

- Patients willing to give consent.
- Age15 – 65 years.
- Either sex.
- ASA I and ASA II patients.

Exclusion Criteria

- Patients not willing to participate in the study.
- ASA III & IV patients.
- Pregnant/breast feeding women.
- Patients allergic to any medication used in the study.

Method of collection of data

Patients posted for elective otolaryngologic surgery under general anaesthesia after an appropriate pre anaesthetic evaluation, were randomly assigned by sealed envelope method into four groups. The study drug for premedication was coded, put in the envelope and sealed, by the person not involved in the study the envelopes were shuffled, patients were asked to pick up a sealed envelope. The drug contained in the envelope was given to the patient by the nurse in the ward. After the investigation the envelope were decoded.

The study drug was administered orally with a sip of water 45 minutes before surgery. A standard balanced anaesthetic technique was followed (using induction with propofol, intermittent doses of fentanyl and atracurium with 1% isoflurane and endotracheal intubation) and patients were evaluated for pain from the time of recovery up to 24 hours of postoperative period and IV Tramadol 50mg was administered as rescue analgesic when VAS was 4 and above or the patient requested for pain relief.

The following variables were recorded:

- **VAS score:** Immediate post extubation (time 0), after 30min, at 1st, 2nd, 3rd, 6th, 12th, 16th and 24th hours.
- Time to 1st dose of Rescue Analgesia and the required dose of rescue analgesic.
- Side effects like nausea, vomiting and sedation.

Statistical Methods: The data collected was analyzed using a descriptive statistical analysis. Results on continuous measurements are presented as Median, Quartiles, Mean and SD (Min- Max) are used to represent the average values of the parameters and results on categorical measurements are presented in Number (%).

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups. The Fisher's exact test looks at a contingency table which displays how different treatments have produced different outcomes. Kruskal – Wallis test has been used to find the significance of VAS score in four groups of patients. Mann – Whitney U is a non-parametric statistical hypothesis test for assessing whether one of two samples of independent observations tends to have larger values than the other. Significance is assessed at 5% level.

Statistical software: The statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Sysdtat 12.0 and R environment ver.2.11.1 were used for the analysis of the data Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

There was no significant difference in age between the four groups (p=0.1), similarly, there was no significant difference in gender distribution (p=0.9) , height and weight analysed among the study groups (p =0.409, p =0.840 respectively).

Study analysis revealed there was a statistically significant association of comorbid conditions and with pain (p =0.015). Evaluation of pain in the 24 hrs postoperative period as shown in the [Table 2], the comparison of VAS score among the four groups in different time periods at 0 min, 30 min, 1st, 2nd, 3rd, 6th, 12th, 16th, 24th hrs with p value of 0.880, 0.069, 0.003**, 0.042*, 0.202, 0.034*, 0.001**, 0.043*, 0.035*.

Analysis on VAS score for pain revealed that there was marked reduction in pain in Group IV, with least VAS score in comparison with Group I. There were similar findings of reduction in pain in Groups II and III patients when compared to Group I. Both these findings were statistically significant. When Group IV was compared with Group II and III, VAS score at different time period 0 min, 30 min, 1st, 2nd, 3rd, 6th, 12th, 16th, 24th hrs was not statistically significant with p value 0.729, 0.412, 0.676, 0.708, 0.964,0.155,0.242,0.169,0.969.

In the current analysis, the VAS score in patients under Group II was comparable with that in group III with no statistical difference in relation to pain relief at different time period.

In the present study, analysis [Table 1] we observed that among those who received rescue analgesia (RA), the time to first RA administration in minutes from extubationis significantly shorter in group I (p=0.004) compared to other groups.

The total dose of rescue analgesia (RA) given was significantly higher in Group I when compared to the other groups (p =0.013). The requirement of rescue analgesia was reduced by 50% in Group IV, when compared to 15%, 25% & 30% in groups I, II and III respectively [Table 3]. However, these results fell short of achieving statistical significance (p=0.1).

With regards to side effects such as nausea and vomiting and sedation [Table 4,5] there was no significant difference between the groups.

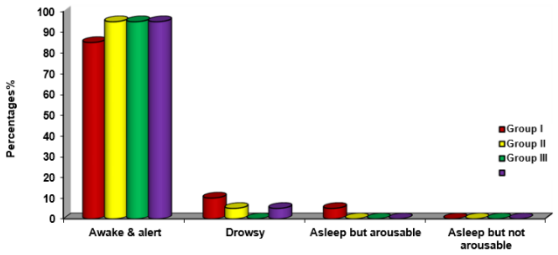

Figure1: Graph showing Sedation score.

Table 1: First rescue analgesia requirement and dosage in different groups.

	Group I	Group II	Group III	Group IV	p value
Rescue Analgesia in min from extubation	30(7.5,60)	150(112.5,360)	120(30,180)	105(10,195)	0.004
Rescue Analgesia Total dose	100(100,175)	50(50,100)	100(50,100)	50(50,112.5)	0.013

Table 2: Comparison of VAS score at different time periods Median (Q1, Q3)

VAS score	Group I	Group II	Group III	Group IV	p value
Baseline	0.00	0.20	0.00	0.00	0.108
0 minute	0(0,4.5)	0(0,2)	0(0,1)	0(0,2)	0.880
30 minutes	3(0,4)	1(0,2.75)	0(0,2)	0(0,2)	0.069
1 hour	3(2.25,4)	1(0,2)	0.5(0,3)	0(0,2)	0.003**
2 hours	3(0.5,3.75)	1.5(0,2.75)	0.5(0,1.75)	0(0,2.75)	0.042*
3 hours	3(0.5,4)	1.5(0,2)	1.5(0,3)	0(0,1.75)	0.202
6 hours	2(1.25,3)	1(0,2.75)	0(0,3)	0(0,1.75)	0.034*
12 hours	2(1.25,3)	1.5(0,2.0)	0.5(0,2)	0(0,1.0)	0.001**
16 hours	2(0,3)	1(0,2.0)	1(0,2)	0(0,1.75)	0.043*

24 hours	2(0,3)	0(0,1.75)	0(0,2)	0(01.75)	0.035*

Table 3: Rescue analgesia requirement in different groups.

Rescue Analgesia	Group I	Group II	Group III	Group IV	p-value
	NO%	NO%	NO %	NO%	
Received	17 (85%)	14 (70%)	15 (75%)	10(50%)	
Nil	3(15%)	6 (30%)	5(25%)	10(50%)	0.1
Total	20(100)	20(100)	20(100)	20(100)	

Table 4: Number of patients with nausea.

Nausea	Group I	Group II	Group III	Group IV	p-value
	No.%	No.%	No.%	No.%	
Yes	5(25%)	1(5%)	2(10%)	1(5%)	
No	15(75%)	19(95%)	18(90%)	19(95%)	0.255
Total	20(100)	20(100)	20(100)	20(100)	

Table 5: Number of patients with Vomiting

Vomiting	Group I	Group II	Group III	Group IV	p-value
	No.%	No.%	No.%	No.%	
Yes	1(5%)	0(0%)	2(10%)	2(10%)	
No	19(95%)	20(100%)	18(90%)	18(90%)	0.747
Total	20(100)	20(100)	20(100)	20(100)	

DISCUSSION

Interest in finding alternatives to opioid analgesics for the treatment and prevention of postoperative pain has led to an increasing use of non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol, of these paracetamol is perhaps the safest and most cost-effective non-opioid analgesic when administered in appropriate analgesic dosages. Oral NSAIDs have long been used for treating non-surgical pain syndromes because of their well-known anti-inflammatory, antipyretic, and analgesic properties.[1] Therefore, we studied the analgesic efficacy and opioid sparing effect of oral paracetamol and diclofenac sodium and a combination of these drugs, based on VAS score in the first 24hrs of postoperative period in eighty adult patients of ASA I & II, who underwent various elective otolaryngologic surgeries under general anaesthesia.

There are various studies in literature on analgesic efficacy and opioid sparing effects of NSAIDs and paracetamol in the postoperative period of various surgical procedures such as dental, otolaryngologic, obstetric, gynaecological, orthopaedic, laparoscopic cholecystectomy, urology, thyroid and cardiac surgery by different routes of administration, during preoperative or postoperative period.[10,11]

Age distribution: In our study, there was no significant difference in age noted between the four groups (p value 0.1), although the majority of patients were between 21 to 30years.

Sex distribution: The study group included 53 (66.3%) males and 27(33.8%) females giving a ratio of 3:2. The sex distribution being comparable in all four groups, there was no significant difference between gender distributions among the study groups with a p value of 0.9. According to Woodrow et al, analysis of pain with respect to age, sex and race showed that pain tolerance decreases with age, men tolerate more pain than women, Caucasians tolerates more pain than Orientals, while Afro-Caribbeans occupy an intermediate position.[12] Our study did not include observation on variation in pain with respect to age, sex and race. Bellville et al, in their study on influence of age on pain relief from analgesics noted that the older age group reported more pain relief in the postoperative period.[13]

In our study analysis as shown in height and weight were equally distributed among all the groups and was not statistically significant respectively. As Stone et al, noted that obese people were considerably more prone to having daily pain.[14] This might be in relation to chronic pain. Similar to our study, Issioui et al, reported, there were no significant difference in pain perception among the four treatment groups with respect to age, weight and sex.[10]

Comorbid condition & ASA grading: Our study analysis shown in the association of comorbid conditions (Diabetes Mellitus, Hypertension, Asthma, Multiple sclerosis & CVA) and ASA grading with nociceptive pain was statistically significant with a 'p' value, and we found that patients with comorbid conditions of ASA grade II were significantly more in Group 1 and Group II compared to Group III and Group IV. This appears to be due to chance, as our patients were randomly allocated in to the four groups by means of sealed envelopes. There are studies in literature showing clinical evidence of association of comorbid conditions with chronic pain such as musculoskeletal pain and neuropathic pain (e g. diabetes mellitus musculoskeletal disorder, HIV, cancers, mental health disorder).[15,16]

Surgical procedure: Shows various otolaryngologic procedures that patients underwent

in the present study. Although otolaryngologic surgery might not be associated with a frequent incidence of severe postoperative pain, we found that 85% of the patients in the Group I required rescue analgesia as they experienced mild to moderate pain in the early postoperative period. Study by Issioui et al, found that 50% of the patients in the Placebo group experienced moderate-to-severe pain in the early postoperative period.[10]

Duration of surgical procedure: In our study, mean duration of surgery was shorter in Groups II and III as compared to Groups I and IV but was not statistically significant (p=0.275).

The dose and route of administration of drugs: In our study, paracetamol 1000mg was used based on the studies done previously. Seideman et al, studied the pharmacokinetics of paracetamol, and demonstrated the relatively lower bioavailability of suppositories compared to oral tablet. The tablets were absorbed faster and had higher peak plasma concentration than suppositories.[17] Studies have shown that oral paracetamol 650–1000 mg, has a significant analgesic effect after dental and oral surgery, and in women who had undergone episiotomy procedures.[18-20]

The perioperative safety of Diclofenac is controversial because of its effect on platelet aggregation, which might increase blood loss, this has been the matter of concern with NSAIDs associated with increased post-operative bleeding.[21-22]

However, several studies have demonstrated the safety of the perioperative use of NSAIDs both after tonsillectomyand adenoidectomy.[23-25] Likewise, in our study we did not find perioperative bleeding to be increased with the use of diclofenac sodium. None of the patients needed re-operation for hemostasis.

VAS score: VAS score among the four groups at different time periods revealed that maximum reduction of pain was statistically significant in Group IV with least VAS score when compared to other groups. Group I had maximum pain score.

When Group IV was compared with Group II and III, VAS score was least in Group IV, although not statistically significant. Combinations of NSAIDs with paracetamol should be more effective than either of the drugs in isolation, as they possess different sites of analgesic action. We need larger future studies to achieve statistically significant difference between the groups.

Analogous to our findings, study done by Issioui et al, showed that a combination of acetaminophen and celecoxib was significantly more effective than placebo in reducing postoperative pain after otolaryngologic surgery.[10] However Naesh et al., found no overall difference in pain scores between the combination group (paracetamol 1.5 g and rofecoxib 50 mg)and a control group (paracetamol 1.5 g and placebo) for adult tonsillectomy.[26]

Similar to our finding, Montgomery et al, randomised control study showed there was no significant difference in VAS score between the study groups (paracetamol 1500mg, diclofenac sodium100mg and combined drugs) after major gynaecological surgery. In this study, the author did not include placebo control and Viitanen et al, Noted there was no improved analgesia with combined drugs (paracetamol and ibuprofen) when compared to individual drug alone after adenoidectomy in the immediate postoperative period.[27,28]

However, Merry et al, showed that combined drugs (acetaminophen 500 mg and ibuprofen 150 mg) provide superior pain relief after oral surgery to paracetamol or ibuprofen alone.[29] Similar results were demonstrated by Hiller et al, Following orthopaedic surgery combined use of acetaminophen and ketoprofen provided better analgesia than either drug alone in the 24-hour postoperative period.[30]

A qualitative systemic review study done by Cliff et al, showed that the combination of paracetamol and NSAIDs was more effective than paracetamol or NSAIDs alone in 85% and 64% of relevant studies, respectively. This study concluded that a combination of paracetamol and NSAIDs may offer superior analgesia compared with either drug alone.[31]

Our current study analysis showed that pain relief was significantly effective in patients under Group II & III compared to Group I. Similar to our study finding Watcha et al, concluded that patient satisfaction with pain management was improved in all three treatment groups rofecoxib (50 mg) or celecoxib (200mg) paracetamol (2000mg) compared with placebo.[32] However Issioui et al, Showed oral celecoxib 200mg or paracetamol 2000mg alone was not significantly more effective than placebo.[28] Whereas Coby et al, demonstrated average pain over 24hrs was lower after diclofenac compared with paracetamol $p<0.01$ & placebo $p<0.08$ respectively.[33]

Furthermore our study showed no statistical difference in relation to pain reduction between Group II & III. The analgesic efficacy of paracetamol and diclofenac sodium sustained release seemed to be at par with each other. Similar to our findings, Dahl et al, demonstrated that no differences were found between the groups received NSAID (ibuprofen 800 mg) and paracetamol l000 mg with respect to reducing postoperative pain and opioid consumption.[34] In contrast to our finding Cooper et al, study reported that NSAIDs (Ibuprofen 400mg) was a more effective analgesic ($p<0.05$ to $p<0.001$) than acetaminophen 1000mg after dental surgery.[35] Watcha et al, demonstrated that patient satisfaction with pain management was higher with celecoxib and rofecoxib compared with acetaminophen,[36] and studies after dental surgery showed that NSAIDs were superior to paracetamol with respect to pain scores.[37,38]

Rescue Analgesia (RA): In the present study analysis we observed that among those who received RA, the time of first RA administration (in

minutes from extubation) was significantly shorter in Group I(p =0.004) compared to the other groups, and the total dose of rescue analgesia was statistically significant between the study groups with(p=0.013), the total dose being maximum in Group I. Study by Watch et al, noted that the dose of RA used was significantly decreased in the COX-2 inhibitor groups compared with either the placebo or the paracetamol treatment groups.[36]

Our study the proportion of patients requiring of rescue analgesia was minimum in Group IV (50%), when compared to 85%, 70% & 75% respectively, in patients belonging to Groups I, II and III. Opioid sparing effect was highest in Group IV at 50% when compared to 15%, 30% & 25% respectively, in patients belonging to Groups I, II and III. However, no statistically significant difference was found between the study groups (p=0.1), although the clinical analgesia requirement was far less in combination group (Group IV) when compared to other groups. Further, evaluation with larger study groups may be required to show statistically significant difference among the study groups.

Study by Viitanen et al, showed that total opioid requirements were significantly less in the groups receiving acetaminophen (19%, p=0.03), ibuprofen (27%, p=0.001), or their combination (28%, p=0.002) when compared with the group receiving placebo.[28] Study by Coby et al, revealed that opioid sparing effect of paracetamol was 36% and of diclofenac was 40%.[33] Another study by Fayaz et al, found that diclofenac alone or combined with paracetamol had significant opioid-sparing effect after CABG, compared with placebo,[39] whereas Montgomery et al, showed that opioid requirement was significantly low in the group who received the combined drugs (paracetamol + diclofenac sodium) p<0.01 when compared with group received paracetamol alone, and found no significant difference with group given diclofenac alone.[27]

In accordance with our findings, a study by Schmidt et al, concluded that there was no significant difference with respect to opioid consumption between groups received diclofenac 50mg and paracetamol 1000 mg after tonsillectomy.[21] Similar results were reported by Dahl et al, wherein no differences were found between the groups received NSAID (ibuprofen 800 mg) and paracetamol l000 mg with respect to opioid consumption.

Side effects: Analysis of our study with respect to side effects, nausea, vomiting [Table 4 &5] showed that no statistically significant difference among the 4 groups (p=0.255), (p=0.747). Similar to our findings, Montgomery et al, noted that there were no differences in the incidence of nausea, vomiting and sedation between the groups,[27] and Watcha et al, reported no significant differences in the incidence of nausea, vomiting, or the requirement for antiemetic rescue medication among the four groups.[32] However, Fayaz et al, reported significantly lower episodes of nausea and vomiting in the combined drugs (diclofenac and paracetamol) and diclofenac groups than in the placebo group.[38] With respect to sedation as shown in [Figure 1] there was no statistically significant difference among the groups whereas Viitanen et al, reported that children given paracetamol were more sedated than those given ibuprofen (p<0.05).[28]

Therefore, analgesic efficacies of paracetamol and diclofenac sodium (NSAIDs) may depend on the type of surgery, patient characteristics, dosage and route of administration of drugs.[18] The results of various studies support the clinical practice of using diclofenac sodium (NSAIDs) or paracetamol and their combination for acute postoperative pain. A qualitative review done by Hyllested et al, on a comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management concluded that paracetamol is a viable alternative to the NSAIDs especially because of the low incidence of adverse effects, and should be the preferred choice in high risk patients, it may be appropriate to combine paracetamol with NSAIDs.[39]

We conclude that oral premedication with paracetamol, diclofenac sodium sustained release and combination of paracetamol and diclofenac sodium sustained release provide effective analgesia in the postoperative period after otolaryngologic surgery. A combination of paracetamol and diclofenac sodium sustained release offers higher opioid sparing effect than either drug by itself. Therefore, current evidence suggests that combined drugs may offer superior analgesia in the postoperative period after otolaryngologic surgery compared to individual drugs. The analgesic efficacy of paracetamol was at par with diclofenac sodium sustained release in providing postoperative analgesia. Hence, paracetamol can be used as an alternative drug in place of diclofenac sodium, when its use is contraindicated for acute postoperative pain.

Drawbacks of the Study

The sample size is small, study of a larger population would give more conclusive results and help in achieving statistical significance in specific areas of the study.

The study sample has included a wide range of surgical procedure. A more focused study sample would yield more specific results.

CONCLUSION

There was significant pre-emptive analgesic efficacy of paracetamol, diclofenac sodium sustained release and their combination compared to placebo after otolaryngologic surgery. The analgesic efficacy of paracetamol and diclofenac sodium sustained-release was at par with each other. Hence, paracetamol can be used as an alternative drug in place of diclofenac sodium, when its use is contraindicated for acute postoperative pain.

REFERENCES

1. White Paul F. The Changing Role of Non-Opioid Analgesic Techniques in the Management of Postoperative Pain. AnesthAnalg 2005; 101:S5–S22.
2. Kehlet H, Dahl JB. Anaesthesia, surgery and challenges in postoperativerecovery. Lancet 2003; 362:1921–8.
3. White PF. Ambulatory anesthesia advances into the new millennium. AnesthAnalg 2000; 90:1234–5.
4. Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery.AnesthAnalg 1997; 85:808–16.
5. White PF. The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery. AnesthAnalg 2002; 94:577–85.
6. Guignard B, Bossard AE, Coste C, et al. Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requirement. Anesthesiology 2000; 93:409–17.
7. Silvasti M, Svartling N, Pitkanen M, Rosenberg PH. Comparison of intravenous patient-controlled analgesia with tramadol versus morphine after microvascular breast reconstruction. Eur J Anaesthesiol 2000; 17:448–55.
8. Rawal N, Allvin R, Amilon A, et al. Postoperative analgesia at home after ambulatory hand surgery: a controlled comparison of tramadol, metamizol, and paracetamol. AnesthAnalg 2001; 92:347–51.
9. Immer FF, Immer-Bansi AS, Tachesel N, et al. Pain treatment with a COX-2 inhibitor after coronary artery bypass operation: a randomized trial. Ann ThoracSurg 2003; 75:490–5.
10. Issioui T, Klein KW, White PF, et al. Efficacy of premedication with celecoxib and acetaminophen in preventing pain after otolaryngologic surgery. AnesthAnalg 2002; 94:1188–93.
11. Korpela R, Korvenoja P, Meretoja OA. Morphine-sparing effect ofacetaminophen in pediatric day-case surgery. Anesthesiology 1999; 91:442-7.
12. Woodrow KM, Friedman GD, Siegelaub AB, et al. Pain Tolerance: Differences According to Age, Sex and Race.PsychosomaticMedicine,1972;34(6):548-556.
13. Bellville WJ, Forrest WH, Miller E, et al. Influence of Age on Pain Relief from Analgesics: A Study of Postoperative Patients. JAMA. 1971; 217(13):1835-1841.
14. Stone AA, Broderick JE. Department of Psychiatry and Behavioral Science, Stony Brook University, Stony Brook, New York, USA Obesity and Pain Are Associated in the United States Epidemiology Obesity (2012); 207: 1491–1495. doi:10.1038/oby.2011.397.
15. Davis JA, Robinson RL, Kim Le T, et al. Incidence and impact of pain conditions and comorbid illnesses. Journal ofPainResearchPublished2011October; 4:331-345.
16. Unpacking the burden: Understanding the relationships between chronic pain and comorbidity in the general population Journal of the International Association for the study of pain. 2010 Feb; 153 (2):293-304.
17. Seideman P, Alván G, Andrews RS.A. Labross relative bioavailability of a paracetamol suppository. Eur J Clin Pharmacol 1980; 17 (6):465-468.
18. Forbes JA, Kehm CJ, Grodin CD, Beaver WT. Evaluation of ketorolac, ibuprofen, acetaminophen, and an acetaminophen/codeine combination in postoperative oral surgery pain. Pharmacotherapy 1990;10(6 (Pt 2)):94S-105S.
19. McQuay HJ, Carroll D, Guest P, et al. A multiple dose comparison of combinations of ibuprofen and codeine and paracetamol, codeine and caffeine after third molar surgery. Anaesthesia 1992; 47:672–7.
20. Mehlisch DR, Sollecito WA, Helfrick JF, et al. Multicenter clinical trial of ibuprofen and acetaminophen in the treatment of postoperative dental pain. J Am Dental Assoc 1990 Aug;121(2):257-63.
21. Schmidt A, Björkman S, Akeson J. Preoperative rectal diclofenac versus paracetamol for tonsillectomy: effects on pain and blood loss. Acta Anaesthesiology Scand. 2001 Jan; 45(1):48-52.
22. Rusy LM, Houck CS, Sullivan LJ, et al. A double-blind evaluation of ketorolac tromethamine versus acetaminophen in paediatric tonsillectomy: analgesia and bleeding. AnesthAnalg. 1995 Feb; 80(2):226-9.
23. Tarkkila P, Saarnivaara L. Ketoprofen, diclofenac or ketorolac for pain after tonsillectomy in adults. Br J Anaesth 1999; 82:56-60.
24. Kokki H, Tuomilehto H, Tuovinen K. Pain management after adenoidectomy with ketoprofen: comparison of rectal and intravenous routes. Br J Anaesth 2000; 85:836-40.
25. Nikanne E, Kokki H, Tuovinen K. Postoperative pain after adenoidectomy in children. Br J Anaesth 1999; 82: 886-9
26. NaeshO,NilesLA,Gilbert JG, et al. A randomized, placebo-controlled study of rofecoxib with paracetamol in early Montgomery JE, Sutherland CJ, Kestin IG, Sneyd JR.Morphineconsumption in patientsreceivingrectalparacetamolanddiclofenacaloneandincombination. Br J Anaesth 1996; 77:445–7.
27. Montgomery JE, Sutherland CJ, Kestin IG, Sneyd JR. Morphine consumption in patients receiving rectal paracetamol and diclofenac alone and incombination. Br J Anaesth 1996; 77:445–7.
28. Viitanen H, Tuominen N, Vaaraniemi H, et al. Analgesic efficacy of rectal acetaminophen and ibuprofen alone or in combination for day-case adenoidectomy. Br J Anaesth 2003; 91:363–7.
29. Merry AF, Gibbs RD, Edwards J, et al. combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: A randomized controlled trial. Br J Anaesth 2010; 104:80-88.
30. Hiller A, Meretoja OA, Korpela R, et al. The Analgesic Efficacy of Acetaminophen, Ketoprofen, orTheir Combination for Pediatric Surgical Patients Having Soft Tissue or Orthopedic Procedure. AnesthAnalg 2006; 102:1365-71.
31. Ong CKS, Seymour RA, Lirk P, et al. Combining Paracetamol (Acetaminophen) with Non-steroidal Anti-inflammatory Drugs: A Qualitative Systematic Review of Analgesic Efficacy for Acute Post operative Pain Anesthesia& Analgesia. 2010 April; 110 (4):1170-1179.
32. Watcha MF, Issioui T, Klein KW, White PF. Costs and Effectiveness of Rofecoxib, Celecoxib, and Acetaminophen for Preventing Pain After Ambulatory Otolaryngologic Surgery. AnesthAnalg 2003; 96:987–94.
33. Cobby TF, Crighton IM, Kyriakides K, Hobbs GJ. Rectal paracetamol has a significant morphine-sparing effect after hysterectomy. Br J Anaesth1999; 83:253–62.
34. Dahl V, Ernø PE, Ræder JC. No analgesic effect of ibuprofen or paracetamol vs placebo for hysterectomies. Eur J Pain 1997; 1: 31–5.
35. Cooper SA, Schachtel BP, Goldman E, et al. Ibuprofen and acetaminophen in the reliefofacutepain:arandomized,double-blind,placebo-controlledstudy.J Clin Pharmacology. 1989 Nov; 29(11):1026-30.
36. Dionne RA. Suppression of dental pain by the preoperative administration of flurbiprofen. Am J Med 1986; 80:41–9.
37. Kiersch TA, Halladay SC, HormelPC. A single - dose, double-blind comparison of naproxen sodium, acetaminophen, and placebo in postoperative dental pain. Clin Ther 1994; 16:394-404.
38. Fayaz MK, Abel RJ, Pugh SC, et al. Opioid-sparing effects of diclofenac and paracetamol lead to improved outcomes after cardiac surgery. J CardiothoracVascAnesth. 2004 Dec; 18(6):742-7.
39. Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: a qualitative review. Br J Anaesth 2002; 88(2) :199-214.