Lababneh MF, Alshiyyab OM, Ibrahim EN, Alshoufi TA, Adaileh MA. (September 2015). The analgesic synergism between paracetamol and tramadol during partial reconstructive osiculoplasty. *Jour of Med Sc & Tech*; 4(3); Page No:

Journal of Medical Science & Technology

Original Article Open Access

The analgesic synergism between Paracetamol and tramadol during partial reconstructive osiculoplasty

Muhannad Fudeil Lababneh*, Osama Mahmoud Alshiyyab, Ethar Najeeb Ibrahim, Tariq Aref Alshoufi, Mohammad Abdelatif Adaileh

Department of anesthesia and intensive care,KHMC, Amman,Jordan.

Abstract

Objective of the study was to evaluate the postoperative pain relief effect between intraoperative intravenous administration of a mixture of paracetamol – tramadol and tramadol only in patients undergoing elective partial reconstructive osiculoplasty. This prospective, randomized and double blind study included 101 patients, of both sexes, aged 32-41 years, classed I-II by the American society of anesthesiologists and scheduled for elective partial reconstructive osiculoplasty under balanced general laryngeal mask airway anesthesia at Prince Ali hospital, Karak, Jordan during the period April 2011-Feb2015. Participants were divided into two groups. Group I patients (n=49) received intraoperative intravenous mixture of paracetamol (10mg/kg) and tramadol (1mg/kg). Group II patients (n=52) received intraoperative intravenous tramadol (1mg/kg) only. Postoperative visual analog score was used to compare the pain relief effect between the two regimens. 22 patients in group I were administered rescue analgesics and 12 patients in group II were administered rescue analgesics ($P<0.05$). The highest pain score was registered at 25 minutes in group II and at 45 minutes in group I. The combination of paracetamol with tramadol increased the pain relief effect more than tramadol only in patients assigned for partial reconstructive osiculoplasty.

Keywords: Intraoperative: paracetamol, tramadol; postoperative: analgesia

*Corresponding Author: Dr Muhannad Fudeil Lababneh, Department of anesthesia, Intensive care and pain management, KHMC, Amman, Jordan. Email: dr.muhannad80@yahoo.com

Received: May 10, 2015 Accepted: June 10, 2015. Published: September 20, 2015.

Introduction

Partial reconstructive osiculoplasty is a surgical technique correlated with pain of intermediate severity. Opiates administered for producing pain relief have multiple adverse effects such as postoperative nausea and vomiting and constipation with negative influence on this type of surgery, although postoperative nausea and vomiting is recorded after tramadol but with less incidence and intensity [1]. Opiates aren't considered an option for this kind of surgical intervention. Postoperative pain is the most frequent cause for demanding medical attention. Analgesia is an ethical obligation of physicians and an essential right for patients. The pathophysiology of pain is complex. The perfect pain relief agent should have less adverse effects and improved pain relief efficiency. Pain relief regimen with two or more drugs can be additive or with synergistic advantages for the management of various mechanisms of pain. Improper pain relief has social, legal, cultural, religious aspects, fundamental knowledge, differences in health care systems and discrepancy in clinical practice [2]. Not treating pain is not a choice and was named as moral outrage. Improper managed pain is correlated with functional impairment, decreased mobility, falls, slower rehabilitation, reduced socialization, improper sleep, poor appetite and modification in mood. It may change quality of life, family and puts a heavy weight on the health care system.

Paracetamol is a safe and efficient pain relief drug used perioperatively for mild to moderate pain. Propacetamol is the water–soluble prodrug of paracetamol which is used if increased efficiency or

more fast onset of action is required. In plasma, this drug is broken to paracetamol and diethylglycin by plasma esterases. Paracetamol passes the blood brain barrier, exerting its central analgesic effect. Paracetamol is degraded from phenacetin, administered for mild to intermediate pain as with tramadol. It is a cyclo-oxygenase inhibitor, inhibiting the production of prostaglandin mainly in the central nervous system than in the periphery. It is used mainly for acute pain control [3, 4].

Tramadol, a synthetic opioid of aminocyclohexanol group. This drug is also efficient on noradrenergic and serotonergic neurotransmission. Tramadol i.v. has a potency which is equal to pethidine and 1/10 of morphine. In patients of more than 1 year it is tolerated well and has no obvious side effect on hemodynamic and respiratory profiles. Tramadol (centrally acting weak opioid analgesic) is a cyclohexanol with weak mu opioid-like receptor agonist activity. Tramadol blocks the reuptake of noradrenaline and enhances the production of serotonin. The monoaminergic is synergistic with opioid, attaining pain relief influence. Tramadol has benefits over other narcotics and nonsteroidal anti-inflammatory drugs [3].

Analgesics may be combined to produce more pain relief than can be attained by increasing doses of singular components. This type of mixtures can enhance toleration .Combinations are most potent when component drugs effect synergistically [5]. Assume paracetamol is combined with tramadol with better pain relief as with tramadol only due to synergism, without added adverse effects. The aim of our investigation was to evaluate the postoperative pain relief effect between intraoperative intravenous administration of a mixture of paracetamol –tramadol and tramadol only in patients undergoing elective partial reconstructive osiculoplasty.

Methods

This prospective, randomized and double blind study included 101 patients, of both sexes, aged 32-41 years, classed I-II by the American society of anesthesiologists and scheduled for elective partial reconstructive osiculoplasty under balanced general laryngeal mask airway anesthesia, after obtaining written informed consent from all patients and approval from the royal Jordanian medical military ethics and research board review committee at Prince Ali hospital, Karak, Jordan during the period April 2011-Feb2015. Patients with preoperative administration of analgesics were ruled out from the investigation.

General anesthesia was induced using Propofol 2 mg/kg, fentanyl 3 mcg/kg and cisatracurium 0.15 mg/kg. Maintenanace of anesthesia was achieved using sevoflurane 2MAC with oxygen l/min and incremental doses of cisatracurium 0.03mg/kg added to fentanyl 1mcg/kg in the middle of surgery. Participants were divided in a random manner into two groups. Group I patients (n=49) received intraoperative intravenous mixture of paracetamol (10mg/kg) and tramadol (1mg/kg). Group II patients (n=52) received intraoperative intravenous tramadol (1mg/kg) only. In both groups, the study analgesics were administered at wound closure. Postoperative visual analog score (0-10)(6) was used to compare the pain relief effect between the two regimens in the postanesthesia care unit(at 0,25 and 45 minutes intervals) and the surgical ward(at 120 minutes interval). Morphine 3mg mg was administered intravenously as rescue pain relief if the patient experienced pain scores of more than 4 on the VAS during the study period.

Statistics: ANOVA was used to assess the VAS pain scores. Chi-square test was used to compare the rescue analgesics between the two groups. $P<0.05$ was considered statistically significant.

Results

Parameter	**Group I (n=49)**	**Group II (n=52)**
Age(yr) range(median)	32-40 (35.4)	33-42 (37.5)
Sex M F	 34 15	 37 15
ASA I II	 43 6	 40 12
Duration of surgery (min) mean ± SD	116 ± 9	121 ± 8

Table I: Patients demographics.

There were no significant differences between the two groups regarding the patient's demographics (Table I). 22 patients in group II were administered rescue analgesics and 12 patients in group I were administered rescue analgesics (P<0.05). At 0 min. immediately after admission in the recovery room, 2patients in group II required analgesia and no one in group I needed analgesia. These requirements increased to 3 and 10 patients in groups I and II, respectively. At 45 min. these needs were 7 and 8 patients in same groups and at 2hours postoperatively, this pattern decreased in both groups to 2 patients in each group. These patients experienced pain scores of 4 or more .The highest pain score was registered at 25 minutes in group II and at 45 minutes in group I. Table II. In group I, mean pain score was 2.21 and in group II, it was 3.05 at 25 minutes postoperatively. This pattern continued at 45 minutes and 120 minutes postoperatively (P<0.05). At 120 minutes postoperatively, mean pain score was 0.21 in group I and 0.73 in group II. No patient experienced in all patients in both groups.

	Group I	**Group II**	**P**
Pain score (mean ± SD) at			
0 min	1.25(2-3)	3.69(3-4)	<0.05
25 min	2.21(2-4)	4.67(4-6)	<0.05
45 min	3.23(3-4)	4.05(4-5)	<0.05
120 min	1.21(2-4)	3.73(3-4)	<0.05
Number of patients who needed rescue analgesics at			
0 min	0	2	<0.05
25 min	3	10	<0.05
45 min	7	8	<0.05
120 min	2	2	>0.05

Table II: Postoperative pain profile.

Discussion

The emotional stress caused by surgery is increased by the intensity of pain after surgery. Pain control after surgery is one of the most important demands which not only gives relief for the patient, but enhances early mobilization. Pain after surgery is a traditional indication for systemic analgesics administration. Opioids are the initial treatment for patients with moderate to severe pain but these are not always easily tolerated and are correlated with dose dependent adverse effects. Partial reconstructive osiculoplasty causes less intense discomfort, but pain correlated with this type of surgery is considered. Prevention and management of pain depends on local anesthesia with the administration of opiates and nonsteroidal anti-inflammatory combination drugs. Local infiltration [7] may be administered for attaining pain relief for this operation.

Different nonsteroidal anti-inflammatory drugs are administered but they are correlated with adverse effects [8]. Opiates are efficient in managing pain after such surgical technique but also with adverse effects. Different treatment approaches are used to decrease pain after such surgery including tramadol and paracetamol [1]. Investigations had shown that pain relief effect and tolerability of intramuscular or intravenous tramadol. Moore RA recorded the safety and dose dependent effect of tramadol in moderate to severe postoperative pain [9]. Tramadol was also administered in obstetric, renal or biliary colic pain and posttraumatic. The pain relief effect of tramadol was superior to fentanyl [10]. It was documented that tramadol 100 mg given during surgery was similar to the administration of fentanyl 100mcg and co-codamol. Tramadol was administered in doses from 1 to 3 mg/kg according to the predicted intensity of postoperative pain [11]. Postoperatively, patients from tramadol group experienced moderate to severe pain while patients from tramadol-paracetamol group experienced mild to moderate pain.

Tramadol is the phenylpiperidine analog of codeine. It is 20%bound to plasma proteins.10%is metabolized to O-desmethyltramadol with more affinity for mu opioid receptor .This effect is weak but is of full agonist. It depresses the neuronal reuptake of norepinephrine, stimulates the release of serotonin resulting in downwards depression of nociception. Paracetamol is the less toxic metabolite of phenacetin. It is not bound significantly to plasma proteins. The effective concentration is 10-20mg/l. There are synergism and addition analgesic properties when combined with opiates.

Combining analgesics with various mechanisms of action and pharmacokinetic picture, efficiency may be improved [12]. Multimodal pain relief protocol improved pain relief efficiency more than unimodal pain relief protocol, decreasing pain after surgery and pain relief needs with early back to daily activity [13]. Tramadol and paractamol showed synergism [6]. Different methods are there to

measure postoperative pain, some are subjective and others are objective. Visual analog pain scale measures pain in a unidimensional way. It measures only the severity of pain but not its quality.

Conclusion

The combination of paracetamol with tramadol increased the pain relief effect more than tramadol only in patients assigned for partial reconstructive osiculoplasty.

References

1. Mohammad A, Fauzia AK. Comparison of analgesic effect of tramadol alone and a combination of tramadol and paracetamol in day care laparoscopic surgery. European J Anesthesiology 2009; 26:475-9.
2. Joseph VPJ, Mart VDL, Richard L, et al. Tramadol/paracetamol fixed dose combination in the treatment of moderate to severe pain. J Pain Res 2012; 5:327-46.
3. Scott LJ, Perry CM. Tramadol: a review of its use in perioperative pain. Drugs 2000; 60:139-76.
4. Bannwarth B, Pehourcq F. Pharmacological rationale for the clinical use of paracetamol: pharmacokinetic and pharmacodynamic issues. Drugs 2003; 63(2):5-13.
5. Tallarida RJ, Raffa RB. Testing for synergism over a range of fixed ratio drug combinations: replacing the isobologram. Life Sci 1996; 58: L23-L28.
6. Katz J, Melzack R. Measurement of pain.Surg Clin North Am 1999; 79:231-51.
7. Palter SF. Office microlaparoscopy under local anesthesia. Obstet Gynecol Clin North Am 1999; 26:109-20.
8. Gotzche PC. Extracts from clinical evidence. Nonsteroidal anti-inflammatory drugs.BMJ 2000; 320:1058-61.
9. Moore RA, Mc Quay HJ. Single patient data meta analysis of 3453 postoperative patients: oral tramadol versus placebo, codeine and combination analgesics. Pain 1997; 69:287-94.
10. Bamigbade TA, Langford RM, Blower AL. Pain control in day surgery: tramadol compared to standard analgesia.BJA 1998; 80:558-9.
11. Van DBAA, Montoya PLF, Halliday EM, et al. Analgesia for adenotonsillectomy in children and young adults: a comparison of tramadol, pethidine and nalbuphine. Eur J Anesthesiol 1999; 16:186-94.
12. Raffa RB. Pharmacology of oral combination analgesics: rational therapy for pain.J Clin Pharm Ther 2001; 26:257-64.
13. Jung YS, Kim DK, Kim MK, et al. Onset of analgesia and analgesic efficacy of tramadol/ acetaminophen and codeine/ acetaminophen/ ibuprofen in acute postoperative pain: a single center, single dose, randomized active controlled parallel group study in a dental surgery pain model. Clin Ther 2004; 26:1037-45.

