



## A COMPARATIVE STUDY OF THE EFFECT OF INTRAVENOUS ADMINISTRATION OF KETOROLAC AND ACETAMINOPHEN ON PAIN RELIEF AFTER UVULOPALATOPHARYNGOPLASTY SURGERY

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### ABSTRACT

**Introduction:** Obstructive sleep apnea (OSA) is a prevalent disorder, and uvulopalatopharyngoplasty (UPPP) is a common surgical intervention. Effective postoperative pain management is crucial for these patients, but minimizing sedation is essential to avoid exacerbating OSA. **Material and Methods:** This study compared the



efficacy and side effects of intravenous ketorolac and acetaminophen for pain management after UPPP in 60 patients. Patients were randomly assigned to receive either ketorolac (0.5 mg/kg) or acetaminophen (15 mg/kg) 30 minutes before the end of surgery and at regular intervals postoperatively. Pain scores (VAS), hemodynamic parameters, water swallowing test (SWT) scores, and side effects were assessed at various time points. **Results:** Results showed no significant difference in demographic variables or hemodynamic parameters between the groups. Ketorolac provided significantly better pain control at 12, 24, and 48 hours postoperatively. The incidence of side effects, including nausea, vomiting, and skin rash, was similar between the groups. Dizziness was significantly higher in the acetaminophen group at 24 hours postoperatively. **Conclusion:** This study suggests that intravenous ketorolac provides superior pain relief compared to acetaminophen after UPPP, without increasing the risk of significant side effects. This finding can guide clinicians in optimizing postoperative pain management for OSA patients undergoing UPPP surgery.

**KEYWORDS:** Obstructive Sleep Apnea, Uvulopalatopharyngoplasty, Pain Management, Ketorolac, Acetaminophen, Postoperative Complications.

#### **HIGHLIGHTS**

- Ketorolac provided superior pain relief compared to acetaminophen after UPPP surgery in OSA patients.
- No significant difference in side effects was observed between the ketorolac and acetaminophen groups, except for dizziness.



- Intravenous ketorolac is a safe and effective analgesic option for managing postoperative pain after UPPP in OSA patients.
- Minimizing opioid use with effective non-opioid analgesics is crucial in OSA patients to avoid respiratory complications.

## UN ESTUDIO COMPARATIVO DEL EFECTO DE LA ADMINISTRACIÓN INTRAVENOSA DE KETOROLACO Y PARACETAMOL SOBRE EL ALIVIO DEL DOLOR DESPUÉS DE LA CIRUGÍA DE UVULOPALATOFARINGOPLASTIA

### RESUMEN

**Introducción:** La apnea obstructiva del sueño (AOS) es un trastorno prevalente y la uvulopalatofaringoplastia (UPPP) es una intervención quirúrgica común. El manejo eficaz del dolor postoperatorio es crucial para estos pacientes, pero minimizar la sedación es esencial para evitar exacerbar la AOS. **Material y métodos:** Este estudio comparó la eficacia y los efectos secundarios del ketorolaco y el paracetamol intravenosos para el tratamiento del dolor después de UPPP en 60 pacientes. Los pacientes fueron asignados aleatoriamente para recibir ketorolaco (0,5 mg/kg) o acetaminofén (15 mg/kg) 30 minutos antes del final de la cirugía y a intervalos regulares después de la operación. Las puntuaciones de dolor (EVA), los parámetros hemodinámicos, las puntuaciones de la prueba de deglución de agua (SWT) y los efectos secundarios se evaluaron en varios momentos. **Resultados:** Los resultados no mostraron diferencias significativas en las variables demográficas o parámetros hemodinámicos entre los grupos. El ketorolaco



proporcionó un control del dolor significativamente mejor a las 12, 24 y 48 horas después de la operación. La incidencia de efectos secundarios, como náuseas, vómitos y erupción cutánea, fue similar entre los grupos. Los mareos fueron significativamente mayores en el grupo de acetaminofén a las 24 horas del postoperatorio. **Conclusión:** Este estudio sugiere que el ketorolaco intravenoso proporciona un alivio del dolor superior en comparación con el paracetamol después de la UPPP, sin aumentar el riesgo de efectos secundarios significativos. Este hallazgo puede guiar a los médicos a optimizar el manejo del dolor posoperatorio en pacientes con AOS sometidos a cirugía UPPP.

**PALABRAS CLAVE:** Apnea obstructiva del sueño, uvulopalatofaringoplastia, manejo del dolor, ketorolaco, acetaminofén, complicaciones posoperatorias.

## INTRODUCTION

Obstructive sleep apnea is one of the most common breathing-related sleep disorders caused by complete or partial obstruction of the upper airway [1].

The prevalence of this disorder is about 2-4% with highest incidence among adult men. Assessment of respiratory, sleep and cardiac parameters for detection of

obstructive events can be used for diagnosis of obstructive sleep apnea [2].

Gender, age, snoring, menopause, and obesity are the main risk factors for obstructive sleep apnea. Positional therapy, oral appliances, and surgical treatment are three main treatments for this disorder [3].



Uvulopalatopharyngoplasty (UPPP) is one of the surgical methods for patients who have not responded to medical treatments. This treatment resect the uvula that lead to improvement of snoring and sleep parameters [4]. Controlling pain and bleeding after this surgery is very important due to improvement of swallowing, easier movement, faster recovery, and improvement of the quality of life. On the other hand, considering that these patients are at high risk of obstructive apnea, the drug used should have the lowest amount of sedation so that the chance of apnea after surgery does not increase in these patients [5-8]. A lot of research has been done in this field, but so far no specific medicine has been introduced that has the least amount of complications. In this study, we aim to compare the effects of intravenous administration of ketorolac and acetaminophen (Apotel) on the improvement of pain in these patients.

## Materials and Methods

This study was done on patients with obstructive sleep apnea (age between 18 to 55 years) referred to Shahid Sadoughi Hospital, Yazd, Iran. These patients underwent Uvulopalatopharyngoplasty (UPPP) surgery. Demographic data (age and weight) was recorded. Inclusion criteria include patients with I & II, ASA, BMI<35. Patients with any heart disease, uncontrolled blood pressure, uncontrolled diabetes, digestive problems including GERD, use of anticoagulant drugs, drug abuse, use of corticosteroids, kidney disease and the duration of the surgery is more than two hours were excluded from the study. Based on the calculation of the sample size, 60 patients were divided into two groups based on the table of random numbers: first group: treatment with 0.5 mg/kg (maximum dose 30 mg) of intravenous ketorolac 30 min before the end of surgery and every 8-24 hours after surgery, and second group: treatment with acetaminophen (Apotel) 15 mg/kg (maximum dose of 1 gram) 30 min before the end of surgery and every 6- 24 hours after surgery. The drugs of

both groups are prepared by the resident and given to the anesthesiologist. The pain level of patients (assessment with visual analog scale (VAS)), bleeding, and side effects such as nausea and vomiting, dizziness and skin rash was examined and recorded in half, 6, 12, 24, and 48 hours

after surgery. In case of VAS > 5, 2 to 4 mg of morphine was prescribed for patients. Water swallowing test (SWT) was also evaluated based on scores summarized in table 1.

**Table 1.** Water swallow test

Water swallow test		
Score	performance	Deficit
1	Can swallow the water smoothly, once in 5s	Normative
2	Can swallow without cough, twice	Minimal
3	Can swallow once, but with cough	Mild
4	Swallow more than twice, with cough	Severe
5	Cough frequently, cannot swallow	Profound

The need for narcotics in two groups was recorded and compared. All patients received 0.1 mg/kg midazolam and 0.2 µg/kg fentanyl as premedication. Induction of general anesthesia was done

with 2 mg/kg propofol and 0.5 mg/kg atracurium. Each patient receives 0.1 mg/kg morphine during surgery and 0.6 mg/kg/hr propofol, N<sub>2</sub>O, and O<sub>2</sub> for anesthesia maintenance. In the last half

hour of surgery, 30 mg of ketorolac or 1 gr of acetaminophen was intravenously infused. Finally, it was reversed and extubated with neostigmine and atropine. Routine monitoring in these patients including noninvasive blood pressure, end-tidal CO<sub>2</sub>, ECG heart monitoring,

pulse oximetry, was done in the operating room and recovery (except ET CO<sub>2</sub>).

**Results**

Demographic data was summarized in Table 2.

**Table 2.** Demographic data of patients in two groups

Variable		N	Mean	SD	P value
Age	Apotel	32	37.75	6.46	0.562
	Ketorolac	30	39.00	10.27	
Gender	Male	Apotel	20		0.31
		Ketorolac	16		
	Female	Apotel	12		
		Ketorolac	16		
BMI	Apotel	32	30.66	2.18	0.082
	Ketorolac	30	31.66	2.38	

This table showed that there is no significant difference between two groups in term of demographic variables. Based on this table, there was no significant difference between two groups in term of

age and BMI (P value > 0.05). Determination and comparison of the Mean arterial pressure (MAP), heart rate (HR), VAS, water swallowing test (SWT)

between two groups was summarized in Table 3&4.

**Table 3.** Determination and comparison of the Mean arterial pressure, heart rate between two groups

		N	Mean	SD	P value
MAP before induction (mmHg)	Apotel	32	96.66	7.76	0.20
	Ketorolac	30	91.04	8.27	
MAP after induction (mmHg)	Apotel	32	92.66	15.44	0.07
	Ketorolac	30	90.95	12.03	
MAP before surgery (mmHg)	Apotel	32	93.91	7.78	0.93
	Ketorolac	30	98.58	8.12	
MAP after extubation (mmHg)	Apotel	32	95.00	8.37	0.108
	Ketorolac	30	99.37	4.89	
MAP 0 min after recovery (mmHg)	Apotel	32	93.68	8.85	0.15
	Ketorolac	30	98.21	8.39	
MAP 15min after recovery (mmHg)	Apotel	32	91.20	8.65	0.46
	Ketorolac	30	96.28	8.90	
MAP 60min after recovery (mmHg)	Apotel	32	90.16	7.98	0.27
	Ketorolac	30	92.87	6.24	
HR/min (before induction)	Apotel	32	86.75	11.39	0.00
	Ketorolac	30	85.53	4.94	
HR/min (after induction)	Apotel	32	77.87	11.90	0.11
	Ketorolac	30	79.25	9.48	
HR/min (before surgery)	Apotel	32	90.37	10.04	0.79
	Ketorolac	30	93.62	12.07	
HR/min (after extubation)	Apotel	32	88.00	7.46	0.49
	Ketorolac	30	95.37	7.30	
HR/min (0 min after recovery)	Apotel	32	90.43	11.58	0.00
	Ketorolac	30	90.50	5.38	
HR/min (15 min after	Apotel	32	86.25	8.25	0.09

recovery)	Ketorolac	30	88.87	6.49	
HR/min (60 min after recovery)	Apotel	32	83.25	5.98	0.68
	Ketorolac	30	83.12	5.71	

**Table 4.** Determination and comparison of the Mean VAS and WST between two groups

		N	Mean	SD	P value
VAS (30 min after surgery)	Apotel	32	8.00	1.01	0.311
	Ketorolac	30	6.87	1.07	
VAS (6 hours after surgery)	Apotel	32	6.75	1.10	0.837
	Ketorolac	30	5.12	1.07	
VAS (12 hours after surgery)	Apotel	32	5.12	1.07	0.013
	Ketorolac	30	3.75	.67	
VAS (24 hours after surgery)	Apotel	32	3.87	.79	0.043
	Ketorolac	30	3.12	.60	
VAS (48 hours after surgery)	Apotel	32	3.62	.70	0.001
	Ketorolac	30	2.28	.45	
WST (6 hours after surgery)	Apotel	32	4.62	.49	0.010
	Ketorolac	30	3.62	.70	
WST (12 hours after surgery)	Apotel	32	3.87	.33	0.729
	Ketorolac	30	3.00	.50	
WST (24 hours after surgery)	Apotel	32	3.12	.60	0.685
	Ketorolac	30	2.37	.49	
WST (48 hours after surgery)	Apotel	32	2.62	.49	0.000
	Ketorolac	30	2.00	.00	

Results showed that Mean arterial pressure had no significant difference between groups in all examined times. Heart rate had significant difference

between two groups in 0 min after recovery. VAS had significant difference between two groups in 12, 24, and 48 min after recovery. Comparison of the average

number of side effects (nausea and vomiting, dizziness and skin rash) indicated that there is no significant difference between two groups in term of mentioned side effects in all examined

times. Only dizziness had significant difference between two groups in 24h after surgery (Table 5).

**Table 5.** Determination and comparison of the nausea and vomiting, dizziness, and rash between two groups

Nausea and Vomiting	6hr		Total	P value
	no	yes		
apotel	4	28	32	0.120
ketorolac	9	21	30	
Total	13	49	62	
	12hr		Total	P value
	no	yes		
apotel	19	13	32	0.183
ketorolac	22	8	30	
Total	41	21	62	
	24 hr		Total	P value
	no	yes		
apotel	24	8	32	>1.000
ketorolac	22	8	30	
Total	46	16	62	
Dizziness	24hr		Total	P value
	no	yes		
apotel	8	24	32	0.002
ketorolac	19	11	30	
Total	27	35	62	
Rash	24hr		Total	P value
	no	yes		
apotel	27	4	32	>1.000



ketorolac	27	4	30	
Total	54	8	62	

### Discussion

Today, pain treatment is based on combined treatment and the use of different drugs due to the multi-mechanism of pain [9, 10]. The approach of reducing pain in various surgeries is one of the main challenges in treatment [11, 12]. Pain reduction should occur with minimal side effects. In this field, the pain relief after UPPP is considered as potent challenge [13]. In this study, we comprised the effect of ketorolac and acetaminophen on pain relief after UPPP surgery. Our data showed that Ketorolac had more effect on pain relief than acetaminophen. VAS scale indicated that Ketorolac significantly reduced the pain more than acetaminophen in 12, 24, and 48 hours after surgery. Literature review has been showed that ketorolac has potent pain relief activity in various surgery [14-17]. Patrocínio *et al.* indicated that ketorolac is more effective than

ketoprofen for pain reduction after UPPP [18]. We showed similar results for this surgery for ketorolac in comparison with acetaminophen. In Rusy *et al.* study, it's found that ketorolac had more effect in the treatment of pain after tonsillectomy in children in comparison with acetaminophen. Watcha *et al.* showed that the use of ketorolac as preoperative agent can provide better postoperative pain control than acetaminophen [19]. Javaherforooshzade *et al.* found that ketorolac has more effect than Paracetamol on pain relief in patients undergoing coronary artery bypass graft surgery without adverse effects [20]. Amini *et al.* showed similar data in congenital cardiac patients [21]. This data was similar to our study. Similar to our data, Forrest *et al.* indicated that the advantages of ketorolac was more than other analgesics for post-operative pain [22]. Some agents such as Paracetamol can change blood pressure.[23] On the



other hand, the hemodynamic safety of diclofenac and related compounds has been reported in various studies [24, 25].

Our data showed similar results in terms of effect on blood pressure. However, a similar result was obtained in the acetaminophen group. Previous articles reported that ketorolac has lower rates of side effects (such as sedation, nausea, vomiting, and respiratory depression) compared to commonly used opioids [26, 27].

Shende *et al.* showed that the use of ketorolac for postoperative pain relief led to a lower rate of vomiting and pain in children compared to the placebo group [28]. Carney *et al.* reported reduction of opioids use and morbidity after use of ketorolac during the first 48 hours after pediatric surgery. It's proven that other related toxicity such as bleeding or kidney toxicity can be reduced after use of ketorolac in comparison with other agents [17]. Our data also showed that the prevalence of nausea, vomiting, and

dizziness in ketorolac was lower than acetaminophen group.

Compared to paracetamol and tramadol, ketorolac provides better analgesia with longer duration in general and orthopedic surgeries [29]. In a study, the effect of 800 mg of ibuprofen and 30 mg of ketorolac was compared in pain after septorhinoplasty [28]. This comparison showed that ibuprofen-treated group had a lower postoperative VAS score, which may be related to the high dose of used ibuprofen in this study. In our study, the WST result was significantly better in the ketorolac group than in the acetaminophen group. In patients who were under Enhanced recovery after surgery (ERAS) protocol, WST had better results than the control group at 6 and 24 hours after UP3 operation [17].

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