# Comparison of Clinical Effects of Dexketoprofen and Paracetamol Used for Analgesia in Endoscopic Retrograde Cholangiopancreatography

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**Objective:** This study aimed to compare 50 mg dexketoprofen vs. 1 g paracetamol that were parenterally administered before endoscopic retrograde cholangiopancreatography (ERCP) under sedoanalgesia with comparable anaesthesia depth regarding haemodynamic, pain, narcotic analgesic requirement, recovery and post-procedural cognitive functions.

Methods: Overall, 80 ASA I-III patients aged 18-75 years who were undergoing scheduled ERCP were randomly assigned into three groups. In all patients, the mini-mental test (MMT) was conducted before the procedure. No drug was administered to controls (Group C; n=26); patients were transferred to ERCP unite 30 min after parenteral dexketoprofen (50 mg) in group D (n=27) and paracetamol (1 g) in group P (n=27). The standard monitoring was applied. After intravenously administering loading doses of midazolam (0.02 mgkg) and propofol (1 mg kg<sup>-1</sup>), propofol infusion was administered at a dose of 2-4 mg kg<sup>-1</sup> h<sup>-1</sup> to maintain a bispectral index value of 50-70. Fentanyl (0.05 µg kg<sup>-1</sup>) was intravenously administered when patients experienced pain. Haemodynamic effects, additional analgesic requirement, adverse effects during procedure, time to reach Aldrete score of 9 and satisfaction of an endoscopist and patient were recorded. MMT was repeated 3 h after completing the procedure.

**Results:** Fentanyl requirement during the procedure was significantly low in group D (p<0.05). Apnoea during the procedure and nausea after the procedure were least common in group D while significantly lower than group C (p<0.05). There was no significant difference with respect to MMT scores and endoscopist's satisfaction, while patient satisfaction was greater in group P.

**Conclusion:** Parenterally administered dexketoprofen provided better haemodynamic effect and pain control, thereby decreasing incidence of adverse events by reducing the requirement for narcotic analgesics.

Keywords: Sedation, endoscopic retrograde cholangiopancreatography, dexketoprofen, paracetamol

#### Introduction

pper gastrointestinal system endoscopy, sigmoidoscopy, colonoscopy and endoscopic retrograde cholangiopancreatography (ERCP) performed in gastrointestinal endoscopy units are diagnostic and treatment procedures that are highly popular today.

The ERCP procedure, which is used for diagnosing and treating disorders in the cystic and pancreatic ducts and periampullary region, is quite painful and disturbing. Additionally, some problems, including hypertension, hypotension, bradycardia, oxygen desaturation, abdominal discomfort and dizziness, can be encountered during this procedure. Therefore, this intervention must be performed under sedation and/or analgesia support for facilitating the work of the endoscopist and for greater patient comfort; also, the patient must be closely monitored using appropriate monitorization techniques (1).

For anaesthetic procedures performed outside the operating room, sedative or narcotic agents cannot be used readily because of their possible side effects (apnoea, hypotension, hypertension, bradycardia and tachycardia). In recent studies, it has been reported that the use of dexketoprofen or paracetamol IV (intravenous) can reduce the need for a narcotic analgesic and sedative agents (2, 3).

In this study, it was aimed to compare patients in whom IV dexketoprofen or IV paracetamol was applied for analysis premedication 30 min before the process, in terms of haemodynamics, additional narcotic analysis need, recovery and post-procedure cognitive dysfunction under propofol infusion and a similar anaesthesia depth in ERCP processes.

# Methods

The study was begun after receiving approval from the Local Ethics Committee in Ümraniye Training and Research Hospital, Istanbul, Turkey, and written informed consent from the patients. Eighty patients, who were between the ages of 18 and 75 years, would undergo ERCP with sedoanalgesia under elective conditions in the Clinic of Gastroenterology and who were in the risk group of the American Society of Anaesthesiology (ASA) I-III, were included in the study.

The patients were evaluated in three groups: Group D (n=27) (those in whom IV 50 mg dexketoprofen was applied 30 min before the process), Group P (n=27) (those in whom IV 1 g paracetamol was applied 30 min before the process) and Group K (n=26) (control group with whom analgesia was not applied before the process).

Patients with uncontrolled hypertension, unstable ischaemic heart disease, decompensated congestive heart failure, serious ventricular arrhythmia, severe chronic lung disease, peptic ulcer, kidney and liver failure, a history of the use of sedative-hypnotic or central acting drugs and a known sensitivity to benzodiazepines, local anaesthetics, propofol and opioid drugs were excluded from the study.

Following 8-h fasting, patients were evaluated through a Mini Mental Test (MMT) before the process.

Within 30 min after the application of dexketoprofen 50 mg IV or paracetamol 1 g IV, the patients were taken into the ERCP unit and standard monitorization (mean arterial pressure, MAP), heart rate (HR) and Bispectral Index (BIS) monitorization were applied. For all the patients, MAP, HR, SpO $_2$  and BIS values and times were recorded at the beginning (30 min before the process) and at 5-min intervals beginning from the 0th (the value before the administration of the drug),  $1^{\rm st}$  and  $5^{\rm th}$  minutes to the  $90^{\rm th}$  minute during the process.

During the process, the patients were laid down in the prone position and their heads were turned toward the endoscopist (to the right). Then, 4 L min<sup>-1</sup> of  $O_2$  support was provided through a nasal  $O_2$  cannula. All the patients were applied propofol 1–3 mg kg<sup>-1</sup> st<sup>-1</sup> infusion so that BIS was 50–70, following a loading dose of midazolam 0.02 mg kg<sup>-1</sup> IV and propofol 1 mg kg<sup>-1</sup> IV.

When the patients experienced pain (wiggling, an increase of 30% and above in HR and MAP), 0.5  $\mu$ g kg<sup>-1</sup> fentanyl was administered at repeating doses and recorded as an additional analgesic dose.

Any side effects, including hypoventilation (<8 respiratory rate/minute and superficial abdominal respiration), apnoea (cessation of breathing for 30 s), hypoxia (SpO<sub>2</sub> value below 90%), hypotension (a decrease of 30 from the initial value), hypertension (an increase of 30% from the initial value), arrhythmia and bradycardia (<50 beat min<sup>-1</sup>), were recorded.

For the patients whose  $\mathrm{SpO}_2$  value decreased below 90%, it was planned to increase the amount of  $\mathrm{O}_2$ , which was given through a nasal cannula, to 6 L min<sup>-1</sup>, to stimulate the patients with verbal and/or tactile stimuli, to provide ventilatory support and, when necessary, to decrease and discontinue infusion. In patients developing hypotension, it was planned to increase fluid infusion primarily and, in case of its continuance, to administer ephedrine 5 mg IV. On the other hand, patients developing bradycardia were planned to be treated by applying 0.5 mg atropine IV.

It was planned to exclude patients whose hypoventilation, apnoea, hypotension, hypertension, arrhythmia and bradycardia still continued despite the treatments.

After the ERCP process, patients with a BIS value of 80 and above were taken into the recovery room and MAP, HR, SpO<sub>2</sub>, their Visual Analogue Scale (VAS) score and their Aldrete Recovery Score (ARS) were evaluated. The time when ARS became 9 was recorded. Patients with an ARS value of 9 and above were given recommendations and transferred to the clinics, where they were followed, in company with a hospital attendant. They were re-evaluated, with MMT performed 3 h after the process.

After ERCP, the satisfaction levels of the endoscopist who performed the procedure and the patients were evaluated (poor, medium, good, excellent).

#### Statistical analysis

For the power analysis, in the measurements for additional analgesic, the delta value was 20 in the evaluation performed according to the results of the preliminary group study and the power was 80%, with a SD value of 27. The number of sampling was at least 26 in the groups, with p=0.05.

While evaluating the data obtained from the study, Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software (Utah, USA) were used for the statistical analyses. In addition to the descriptive statistical methods (the mean, standard deviation, median, frequency, rate), for comparing quantitative data, a one-way analysis of variance (ANOVA) test was used for the normally distributed parameters, whereas the Kruskal-Wallis test was used for the non-normally distributed parameters between the groups. The Mann-Whitney U test with Bonferroni correction was employed for the post hoc comparisons. For comparing the normally distributed parameters within groups, the Paired Samples t-test was utilized. The Pearson chi-square test was used for comparison of the qualitative data. The results were evaluated at the 95% confidence interval and at the significance level of p<0.05.

### Results

The ages of patients were between 15 and 84 years (52.8±17.2). Of these patients, 63.8% (n=51) were female and 36.3% (n=29) were male. No patient was excluded during the study.

	_		Groups		_
		Control n=26	Dexketoprofen n=27	Paracetamol n=27	
	_	Mean±SD	Mean±SD	Mean±SD	a <sub>p</sub>
Age (years)		54.25±18.09	54.45±18.38	50.03±15.54	0.572
Body weight (kg)		71.96±11.13	70.69±11.99	73.86±12.81	0.808
Duration of proce	edure (min)	34.18±9.52	35.21±7.87	33.62±8.95	0.639
		n (%)	n (%)	n (%)	ьp
ASA	I	8 (30.8)	10 (37.0)	10 (38.5)	0.543
	II	13 (50.0)	13 (48.1)	15 (57.7)	
	III	5 (19.2)	4 (4.8)	1 (3.8)	
Gender	Female	17 (65.4)	15 (55.6)	19 (70.4)	0.515
	Male	9 (34.6)	12 (44.4)	8 (29.6)	

In our study, there was no statistically significant difference in terms of age, weight, duration of procedure (the time from the oropharyngeal application of local anaesthetic until removal of the endoscope), ASA scores and the gender distributions (p>0.05) (Table 1).

There was no significant difference among the groups in terms of MAP levels at all the measurement times during the process and at the post-procedure 5<sup>th</sup>, 10<sup>th</sup>, 15<sup>th</sup> and 30<sup>th</sup> minutes. The values at the 20<sup>th</sup> and 25<sup>th</sup> minutes were significantly lower in the D group than in the K group (p<0.05). There was no difference between the other groups. In the comparisons within the groups, no statistically significant difference was found at all the measurement times compared to the basal values (Figure 1), and all the values were within normal intervals.

At all the measurement times during the process, no statistically significant difference was observed among the groups with regard to HR. In the within-group comparisons, while there was no difference at all the measurement times in the K group, there were significant decreases at the 15<sup>th</sup>, 20<sup>th</sup> and 30<sup>th</sup> minutes in the D group and at the 30<sup>th</sup>, 35<sup>th</sup> and 45<sup>th</sup> minutes in the P group compared to the basal values (p<0.05) (Figure 1). However, all the values were within normal intervals.

Although there was a statistically significant difference in the comparisons of  ${\rm SpO_2}$  values between and within the groups (p<0.05), all the values were between normal intervals. The value of  ${\rm SpO_2}$  did not decrease below 94% in any patient.

While the VAS levels were not different in the groups at the 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup>, 25<sup>th</sup>, and 30<sup>th</sup> minutes after the process, the 15<sup>th</sup> minute VAS levels were significantly higher in the K group

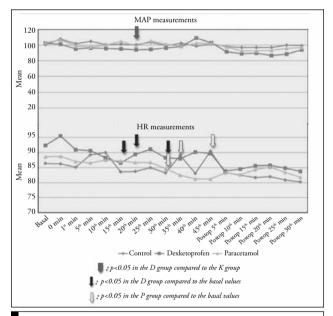


Figure 1. Evaluation of MAP and HR measurements according to the groups.

MAP: mean arterial pressure; HR: heart rate

than in the D and P groups (p<0.01) (Table 2). In all the patients, the VAS value was below 3.

In the evaluation of sedation levels, no significant difference was found among the groups with regard to the post-procedure ARS values at the  $10^{th}$ ,  $15^{th}$ ,  $20^{th}$  and  $30^{th}$  minutes. However, the ARS values at the  $5^{th}$  and  $25^{th}$  minutes in the K group were significantly higher than in the D and P groups (p<0.01) (Table 3).

In terms of additional analgesic (fentanyl) used during the process, there was a significant difference among the groups (p<0.05). The amount of fentanyl in the D group was signifi-

cantly lower than in the K and P groups (p=0.004; p=0.016). On the other hand, there was no statistically significant difference between the K group and P group. Moreover, no significant difference was observed in terms of the total amount of propofol used during the procedure (Table 4).

In the evaluation of cognitive functions, no statistically significant difference was detected among the three groups with regard to initial MMT and final MMT values and the time when the Aldrete score became 9 (Table 5).

Considering the side effects, there was a statistically significant difference between the frequency rates of nausea and apnoea in the groups (p<0.05). The rate of nausea (p=0.03) and apnoea (p=0.003) after the process was significantly higher in the K group than in the D group, but there was no significant difference among the other groups.

In terms of the vomiting rates, no statistically significant difference was observed among the groups. The numbers with vomiting were 10 in the K group and 4 in each of the P and D groups (Table 6).

		Groups		
	Control- dexketoprofen	Control- paracetamol	Dexketoprofen- paracetamol	
	ap	<sup>a</sup> p	<sup>a</sup> p	
VAS 15 <sup>th</sup> min	0.071	0.003**	0.137	
		Groups		
	Control	Dexketoprofen	Paracetamol	ьp
	Mean±SD (Median)	Mean±SD(Median)	Mean±SD(Median)	
VAS 15 <sup>th</sup> min	1.41±0.71 (1.00)	1.12±0.45 (1.00)	1.00±0.00 (1.00)	0.006**

		Groups			
	Control -dexketoprofen	Control -paracetamol	Dexketoprofen -paracetamol		
	°p	e <b>p</b>	°p		
Aldrete 5th min	0.002**	0.235	0.010*		
Aldrete 25 <sup>th</sup> min	0.034*	0.005**	0.443		
		Groups			
	Control	Arveles	Paracetamol		
	Mean±SD (Median)	Mean±SD (Median)	Mean±SD (Median)	$^{\mathrm{d}}\mathbf{p}$	
Aldrete 5th min	6.65±1.40 (7.00)	5.33±1.34 (5.00)	6.26±1.13 (6.00)	0.003**	
Aldrete 25 <sup>th</sup> min	9.50±0.51 (9.50)	9.21±0.41 (9.00)	9.12±0.34 (9.00)	0.009**	

Table 4. Total amounts of propofol and analgesics according to the group						
		Groups				
	Control	Dexketoprofen	Paracetamol			
	Mean±SD	Mean±SD	Mean±SD	<sup>a</sup> <b>p</b>		
Total Propofol (mg)	230.59±88.23	256.04±117.47	243.15±114.79	0.700		
Fentanyl (mcg) (median)	35.55±30.67 (50)	12.50±26.58(0)	31.03±31.09(50)	<sup>b</sup> 0.036*		
<sup>a</sup> One-Way ANOVA test, <sup>b</sup> Kruskal–Wal	lis test, *p<0.05. SD: standard deviati	on				

Table 5. Initial and final MMT measurements and the times of ARS 9-10 according to the group

	Groups			
_	Control	Dexketoprofen	Paracetamol	
	Mean±SD	Mean±SD	Mean±SD	<sup>a</sup> p
	26.40±3.46	25.71±3.08	26.82±2.75	0.437
	25.78±3.48	25.91±3.65	26.88±2.98	0.440
bр	0.054	0.462	0.409	
	11.12±3.96	11.31±4.14	12.92±4.59	0.256
	<sup>b</sup> p	Mean±SD 26.40±3.46 25.78±3.48  bp 0.054	Control         Dexketoprofen           Mean±SD         Mean±SD           26.40±3.46         25.71±3.08           25.78±3.48         25.91±3.65           bp         0.054         0.462	Control         Dexketoprofen         Paracetamol           Mean±SD         Mean±SD         Mean±SD           26.40±3.46         25.71±3.08         26.82±2.75           25.78±3.48         25.91±3.65         26.88±2.98           bp         0.054         0.462         0.409

Table 6. C	Complications	according to	the group
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		Groups		
	Control	Dexketoprofen	Paracetamol	_
	n (%)	n (%)	n (%)	- <sup>a</sup> p
Nausea	14 (53.8)	4 (14.8)	9 (33.3)	0.011*
Vomiting	10 (38.5)	4 (14.8)	4 (14.8)	0.060
Apnoea	11 (42.3)	2 (7.4)	5 (18.5)	0.008**
		Groups		
	Control- dexketoprofen	Control- paracetamol	Dexketoprofen- paracetamol	
	p	p	p	_
Nausea	0.003**	0.132	0.111	
Vomiting	0.051	0.051	1.000	
Apnoea	0.003**	0.059	0.224	

With regard to the satisfaction levels of the endoscopist, there was no difference among the groups (p>0.05). On the other hand, with regard to patient satisfaction, the difference was not statistically significant but was close to being significant (p=0.055) (Table 7).

<sup>a</sup>Pearson chi-square, \*p<0.05; in the comparison of three groups \*\*p<0.01; in the comparison of two groups

# Discussion

During ERCP, patients must be kept under deep sedation without suppressing the protective airway reflexes, their retching reflex must be prevented with coughing and analgesia must be provided. The most appropriate agent for sedation and the level of sedation differ for each patient. Age, general health state and the experience of the endoscopist and anaesthetist are important for choosing the proper drug (1). With this aim, barbiturates, benzodiazepines, hypnotics and opioids are frequently used today, but the doses of these drugs must be adjusted carefully because of their side effects (2, 3).

Non-steroid anti-inflammatory drugs (NSAIDs) are commonly used in outpatient surgeries because they have fewer

side effects and have analgesic efficiency (paracetamol 95%, other NSAIDs 73%) (4).

Although many NSAIDs have oral and rectal forms, they do not have a parenteral form. Dexketoprofen trometamol and paracetamol IV forms are non-opioid analgesic agents that are also available in Turkey (5). In the studies conducted on the parenteral formulation of paracetamol, it has been demonstrated that: analgesic efficiency is similar to that in the agents from the same group, it decreases the use of opioid required in postoperative analgesia, it reduces the incidence of nausea and vomiting, it improves sleep quality and it causes less sedation (6, 7). It has also been stated that dexketoprofen is an important alternative in parenteral applications due to the rapid onset of action of its parenteral form and as it is efficient and safe (8).

In the implementations of ERCP, propofol and/or midazolam and fentanyl are generally applied at different doses and protocols. Large-scale studies revealed that the sedation process with propofol was superior to that with benzodiazepines and opioids (9).

Table 7. Comparison of satisfaction levels in the endoscopists and patients according to the group

		Groups			
		Control	Dexketoprofen	Paracetamol	
		n (%)	n (%)	n (%)	<sup>a</sup> p
Endoscopist satisfaction	Very good	10 (38.5)	16 (59.3)	15 (55.6)	
	Good	12 (46.2)	9 (33.3)	12 (44.4)	0.191
	Moderate	4 (15.4)	2 (7.4)	0 (0)	
Patient satisfaction	Very good	17 (65.4)	18 (66.7)	24 (88.9)	
	Good	9 (34.6)	7 (25.9)	2 (7.4)	0.055
	Moderate	0 (0.0)	2 (7.4)	1 (3.7)	

\*Pearson chi-square test, \*p<0.05: in the comparison of three groups. It is remarkable that the satisfaction level of patients using paracetamol is very good despite the absence of a statistically significant difference among the groups (p>0.05).

Pratila et al. (10) investigated the effects of midazolam and propofol on haemodynamics, sedation and recovery in children undergoing inguinal hernia repair under local anaesthesia. They applied 0.02 mg kg<sup>-1</sup> bolus midazolam or 1 mg kg<sup>-1</sup> IV bolus propofol, which provided adequate intraoperative sedation in both groups. They reported that recovery was more rapid in the propofol group and postoperative sedation and psychomotor insufficiency were prolonged, while amnesia was significantly higher in the midazolam group.

The agents used for sedation can often cause haemodynamic depression. In the study of Sarıkaya et al. (11), 40 patients who underwent endoscopic sinus surgery under local anaesthesia were applied remifentanil (0.1  $\mu g\ kg^{-1}\ min^{-1}$  infusion following 1  $\mu g\ kg^{-1}$  bolus) and remifentanil+propofol (0.05  $\mu g\ kg^{-1}\ min^{-1}$  infusion and 50  $\mu g\ kg^{-1}\ min^{-1}$  propofol following 0.5  $\mu g\ kg^{-1}$  bolus) infusion. They found no significant difference between the groups with regard to SAB, DAB, MAP, HR, respiratory rate and SpO $_2$  values.

In our study, comparisons of groups during and after the process revealed no statistically significant difference in terms of MAP and HR. However, the MAP values during the process were lower in the D group than in the P and K groups. In the HR values, significant decreases were observed in the D and P groups compared to the basal values. We think that this might have resulted from the pre-emptive analgesic effects of dexketoprofen and paracetamol.

It has been reported that oral paracetamol is an effective and well-tolerated agent in postoperative pain control in various surgeries (12). In the combination studies on paracetamol, it was found that it had a sparing effect on opioid and it reduced the need for opioid in total. However, the postoperative use of oral paracetamol is limited. Furthermore, it has been reported that the use of parenteral paracetamol involves a more rapid onset of impact and a longer action time (14). Based on this information, paracetamol was given IV 30 min before the process to provide a pre-emptive effect

and to benefit from its analgesic effect during the process in our study.

Berti et al. (15) compared the administrations of oral dexketoprofen (25 mg, 3 times a day), ketoprofen (50 mg, 3 times a day) and paracetamol (500 mg, 4 times a day) for postoperative pain treatment in patients undergoing outpatient knee arthroscopy with a combined sciatic-femoral block. They found that the analgesic effects of 75 mg day<sup>-1</sup> dexketoprofen and 150 mg day<sup>-1</sup> ketoprofen were similar and that both agents were more effective than paracetamol.

In the study of Gülhaş et al. (16) on 120 patients who underwent total abdominal hysterectomy, it was detected that IV forms of dexketoprofen (50 mg), paracetamol (1 g) and lornoxicam (8 mg) given 30 min before the end of operation and at the postoperative 8<sup>th</sup>–16<sup>th</sup> hours decreased the amount of fentanyl consumed with patient-controlled analgesia (PCA) at similar rates.

In the studies conducted for postoperative pain control in the literature, it was reported that paracetamol IV increased the analgesic effect, decreased the use of opioid and increased patient satisfaction in different surgical interventions (17). However, in our literature review, we found no studies on the use of dexketoprofen IV with the aim of analgesia in procedures with sedation (either with ERCP or interventional endoscopic procedures).

In our study, it was found that parenteral dexketoprofen used 30 minutes before the procedure in ERCP applications reduced the need for an additional dose of fentanyl compared to the paracetamol and control groups, and that dexketoprofen was superior to paracetamol with regard to this point.

Although we encountered some studies comparing the effects of regional and general anaesthesia on cognitive functions and recovery in our literature review, no studies comparing the effect of sedo-analgesia on cognitive functions were found. Moreover, the effects of paracetamol and dexketoprofen, add-

ed to a combination of propofol and midazolam, were also investigated in our study.

The Aldrete Recovery Score (ARS) was used herein for evaluating patients in the early-recovery stage. There was no statistically significant difference among the groups in terms of ARSs in the first 30 min after the end of the process (though the scores were higher in the control group at the 5<sup>th</sup> and 25<sup>th</sup> minutes than in the other groups) (p>0.05). The time when ARS became 9 was similar in all three groups.

In the study groups, MMT, which was developed by Folstein et al. (18) in 1975 and is used for evaluating cognitive disorders, disease course and treatment, orientation, attention, calculating ability, memory (recording memory and recent memory), recall, linguistic and visual states, was applied at the preoperative 30<sup>th</sup> minute and at the postoperative 3<sup>rd</sup> hour.

Cheung et al. (19) compared dexmedetomidine (80.88 mg kg<sup>-1</sup>) and midazolam (0.07 mg kg<sup>-1</sup>) in 60 patients through MMT at the preoperative and postoperative 2<sup>nd</sup> hours, and they found no difference. Bustillo et al. (20) reported that adequate sedation was provided with dexmedetomidine in all cases with cerebral arteriovenous malformation embolism, and that the patients woke up in 10 min after the cessation of infusion, but impairment was observed in the cognitive test results and this continued until the postoperative 45<sup>th</sup> minute.

Özhan et al. (21) investigated the effects of propofol and a 0.25 mg<sup>-1</sup> kg<sup>-1</sup> dose of ketamine added to propofol on post-operative cognitive functions in 60 patients who were applied laparoscopic cholecystectomy. They did not detect any significant difference between the groups in terms of the results of MMT performed at the postoperative 24<sup>th</sup> hour.

In our study, there was no statistically significant difference among the groups in terms of MMT scores at the preoperative 30<sup>th</sup> minute and at the postoperative 3<sup>rd</sup> hour (p>0.05), and all the values were at the level of 'normal cognitive functions'.

The risk of bleeding has been found to be lower in dexketoprofen than with other NSAIs or is never seen; thus, it has been specified that dexketoprofen has a safe profile (22-24).

In our study, no coagulation problems associated with NSAIDs were observed, and none of patients had gastrointestinal system (GIS) bleeding or similar complaints during or after the procedure.

Another complication that can commonly occur during the postoperative period is nausea-vomiting. Its severity and frequency can differ depending on gender, smoking, the type and duration of surgery, the anaesthesia technique, the use of inhalation anaesthetics or the use of opioids (25).

In a study comparing lornoxicam, paracetamol and dexketoprofen trometamol in total abdominal hysterectomy surgeries, although the use of postoperative fentanyl was higher in the control group, there was no significant difference in terms of gastrointestinal side effects and nausea-vomiting (16).

In the study performed by Gülhaş et al. (16) on 120 patients who were planned to undergo total abdominal hysterectomy, the IV forms of dexketoprofen trometamol, paracetamol and lornoxicam, which were applied 30 min before the end of operation and at the postoperative 8th-16th hours, decreased the rate of fentanyl used with PCA at similar rates and, thus, the side effects including respiratory depression, change in mental state, ileus, constipation and nausea-vomiting were similar to those in IV PCA, while their frequencies were lower.

In our study, the incidence of nausea was higher in the K group, and this was attributed to the fact that the use of additional fentanyl was higher in the K group than in the D group. Vomiting was observed in 10 patients in the K group, in 4 patients in the D group and in 4 patients in the P group, and no statistically significant difference was found among the groups.

In addition, although 11 patients in the K group had apnoea during the process, this number was 2 in the D group and 5 in the P group. Spontaneous ventilation re-occurred with increased  $\rm O_2$  (6 L min<sup>-1</sup>) and verbal-tactile stimuli. In none of patients did the value of  $\rm SpO_2$  fall below 94%. The incidence of apnoea was higher in the K group than in the D group (p<0.01), which was attributed to the higher amount of additional opioids in the K group.

Another important criterion is the satisfaction levels of the patient and the endoscopist, which was one of the parameters investigated in our study. In our literature review, most studies were generally about postoperative analgesia and patient satisfaction (17, 25). We did not encounter any studies on this issue regarding interventional endoscopic procedures.

In our study, no statistically significant difference was detected among the groups in terms of endoscopist satisfaction (p>0.05). On the other hand, with regard to patient satisfaction, the difference was not statistically significant, but was near significant (p=0.055, p>0.05). The satisfaction level was 'very good' in Group P patients and 'good' in Group D patients, which was suggested to be associated with the effect of fentanyl, which was administered at a higher rate in the P group than in the D group.

#### Conclusion

In our study, it was observed that dexketoprofen parenterally administered before the process significantly reduced the need for analysesics and thus reduced the undesirable side effects in patients who were administered sedation with propofol and midazolam at similar anaesthesia depths in ERCP

interventions compared to a paracetamol group and control group. Moreover, it was revealed that it did not cause cognitive dysfunction or affect the recovery period. It is suggested that further studies with a larger population are needed on this subject.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ümraniye Training and Research Hospital.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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## References

- Türk Anestezi ve Reanimasyon Derneği, TARD uygulama klavuzları, Ameliyathane dışı anestezi uygulamaları 2005; 67.
- Campo R, Brullet E, Junquera F, Puig-Diví V, Vergara M, Calvet X, et al. Sedation in digestive endoscopy. Results of a hospital survey in Catalonia (Spain). Gastroenterol Hepatol 2004; 27: 503-7. [CrossRef]
- 3. Jung M, Hofmann C, Kiesslich R, Brackertz A. Improved sedation in diagnostic and therapeutic ERCP: propofol is an alternative to midazolam. Endoscopy 2000; 32: 233-8. [CrossRef]
- Segerdahl M, Warren-Stomberg M, Rawal N, Brattwall M, Jakobsson J. Clinical practice and routines for day surgery in Sweden: results from a nation-wide survey. Acta Anaesthesiol Scand 2008; 52: 117-24. [CrossRef]
- Walczak JS. Analgesic properties of dexketoprofen trometamol. Pain Manag 2011; 1: 409-16. [CrossRef]
- Arici S, Gurbet A, Türker G, Yavaşcaoğlu B, Sahin S. Preemptive analgesic effects of intravenous paracetamol in total abdominal hysterectomy. Agri 2009; 21: 54-61.
- Cakan T, Inan N, Culhaoglu S, Bakkal K, Basar H. Intravenous paracetamol improves the quality of postoperative analgesia but does not decrease narcotic requirements. J Neurosurg Anesthesiol 2009; 20: 169-73. [CrossRef]
- 8. Yazar MA, Inan N, Ceyhan A, Sut E, Dikmen B. Postoperative analgesic efficacy of intravenous dexketoprofen in lumbar disc surgery. J Neurosurg Anesthesiol 2011; 23: 193-7. [CrossRef]
- Koshy G, Nair S, Norkus EP, Hertan HI, Pitchumoni CS. Propofol versus midazolam and meperidine for conscious sedation in GI endoscopy. Am J Gastroenterol 2000; 95: 1476-9. [CrossRef]
- 10. Pratila MG, Fischer ME, Alagesan R, Reinsel RA, Pratilas D. Propofol versus midazolam for monitored sedation: a compa-

- rison of intraoperative and recovery parameters. J Clin Anesth 1993; 5: 268-74. [CrossRef]
- 11. Sarıkaya HG, Dinçer E, Özgültekin A, Turan G, Turan E. Fonksiyonel endoskopik sinüs cerrahisinde sedoanaljezi amacıyla remifentanil ve remifentanil+propofol kombinasyonunun karşılaştırılması. J Kartal TR 2011; 22: 1-6. [CrossRef]
- 12. Moller PL, Juhl GI, Payen-Champenois C, Skoglund LA. Intravenous acetaminophen (paracetamol): comparable analgesic efficacy, but better local safety than its prodrug, propacetamol, for postoperative pain after third molar surgery. Anesth Analg 2005; 101: 90-6. [CrossRef]
- Türkoğlu, M. Ağrının tanımlanması ve ölçümü. Ed. İ. Yegül, Ağrı ve Tedavisi, Yapım Matbaacılık, İzmir, 1993: 19-27.
- 14. Aksoy EA, Polat Ş, Serin GM, Öz F, Kaytaz A. Termal welding sistemi ile tonsillektomi sonrası ağrı değerlendirilmesi. Acıbadem Üniversitesi Sağlık Bilimleri Dergisi 2011; 2: 75-9.
- Berti M, Albertin A, Casati A, Palmisano S, Municino G, da Gama MM, et al. A prospective, randomized comparison of dexketoprofen, ketoprofen or paracetamol for postoperative analgesia after outpatient knee arthroscopy. Minerva Anestesiol 1999; 66: 549-54.
- 16. Gülhaş N, Durmuş M, Yücel A, Şahin T, Erdil FA, Yoloğlu S, et al. Comparasion of the analgesic effects of intravenous Dexketoprofen Trometamol, Lornoxicam and Paracetamol on postoperative pain after total abdominal hysterectomy. Turk J Anaesth Reanim 2011; 39: 176-81. [CrossRef]
- Ekmekçi P, Kazak Bengisun Z, Kazbek BK, Öziş SE, Taştan H, Süer AH. The efficacy of adding dexketoprofen trometamol to tramadol with patient controlled analgesia technique in postlaparoscopic cholecystectomy pain treatment. Agri 2012; 24: 63-8. [CrossRef]
- 18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr 1975; 12: 189-98. [CrossRef]
- Cheung CW, Ying CLA, Chiu WK, Wong GTC, Ng KFJ, Irwin MG. A comparison of dexmedetomidine and midazolam for sedation in third molar surgery. Anaesthesia 2007; 62: 1132-8. [CrossRef]
- Bustillo MA, Lazar RM, Finck AD, Fitzsimmons B, Berman MF, Pile-Spellman J, et al. Dexmedetomidine may impair cognitive testing during endovascular embolization of cerebral arteriovenous malformations: a retrospective case report series. J Neurosurg Anesthesiol 2002; 14: 209-12. [CrossRef]
- Özhan Y, Bakan N, Karaoren G, Tomruk SG, Topaç Z. Effects of Subanesthetic Ketamine on Pain and Cognitive Functions in TIVA. J Clin Anal Med 2013; DOI: 10.4328/JCAM.2161. [CrossRef]
- Laporte JR, Ibanez L, Vidal X, Vendrell L, Leone R. Upper gastrointestinal bleeding associated with the use of NSAIDs. Drug Saf 2004; 27: 411-20. [CrossRef]
- 23. Barbanoj MJ, Antonijoan RM, Gich I. Clinical pharmacokinetics of dexketoprofen. Clin Pharmacokinet 2001; 40: 245-62. [CrossRef]
- 24. Hanna MH, Elliott KM, Stuart-Taylor ME, Roberts DR, Buggy D, Arthurs GJ. Comparative study of analgesic efficacy and morphine-sparing effect of intramuscular dexketoprofen trometamol with ketoprofen or placebo after major orthopaedic surgery. Br J Clin Pharmacol 2003; 55: 126-33. [CrossRef]
- Arici S, Gurbet A, Türker G, Yavaşcaoğlu B, Sahin S. Preemptive analgesic effects of intravenous paracetamol in total abdominal hysterectomy. Agri 2009; 21: 54-61.