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The impact of intravenously administered dexketoprofen trometamol on analgesia and recovery in ambulatory dilatation and curettage procedures: a retrospective analysis

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Abstract

Background: Achieving adequate pain control during and after the uterine D/C (dilatation and curettage) procedure is crucial for a good recovery process and early discharge.

The study was conducted to find out whether intravenous dexketoprofen trometamol is more effective than tramadol and paracetamol in easing pain during the D/C procedure as well as to assess its effectiveness in the recovery period.

Results: Significant differences were determined between the groups regarding the values of Ramsey sedation scores (p=0.048). VAS (visual analog scale) mean values of group T were higher compared to the VAS mean values of group D (p=0.02). A significant difference was found between group P and group D (p=0.016), the mean VAS values of group P were higher than group D.

Conclusions: We found out that preemptive intravenous 25 mg dexketoprofen trometamol administered in the daily D/C procedure provides good quality postoperative analgesia with minimal adverse effects by reducing the need for rescue analgesia, and is more effective in postoperative analgesia than paracetamol and tramadol.

Keywords: Pain, Dexketoprofen trometamol, Ambulatory surgery, Sedation, Uterine dilatation and curettage

Background

D/C are the most commonly performed ambulatory minor surgical procedures in the practice of obstetrics and gynecology (Sethi et al. 2015). Although it is a procedure performed in a short time, severe pain during the procedure requires adequate analgesia, rapid onset, and anesthesia that enables a rapid recovery (Taş et al. 2014). The selection of anesthesia and analgesia depends on the effectiveness, cost, safety, adverse effects, and patient, as well as on the preference of the physician (Mittal and Goyal 2015). In the previous studies, it has been revealed that only 10% of the clinics performed the procedure under general anesthesia, while 58% of them preferred local anesthesia, and 32% performed it under local anesthesia and sedation anesthesia (Lichtenberg et al. 2001).

Pain is a complicated experience involving a particular sensation and the responses it evokes. Conventional analgesics either inhibit elevated nociceptive stimuli or suppress interpretations within the CNS (central nervous system) (Becker 2010). Postoperative pain occurs in

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more than 85% of patients who underwent surgery, and in 75% of such patients, pain occurs immediately after surgery with moderate or severe intensity (Hanna and Moon 2019). Adequate treatment of acute pain improves clinical and economic outcomes, hence, in the last 2 decades, there has been increasing emphasis on this issue to improve postoperative pain management (Gan et al. 2014).

During dilatation and curettage procedures, various analgesic drugs are administered for the prevention of intraoperative and postoperative pain. NSAIDs (nonsteroidal anti-inflammatory drugs), which are non-opioids with a short duration of action and few cardiovascular and respiratory system side effects, or synthetic weak-acting opioid agents have often been the preferred analgesics in these procedures, as they are ambulatory surgery procedures and discharge is scheduled as soon as possible.

Dexketoprofen trometamol is a relatively novel NSAID and is the active enantiomer of racemic ketoprofen (Akil et al. 2014). The tromethamine salt of dexketoprofen (dexketoprofen trometamol) is rapidly absorbed and peak plasma concentrations are reached in a short duration. Compared with ketoprofen, dexketoprofen has the advantages of faster onset of action, increased effectiveness, and less gastrointestinal side effects. As an advantage, dexketoprofen trometamol has been clinically shown to produce effective analgesia with rapid onset of action in the treatment of moderate to severe pain (Hanna and Moon 2019; Rodríguez et al. 2008). In a study scrutinizing the use of dexketoprofen in minor gynecological surgery, it was found to provide a satisfactory level of analgesia similar to that achieved with a paracervical block during diagnostic hysteroscopy in postmenopausal women (Mercorio et al. 2002). While its oral form has been approved since 1998, its parenteral form has been introduced to the market in 2002 and is licensed in many countries around the world (Moore and Barden 2008). Following the recent introduction of intravenously administered dexketoprofen trometamol, studies revealing its post-operative effectiveness in orthopedic surgery, lumbar disc herniation surgery, and gynecological surgery have been published (Koçum et al. 2014).

In this study, it was aimed to compare the effectiveness of opioid analgesics, namely tramadol, non-opioid analgesic agents, paracetamol, and dexketoprofen trometamol, which are routinely administered intravenously, on pain and sedation of the patients, who underwent outpatient elective dilatation and curettage, in the intraoperative and postoperative recovery period. However, the use of intravenous dexketoprofen trometamol in similar operations is included in a limited number of studies. Previous studies have investigated its oral use in dilatation and curettage procedures. Hence, in our study, we primarily aimed to investigate the effectiveness of intravenous dexketoprofen trometamol administered under sedation anesthesia by comparing it with previous analgesics used in similar cases.

Methods

The study was started as a retrospective study following the approval of the University of Health Sciences Kanuni Sultan Suleyman Training and Research Hospital Ethics Committee (KAEK/2018.4.15). It was designed to investigate the effects and effectiveness of analgesic drugs, which are routinely administered in dilatation and curettage operations in accordance with the hospital protocol, on intraoperative, postoperative, and recovery periods. Patients, who were operated under elective circumstances under sedation anesthesia in the non-operating room gynecological septic intervention room, were included in the study. Patients in the ASA (American Society of Anesthesiology) I–II group, those who aged 18–65 years, underwent elective surgery, and no routine analgesic use in the last 24 h, were included in the study, whereas patients under 18 years old, and over 65 years old, and in the classification of ASA III and above, with a known heart, kidney, liver, hematological, psychiatric disease, anemia, analgesic hypersensitivity, operated under emergency conditions, morbidly obese, patients who developed any complications during or after surgery, and could not cooperate in the postoperative period, were excluded from the study.

As the Anesthesiology and Reanimation clinic, we routinely administer analgesic medication to prevent pain in addition to the sedation anesthesia generated using propofol, since it is a painful intervention. All procedures performed are recorded in the anesthesia and recovery follow-up forms. Through the examination of these data, patients who met the inclusion criteria who underwent elective dilatation and curettage between February 01, 2017, and April 01, 2017, were retrospectively reviewed. The number of cases included in the study was determined as a minimum of 60 with 90% accuracy, through the "power analysis" with α: 0.90 and β: 0.05 values performed before the study. A total of 180 patients were divided into three groups, 60 of whom were administered intravenous 25 mg of dexketoprofen trometamol (group D), 60 of who were administered 1000 mg of intravenous infusion of paracetamol (group P), and 60 of whom were administered intravenous tramadol at 1 mg/kg (group T).

Patient's demographic data, ASA physical status, diagnosis, duration of the procedure, the total and additional dose of propofol, baseline values, as well as SAP (systolic arterial pressures), DAP (diastolic arterial pressures) every 3 min during the operation, MAP (mean arterial

pressures), HR (heart rates), SpO_2 (peripheral oxygen saturation) and Ramsey sedation scores, VAS values of the patients before surgery, at onset and the 30th minute and 1 h after the procedure, onset, 15th, 30th minute, 1st hour, and 2nd hour Aldrete recovery scores in the recovery period and the period when the Aldrete recovery score was 10 points, additional analgesia in the postoperative period, any side effects if developed, and patient and surgeon satisfaction were recorded by reviewing the anesthesia and recovery follow-up forms. Analyzed parameters were compared between groups.

In order to prevent acute pain in dilatation and curettage procedures, different groups of analgesic drugs are used. Dexketoprofen trometamol, used in minor gynecological surgery, has been shown to provide effective analgesia with rapid onset of action. The primary outcome of this study effects of intravenously administered dexketoprofen trometamol on postoperative analgesia and patient satisfaction was good. Also, the secondary outcome of this study showed that intravenous dexketoprofen trometamol administered preemptively in dilatation and curettage operations provides more effective sedation.

Statistical analysis

Descriptive statistics were presented as percentages and mean ± SD (standard deviation). Statistical analyzes of the groups were conducted using paired Student's t-test, repeated measures, and unpaired ANOVA post hoc test. Moreover, the Kruskal-Wallis test was used to analyze non-parametric variables. Continuous numerical variables were analyzed via the Mann-Whitney *U* test. Besides, the chi-square test was used to compare the categorical variables. The results were considered statistically significant at $P<0.05$.

Results

All three groups were comparable between themselves in terms of demographic and clinical characteristics (Table 1). Significant differences were found between the groups with dexketoprofen trometamol and paracetamol in terms of age and R/C percentage (p<0,033 ; <0,007 respectively).

Between groups, heart rate, systolic, diastolic, and mean arterial pressures, and SpO_2 were comparable hemodynamic parameters. Regarding the comparison between the groups, no significant difference was found between the groups in terms of Sp02, HR, DAP, and MAP values (p=0.834; 0.331; 0.934 and 0.390, respectively). Significant differences were observed between the groups in terms of SAP values (p=0.02). Accordingly, a significant difference was found between group T and group D (p=0.02), mean SAP values of group T were found to be higher than group D. Similarly, the mean SAP values of group T were higher than group P, though the difference was not significant.

Significant differences were determined between the groups regarding RSS values (p=0.048). All three groups show a similar increase until the 6th minute, whereas until the 9th minute, a decrease was observed in the control group, stagnation in group P, and an increase in group D. When the relations between consecutive RSS measurements were analyzed, it was found that the increase at the 3rd minute was significant (Fig. 1).

Furthermore, the difference between VAS measurements at different times was determined to be significant

Table 1 Demographic and clinical data for each group

	Grup T (n=60)	Grup P (n=60)	Grup D (n=60)	p-value
Age (year)	35.50±8.8	36.68±10.5	32.30±8.7[a]	0.033
Height (cm)	160.32±5.7	160.28±5.0	160.18±6.1	0.991
Weight (kg)	70.10±12.3	69.15±13.9	69.15±13.8	0.905
BMI	27.22±4.1	26.85±4.9	27.00±5.4	0.916
ASA (I/II) (n)	53/7	49/11	47/13	0.336
R/C (%)	76.7	66.7	91.7	0.007[£]
Duration of anesthesia (min)	6.35±3.0	7.07±3.7	6.93±3.5	0.484
Duration of operation (min)	5.83±3.0	6.05±3.7	6.32±3.0	0.725
First dose of propofol (mg/kg)	1.51±0.52	1.52±0.39	1.51±0.47	0.905
Additional dose of propofol (mg/kg)	0.66±0.57	0.74±0.60	0.68±0.52	0.744
Total dose of propofol (mg/kg)	2.18±0.56	2.26±0.61	2.19±0.53	0.678

Values are expressed as mean ± standard deviation or *n*. [a] Groups with dexketoprofen trometamol and paracetamol were found to have significant differences. £ Since the significance value was 0.007, the relationship between the patient diagnosis and the groups was statistically significant

ASA American Society of Anesthesiologists, *T* tramadol, *P* paracetamol, *D* dexketoprofen trometamol, *R/C* revision curettage (pregnancy termination)

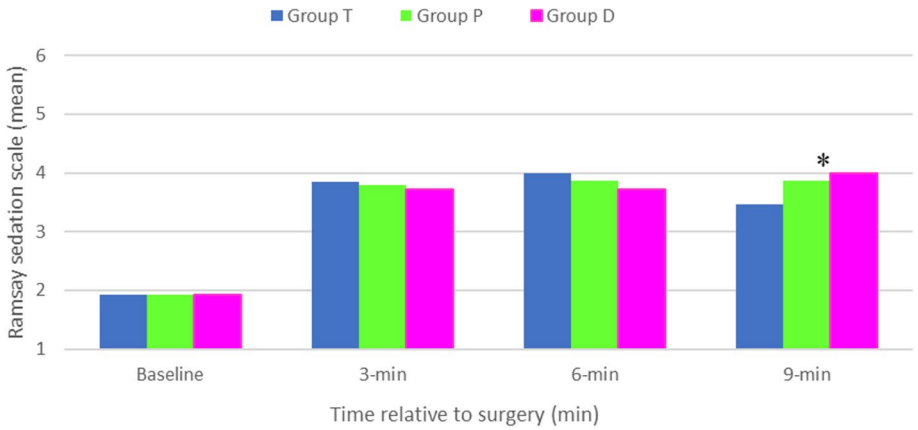

Fig. 1 Time course of the level of Ramsay sedation scale. Data are mean (SD), * p<0,05 refers to between groups comparisons (T, tramadol group; P, paracetamol group; D, dexketoprofen trometamol group; min, minute)

(p<0.01). Significant differences were found between the groups in terms of VAS values (p<0,01). When group T and group D were compared in terms of VAS, a significant difference was found (p=0.02), and group T mean VAS values were found to be higher than group D. Moreover, a significant difference was found between group P and group D (p=0.016), and mean VAS values of group P were higher than group D (Fig. 2).

Patients in all three groups obtained an Aldrete recovery score of 10, on average, 8 min after the procedure. The correlation between the duration of recovery and the groups was not significant, as the significance value was found to be 0.801 (Fig. 3). No significant difference was found between the groups in terms of Aldrete recovery score values (p=0.627) (Fig. 4).

Of the adverse effects, nausea was observed as moderate in one patient each in group T and group D and was treated with antiemetic medications. It cannot be stated that the correlation between nausea and the groups is significant (p=1). Hypotension was observed only in two patients in the control group, namely group T (p=0.33). Complications such as vomiting, bradycardia, and allergic reaction were not detected in any of the patients.

Fig. 2 Graphical presentation of the VAS (visual analog scale) values of the groups. Data are mean (SD), * p<0,05 refers to between groups comparisons. † p<0,05 refers to comparison between group T and group D, ‡ p<0,05 refers to comparison between group P and group D. VAS, vizuel analog scale; postop, postoperative; T, tramadol group; P, paracetamol group; D, dexketoprofen trometamol group; min, minute; h, hour

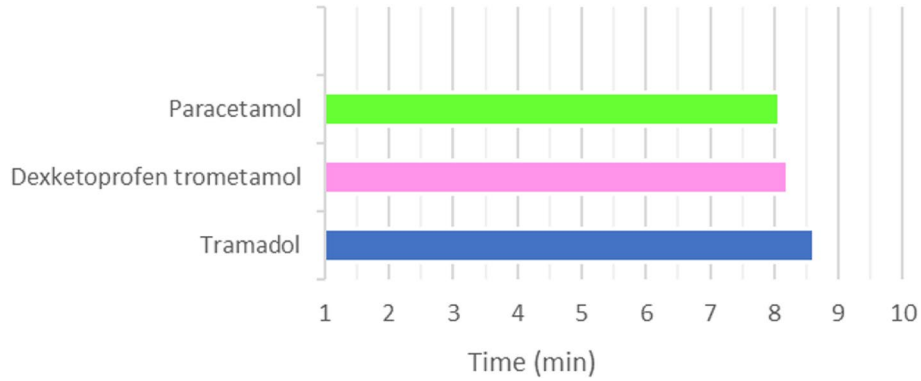

Fig. 3 Graphical presentation of recovery time to Aldrete recovery score point 10 (min). Data are mean (SD), p=0,801 refers to between groups comparisons, min, minute

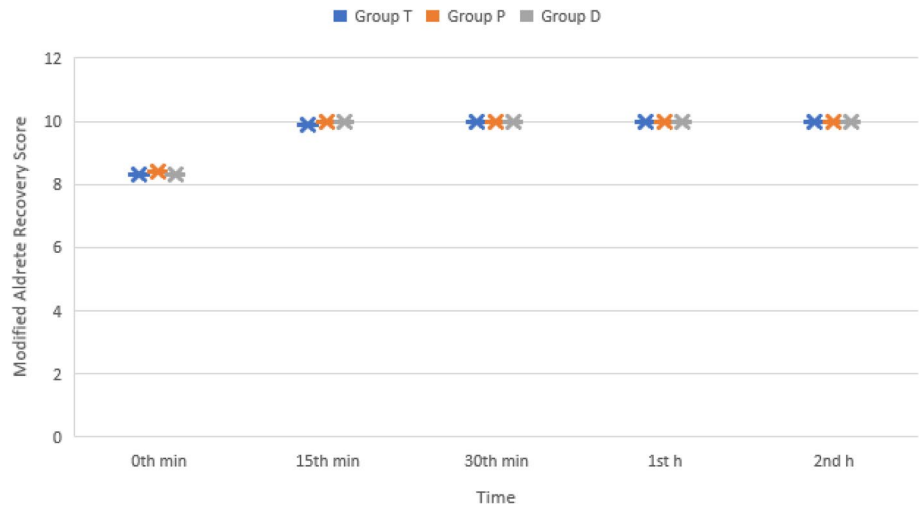

Fig. 4 Graphical presentation of the Modified Aldrete Recovery scores mean values of the groups. Data are mean (SD), T, tramadol group; P, paracetamol group; D, dexketoprofen trometamol group; min, minute; h, hour

Regarding the additional analgesia, when the groups were compared, it was determined that additional analgesia was used in 10 patients in group T, 14 patients in group P, and 3 patients in group D. The correlation between additional analgesia and the groups was found to be significant (p=0.017) (Fig. 5).

Besides, it was noticed that the correlation between the groups in terms of patient satisfaction was significant (p<0.01) (Fig. 6). No significant difference was found in the relationship between surgeon satisfaction and the groups (p= 0.096).

Discussion

Recent advances in anesthesia and surgical techniques have resulted in an escalation in surgical procedures worldwide as ambulatory practices, along with increased healthcare costs (Rawal 2001). The concept of ambulatory surgery emerged in the early 1990s to facilitate early recovery and discharge from the hospital and early resumption of normal daily activities following elective surgical procedures (Jafra and Mitra 2018).

In the practice of obstetrics and gynecology, the most prevalent outpatient anesthesia administration is the

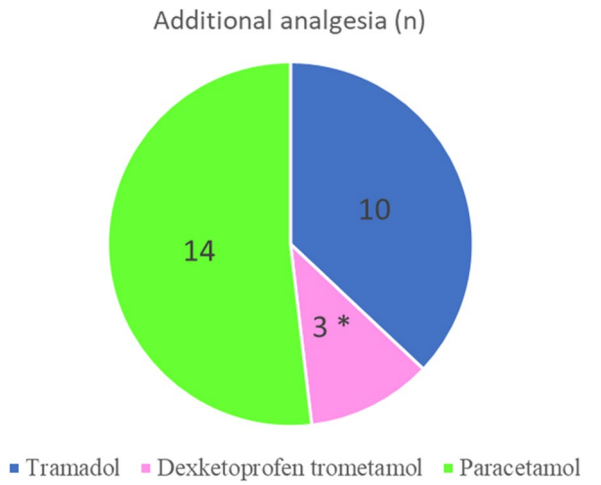

Fig. 5 Graphical presentation of additional analgesia. * $p<0,05$ refers to between groups comparisons

dilatation and curettage procedure. In this procedure, sedation anesthesia is often administered and propofol is one of the most popular intravenous agents used for this purpose. It requires us to pay as much attention as possible, especially to respiratory depression and cardiovascular collapse that can be induced by medications. The painful nature of the procedure makes the administration of analgesia inevitable during and following the procedure. Hitherto, various analgesia techniques and anesthetics have been utilized. Existing analgesic drugs and applications in the control of perioperative pain continue to develop rapidly.

Wall, Woolf, and Chong hypothesized in their study, which was based on scientific evidence and supported by animal experiment evidence, that a preemptive treatment could prevent the occurrence of central hypersensitivity, reduce the incidence of hyperalgesia, and reduce the intensity of postoperative pain. Remarkably, preemptive treatment is a procedure that starts before a surgical procedure and has been described as an antinociceptive intervention that is more effective than the same practice initiated postoperatively (Wall 1988; Woolf and Chong 1993; Pogatzki-Zahn and Zahn 2006).

We compared the impacts of dexketoprofen trometamol, which is routinely administered preemptively in our clinic for perioperative analgesia, on acute pain in minor gynecological procedures, by comparing it with paracetamol and control group tramadol.

Management of pain during curettage is of great importance for the patient. During dilation and curettage, the pain usually manifests itself in the cervical block injection procedure, with cervical dilation, suction aspiration, and postoperative uterine cramping (Meckstroth and Mıshra 2009). Even with conscious sedation, mean pain scores range from 3.4 to 4.9 at 10 cm on the VAS (visual analog scale) during dilatation, while it ranges from 3.8 to 7.1 cm with curettage (Mankowski et al. 2009). In a report involving 825 women who had a curettage in the first trimester, the mean pain score was determined to be 5.4 on an 11-point scale (Wiebe et al. 2005). Depression and anxiety scores were found to be positively correlated with pain perception (Rawling and Wiebe 2001). This points out the need for better analgesia for the revision curettage procedure. In our study, the younger age of the patients in the dexketoprofen trometamol group and the more intensive revision curettage procedure in this group indicates that more anxious patients and more painful procedures are common compared to the literature. Nevertheless, the similarity of induction and additional doses of propofol administered in all three groups under deep

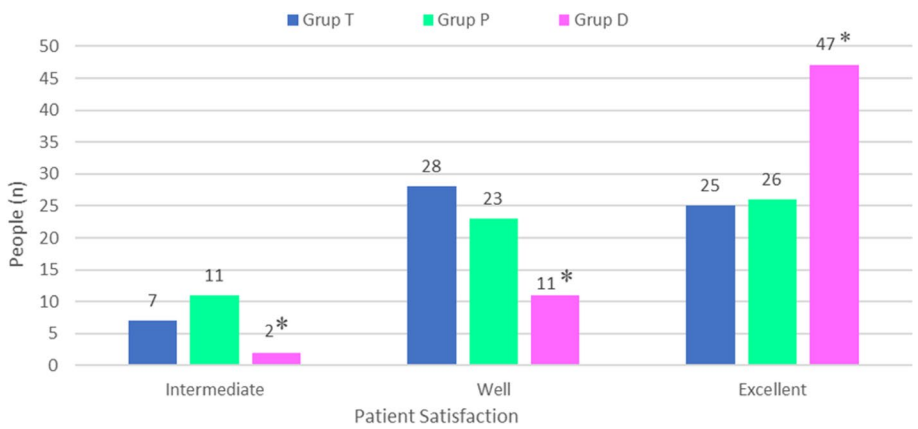

Fig. 6 Graphical presentation of patient satisfaction. * $p<0,05$ refers to between groups comparisons. T, tramadol group; P, paracetamol group; D, dexketoprofen trometamol group

sedation suggests that Dexketoprofen trometamol might play a role in sedation as well as its analgesic activity.

In our study, we assessed the impact of analgesics administered with propofol sedation anesthesia on intraoperative RSS (Ramsey sedation scores). In the study of Yazar et al., in which the postoperative analgesic efficacy of i.v. dexketoprofen trometamol in lumbar disc surgery was assessed, and RSS results were found to be similar to placebo (Yazar et al. 2011). In another study by Hanna et al. in which intramuscular dexketoprofen trometamol was compared with ketoprofen, it was revealed that the 2nd and 13th-hour values of patients who underwent major orthopedic surgery had higher sedation scores for both agents compared to placebo (Hanna et al. 2003). The results of the study conducted by Calvo et al. on dogs demonstrated that dexketoprofen and methadone produced similar sedation during orthopedic surgery with similar isoflurane concentration and similar doses of fentanyl and propofol (Navarrete-Calvo et al. 2016).

We consider that the increase in the sedation scores of the dexketoprofen trometamol group during the procedure compared to the control and paracetamol groups in our study might be due to the analgesic quality or pharmacokinetic drug-drug interactions that cause relaxation or sleep, as in the study of Hanna et al. (2003).

Kesimci et al. revealed that oral dexketoprofen trometamol 25 mg administered preemptively during the first 24 h following lumbar disc surgery was associated with a reduction of up to 35% in morphine consumption compared to placebo, whereas paracetamol 500 mg did not show the expected opioid-sparing effect comparatively (Kesimci et al. 2011).

In their comparative study of oral 25 mg dexketoprofen trometamol administered perioperatively in elective knee arthroplasty operations with placebo, Lohom et al. found out that the VAS scores at the postoperative 15th hour were lower in the dexketoprofen trometamol group and suggested that dexketoprofen trometamol significantly improved analgesia for 8 h and reduced the need for opioids (Iohom et al. 2002).

In another study by Ozer et al., it was observed that all groups that received dexketoprofen achieved significantly lower tramadol consumption for 24 h after surgery and during recovery room follow-ups, with lower VAS scores compared to the control group. They stated that the effects of intravenously administered dexketoprofen on postoperative analgesia and patient satisfaction in septorhinoplasty operations were favorable; however, no significant difference was found between preoperative and intraoperative practices (Ozer et al. 2012).

Likewise, in our study, similar to the literature, we observed that postoperative VAS values of dexketoprofen trometamol were significantly lower than both paracetamol and tramadol groups, and postoperative additional analgesia needs were significantly lower than both other groups.

Our study has several limitations. The study is a report of our own clinical experience. Data were collected retrospectively from clinical charts, forms, and electronic data designed for clinical purposes.

Conclusions

In conclusion, this study demonstrated that intravenous dexketoprofen trometamol administered preemptively in dilatation and curettage operations provides more effective sedation, decreases VAS scores in the postoperative period, increases patient satisfaction, and reduces the need for additional analgesia. There is a need for further larger prospective studies that focus on the potential effectiveness of dexketoprofen trometamol administration on sedation in different procedures.

Abbreviations

D/C: Dilatation and curettage; VAS: Visual analog scale; CNS: Central nervous system; NSAIDs: Nonsteroidal anti-inflammatory drugs; ASA: American Society of Anesthesiology; SAP: Systolic arterial pressures; DAP: Diastolic arterial pressures; MAP: Mean arterial pressures; HR: Heart rates; SpO_2: Peripheral oxygen saturation; SD: Standard deviation; RSS: Ramsey sedation scores.

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Authors' contributions

Author NY and author AŞ have given substantial contributions to the conception or the design of the manuscript, author BS to acquisition, analysis and interpretation of the data, author NY to review literatüre and write manuscript, author AD and author ZS to review critical. All authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was started as a retrospective study following the approval of the University of Health Sciences Kanuni Sultan Suleyman Training and Research Hospital Ethics Committee (KAEK/2018.4.15). Informed written consent to participate in the study was provided by all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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