



RESEARCH ARTICLE

The effect of intravenously given dexketoprofen trometamol on postoperative pain in ovariohysterectomized dogs

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Özet

Saritas ZK, Korkmaz M, Yilmaz O. Ovariohisterektomi yapılan köpeklerde intravenöz deksketoprofen trometamol'ün postoperatif ağrı üzerine etkisi. *Eurasian J Vet Sci*, 2014, 30, 1, 5-10

Amaç: Bu çalışmanın amacı ovariohisterektomi yapılan köpeklerde intravenöz deksketoprofen trometamolün postoperatif ağrı üzerine olan etkisinin araştırılmasıdır.

Gereç ve Yöntem: Ergin 17 dişi köpek rastgele iki gruba ayrıldı. Deksketoprofen trometamol (DEX) grubuna (n=10, 1mg/kg, IV) anesteziyenin uyanma sonrası deksketoprofen trometamol uygulanırken, kontrol (C) grubuna (n=7) herhangi bir analjezik uygulanmadı. Bütün köpeklerin ovariohisterektomileri median laparotomi ile aynı araştırmacı tarafından gerçekleştirildi. Postoperatif periyod süresince kalp frekansı, solunum sayısı ve vücut ısısı ölçüldü. Operasyon sonrası 0, 1, 4 ve 6. saat ağrı düzeyleri iki araştırmacı tarafından değerlendirildi. İki grubun ağrı düzeylerinin değerlendirilmesinde modifiye Melbourne Üniversitesi ağrı skalası (UMPS) kullanıldı.

Bulgular: Modifiye UMPS test sonuçlarına göre DEX grubunda postoperatif birinci saat ağrı skorunun istatistiksel olarak önemli derecede ($P<0.05$) azaldığı belirlendi. DEX grubunda 6. saat ağrı skorunun daha düşük olmasında rağmen diğer ölçüm zamanlarında önemli bir fark ($P>0.05$) belirlenmedi.

Öneri: Deksketoprofen uygulamasında vital bulguların stabil olması umut verici bir bulgudur. Ağrı skorunda gösterdiği klinik avantaj ile deksketoprofen köpeklerde postoperatif ağrı kontrolü için kullanım yeri bulabilir.

Anahtar kelimeler: Deksketoprofen, köpek, ovariohisterektomi, postoperatif ağrı.

Abstract

Saritas ZK, Korkmaz M, Yilmaz O. The effect of intravenously given dexketoprofen trometamol on postoperative pain in ovariohysterectomized dogs. *Eurasian J Vet Sci*, 2014, 30, 5-10

Aim: The aim of this study was to investigate the postoperative analgesic effect of dexketoprofen trometamol in dogs subjected to ovariohysterectomy.

Materials and Methods: Seventeen adult bitches were randomly allocated to two groups. Dexketoprofen trometamol (n=10, 1 mg/kg, IV) was administered to DEX group after recovery of anaesthesia, while those assigned to the control (C) group (n=7) were not given any analgesic after recovery of anaesthesia. The ovariohysterectomy procedure was performed on all dogs by the same researcher using a median laparotomy access. Heart rate (HR), respiratory rate (RR) and body temperature were measured during the postoperative period. Pain level was assessed by two researchers 0, 1, 4 and 6 hours after surgery. A modified University of Melbourne Pain Scale (UMPS) was used to evaluate pain in both groups.

Results: According to modified UMPS test, postoperative first hour pain score decreased statistically significant ($P<0.05$) in the DEX group. Although at 6th hour pain scale is lower in DEX group, no significant difference was ($P>0.05$) determined at other measurement times.

Conclusions: The presence of stable vital signs of dexketoprofen administration is a promising finding. Dexketoprofen may be used for postoperative pain management in dogs due to its clinical advantage shown by the pain scale.

Keywords: Dexketoprofen, dog, ovariohysterectomy, postoperative pain.



Introduction

The recovery time commonly delays under adverse effect of postoperative pain such as loss of appetite, self-trauma, maladaptive physiological responses or maladaptive behaviors (Mathews 2000, Pascoe 2000, Morgaz et al 2013).

Ketoprofen is a non-steroidal anti-inflammatory drug (NSAID) (Piparot et al 1997) which has been generally used as an analgesic in dogs (Grisneaux et al 1999, Lemke et al 2002, Morgaz et al 2013). Ketoprofen shows its activity by inhibiting cyclooxygenase enzyme-1 (COX-1) and/or COX-2, thereby inhibiting the synthesis of prostaglandins in inflammation, but also in the healthy tissue (Streppa et al 2002, Morgaz et al 2013). Dexketoprofen trometamol is an S-isomer of racemic non-steroidal anti-inflammatory drug ketoprofen (Mauleon et al 1996, Leman et al 2003).

The absorption of dexketoprofen is increased by the addition of trometamol in the formulation. Recently, it has been widely used in human medicine to prevent postoperative pain, since the parenteral form is commercially available (Mauleon 1996, Zippel and Wagenistz 2006). There are few reports available on analgesic efficacy of dexketoprofen in veterinary medicine (Morgaz et al 2013).

This study was designed to evaluate the effect of a widely used NSAID, dexketoprofen trometamol, on the control of postoperative pain in dogs undergoing ovariohysterectomy (OHE).

Materials and Methods

Animals

Seventeen adult bitches of various breeds were randomly divided into two groups. In the first group (Control group, n=7) the mean weight of dogs was 19.3 ± 7.5 kg and mean of ages was 2.8 ± 0.9 years and in the Dexketoprofen group (DEX, n=10) the mean weight was 23 ± 3.7 kg and the age was 3 ± 1 years. The ethical permission of this study was registered to the Local Ethics Committee of Afyon Kocatepe University by reference number (01.03.2011 and 07-11). Owners were informed and signed voluntary consent for the patients to be included in the study.

Anesthesia

Dogs were fasted 12 hours before the study. Atropine, 0.04 mg/kg (Atropin, Vetas, Turkey), was given via SC 30 minutes prior to general anesthesia. Premedication consisted in IM administration of 2 mg/kg xylazine HCl (Rompun 2%, Bayer, Germany) and general anesthesia was achieved with ketamine HCl (Alfamine 10%, Ege Vet, Turkey) 15 mg/kg IM.

Surgical procedure

Following preparation for aseptic surgery, OHE was performed through a ventral midline approach. All OHE procedures were performed by same practitioner to avoid bias between groups. Procedure duration was 30 ± 5 and 29 ± 8 min, respectively, in the control and DEX groups.

Vital parameters

Heart rate (HR), respiratory rate (RR) and body temperature were measured preoperatively at baseline (T0), and at postoperative 0 (T1), 30 (T2), 60 (T3), 90 (T4), 240 (T5) and 360 (T6) minutes.

Postoperative pain control

Postoperatively 1 mg/kg IV dexketoprofen trometamol was applied to the bitches in the DEX group and no additional dose applied until 6th hour. After 6th hour, dexketoprofen trometamol was applied intravenously bitches that suffering from pain in both of the groups.

Pain assessment

The degree of pain was assessed at 0, 1, 2, 4 and 6 hours after surgery by the same researchers. The modified University of Melbourne Pain Scale was used of this evaluation in all dogs (Table 1).

Statistical Analysis

Data were analyzed with Student's t-test for paired samples and ANOVA for repeated measurements (SPSS for Windows, 16.0). Values were described by their average mean \pm Standard Deviation (SD). A p-value less than 0.05 was considered to be statistically significant

Results

Vital parameters of the groups were shown in Table 2. Heart rates, body temperatures and respiratory rates were between normal ranges before the operation. At the postoperative 0. minute and T4 heart rate was significantly ($P < 0.05$) decreased in the Control group and significantly ($P < 0.05$) increased at T5 and T6. Respiratory rate was significantly increased in the Control group at T4 and T6 times ($P < 0.05$). Body temperatures were in normal ranges at measured times.

Postoperative pain level was evaluated with Modified UMPS (Table 1) and the results were shown in Table 3 and Figure 1. Postoperative pain was significantly ($P < 0.05$) decreased only at postoperative first hour in DEX group (Control and DEX group; 7.1 ± 1.2 and 4.9 ± 1.5). There was no significant



Table 1. Modified University of Melbourne Pain Scale (Odette and Lesley 2013).

Dog Name/ID: _____ Date: _____ Time Point: _____	
Breed: _____ Total UMPS Score: _____	
Category and descriptor Score _____	
From outside the cage:	
Vocalization (choose only one)*	
Not vocalizing	0
Slight vocalization but dysphoric	1
Intermittent vocalization	2
Continuous vocalization	3
Posture	
a) Guarding or protecting affected area	2
b) Position (choose only one)	
Lateral recumbency	0
Sternal recumbency	1
Sitting, standing, or comfortable	1
Standing with head hanging	2
Moving	1
Abnormal posture and/or uncomfortable, continuous position change	2
Activity (choose one)	
At rest	
Sleeping	0
Semi-conscious	0
Awake	1
Eating	0
Restless (pacing continuously; getting up and down)	2
Rolling and thrashing	3
From inside the cage:	
Mental status (choose only one)** Baseline minus current score = overall score	
Too sedate to evaluate or dysphoric	0
Submissive	1
Uninterested in people (unusual for this dog)	2
Overtly friendly	3
Wary or Aggressive	4
Response to palpation (choose only one)***	
Normal, allows palpation of surgical site	0
Allows but then moves away, tenses or looks when surgical area touched	1
Increased whining or painful expression when surgical area touched	2
Will not allow general surgical area to be touched	3
Vocalization (choose only one)*	
Not vocalizing	0
Vocalizing but responds to quiet voice and/or stroking	1
Vocalizing when touched	2
Intermittent vocalization	2
Continuous vocalization	3

The minimum possible score is 0; the maximum possible score is 20. * Does not include alert barking.

** For this category, score recorded is the score obtained after surgery minus the score obtained before surgery. *** Palpate around the general surgical area starting at the dorsal end and working toward incision site.



Table 2. Vital parameters in Control and Dexketoprofen group (mean±SD).

Time/Group	Heart Rate (Pulse/Min)	Respiratory Rate (Min)	Body Temperature (°C)
T0 / Baseline			
Control	85.8±12.4 ^{abc}	19.4±2.5	38.6±0.9 ^a
Dexketoprofen	88.2±17.2	16.4±3.9 ^{ab}	38.3±0.3 ^a
T1			
Control	77.7±9.7 ^{bc}	18.5±2.7	38.2±0.8 ^{abc}
Dexketoprofen	85.6±13.8	16.4±3.1 ^{ab}	37.8±0.3 ^{bc}
T2			
Control	74.7±5.3 ^c	17.1±2.7	37.8±0.5 ^{bc}
Dexketoprofen	83.2±9.9	15.6±3 ^b	37.4±0.4 ^c
T3			
Control	79.5±6.1 ^{abc}	18.5±7.4	37.7±0.4 ^c
Dexketoprofen	87.6±12.8	16.5±3.02 ^{ab}	37.6±0.5 ^c
T4			
Control	83.5±10.7 ^{abc*}	20.4±6.1 [*]	37.7±0.4 ^c
Dexketoprofen	89.2±12.1	17.2±2.8 ^{ab}	37.8±0.6 ^c
T5			
Control	90.5±17 ^{ab*}	19.7±3.3	38.1±0.4 ^{abc}
Dexketoprofen	84.3±8.9	19.1±2.6 ^a	38.2±0.7 ^{ab}
T6			
Control	92±9.8 [*]	20.5±1.5 [*]	38.5±0.4 ^{ab}
Dexketoprofen	88.1±14.5	18.3±2.1 ^{ab}	38.4±0.2 ^a

^{a,b,c} Indicates a statistical difference between or among values marked by the different letter in the same column within groups (P<0.05). *Indicates a statistical difference between groups (P<0.05).

difference (P>0.05) between the groups at other measurement times but at the 6th hour pain scale was lower in the DEX group

Discussion

Ovariohysterectomy which causes moderate or severe postoperative pain, is a surgical procedure widely used for evaluating analgesic effect in dogs (Slingsby et al 2011, Morgaz et al 2013). Surgical trauma activates COX-2 and prostaglandin synthesis, respectively intervening in peripheral and central nervous system sensitization (Kara et al 2011). The main enantiomer of ketoprofen is responsible for analgesic effect and this enantiomer is known as dexketoprofen [S(+)-ketoprofen] which cause fewer adverse effects than racemic ketoprofen (Mauleon et al 1996, Neirinckx et al 2011, Morgaz et al 2013). In human practice, dexketoprofen is used for postoperative analgesia by the oral (Iohom et al 2002), intramuscular (Hanna et al 2003, Jamdade et al 2011) or intravenous routes (Zippel and Wagenitz 2006, Yazar et al 2011).

In this study, dexketoprofen trometamol was applied to DEX group for pain control and the bitches were observed for 6 hours. In the study by Morgaz et al (2013), buprenorfin, dexketoprofen or tramadol were given preoperatively to prevent postoperative pain in dogs. HR and RR were recorded every 15 min for 120 min during the procedure. No statistical difference was observed among the measurements of the three groups. In our study, HR, RR and body temperature were recorded before surgery, 0, 30, 60, 90, 240 and 360 minutes thereafter. At the postoperative 0. minute and T4 heart rate was significantly (P<0.05) decreased in the control group and significantly (P<0.05) increased at T5 and T6. And all these measurements were in normal ranges. Intraoperative measurements were disregarded in this study due to the short surgery duration (average 30 min.). Body temperature, recorded in our study, was not available in the study of Morgaz et al (2013). Body temperatures were in normal ranges at measured times.

Ketoprofen is used postoperatively in dogs for its non-se-



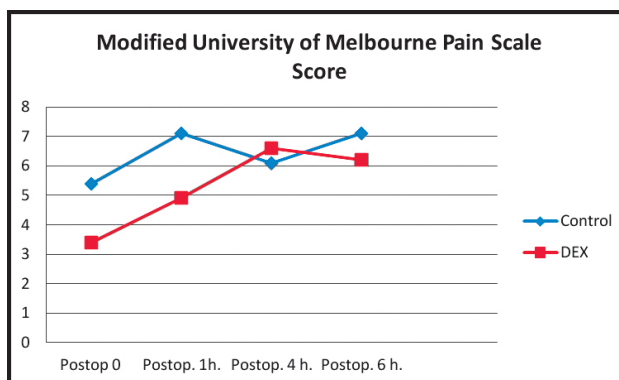


Figure 1. Postoperative pain score in Control and Dexketoprofen (DEX) group.

lective COX inhibition (Lamont and Mathews 2007, Morgaz et al 2013). Luna et al (2007) studied the negative effects of the chronic use of ketoprofen, etodolac, meloxicam, caprofen and flunixin. They reported that ketoprofen and etodolac increased clotting time, predisposing patients to gastrointestinal bleeding. This effect on haemostasis also creates a surgical handicap by increasing the chances of intraoperative bleeding (Lamont and Mathews 2007, Morgaz et al 2013). Some authors reported, however, that this defect was not clinically relevant (Deneuche et al 2004, Morgaz et al 2013). In human medicine, dexketoprofen is considered an excellent analgesic (Yazar et al 2011).

In the current study, vital parameters showed limited variation in dogs given postoperative dexketoprofen. Adverse effects linked to NSAID are primarily renal, gastrointestinal and coagulation disorders. None of these were encountered in the first week of the study by Morgaz et al (2013). No intraoperative or postoperative bleeding or diarrhoea was seen in the Control and DEX group in our study.

Pain measurement is a subjective procedure in veterinary medicine, as it may be in neonatology. The veterinary anaesthesiologist is obliged to evaluate behaviour to assess postoperative pain (Morgaz et al 2013). Different pain scales

are used in veterinary medicine. Moll et al (2011) used SC and transdermal buprenorphin as a pre-emptive analgesic in dogs undergoing OHE, evaluating postoperative pain by modified UMPS. A study of epidural morphine and transdermal fentanyl in OHE dogs (Pekcan and Koc 2010) postoperative analgesic efficacy was estimated by a modified scale used by both Grisneaux et al (1999) and Robinson et al (1999). As for Morgaz et al (2013), they used two different evaluation systems for postoperative pain evaluation: A dynamic and interactive visual analogue scale (DIVAS) and the short-form Glasgow Composite Measure Pain Score (CMPS-SF). In this study the modified UMPS was used for 6 hours following surgery; the score was found significantly lower in the DEX group compared to controls at 1th and 4th hours. We previously found that dexketoprofen decreased the pain scores significantly in ovariohysterectomized bitches (unpublished data).

Conclusion

Considering its ease of administration, the stability of vital signs and the lower pain scores in DEX group, it may be concluded that dexketoprofen trometamol may be used management of postoperative pain in dogs. Moreover it is concluded that new studies needed to estimate postoperative analgesic requirement with longer observation periods.

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Table 3. Postoperative modified University of Melbourne Pain Scale scores in Control and Dexketoprofen Group (Mean±SD).

Time	Control Group (n=7)	Dexketoprofen Group (n=10)
Postop. 0 min+	5.4±1.5	3.4±1.3
Postop. 1 h	7.1±1.2	4.9±1.5*
Postop. 4 h	6.1±2.4	6.6±3.1
Postop. 6 h	7.1±2.9	6.2±2.8

+: 0. min: dexketoprofen administration. *: Indicates a statistical difference between groups (P<0.05).



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