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EFFICACY OF PRE-EMPTIVE MELOXICAM AND LOCAL ANESTHESIA IN LAME DAIRY COWS UNDERGOING RESECTION OF THE DISTAL INTERPHANAGEAL JOINT

BY

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ABSTRACT

The present study aimed to determine the analgesic effect of meloxicam administration on the stress and pain response induced during resection of the distal interphalangeal joint (DIJ) in lame dairy cows. In a prospective, blinded, randomized and placebo-controlled clinical trial, 19 German Holstein Frisian cows were used. All cows suffered from unilateral lameness due to septic arthritis of the coffin joint. Cows were allocated into either meloxicam group (M, n= 9) or control group (P, n= 10) and received an intravenous injection (IV) of meloxicam in a dose of 0.5 mg kg^{-1} BW 15 min before surgical resection of the DIJ or an equal volume of saline solution. All cows received a retrograde intravenous local anaesthesia (LA; 20 mL 2% procaine). In a regular pre-set time intervals (15 minutes before drug application until 5 hours post-surgery) Heart rate (HR), respiratory rate (RR), mean arterial blood pressure (MAP), body temperature, arterial blood gases, plasma levels of cortisol, glucose, lactate and non-esterified fatty acids (NEFA) were measured as well as clinical signs of analgesia. Pre-emptive administration of meloxicam provoked no significant difference between both groups during the surgical intervention while in the immediate post-operative period (5 hours post-surgery) it demonstrated significant alleviation of the surgical stress and produce additional analgesic effect to LA by reduced plasma level of cortisol, NEFA and lactate. It was concluded that, pre-emptive administration of meloxicam in dairy cows

undergoing resection of the DIJ can alleviate surgical stress and is able to produce additional analgesic effects to LA without provoking considerable adverse effect.

Key words: analgesia, cattle, distal interphalngeal joint, meloxicam, pain, stress.

INTRODUCTION

Lameness in cattle has a great economic impact on the dairy industry; it is ranked as the third most important problem after mastitis and reproductions disorders **(Clarkson et al. 1996).** With the common claw disorders profound septic inflammatory and necrotic processes of the corium or laminar tissues can develop. These septic processes can spread to neighbouring structure like the flexor tendons, podotrochlear bursa, distal and middle phalanges, distal sesamoid bone and may result in septic arthritis of the distal interphalangeal joint **(Starke et al. 2007).** The claw health disorders lead to traumatisation of tissue which is perceived by the affected animal as a pain **(Hassal 1993).**

Analgesia and anaesthesia during orthopaedic surgery of extensive claws disorders alleviate the surgical stress as well as reduce and abolish the perception of pain during surgery **(Whay et al. 2005)**. For optimal pain relief it has been recommended to combine sedation, local anesthesia and a non steroidal anti-inflammatory drug (NSAID) as suggested in several surgical husbandry procedures in cattle **(McMeekan, et al. 1998; Sylvester et al. 1998; Stafford et al. 2002; Offinger et al. 2013).**

Retrograde intravenous application of local anaesthetic proved to successfully diminish pain caused by surgical manipulation for a period of approximately 2 hours **(Antalovsky, 1965, Rizk *et al.*, 2012a, Offinger et al., 2013)**. After this period the animal is left without pain relief if no long-lasting analgesic is applied. It also allows intravenous administration of a water soluble antibiotic together with the local anaesthetic **(Stanek 1994).** Meloxicam is a NSAID of the oxicam class, which preferentially inhibits the synthesis of the inducible cyclo-oxygenase (COX-2) **(Heinrich *et al.*, 2009)**. Repeated meloxicam application demonstrated effective analgesia in the post surgical period after resection of septically infected coffin joints in dairy cows without indications of evoking adverse effects on abomasal integrity **(Offinger et al.2013).**

We hypothesized that the analgesic effect of meloxicam would alleviate stress response and has additional analgesic effect to local anaesthesia on the pain perception in lame dairy cows undergoing resection of coffin joint. Thus, the aim of the study was to evaluate the influence of pre-emptive meloxicam administration on cardio-respiratory, hormonal and metabolic stress response intra-operatively in lame dairy cows undergoing resection of the septically infected coffin joint.

MATERIALS AND METHODS

The experimental protocol was approved by the Animal Care Committee of the Federal State of Lower Saxony, Germany (research permit number 33.9-42502-04-08/ 1462).

Animal's inclusion criteria

The study was conducted on 19 clinically lame German Holstein Frisian cows (mean ± SD; age = 5.7 ± 2.8 yr, BW 536 ± 98 kg). All cows suffered from lameness due to septic arthritis of the coffin joint involving one claw on one hind limb and were referred to the Clinic for Cattle, University of Veterinary Medicine Hannover, Germany, for adequate surgical claw treatment. Cattle were excluded if profound defects at the claw of the opposite limb or at both claws of the affected limb were found or if the animals suffered from diseases of the other organ. According to the owner no steroidal or nonsteroidal analgesics were given within one week before admission to the clinic.

Experimental Procedure and Treatments

The present trial was performed as blinded, randomized, prospective and placebo-controlled clinical study. Septic arthritis of the coffin joint was diagnosed *the day before surgery* by means of clinical examination, radiography, arthrocentesis and sonography **(Starke *et al.*, 2007)**. All examinations were performed in lateral recumbency (LR) on a surgical tipping table without prior application of sedatives. After diagnosis of septic arthritis cows were fitted with an indwelling jugular vein catheter (Baruth /Mark, Germany).

On the day of operation: one hour before commencing the operation, the arterial catheter (Vygon®, France) was inserted into right caudal auricular artery using the Seldinger technique, secured with tape, and immediately connected to a calibrated electro-mechanical transducer via a fluid filled extension set. For maintaining patency catheters were flushed with

heparinised 0.9% saline solution after insertion and each blood sampling. Catheters were removed with the last blood sampling.

Cows were randomly allocated to either the meloxicam group (M; n = 9) or placebo (control) group (C; n = 10), receiving meloxicam (0.5 mg/kg BW IV; Metacam, Boehringer Ingelheim, Germany) or an equal volume of sterile isotonic saline solution (0.9% sodium chloride solution IV, NaCl 0.9 % ad.us.vet. B.Braun), respectively. The treatment took place in the stable before surgery. Fifteen min after drug application cows were moved to the surgical room and turned into LR for surgical intervention. All cows, regardless of their allocated group, received a retrograde intravenous local anaesthetic (20 mL 2% procaine) combined with 3,000,000 U sodium penicillin G dissolved (Dietz *et al.,* 1980) in 10 mL sterile sodium chloride solution (300,000 U/mL, Aulicin Albrecht, Germany) using the technique of **Antalovsky (1965)**. Thereafter, surgical resection of the affected coffin joint was performed **(Starke *et al.,* 2007).** After turning into standing position cows were moved back to the stable.

All cows received systemic antibiotic treatment (10mg/kg ampicillin trihydrate SC, Alvetra, Germany,) twice daily for 5 days.

Measured parameters

Clinical signs

Salivation and teeth grinding were scored (score0: no change, 1: mild, 2: moderate, 3: severe and 4 highly severe).

Mean arterial blood pressure (MAP)

Mean arterial blood pressure was continuously recorded by means of a fluid filled extension connected to the arterial catheter and a mechanical-electrical transducer (Supermon Module 7272, Kontron instruments, England). The zero pressure point was taken at the level of the scapulo-humeral joint in the standing animal and the centre of the thorax in LR.

Heart rate (HR) was recorded by counting the heart beats in one min by auscultation,

Respiratory rates (RR) were measured by counting thoracic excursions for a period of 1 minute.

Rectal temperature was recorded by a digital thermometer.

Blood gas analysis of the arterial blood which collected anaerobically in heparinised syringes from catheter and placed on ice after withdrawal and it was analysed (Rapid lab.™ 348, Bayer health care Diagnostic) within 15 min after collection. Results were corrected to body temperature and haemoglobin level which was measured automatically (Cell tac MEK, Nihon- Kohdan). Arterial partial pressure of oxygen tension (PaO2, mmHg), and carbon dioxide tension (PaCO2, mmHg) were recorded as well as oxygen saturation (SaO2 %), and blood Ph.

Hormonal and metabolic parameters

Heparinised venous blood samples were collected and centrifuged at 1.500g (for 10 min) immediately after collection. Plasma was stored at -20°C until analysis of cortisol (Chemiluminescent enzyme immunoassay, Siemens, Germany). Plasma glucose, nonesterified fatty acids (NEFA) and lactate were measured on an automated analyser (ABX Pentra 400, France) using commercial test kits.

Study protocol

Baseline values were determined 15 min after arterial catheter insertion. Cardiopulmonary parameters, blood samples for analysis of blood gases and endocrine-metabolic parameters were evaluated 10 and 45 minutes after LR on the surgical tipping table and at thereafter all the mentioned parameters were recorded at 30, 60, 120, 180 and 300 minutes post-surgery.

Statistical Analysis

Statistical analyses were performed with SAS (version 9.2; SAS Institute, 2002). All parameters were tested for deviation from normal distribution within groups by means of the Shapiro-Wilk-Test (Proc Univariate). The level of statistical significance was set at $P < 0.05$.

RESULTS

Clinical signs

There was no significant ($P < 0.05$) different between both treated groups in the degree of salivation and teeth grinding, while the later was lower but not significant in meloxicam treated cows.

Endocrine-metabolic stress response

Average mean plasma concentration of cortisol were significantly higher in both treatment groups during the surgical resection of the infected coffin joint compared to baseline, while it reduced significantly after meloxicam pre-treatment at 2 and 5 hours post-surgery compared to controls (P= .01 and .005 respectively; Table 1).There were a significant group (P= .048) and time (P <.0001) effects while no group x time effect were found for plasma cortisol.

During surgery, the mean plasma glucose was significantly higher in meloxicam treated cows compared to baseline. While in controls it showed a significant increase for one hour post-surgery compared to baseline (Table 1). There was a significant time effect (P <.0001) while no group and group x time effects.

Mean plasma NEFA and lactate concentrations were significantly higher in both pre-treated cows groups during surgical intervention compared to baseline and continued for one hour post-surgery in meloxicam treated cows (Table 1). In the immediate post-operative period (for 5 hours) both cows groups showed a significantly decrease in plasma lactate concentration compared to baseline (Table 1). There was a significant time effect (P <.0001) for plasma NEFA and lactate concentration while no group and group x time effects.

Cardio-respiratory parameters

The mean average of HR and body temperature were not affected by meloxicam treatment and there was no significant different between both groups (Table 2). Statistically, there was a significant time effect (P = .017) for body temperature while no group and group x time effect were found.

Mean RR increased significantly in meloxicam treated cows during the surgical intervention on the tipping table, while it was reduced significantly in the same group in the immediate period post surgery (for 5 hours after standing; Table 2). There was a significant time effect (P <.0001) for RR while no group and group x time effect were found.

Cows in both groups showed a significantly higher mean MAP during the time of surgical resection of coffin joint compared to baseline values (Table 2). The median average of MAP were significantly (P =.03) reduced 2 hours post-surgery after meloxicam treatment compared to controls at the same time. There was a significant time effect (P =.002) for MAP while no group and group x time significant effect were found.

Mean arterial Ph remained nearly unchanged during both treatment protocols throughout the experimental period (Table 3).

During the period of surgical intervention, we found a significant reduction in the mean PaO_2 and SaO_2 compared to baseline values in both group. While no animals after meloxicam and placebo treatment showed SaO_2 values of less than 92% (Table 3). There were a significant time effect (P <.0001) for both PaO_2 and SaO_2 while no group and group x time effect. The mean $PaCO_2$ remained almost unchanged in placebo treated cows, while it showed a significant reduction during the surgical intervention in meloxicam treated cows compared to baseline values (Table 3). It was significantly decreased (P = .02) after meloxicam treatment 30 min post-surgery compared to controls.

DISCUSSION

The objective were to study the effect of pre-emptive meloxicam administration before resection of the sepically infected coffin joint in lame dairy cows on surgical stress alleviation and to evaluate its additional analgesic effect to local intravenous analgesia. Because it is well known that claw surgery for severe septic claw disorders with only local anaesthesia causes pain and an acute stress response **(Whay et al., 2005; Huxley& Whay 2006).**

Meloxicam is a selective COX-2 inhibitor derived from enolic acid**.** It has been documented to be effective in decreasing the local inflammatory response in a shoulder synovitis model in dogs and in attenuating stifle synovitis. Meloxicam significantly reduced specific lameness, general stiffness, painful rise, and exercise intolerance of the dogs **(Doig et al., 2000)**. To the authors knowledge, this is the first report describe the effectiveness of meloxicam on stress alleviation and pain perception in lame dairy cows with septic arthritis of the coffin joint .

This study demonstrated a significant rise in plasma cortisol concentration in both treatment groups during surgical intervention, which itself is a stressful and painful procedure, after the LA resection of the joint were performed and naturally nociceptors were stimulated in surgical area. Thus, we assume that the HPA-axis was activated despite meloxicam pre-treatment by strong stimulation of nociceptors during the surgical intervention of the joint, although all cows received regional intravenous anaesthesia, which is seen as the most effective analgesic regime in surgeries on the distal limb in cattle **(Antalovsky, 1965; Nuss,**

2004). Higher plasma cortisol concentration after septic claw disorders was reported in cows **(El-Ghoul & Hofmann 2002)** and in sheep **(Ley et al., 1991)**. Furthermore, we found that pre-emptive meloxicam administration induced a significant reduction in plasma cortisol in the immediate post-operative period compared to controls, which probably was an indicative that meloxicam can alleviate stress and excitement as well as decrease pain perception in the postoperative period. Similar results were also observed in clinical evaluation of postoperative pain using meloxicam in dogs **(Deneuche et al., 2004)** and cattle **(Rizk et al.,2012b, Offinger et al., 2013)** undergoing orthopaedic surgery. Changes in animal behaviour and clinical parameters such as heart rate are seen as more sensitive indicators of pain than plasma cortisol **(Anderson and Muir, 2005).**

In the present study, both treated cows groups showed in average unchanged HR also both groups showed a significant increase of MAP during surgical intervention. We attribute the mild hypertension to the surgical stress induced secretion of catecholamine during resection of the coffin joint inducing peripheral vasoconstriction and an increase in systemic vascular resistance **(Boandl et al. 1989; Tagawa et al.1994; Rizk et al. 2012a,b)**. In the immediate period post-surgery meloxicam induced a significant decrease in the MAP.

The painful surgical intervention of the claw induced an increase in RR in cows although meloxicam treatment, which my related to excitement, discomfort or struggling during restraint also attributed to the severity of pain during surgery. Similar observation previously reported in cattle **(Klein and Fisher 1988, Rizk et al., 2012a,b)** and ponies **(Hall 1984)** undergoing different surgical interventions in lateral and dorsal recumbency.

Despite the increased RR in both treated cows groups during surgery PaO2 and SaO2 fell whereas PaCO2 remained almost unchanged. Large animals are particularly susceptible to compression of the lung because of the weight of abdominal viscera pressing against the diaphragm during LR **(Wagner et al. 1990)**. Hypoventilation of compressed lung areas and ventilation–perfusion mismatch during lateral recumbency may lead to insufficient oxygenation of the blood. To shunt the blood into well ventilated areas of the lung, vasoconstriction will occur in the hypoxic lung areas **(Hornof et al., 1986)** which may result in mixing un-oxygenated blood from hypoxic lung areas and well-oxygenated blood from well-ventilated lung areas in the left side of the heart **(Wagner et al. 1990)**. As a result, the PaO2 can decrease by 35 % in cows positioned in dorsal or lateral recumbency **(Wagner et al. 1990; Rizk et al.,2012a).**

The stress provoked cortisol and catecholamine release commonly induces lipolysis and thereby increased plasma NEFA concentration **(Chacon et al.2005)**. In this study, the mean plasma NEFA concentration was significantly higher in both groups during surgical resection of the coffin joint and for one hour post surgery, this reflect that meloxicam has no effects on liypolysis process and this increase was attributed to the stress and severity of pain induced catecholamine release.

In this study we found a significant increase in plasma lactate during claw surgery , a mild increase in blood lactate concentration were reported in cattle during different surgical intervention such as claw treatment**(El-Ghoul & Hoffmann 2002)** and abdominal surgeries **(Mudron et al.2005)** and were attributed to stress induced vasoconstriction and reduced tissue oxygenation.

CONCLUSION

Result of this study indicated that, the pre-emptive intravenous meloxicam treatment in dairy cows undergoing resection of the distal interphalangeal joint due to septic arthritis can alleviate experienced surgical stress and has little additional analgesic effects to local anaesthesia at the immediate post-operative period without provoking considerable adverse effect.

Acknowledgement

Table 1. Results of Plasma glucose, cortisol, lactate and non-esterified fatty acid (NEFA) concentrations in dairy cows measured at baseline, (10 and 45 min) after lateral recumbency(LR) and at 30, 60, 120,180 and 300 min after surgery. All cows received IVRA with 20ml of procaine and either meloxicam (0.5 mg kg⁻¹ BW; IV; N=9) or sodium chloride (controls; N=10) in an equal volume 30 min before the intervention.

Variable	Groups	Baseline	LR+10	LR+45	Stand +30	Stand +60	Stand +120	Stand +180	Stand +300	Main	effects
Glucose	Controls	4.09[b]	4.13	4.55	**5.01**	4.86	**4.57**	4.08	4.12	G	.94
		(3.7-5.4)	(3.7-5.6)	(3.9-5.8)	(3.8-6.2)	(3.2-6.3)	(4.1-5.5)	(3.8-6.1)	(3.8-6.2)		
[mmol L⁻¹]	Meloxicam	4.13	4.19	**4.67**	**4.98**	**4.82**	4.55	4.36	**4.58**	T	<.0001
		(3.8-4.9)	(3.9-4.7)	(4.1-4.9)	(4.2-5.5)	(3.9-5.3)	(3.6-5.1)	(3.5-5.1)	(3.8-4.8)		
	Group difference[a]	.91	.73	.54	.81	.73	.37	.87	.63	G x T	.67
Cortisol	Controls	8.25	39.9	33.9	13.02	8.95	13.9	8.35	13.1	G	.048
		(7.0-12.8)	(21.2-77.4)	(13.4-127.5)	(6.65-62.1)	(5.2-29.3)	(3.4-30.4)	(2.7-28.2)	(10.1-38.9)		
[ng ml⁻¹]	Meloxicam	5.95	44.2	**33.2**	15.7	6.5	5.3	8.3	8.2	T	<.0001
		(2.2-17.5)	(22.9-71.3)	(17.9-73.3)	(4.2-31.3)	(2.9-15.4)	(1.5-14.4)	(3.3-12.4)	(4.9-16.7)		
	Group difference	.21	.65	.72	.54	.17	.01	.42	.005	G x T	.079
Lactate	Controls	0.70	**0.95**	**1.12**	0.78	0.60	**0.50**	0.47	0.44	G	.229
		(.47-1.23)	(.81-1.51)	(.63-2.02)	(.48-1.64)	(.36-1.08)	(.27-.73)	(.25-.85)	(.23-1.35)		
[mmol L⁻¹]	Meloxicam	0.61	0.86	0.76	0.76	0.58	0.48	**0.36**	**0.36**	T	<.0001
		(.46-1.22)	(.70-1.66)	(.58-1.82)	(.54-1.07)	(.38-.95)	(.34-.69)	(.22-.55)	(.20-.52)		
	Group difference	.26	.90	.27	.27	.36	.57	.19	.17	G x T	.693
NEFA	Controls	159.2	**377.5**	490	**228.7**	216.5	181	186.5	**237.5**	G	.777
		(46-446)	(98-750)	(127-963)	(84-1030)	(58-716)	(95-496)	(62-663)	(66-840)		
[µmol L⁻¹]	Meloxicam	150	**351**	**536.5**	**224.5**	176	168	183	217	T	<.0001
		(51-522)	(256-586)	(360-747)	(91-608)	(53-778)	(45-472)	(47-484)	(64-506)		
	Group difference	.73	.89	.79	.35	.79	.98	.87	.62	G x T	.585

2f-analysis of variance: T = time effect; G = group effect; G x T = group x time effect; Bold values differ significantly at specific time points.

a: P-value of group differences in corresponding means (P < 0.05) from baseline.

b: medians (with 25% and 75 percentils)

Table 2. Results of Heart rate(HR), respiratory rate (RR), mean blood pressure (MAP) and body temperature in dairy cows measured at baseline, (10 and 45 min) after lateral recumbency(LR) and at 30, 60, 120,180 and 300 min after surgery. All cows received IVRA with 20ml of procaine and either rmeloxicam (0.5 mg kg^{-1} BW; IV; N=9) or sodium chloride (controls; N=10) in an equal volume 30 min before the intervention.

Variable	Groups	Baseline	LR+10	LR+45	Stand +30	Stand +60	Stand +120	Stand +180	Stand +300	Main Effects	
HR Beat/ min	Controls	79[b] (64-94)	78 (64-102)	77 (61-100)	81 (66-98)	76 (68-104)	80 (68-92)	77 (64-88)	80 (64-92)	G	.689
	Meloxicam	71 (68-86)	80 (66-96)	**82** (68-98)	**82** (62-94)	76 (56-100)	72 (64-104)	76 (68-92)	72 (68-88)	T	.22
	Group difference[a]	.26	.83	.64	.83	.54	.62	.87	.22	G x T	.567
RR Breath/min	Controls	43 (23-78)	44 (27-70)	42 (34-78)	45 (19-72)	38 (20-68)	42 (20-64)	38 (20-68)	42 (20-68)	G	.916
	Meloxicam	48 (21-66)	**54** (36-72)	**54** (36-74)	44 (32-58)	44 (24-52)	44 (20-52)	44 (20-52)	44 (22-52)	T	< .0001
	Group difference	.75	.31	.29	.95	.48	.45	.95	.71	G x T	.066
MAP mmHg	Controls	113 (103-136)	**139** (106-157)	**136** (114-158)	121 (96-160)	118 (98-160)	**145** (108-171)	**134** (100-156)	**130** (100-145)	G	.084
	Meloxicam	114 (105-141)	**130** (117-151)	**131** (109-151)	114 (95-131)	115 (96-146)	117 (110-139)	122 (111-158)	122 (94-153)	T	.002
	Group difference	.98	.59	.40	.25	.45	.03	.24	.29	G x T	.689
Temperature C°	Controls	38.8 (38.5-39.3)	38.9 (38.4-39.3)	38.9 (38.6-39.3)	38.8 (38.3-39.5)	38.8 (38.4-39.3)	38.8 (38.2-39.3)	38.9 (38.4-39.4)	39.0 (38.5-39.6)	G	.77
	Meloxicam	38.9 (38.7-39.5)	39.1 (38.8-39.4)	38.9 (38.4-39.4)	38.9 (38.7-39.4)	38.8 (38.3-39.2)	38.9 (38.5-39.2)	**38.9** (38.5-39.3)	39.0 (38.3-39.7)	T	.017
	Group difference	.22	.23	.82	.64	.77	.91	.88	.81	G x T	.606

2f-analysis of variance: T = time effect; G = group effect; G x T = group x time effect; Bold values differ significantly(P < 0.05) from baseline.
a: P-value of group differences in corresponding means at specific time points.
b: medians (with 25% and 75 percentils)

Table 3. Results of arterial blood gases in dairy cows measured at baseline, (10 and 45 min) after lateral recumbency(LR) and at 30, 60, 120,180 and 300 min after surgery. All cows received IVRA with 20ml of procaine and either meloxicam (0.5 mg kg^{-1} BW; IV; N=9) or sodium chloride (controls; N=10) in an equal volume 30 min before the intervention.

Variable	Groups	Baseline	LR+10	LR+45	Stand +30	Stand +60	Stand +120	Stand +180	Stand +300	Main	Effects
Ph	Controls	7.44[b]	7.46	7.46	7.43	7.44	7.44	7.43	7.43	G	.275
		(7.37-7.51)	(7.43-7.51)	(7.44-7.50)	(7.37-7.49)	(7.40-7.51)	(7.34-7.52)	(7.39-7.48)	(7.36-7.48)		
	Meloxicam	7.43	**7.46**	**7.46**	**7.45**	7.43	7.44	**7.41**	7.43	T	.221
		(7.41-7.46)	(7.45-7.50)	(7.41-7.48)	(7.41-7.46)	(7.41-7.46)	(7.40-7.48)	(7.39-7.44)	(7.38-7.46)	G x T	.321
	Group difference[a]	.56	.44	.28	.30	.44	.90	.06	.78		
PaO2	Controls	103	86.4	89.1	**100**	105	103	103	101	G	.348
		(98-112)	(69-101)	(71-104)	(94-108)	(90-112)	(97-114)	(95-109)	(89-112)		
[mmHg]	Meloxicam	105	89.8	89	105	103	106	104	105	T	<.0001
		(99-110)	(75-108)	(70-104)	(99-109)	(92-111)	(92-112)	(97-111)	(96-114)	G x T	.501
	Group difference	.58	.32	.89	.06	.85	.96	.44	.08		
PaCo2	Controls	44.4	42.8	43.8	46.6	45.6	44.8	44	43.1	G	.083
		(41-51)	(38-51)	(39-47)	(41-52)	(41-51)	(39-55)	(42-47)	(39-52)		
[mmHg]	Meloxicam	44.6	40.4	**42.8**	43.6	44.7	43.9	45	**41.5**	T	.0015
		(39-49)	(38-43)	(37-44)	(42-46)	(40.7-47.8)	(41-47)	(41-46)	(39-45)	G x T	.724
	Group difference	.49	.08	.13	.02	.55	.43	.70	.20		
HCO3	Controls	29.8	30.5	31.4	30.3	29.8	29.7	28.7	**28.5**	G	.092
		(27.5-32.4)	(26.7-33)	(26.8-33.6)	(26.2-33.5)	(26.6-34.2)	(26.2-33.8)	(26.1-32)	(25.2-29.8)		
[mmol L⁻¹]	Meloxicam	29.4	28.1	28.7	28.8	28.7	29.2	**26.9**	**26.9**	T	<.0001
		(25.4-31.1)	(25.5-32.4)	(25.8-32.6)	(24.8-32.4)	(26.3-33.1)	(26.6-30.7)	(24.5-30.1)	(23.6-30.0)	G x T	.866
	Group difference	.16	.27	.039	.19	.31	.26	.095	.28		
O2 Sat	Controls	97.4	96	96	97	97	97	97	97	G	.45
		(97-98)	(92-97)	(94-97)	(96-97)	(96-98)	(95-98)	(96-97)	(95-97)		
%	Meloxicam	97.4	96	96	97	97	97	97	97	T	<.0001
		(97-97.8)	(95-97)	(93-97)	(96-97.7)	(96-97.8)	(96.5-97.8)	(97-97.6)	(96.9-97.9)	G x T	.401
	Group difference	.91	.25	.82	.22	.83	.87	.98	.11		

2f-analysis of variance: T = time effect; G = group effect; G x T = group x time effect; Bold values differ significantly (P < 0.05) from baseline.
a: P-value of group differences in corresponding means at specific time points.
b: medians (with 25% and 75 percentils)

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الملخص العربى
تأثير إستخدام عقار الميلوكسيكام والتخدير الموضعى على مدى تسكين الألم
الناتج اثناء الأستئصال الجزئى لمفصل الحافر فى الابقار الحلابة المصابة بالعرج

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تهدف هذه الدراسة إلى تحديد مدى تأثير استخدام عقار الميلوكسيكام على الإجهاد والألم الناتج أثناء الأستئصال الجزئى لمفصل الحافر في الأبقار الحلابة التى تعانى من العرج. في دراسة سريرية عشوائية تم استخدام عدد ١٩ بقرة هولشتين فريزيان ألمانى تعانى من التهاب تقيحى فى مفصل الحافر فى ناحية واحدة من الظلف. تم تقسيم الحيوانات الى مجموعتين الاولى تحتوي علي ٩ حيوانات تم حقنهم بعقار الميلوكسيكام بجرعة ٥،٠ مجم/كجم من وزن الحيوان ١٥ دقيقة قبل التدخل الجراحي. اما المجموعه الثانية والتي تحتوي علي ١٠ حيوانات حقنت بجرعة مماثلة من محلول ملحي (Placebo). كل الحيوانات تم حقنها بالمخدر الموضعي الوريدي (IVRA) بجرعة ٢٠ مل من بروكايين ٢ ٪ ويصفة دورية لمدة ٥ ساعات بعد التدخل الجراحي تم قياس كلا من معدل ضربات القلب والتنفس، ضغط الدم الشرياني، درجة الحرارة، معدل غازات الدم،نسبة الكورتيزول، اللاكتات و الاحماض الامينية الغير مشبعة في الدم بالاضافة الي الاعراض الاكلينيكية لتسكين الالم ومقارنتها بما هو قبل التدخل الجراحي.

أوضحت النتائج ان استخدام عقار الميلوكسيكام قبل التدخل الجراحي للأستئصال الجزئى لمفصل الحافر أدي الي ازالة التوتر الجراحي وتسكين الالم بشكل معنوي كما انه اضاف تاثيرا ملحوظا لتسكين الالم مع التخدير الموضعي وذلك من خلال الانخفاض المعنوي في معدل نسبة الكورتيزول، الاحماض الامينية الغير مشبعة واللاكتات كمؤشرات للالم.بالاضافة الى ذلك ان استخدام عقار الميلوكسيكام في الابقار الحلابة ليس له أعراض جانبية.