The effect of flunixin meglumine on eating and rumination variables in cows after omentopexy for correction of left displaced abomasum

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Summary

Eating and rumination variables were recorded using a pressure sensor integrated into the noseband of a halter in 60 cows with left displaced abomasum (LDA) before and after postoperative administration of flunixin meglumine (FM). Group 1 comprised 9 healthy control cows that were used to establish reference intervals. Group 2 included 60 cows with LDA that received one of the following three treatments: intravenous saline solution (2A, n=20), 1.1 mg/kg FM (2B, n=20) or 2.2 mg/kg FM (2C, n=20) once daily for 3 days after right-flank omentopexy. Median eating times on the day before surgery were 93 (2A), 80 (2B) and 114 (2C) min, which were below the reference interval (246 to 381 min). On the day after surgery, eating times had increased significantly to 201 (2A), 172 (2B) and 216 (2C) min, after which time they continued to increase. Eating and rumination times, numbers of regurgitated feed boluses per day and chewing cycles per bolus did not differ among treated groups. Postoperative administration of FM did not affect eating and rumination variables in this study, and normalisation of these variables was attributable to surgical correction of LDA.

Keywords: Cattle, eating, rumination, left displaced abomasum, flunixin meglumine

Untersuchung über den Einfluss von Flunixin meglumin auf Fressen und Wiederkauen bei Kühen nach Omentopexie infolge linksseitiger Labmagenverlagerung

Die Fress- und Wiederkauparameter von 60 Kühen mit linksseitiger Labmagenverlagerung (LLV) wurden nach postoperativer Verabreichung von Flunixin meglumin (FM) mittels Drucksensors im Halfter untersucht. Die Gruppe 1 bestand aus 9 gesunden Kühen für die Normalbereichsermittlung. Die Gruppe 2 umfasste 60 LLV-Kühe, die nach Omentopexie 3mal in 24-stündigen Abständen mit NaCl (2A), 1.1 (2B) oder 2.2 mg FM/kg (2C) behandelt wurden. Bei den LLV-Kühen lag die Fressdauer (Medianwert) bei den 3 Gruppen am Tag 0 mit 93, 80 und 114 Min. unterhalb des Normalbereichs von 246 bis 381 Minuten. Bereits am Tag 1 nach der Operation war sie mit 201, 172 und 216 Min. signifikant länger und stieg danach weiter an. Die Werte der 3 Behandlungsgruppen unterschieden sich nicht signifikant. Ähnliche Ergebnisse wurden für Wiederkaudauer, Anzahl Wiederkauboli und Kauschläge pro Wiederkaubolus ermittelt. Die Verabreichung von FM beeinflusste die Fress- und Wiederkauparameter in der vorliegenden Untersuchung nicht. Vielmehr war für die rasche Normalisierung die Omentopexie entscheidend.

Schlüsselwörter: Rind, Fressen, Wiederkauen, linksseitige Labmagenverlagerung, Flunixin meglumin

Short communication

Left displacement of the abomasum (LDA) in cattle is a disorder characterised by reduced feed intake, impaired rumination and probable visceral pain. Surgical treatment of LDA can decrease visceral pain by virtue of reducing the displacement, but the surgical incision may cause somatic pain with inadequate analgesia.[14] Pain control of surgical correction of LDA includes non-steroidal anti-inflammatory drugs (NSAIDs) such as, carprofen, flunixin meglumine and ketoprofen.[5,7,8,15] Pre- and postsurgical administration of carprofen improved the wellbeing of cows after LDA surgery, reduced pain-associated behaviours and increased rumination times.[7] Operated cows that received flunixin meglumine before surgery had a better clinical recovery, which was evidenced by increased feed intake and rumination [5] and significantly higher rumen contraction rates[15] compared

with control cows. Cows that received ketoprofen postoperatively tended to eat immediately after surgery when fresh feed was provided compared with non-treated cows.[8] It has long been suspected that there are differences in the pharmacokinetics of flunixin meglumine between cattle and other domestic animal species.[6] A recent review of the use of nonsteroidal anti-inflammatory drugs for pain control during castration and dehorning of calves reports doses of flunixin meglumine ranging from 1.1 to 3.3 mg/kg.[13]

The goal of the present study was to examine eating and rumination variables in 60 cows undergoing omentopexy for correction of LDA in relation to the postoperative administration of flunixin meglumine (FM) at two different doses; the methodology and results have been described in detail.[11] Our hypothesis was that the administration of flunixin meglumine to cows after surgical correction of left displaced abomasum has a positive effect on eating and rumination behaviours. Group 1 (controls) comprised nine healthy cows, aged 4.6 ± 1.2 years, which served to establish reference intervals for eating and rumination variables. Group 2 (experiments) comprised 60 cows (32 Holstein Friesian, 26 Swiss Fleckvieh, 2 Brown Swiss; 5.1 ± 1.8 years of age; 2 to 108 days in milk) with LDA, which were used to investigate the effect of FM on eating and rumination. The cows were referred to the Department of Farm Animals, University of Zurich, by practicing veterinarians for examination and treatment, and assigned to groups 2A, 2B or 2C, each comprising 20 cows, in a randomised double-blind study. The diagnosis of LDA was made clinically and confirmed ultrasonographically (day 0).[1] Right-flank omentopexy[2] was carried out 9 to 24 h (median = 20.5 h) after admission, which allowed the recording of preoperative eating and rumination variables. Immediately after surgery (defined as start of day 1) and 24 and 48 h later, the cows received isotonic NaCl solution (group 2A) or FM (Flunixine®, Biokema SA, Crissier) at a dose of 1.1 (group 2B) or 2.2 mg/kg body weight (group 2C) intravenously. In addition, cows received 10 litres of a solution containing 9 g sodium chloride and 50 g glucose per litre administered via an indwelling jugular vein catheter during surgery and then daily for three days, and antibiotics administered intramuscularly for three days. Serum electrolyte deficiencies were corrected as needed.[11] Eating and rumination variables were obtained as described using a pressure sensor integrated into the noseband of a horse halter.[3] The sensor recorded the pressure changes that occurred with each jaw movement. The sensor was connected to a data logger, which contained a secure digital (SD) card to store the data. At the end of one measuring period, the data were uploaded from the logger to a personal computer using the SD card. A special software program (R V2.12.1, MSR Electronics) was used to evaluate the data. The analysis was done as described.[3] The measured variables included duration of eating and rumination, number of regurgitated feed boluses per day and chewing cycles per bolus. Variables were recorded in the controls for five days to establish reference intervals. In the cows with LDA, recording was started on day 0 immediately after the initial examination and continued for five days. The conclusion of surgery 9 to 24 h after the start of recording was defined as the end of day 0, and recording ended 96 h later. When the preoperative recording phase (day 0) was shorter than 24 h, the results were extrapolated to a period of 24 h. Recordings were repeated on day 14 after surgery, at which time the owners of the cows applied the programmed halter for a 24 h period. Duration of eating and rumination, the number of regurgitated boluses and the number of chewing cycles per bolus were deduced from the pressure data on the data logger on a daily basis.[3,11] During hospitalisation, the cows were housed in straw-bedded tie-stalls and fed a total mixed ration (TMR) at 7:00, 10:00, 14:00, 17:00 and 20:00 and concentrate at 10:00 and 17:00; details of the TMR and the concentrate have been published.[11] All cows underwent daily clinical examination and measurement of ketone levels in the urine. The cows were discharged 5 to 7 days after surgery. The Shapiro-Wilk test was used to test the data for normality. Normal data (age, milk yield) were presented as mean ± standard deviation and non-normal data (eating and rumination variables) were given as 5th, 50th (median) and 95th percentiles. Differences in non-normal variables between groups were analysed using the Kruskal-Wallis test. A generalised linear model was used to identify changes in the variables during the study period. The effects of repeated measures were accounted for by using xtmixed procedure from the GLM family provided by STATA (<xtmixed vary varx time || time:>; StataCorp., 2017; Stata Statistical Software: Release 15.1; College Station, Texas, USA). Statistical power was calculated for the variables *rumination time* and *number of regurgitated boluses per day* using the sampling procedure of the STATA program (StataCorp LP, College Station, Texas, USA). Differences were considered significant at $P < 0.05$. The 90% confidence interval was calculated for each variable using the data obtained from the controls during the 5-day recording period, and defined as the reference interval.

The reference intervals obtained from the controls were 246 to 381 min for daily eating and 362 to 551 min for rumination time. The numbers of regurgitated feed boluses per day ranged from 473 to 705, and the numbers of chewing cycles per bolus from 49 to 69. On day 0, median eating time of cows with LDA was below the reference interval and was 93 min in group 2A, 80 min in group 2B and 114 min in group 2C (Table 1). By day 1, it had increased significantly to 201 min (Group 2A),

172 min (Group 2B) and 216 min (Group 2C) ($P < 0.01$) and was in the reference interval from day 2 onward. It increased further by day 30 reaching values of 305, 310 and 313 min, respectively. Eating times of the 3 groups did not differ significantly. The results for daily rumination time and number of regurgitated boluses were similar (Table 1); the values for both variables were significantly greater on day 1 than on day 0 ($P < 0.01$), the median values were in the reference interval from day 2 onward, and the values of the 3 groups did not differ significantly. The number of chewing cycles per bolus before surgery was in the reference interval near the lower limit in all three groups with 49 (Group 2A and 2B) and 50 (Group 2C) cycles (Table 1). From day 2 onward, the numbers of chewing cycles per bolus were significantly greater than on day 0 ($P < 0.05$) and did not differ significantly among the 3 groups. Depending on the variability in the different variables, the statistical power varied widely at the level of significance of 0.05 and ranged from 0.06 to 0.09 for the rumination time and number of regurgitated boluses per day respectively.

Eating and rumination variables of the control cows were largely in agreement with those of numerous other reports, which were summarised.[3] We were aware that the extrapolation of the recordings on day 0 from an observation period shorter than 24 h was associated with a certain inaccuracy. However, for study-related and ethical reasons, we did not insist on a pre-surgical recording period of 24 h in all cases. The increase in the eating and rumination variables from the day of admission before surgery to the day after surgery in all three groups largely reflects the positive effect of the surgical correction of the abomasal displacement. Rumination variables reached maximum values as early as three days after surgery. Eating and rumination times and the number of regurgitated boluses per day during the first two days after surgery were numerically greater in the cows that received the higher FM dose but the differences among groups were not significant throughout the study period. The high variability of the studied variables was most likely related to the fact that cows with left displaced abomasum usually have comorbidities such as ketosis, metritis or lameness and that left displaced abomasum does not occur as an isolated disorder. Therefore, randomization and a double-blinded study approach were used to neutralize the effects of comorbidities among the three groups. Furthermore, the urine concentration of ketone bodies and the BHB and NEFA concentrations in blood did not differ among the three groups on the day of admission (details are published in the dissertation of Schwellinger[11]). The lack of a positive effect of ketoprofen on eating behaviour after LDA surgery in an earlier study was explained in part by the short half-life of the drug.[8] We failed to observe a positive effect of FM even though its half-life (3 to 8 h) is longer than that of ketoprofen (1.5 to 2h)[10] and its duration of action can be expected to be prolonged.[9] Cows with LDA that had been treated with carprofen preoperatively had significantly greater rumination activities during the 24-h postoperative period than non-treated control cows.[7] Likewise, cows with LDA that had received xylazine before omentopexy had significantly greater numbers of chewing cycles per regurgitated bolus than non-treated cows (55.5 vs 46.6).[12] These findings support the recommendation of others

Table 1: Eating and rumination times, numbers of regurgitated feed boluses and numbers of chewing cycles per bolus in 60 cows with left displacement of the abomasum (medians, 5th and 95th percentiles in brackets).

		Reference	Days post surgery					
Variables	Group	interval[1]	0	1	2	3	4	14
Eating time (min/day)	2A	246–381	93 (17–192)	201 (29–306)**	260 (204–335)**	268 (164–307)**	267 (204–322)**	280 (180–380)**
	2B		80 (10–263)	172 (35–355)**	267 (138–367)**	258 (177–379)**	255 (128–369)**	280 (160–397)**
	2C		114 (21–197)	216 (106–325)**	286 (135–402)**	263 (151–363)**	247 (147–338)**	276 (152–432)**
Rumination time (min/day)	2A	362–551	126 (0–403)	344 (5–580)**	477 (161–642)**	499 (248–695)**	537 (362–633)**	511 (375–628)**
	2B		28 (0–323)	366 (46–486)**	460 (195–579)**	539 (231–690)**	551 (59–657)**	546 (310–621)**
	2C		97 (0–447)	424 (169–585)**	478 (222–604)**	543 (239–657)**	497 (372–612)**	489 (165–729)**
Boluses per day	2A	473–705	156 (0–483)	426 (7–603)**	522 (208–705)**	526 (319–751)**	601 (410–738)**	566 (489–766)**
	2B		44 (0–461)	450 (73–598)**	541 (266–648)**	633 (282–784)**	636 (61–729)**	595 (376–761)**
	2C		161 (0–640)	496 (236–704)**	573 (197–676)**	643 (208–787)**	604 (393–727)**	560 (339–873)**
Chewing cycles per bolus	2A	49–69	50 (29–71)	50 (26–69) ns	56 (42–65)*	58 (42–73)**	58 (50–69)**	61 (49–81)**
	2B		49 (30–58)	50 (37–65) ns	54 (41–69)*	57 (43–74)**	59 (46–71)**	59 (46–72)**
	2C		49 (34–67)	52 (38–71) ns	55 (44–71)*	59 (46–73)**	55 (45–75)*	60 (31–86)**

[1]The reference intervals were calculated from the recordings in the healthy controls (group 1) during 5 days and represent the 90% confidence intervals for each variable

nsWithin rows, values with this superscript do not differ from value on day 0 ($P > 0.05$)

*Within rows, values with this superscript differ from value on day 0: $P < 0.05$

**Within rows, values with this superscript differ from value on day 0: $P < 0.01$

to administer FM before surgical correction of LDA.[5] It is possible that the numerical differences observed in our study would have been significant had we started FM treatment before surgery. A power of 0.8 is considered a standard for adequacy. If the power value is lower than 0.8, it may be increased by increasing the sample size.[4] To get a significant result with alpha ≤ 0.05 and a power ≥ 0.8, a sample size of 2887 for the rumination time and 391 for boluses per day had been needed. These sample sizes are fare behind the possibilities of such a study. Summarising, this study has shown that FM administered to cows after omentopexy for correction of LDA had a non-significant effect in this study on eating and rumination behaviours and therefore we rejected our hypothesis. Surgical correction was the main determinant for normalisation of eating and rumination behaviour. Pending further studies on pain prevention in cows undergoing surgery, it is recommended that treatment with FM be initiated preoperatively and continued for two days.

Effet de la flunixine méglumine sur les variables d'alimentation et de rumination chez les vaches après omentopexie pour la correction d'un déplacement à gauche de la caillette

Les variables d'alimentation et de rumination ont été enregistrées à l'aide d'un capteur de pression intégré à la muserolle d'un licol chez 60 vaches avec déplacement à gauche de la caillette (LDA) avant et après l'administration postopératoire de flunixine méglumine (FM). Le groupe 1 comprenait 9 vaches témoins en bonne santé qui ont été utilisées pour établir des intervalles de référence. Le groupe 2 comprenait 60 vaches avec LDA qui ont reçu l'un des trois traitements suivants : solution saline intraveineuse (2A, n=20), 1,1 mg/kg FM (2B, n=20) ou 2,2 mg/kg FM (2C, n= 20) une fois par jour pendant 3 jours après omentopexie par le flanc droit. La durée médiane des repas la veille de la chirurgie était de 93 (2A), 80 (2B) et 114 (2C) minutes, ce qui était inférieur à l'intervalle de référence (246 à 381 min). Le lendemain de la chirurgie, la durée des repas avait augmenté de manière significative à 201 (2A), 172 (2B) et 216 (2C) minutes, après quoi elle a continué à augmenter. Les temps de repas et de rumination, le nombre de bolus alimentaires régurgités par jour et les cycles de mastication par bolus ne différaient pas entre les groupes traités. L'administration postopératoire de FM n'a pas affecté les variables d'alimentation et de rumination dans cette étude et la normalisation de ces variables était attribuable à la correction chirurgicale de la LDA.

Mots clés: Bovins, alimentation, rumination, déplacement à gauche de la caillette, flunixine méglumine

L'effetto della flunixina meglumine sulle variabili di alimentazione e ruminazione nei bovini dopo un'omentopessi per correggere l'abomaso dislocato sulla sinistra

Le variabili di alimentazione e ruminazione sono state registrate utilizzando un sensore di pressione integrato nella fascia nasale di una cavezza in 60 vacche con abomaso dislocato a sinistra (LDA) prima e dopo la somministrazione post-operatoria di flunixina meglumine (FM). Il gruppo 1 comprendeva 9 vacche di controllo sane che sono state utilizzate per stabilire gli intervalli di riferimento. Il gruppo 2 comprendeva 60 vacche con LDA che avevano ricevuto uno dei seguenti tre trattamenti: soluzione salina per via endovenosa (2A, n=20), 1,1 mg/kg FM (2B, n=20) o 2,2 mg/kg FM (2C, n=20) una volta al giorno per 3 giorni dopo l'omentopessi del fianco destro. I tempi mediani per mangiare il giorno prima dell'intervento erano di 93 (2A), 80 (2B) e 114 (2C) min, e risultavano inferiori dell'intervallo di riferimento (da 246 a 381 min). Il giorno dopo l'intervento, i tempi di alimentazione erano aumentati significativamente a 201 (2A), 172 (2B) e 216 (2C) min, dopo di che hanno continuato ad aumentare. I tempi di alimentazione e di ruminazione, il numero di boli di mangime rigurgitati al giorno e i cicli di masticazione per bolo non differivano tra i gruppi trattati. La somministrazione post-operatoria di FM non ha influenzato le variabili di alimentazione e ruminazione in questo studio, e la normalizzazione di queste variabili era attribuibile alla correzione chirurgica della LDA.

Parole chiave: Bovini, alimentazione, ruminazione, abomaso dislocato a sinistra, flunixina meglumine

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Ethics approval

The study was approved by an ethical committee of the canton of Zurich, Switzerland.

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