



Gastroduodenal toxicity prevention in dogs associated with Nonsteroidal Antiinflammatory Drugs: Comparison of Omeprazole, Ranitidine and Misoprostol
(Prevención de la toxicidad gastroduodenal en perros asociada al consumo de AINES: comparación entre el Omeprazol, Ranitidina y Misoprostol)

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Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for the treatment of musculoskeletal disease in veterinary medicine. However, most NSAIDs also have various adverse effects including gastrointestinal irritation or ulcers in dogs.

Material and Methods: 107 dogs with musculoskeletal disease and without gastroduodenal mucosal injuries were medicated with 20mg per day of piroxicam during ten days. They had a weight between 20 and 40 Kilograms and were randomly assigned to double-blind treatment in four groups: A (omeprazole 20 mg orally per day) B (ranitidine 300 mg orally per day), C (Misoprostol 400µg orally per day) and D (placebo) for ten days. Group A had 15 dogs, B 17 dogs, C 13 dogs and D 22 dogs. Upper endoscopy was used the eleventh day to detect surrogate end points of NSAID-induced gastrointestinal toxic effects and the first day to exclude dogs with gastroduodenal mucosal injuries.

Results: At eleventh day the prevalence of gastroduodenal mucose abnormalities was: 47.63% in Placebo or D group, 22.22% in Ranitidine or B group, 8.69% in Misoprostol or C group and 8% in Omeprazole or A group. Omeprazole and Ranitidina were associated with a better tolerance than Misoprostol because group C had some diarrhea complications in 34.78% of the dogs.

Conclusions: In dogs, gastroduodenal toxicity associated to NSAIDs, specifically to Piroxicam can be very high, about 40%. For that reason vets would have to prevent this situation. Comparing with placebo, Omeprazole and Misoprostol reduce the prevalence of gastroduodenal mucosal abnormalities associated with NSAIDs toxicity by 5 times and Ranitidina by 2 times. Due to the fact that Misoprostol has diarrhea complications and it is a more expensive drug, the best drug for prevention of NSAIDs gastroduodenal toxicity is Omeprazole.

Keywords: gastroduodenal ulcers | H2-receptor antagonists | misoprostol | NSAIDs | omeprazole | proton pump inhibitors | ranitidine

Resumen

Los antiinflamatorios no esteroides (AINEs) se usan con frecuencia en veterinaria para el tratamiento de los problemas musculoesqueléticos. No obstante, en perros la mayoría de ellos tiene el problema de que suelen provocar úlceras e irritaciones gastrointestinales.

Material y Métodos: un total de 107 perros (58 machos y 49 hembras) con problemas musculoesqueléticos y sin afectación de la mucosa gastroduodenal fue tratado con 20mg de Piroxicam al día durante un total de 10 días. Los perros estudiados tenían un peso de entre 20 y 40 kilogramos y se les asignó de forma randomizada y a doble ciego un determinado grupo de tratamiento preventivo: A (Omeprazol oral a 20mg por día), B (Ranitidina oral a 300mg por día), C (Misoprostol oral a 400µg por día), D (Placebo).

Se realizó una endoscopia alta el día 1 para excluir del estudio los perros con afectación gastroduodenal y el día 11 para valorar los efectos lesivos gastroduodenales.

Resultados: El undécimo día la prevalencia de problemas gastroduodenales era: del 40.63% en el grupo D o Placebo, del 22.22% en el grupo B o de la Ranitidina, del 8.69% en el grupo C o del Misoprostol y del 8% en el grupo A o del Omeprazol. El Omeprazol y Ranitidina se asociaron a una mejor tolerancia que el Misoprostol ya que éste provocó complicaciones diarreicas en el 34.78% de los perros tratados.

Conclusiones: en los perros la toxicidad gastroduodenal asociada al consumo de AINES, concretamente al Piroxicam puede ser muy alta, en torno al 40%. Por este motivo los médicos veterinarios deberían de prevenir esta situación. Comparado con el placebo, el Omeprazol y Misoprostol reducen al quintuple los daños en la mucosa gastroduodenal asociados al consumo de AINES, mientras que en la Ranitidina esta reducción es de tan sólo al doble. Debido a que el Misoprostol es más caro que el Omeprazol y resulta peor tolerado por tener asociadas complicaciones de tipo diarreico, la mejor opción terapéutica es el empleo del Omeprazol.

Palabras clave: AINES | antagonistas H2 | inhibidores de la bomba de protones | misoprostol | omeprazol | ranitidina | úlceras gastroduodenales

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for the treatment of musculoskeletal disease in veterinary medicine and are recognized for their analgesic, antipyretic and anti-inflammatory properties (Jonston et al., 1997; Lawson et al., 1971). However, most NSAIDs also have various adverse effects including gastrointestinal irritation or ulcers in dogs (Daehler, 1986; Dow et al., 1990; Vonderhaar and Salisbury, 1993) caused by the suppression of Cyclooxygenase 1 (COX-1), which produces PGs for physiological roles within these tissues and cells (Seibert et al., 1997).

There are differences between the gastrointestinal toxicity of anti-inflammatory drug: Nabumetone and ibuprofen appear to have ones of the lowest risks for severe gastrointestinal toxicity. In contrast, NSAIDs with the highest risks during long-term oral use are piroxicam, flurbiprofen, meclofenamate sodium and ketorolac tromethamine (Henry et al., 1996; Macdonald et al., 1997; Singh, 1998; Garcia Rodriguez et al., 1998).

In human medicine there are several drugs as protective agent to mitigate the adverse effects of NSAIDs in gastrointestinal level like Misoprostol, Proton Pump Inhibitors and Anti H2. The question is: which is the best option in dogs?

Materials and Methods

107 dogs with musculoskeletal disease (58 males and 49 females) and without gastroduodenal mucosal injuries were medicated with 20mg per day of piroxicam during ten days. They had a weight between 20 and 40 Kilograms and were randomly assigned to double-blind treatment in four groups: A (omeprazole 20 mg orally per day) B (ranitidine 300 mg orally per day), C (Misoprostol 400µg orally per day) and D (placebo) for ten days. Group A had 15 dogs, B 17 dogs, C 13 dogs and D 22 dogs.

Upper endoscopy was used the eleventh day to detect surrogate end points of NSAID-induced gastrointestinal toxic effects and the first day to exclude dogs with gastroduodenal mucosal injuries. These end points include the following mucosal abnormalities: ulcers (mucosal breaks greater than 3 mm with unequivocal depth), erosions (mucosal breaks of any size with no depth) or mucosal hemorrhages.

The dogs with one of these mucosal abnormalities was classified as a positive case. Groups were analysed and compared using contingency table Chi-square analysis with a 95% confidence interval because they have a normal distribution.

Table 1. Chi-square analysis to "dogs with gastroduodenal injuries in each group"

Group	N (total dogs/group)	n (+ dogs/group)	% + Dogs/group
A	25	2	8.000%
B	27	6	22.222%
C	23	2	8.696%
D	32	13	40.625%

*P<0.0001

Results

Chi-square analysis showed highly significant differences between the groups ($p < 0.0001$). Nevertheless group A and C were significant equals. At eleventh day the prevalence of gastroduodenal mucose abnormalities was: 47.63% in Placebo or D group ($n=13$), 22.22% in Ranitidine or B group ($n=6$), 8.69% in Misoprostol or C group ($n=2$) and 8% in Omeprazole or A group ($n=2$). Table 1 represents these results. Medications were well tolerated although Omeprazole and Ranitidina were associated with a better tolerance than Misoprostol because group C had some diarrhea complications in 34.78% of the dogs ($n=8$). On the contrary diarrhea complications in Groups A and B were statistically equal: 4% in Omeprazole or A group ($n=1$) and 3.7% in Ranitidina or B group ($n=1$).

Discussion

Hawkey et al. (1998) compared omeprazole with misoprostol for ulcers and erosions associated with nonsteroidal antiinflammatory drugs. They found that the overall rates of successful treatment of ulcers, erosions, and symptoms associated with NSAIDs were similar for the two doses of omeprazole and misoprostol. Maintenance therapy with omeprazole was associated with a lower rate of relapse and a better tolerance than misoprostol. Yeomans et al. (1998) compared Omeprazole with Ranitidine for Ulcers Associated with Nonsteroidal Antiinflammatory Drugs and found that in patients who use NSAIDs regularly, Omeprazole healed and prevented ulcers more effectively than did Ranitidine. We agree with both studies because we found that Omeprazole is as effective as Misoprostol, it is more effective than ranitidine and it has a better tolerance than Misoprostol.

Conclusions

In dogs, gastroduodenal toxicity associated to NSAIDs, specifically to Piroxicam can be very high, about 40%. For that reason vets would have to prevent this situation. Comparing with placebo, Omeprazole and Misoprostol reduce the prevalence of gastroduodenal mucosal abnormalities associated with NSAIDs toxicity by 5 times and Ranitidina by 2 times. Due to the fact that Misoprostol has diarrhea complications and it is a more expensive drug, the best drug for prevention of NSAIDs gastroduodenal toxicity is the Omeprazole.

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