Evidence-based Clinical Question

Evidence for dimethyl sulphoxide (DMSO) use in horses. Part 2: DMSO as a parenteral anti-inflammatory agent and as a pharmacological carrier

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Introduction

The evidence for the use of dimethyl sulphoxide as a topical anti-inflammatory agent, and for intra-articular use, was examined in Part 1 (Schleining and Reinertson 2007). Part 2 examines the use of DMSO as a parenteral anti-inflammatory agent, and as a pharmacological carrier.

Parenteral anti-inflammatory

The observation of the ability of DMSO to scavenge oxygen-derived free radicals has lead to an interest in its use to prevent reperfusion injury following ischaemia to the gastrointestinal tract. Many of the studies in this area utilise either a low-flow or complete arterial and venous occlusion model of either the small or large intestine. The first study was published in 1989 and included 18 ponies that underwent 1 h of jejunal ischaemia followed by 1 h of reperfusion. The ponies in the DMSO group received 1 g/kg bwt DMSO in 1 l of lactated Ringer's solution i.v. immediately prior to reperfusion. There were no differences in the variables studied, and the authors concluded DMSO was not effective in preventing equine jejunal injury resulting from complete arterial occlusion followed by reperfusion (Arden *et al.* 1989). The results of that study were supported by a concurrent study by the same authors utilising a similar model, but evaluating the effect of DMSO utilising histological sampling of the jejunum. Again, DMSO was ineffective in preventing ischaemia-reperfusion injury (Arden *et al.* 1990).

Further research failed to show a benefit of i.v. DMSO in both an arteriovenous obstruction and a venous obstruction model in equine jejunum up to 48 h following reperfusion (Horne *et al.* 1994). In a conflicting report, microvascular permeability and morphology of the equine jejunum was evaluated following i.v. DMSO administration in a jejunal low-flow ischaemia model. Although serosal and submucosal layer oedema was significantly increased after DMSO treatment, the oedema was significantly less than that observed in lactated Ringer's and U-74389G treatment groups. Jejunal microvascular permeability was significantly lower after DMSO treatment. Because of these results the authors concluded that DMSO may have a protective effect against ischaemia-reperfusion injury (Dabareiner *et al.* 2005). Using a large intestinal ischaemia and reperfusion model, 16 horses underwent a period of either haemorrhagic or ischaemic strangulation obstruction followed by reperfusion. A 20% DMSO solution was administered i.v. 10 min prior to reperfusion and samples were obtained for histological evaluation, immunohistochemical staining, and indirect measures of oxygen free radical production. The results indicated there was no benefit of DMSO treatment when compared to control segments (Reeves *et al.* 1990).

This was supported by a second study where 6 horses underwent low-flow ischaemia and reperfusion of the large colon. DMSO was administered i.v. 30 min prior to reperfusion. Numerous variables including eicosanoid production, endotoxin production, lactate concentration, and full thickness biopsy specimens were examined. They found no beneficial effect of DMSO against the oxygen-derived free radical-mediated damage to colonic mucosa, but deleterious haemodynamic effects were not observed consequent to its use (Moore *et al.* 1995). In a separate experimental design study using jejunal low-flow ischaemia in foals, the use of DMSO was investigated as a preventative for the formation of intestinal adhesions post operatively. In that study, DMSO was administered i.v. starting at the time of reperfusion and repeated every 12 h for 72 h. In the 4 foals in the DMSO group, no adhesions were observed at the time of necropsy 10 days post operatively. It is interesting to note, however, that the 4 foals in the group that received flunixin meglumine, penicillin and gentamicin post operatively also failed to develop adhesions. From these results it was concluded that DMSO had anti-inflammatory properties that

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prevented adhesions in foals that underwent ischaemia and reperfusion (Sullins *et al.* 2004).

DMSO is also commonly used as a parenteral or enteral anti-inflammatory agent in the treatment of various conditions such as laminitis or neurological trauma. There appears to be no evidence obtained in horses to support such use. Doses vary widely, and such evidence as appears is anecdotal (Slater *et al.* 1995). Of interesting note, there is no available evidence examining DMSO in its widespread use as an oxygen free radical scavenger or anti-inflammatory in the treatment of equine endotoxaemia.

Pharmacological carrier

The novelty of DMSO as a solvent has expanded to investigation of its use as a carrier for other therapeutic agents. In horses, corneal uptake of topical itraconazole was increased 7-fold when combined with DMSO compared with itraconazole alone (Ball *et al.* 1997). When used clinically for treatment of keratomycosis, 80% of the horses in the study population were treated successfully using this combination (Ball *et al.* 1997). However in a group of mares that were pretreated with DMSO i.v. immediately prior to an i.v. dose of trimethoprim and sulphamethoxazole, there was no difference in mean serum or cerebrospinal concentrations of the drug (Green *et al.* 1990). Additionally, mercury toxicity was described in 2 horses in which DMSO was used concurrently under a mercuric blister bandage (Schuh *et al.* 1988).

Conclusions

When interpreting studies for their level of evidence, one should recall the evidence pyramid that illustrates the weight of different study types. At the bottom of the pyramid lies *in vitro* research. Case reports and case series are classified in the middle, while randomised, controlled, double-blind studies carry the most weight (Innes 2007). Despite the wealth of information on the extensive uses of DMSO in the human literature, there is a lack of consistency in its effectiveness. Although DMSO is used frequently in equine veterinary medicine it appears that the evidence to support its beneficial use as an anti-inflammatory in the treatment of clinical disease is primarily anecdotal and, therefore, weak evidence.

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