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Practical use of Dantrium

Charlie Schreiber
O’Gorman, Slater, Main and Partners, Donnington Grove Veterinary Surgery, Oxford Road, Newbury, Berkshire RG14 2JB, UK.

Introduction
The use of Dantrium has been well documented as a treatment for exertional rhabdomyolysis in the horse. Estimates of the prevalence of exercise associated rhabdomyolysis in Thoroughbreds suggests that 5–7% are affected at any one time (MacLeay et al. 1999; McGowan et al. 2002; Cole et al. 2004).

There is a sex predilection which was estimated by Wilsher et al. in a survey in 2001, when of 514 2-year-olds in training, 27 were clinically affected, of which 78% were fillies (Wilsher et al. 2006).

Mechanism of action
An abnormality in muscle calcium regulation in Thoroughbreds with recurrent exertional rhabdomyolysis (RER) has been detected which bears close similarity to the condition recognised in man and other species known as malignant hyperthermia (MH). In particular, muscle from horses with RER and individuals susceptible to MH share a sensitivity to some agents (caffeine and halothane). These agents stimulate the release of calcium from the sarcoplasmic reticulum where it is stored within the cell. Although the exact mechanism of release site in RER has still to be clarified, dantrolene is capable of blocking this channel and hence prevents the release of excessive quantities of calcium into the cell. High intracellular calcium concentrations is thought to cause the clinical condition that practitioners recognise as ‘tying-up’. Although the exact mechanism is still poorly understood, dantrolene is classified as a direct acting muscle relaxant.

Use and dosage
In human medicine, dantrolene is used for the relief of muscular soreness, cramping, spasticity and even neuromuscularly based muscular pain. For these conditions, a total dose rate starting at 25 mg working up to 100 mg q.i.d. is used to reduce symptoms.

The use of Dantrium has been well documented as a treatment for exertional rhabdomyolysis in the horse. Estimates of the prevalence of exercise associated rhabdomyolysis in Thoroughbreds suggests that 5–7% are affected at any one time (MacLeay et al. 1999; McGowan et al. 2002; Cole et al. 2004).

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Treatment regimes have varied, but generally the use of dantrolene has allowed levels of muscle enzymes (CK and AST) to be eliminated from the body at expected rates despite the continuation of exercise which would normally lead to further episodes of tying-up.

This proves to be a very useful tool in the training of racehorses, especially fillies, who can otherwise get into a vicious cycle of a constantly interrupted exercise programme in turn increasing the probabilities of tying-up.

Withdrawal period and detection times
There is currently no advice on either the British Horseracing Authority (BHA) or European Horserace Scientific Liaison Committee (EHSLC) websites regarding the withdrawal of Dantrium medication prior to racing. The paper by DiMaio Knych (2010) on the pharmacokinetics and metabolism of Dantrium does offer some indication as to the detection time of a 500 mg dose. Elimination from plasma appears to have taken place within 48 h of administration, although 7 days were required for levels in urine to fall below that which is detectable.

References


TABLE 1: Doses of dantrolene reported for use in the horse

<table>
<thead>
<tr>
<th>Source/reference</th>
<th>Dose rate</th>
<th>Total dosage</th>
<th>No. of capsules of Dantrium</th>
<th>Time before exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards et al. 2003</td>
<td>1.6 mg/kg bwt</td>
<td>800 mg</td>
<td>8</td>
<td>1 h</td>
</tr>
<tr>
<td>McKenzie et al. 2004</td>
<td>4.0 mg/kg bwt</td>
<td>2000 mg</td>
<td>20</td>
<td>1.5 h</td>
</tr>
<tr>
<td>DiMaio Knych et al. 2010</td>
<td>1.0 mg/kg bwt</td>
<td>500 mg</td>
<td>5</td>
<td>3.8 h</td>
</tr>
<tr>
<td>Donnington Grove Veterinary Surgery</td>
<td>2.0 mg/kg bwt</td>
<td>1000 mg</td>
<td>10</td>
<td>1.5 h</td>
</tr>
</tbody>
</table>