

## Hydroxycarbamide (hydroxyurea) toxicity in dogs

MADAM

Wray (2007) reports a canine case of hydroxycarbamide toxicity characterised by severe methaemoglobinaemia. There appear to be no other cases of hydroxycarbamide toxicity in dogs reported in the literature and the Veterinary Poisons Information Service (London) (VPIS) would like to present additional data from the small number of canine cases of hydroxycarbamide toxicity on its database.

The VPIS was consulted about the case reported by Wray prior to referral to the Centre for Small Animal Studies, Animal Health Trust and have information on a further seven cases. Of these cases only two dogs remained asymptomatic; one had reportedly ingested only 33 mg/kg (less than the therapeutic dose) and the other, a 12-month-old cross breed of unknown weight, had taken 3.5 g.

Of the remaining five dogs all developed cyanosis. Other signs reported included collapse (two dogs), methaemoglobinaemia (two), tachycardia (one), dyspnoea (one) and thrombocytopenia (one). The onset of clinical signs appears to be rapid; where the time of onset was reported it was within 1-2 hours of ingestion.

The reported dose of hydroxycarbamide taken in symptomatic cases varied from 80 to 400 mg/kg. Three dogs were treated with methylthionium chloride (methylene blue). Four dogs recovered but the fifth case was ongoing at the time of follow up and the final outcome was not determined.

Methaemoglobinaemia is the main concern following ingestion of hydroxycarbamide in dogs. This is not the case in humans

where toxicity is typically characterised by mild bone marrow suppression without causing methaemoglobinaemia. Any dog that has ingested an overdose of hydroxycarbamide should be urgently assessed for methaemoglobinaemia and hypoxia. Methaemoglobin concentrations will not be readily available in most cases and methaemoglobinaemia should be suspected if the blood is chocolate brown and does not change on exposure to air, dyspnoea is unresponsive to oxygen and the animal has normal oxygen saturation. As Wray discusses in the case report it should be emphasised that neither pulse oximetry or blood gas analysis of PaO<sub>2</sub> are useful in the assessment of methaemoglobinaemia; co-oximetry is required. In addition oxygen therapy is most effective once methaemoglobinaemia has been corrected.

Methylthionium chloride is an antidote for methaemoglobinaemia and only pharmaceutical grade should be used. It should be reserved for cases where methaemoglobinaemia is confirmed or strongly suspected as its use is not without risks (e.g. Heinz body formation, red blood cell morphology changes and reduced lifespan). Recommended doses of methylthionium chloride are very variable. Doses of 1 to 10 mg/kg by slow intravenous injection have been used but in view of the risk of adverse effects the lowest effective dose should be given.

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### Reference

WRAY, J. D. (2007) Methaemoglobinaemia caused by hydroxycarbamide (hydroxyurea) ingestion in a dog. *Journal of Small Animal Practice* **9**, 211-215



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