Evaluation of a novel rodenticide: welfare assessment of fatal methaemoglobinaemia in adult rats (Rattus norvegicus)

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Abstract

This study assessed the welfare of rats (Rattus norvegicus) poisoned with a lethal dose of the methaemoglobin (MetHb) inducing compound para-aminovalerophenone (PAVP). Twenty rats were orally gavaged with either PAVP (treated) or the vehicle only (control). Spontaneous and evoked behaviours were recorded and blood samples collected post mortem for analysis of MetHb%. Female and male rats received a mean (± SEM) dose of 263 (± 3) and 199 (± 6) mg PAVP kg⁻¹, respectively. Mean (± SEM) time to death was 67 (± 16) and 354 (± 71) min for female and male rats, respectively. Control animals did not show any signs of intoxication. The time to death from methaemoglobinaemia in rats was significantly shorter than that reported for anticoagulants and there were no obvious signs of distress or pain.

Keywords: animal welfare, death, hypoxaemia, methaemoglobin (MetHb), methaemoglobinaemia, rat

Introduction

Rodenticides are the predominant method of controlling rodent pests, such as rats and mice. Following the withdrawal of several rodenticide products from the UK market, there is now more reliance on anticoagulants. While often very effective (PSD 1997; Mason & Littin 2003), there is widespread concern about the humaneness of anticoagulant poisons (PSD 1997; Littin et al 2000; Mason & Littin 2003; Gregory 2004a; Fisher et al 2010) and the risk that second-generation anticoagulants, in particular, pose to non-target species through greater persistence and through primary and secondary poisoning routes (Eason et al 2002; Sanchez-Barbudo et al 2012; Langford et al 2013). Specific welfare issues associated with anticoagulant intoxication are: the prolonged time to death, dehydration, pain associated with bleeding in joints and other enclosed spaces within the body, haemorrhage in the respiratory tract and associated laboured breathing, episodic struggling, reduced activity, effects on general condition and paralysis (PSD 1997; Littin et al 2000). The mean time from ingestion of a second-generation anticoagulant (brodifacoum) to the beginning of clinical signs of toxicity (reduced feed intake) has been reported as four days in rats (Littin et al 2000), and the period from the onset of clinical signs to death is between three to four days (PSD 1997; Littin et al 2000). It has also been reported in electroencephalographic (Rowsell et al 1979) and behavioural (PSD 1997; Littin et al 2000) studies that generally the animals remain conscious and responsive during the sickness period until immediately before death.

Novel vertebrate pesticides are now being developed, with the aim of improving humaneness and minimising the risk to non-target species without compromising efficacy. Methaemoglobin-inducing compounds have been evaluated as vertebrate pesticides for the control of feral pigs (Sus scrofa) (Anon 2010), stoats (Mustela erminea) (Fisher et al 2005; Eason et al 2010; Dilks et al 2011), ferrets (M. furo) (Fisher & O’Connor 2007), brushtail possums (Trichosurus vulpecula) (Fisher et al 2008) and feral cats (Felis catus) (Murphy et al 2007). In mammalian species, these compounds target red blood cells and induce the formation of methaemoglobin (MetHb), which reduces the capacity of blood to carry oxygen to tissues causing hypoxia and respiratory depression leading to death over a shorter time-period than anticoagulant agents (Eason et al 2014). The mode of action of MetHb inducers is the oxidation of the haem iron in red blood cells from the ferrous state (Fe²⁺) to the ferric state (Fe³⁺) to form MetHb (Rennison et al 2013). However, rodents appear to have a high MetHb reductase activity after treatment with sodium nitrite (Stolk & Smith 1966) or para-aminopropiophenone (PAPP) (Scawin et al 1984), and this could reduce the effectiveness of those pesticides in this group of animals. More recently, analogues of PAPP have shown promise during in vitro and in vivo testing as being more toxic than PAPP in rodents. Of these analogues, para-aminovalerophenone (PAVP) has so far been found to have the highest toxicity in vivo with reported oral LD50 values of 84 (CI 56–126) mg kg⁻¹ (Pan et al 1983) and 85 (± 31) mg kg⁻¹ (Rennison et al 2013) in