Veterinary Anaesthesia and Analgesia 2017, **xxx**, 1–9 http://dx.doi.org/10.1016/j.vaa.2016.06.004

RESEARCH PAPER

Alfaxalone for maintenance of anaesthesia in ponies undergoing field castration: continuous infusion compared with intravenous boluses

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Abstract

Objective To compare alfaxalone as continuous intravenous (IV) infusion with intermittent IV injections for maintenance of anaesthesia in ponies undergoing castration.

Study design Prospective, randomized, blinded clinical study.

Animals A group of 33 entire male Welsh ponies undergoing field castration.

Methods After preanaesthetic medication with IV detomidine (10 μg kg^{-1}) and butorphanol (0.05 mg kg^{-1}), anaesthesia was induced with IV diazepam (0.05 mg kg^{-1}) followed by alfaxalone (1 mg kg^{-1}). After random allocation, anaesthesia was maintained with either IV alfaxalone 2 mg kg^{-1} $hour^{-1}$ (group A; $n = 16$) or saline administered at equal volume (group S; $n = 17$). When necessary, additional alfaxalone (0.2 mg kg^{-1}) was administered IV. Ponies were breathing room air. Using simple descriptive scales, surgical conditions and anaesthesia recovery were scored. Total amount of alfaxalone, ponies requiring additional alfaxalone and time to administration, time from induction to end of infusion; and end of infusion to standing were noted. Indirect arterial blood pressure, pulse and respiratory rates, end-expiratory carbon dioxide partial pressure and arterial haemoglobin oxygen saturation were recorded every 5 minutes. Data were analysed using Student *t*, Mann–Whitney *U* and chi-square tests, where appropriate ($p < 0.05$).

Results Total amount of alfaxalone administered after induction of anaesthesia (0.75 ± 0.27 *versus* 0.17 ± 0.23 mg kg^{-1}; $p < 0.0001$) and time to standing (14.8 ± 4 *versus* 11.6 ± 4 minutes; $p = 0.044$) were higher in group A compared to group S. Ponies requiring additional alfaxalone boluses [four (group A) *versus* seven (group S)] and other measured variables were similar between groups; five ponies required oxygen supplementation [three (group A) *versus* two (group S)].

Conclusion and clinical relevance Continuous IV infusion and intermittent administration of alfaxalone provided similar anaesthesia quality and surgical conditions in ponies undergoing field castration. Less alfaxalone is required when used intermittently.

Keywords alfaxalone, castration, continuous rate infusion, equine.

Introduction

The neurosteroid anaesthetic agent alfaxalone (3α-hydroxy-5α-pregnane-11,20-dione), solubilized in 2-hydroxypropyl-β-cyclodextrin (Alfaxan), is licensed for intravenous (IV) induction and maintenance of anaesthesia in dogs and cats, but has no Market Authorisation for this purpose in horses.

The successful use of alfaxalone for total intravenous anaesthesia has been described in dogs (Ambros et al. 2008; Suarez et al. 2012; Herbert et al. 2013), cats (Beths et al. 2014; Campagna et al. 2015) and small ruminants (Moll et al. 2013; Ndawana et al. 2015), providing good cardiovascular stability. However, in equine anaesthesia its use has only sporadically been reported (Leece et al. 2009; Klöppel & Leece 2011; Keates et al. 2012; Wakuno et al. 2017). Leece et al. (2009) and Klöppel & Leece

Please cite this article in press as: Deutsch J, Ekiri A, de Vries A Alfaxalone for maintenance of anaesthesia in ponies undergoing field castration: continuous infusion compared with intravenous boluses, Veterinary Anaesthesia and Analgesia (2017), http://dx.doi.org/10.1016/j.vaa.2016.06.004

(2011) described induction and maintenance of anaesthesia by IV boluses of alfaxalone, after preanaesthetic medication with IV romifidine and butorphanol, for castration of ponies under field conditions. In their studies, additional alfaxalone boluses of 0.2 mg kg^{-1} were necessary to maintain a stable plane of anaesthesia in 58.8 and 33.3% of the cases, respectively. Overall, surgical conditions as well as recovery scores were described as good to excellent. Goodwin et al. (2010, 2013) reported the use of alfaxalone as continuous infusion in adult horses under research and field conditions, respectively. In both studies, horses were administered acepromazine and either xylazine or medetomidine as preanaesthetic medication, followed by IV guaifenesin and alfaxalone for induction of anaesthesia. In their dose finding study, Goodwin et al. (2010) administered alfaxalone at a mean dose rate of 3 mg kg $hour^{-1}$ IV over a period of 3 hours. Although this protocol proved to be effective for anaesthesia, brief excitement and hyperaesthesia as well as twitching and increased muscle rigidity were noticed during the recovery period. Despite these reported side effects, all horses achieved standing position after just one to two attempts. When alfaxalone (2 mg kg $hour^{-1}$) was administered together with medetomidine at a rate of 5 μg kg^{-1} $hour^{-1}$ in colts undergoing castration, a stable plane of anaesthesia was provided for 45 minutes with good to excellent recoveries (Goodwin et al. 2013).

To date, no studies have been published in which the continuous infusion of alfaxalone is compared with intermittent IV injections of alfaxalone for maintenance of anaesthesia in horses. Because peaks and troughs of plasma concentration and subsequently of anaesthetic depth are avoided with a continuous infusion, quality of anaesthesia and surgical conditions may be better when anaesthesia is maintained in this way.

The aim of this study was to compare the quality of anaesthesia provided by alfaxalone, either administered as IV bolus(es) or by continuous IV infusion. The hypothesis was that continuous IV infusion of alfaxalone would provide adequate anaesthesia and better anaesthetic and surgical conditions for field castration in ponies compared to the intermittent IV administration.

Materials and methods

Approval of the study was granted by the Veterinary Medicines Directorate (animal test certificate number 25296/4000) and the Animal Health Trust Clinical Research Ethics Committee (AHT 02-2014). The study was designed as a randomized clinical trial and was performed by two anaesthetists, of whom one was responsible for preparation and administration of medications and one who was unaware of treatment and undertook all monitoring, measuring and scoring as per the protocol.

For maintenance of anaesthesia, the ponies were randomly allocated to be administered with either a continuous IV infusion of alfaxalone (Alfaxan, 10 mg mL^{-1}; Jurox Ltd., UK) (group A) at a set rate of 2 mg kg^{-1} $hour^{-1}$ or an IV infusion of saline 0.9% (Aqupharm 1, sodium chloride 0.9% w/v; Animalcare Ltd., UK) (group S) at an equal volume. Both alfaxalone and saline were infused by means of a syringe driver (Cardinal Health Alaris GS Syringe Driver; Avensys UK Ltd., UK). Randomization was achieved by blindly drawing a closed envelope containing the group allocation from a bag. All scoring was performed according to simple descriptive scales modified from Klöppel & Leece (2011), with the scales ranging from 1 to 4 for quality of sedation, ease of intubation and surgical condition; and 1 to 5 for both quality of induction and recovery, with 1 always representing the best score (Appendix 1).

A total of 39 feral, 9-month-old, entire male Welsh section A ponies undergoing field castration were included in the study. Sample size was limited by the herd size. Considering the nature of the ponies, the ponies were kept in a field during the night and only confined to a smaller area without grass and straw the morning of the procedure. Therefore, the period of fasting before anaesthesia was approximately 2–6 hours, with *ad libitum* access to water. Based on clinical examination, all ponies were classified according to the American Society of Anesthesiologists as grade I. Preanaesthetic medication consisted of detomidine hydrochloride (Domosedan, 10 mg mL^{-1}; Eurovet Animal Health BV, The Netherlands) 10 μg kg^{-1} and butorphanol tartrate (Torbugesic, 10 mg mL^{-1}; Pfizer Ltd., UK) 0.05 mg kg^{-1} mixed in the same syringe and administered by IV injection. After clipping, surgical preparation and subcutaneous (SC) infiltration of the skin with 10 mg mepivacaine (Intra-Epicaine, 20 mg mL^{-1}; Dechra Ltd., UK), a 14 gauge catheter (Intraflon 2; Vygon Ltd., UK) was placed in the left jugular vein. Quality of sedation was scored after 5 minutes; an additional IV dose of detomidine 5 μg kg^{-1} was administered if the sedation score was $\geq$ 3. Subsequently, baseline measurements of pulse rate (PR), respiratory rate (f_R) as

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