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SHORT COMMUNICATION

Effects of intramuscular alfaxalone alone or in combination with diazepam in swine

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Abstract

Objective To describe the use of intramuscular (IM) premedication with alfaxalone alone or in combination with diazepam in pigs.

Study design Randomised-controlled trial.

Animals Twelve healthy 2 month-old Landrace x Large White pigs weighing 21.3 ± 2.4 kg.

Methods Animals were distributed randomly into two groups: group A ($n = 6$) 5 mg kg^{-1} of IM alfaxalone; and group AD ($n = 6$) 5 mg kg^{-1} of IM alfaxalone + 0.5 mg kg^{-1} of IM diazepam mixed in the same syringe. The total volume of injectate was standardized at 14 mL by dilution in 0.9% sodium chloride. Pain on injection, the degree of sedation and the quality of and time to induction of recumbency were evaluated. Once pigs were recumbent, reflexes were evaluated. Pulse and respiratory rates and arterial oxygen saturation were recorded at 5 and 10 minutes after drug administration. Pigs were then moved to another room for subsequent anaesthesia.

Results Two animals of group A and one of group AD showed slight pain on drug injection. Time to lateral recumbency (in seconds) was shorter in group AD (mean 203 ± SD 45 range 140–260) than group A (302 ± 75, range 220–420; $p < 0.05$). In group AD sedation was deeper, and on recumbency there was better muscle relaxation. When moved for anaesthesia, two pigs in Group A showed slight resistance but did not vocalize. There were no differences in physiologic measurements between groups, although in both groups, respiratory rate was significantly lower at ten compared with five minutes post drug injection. There was no apneoa.

Conclusions and clinical relevance IM administration of alfaxalone combined with diazepam resulted in a rapid onset of recumbency and deep sedation, with minimal side effects. The combination might be useful for premedication, but volume of injectate will limit its use to small pigs.

Keywords alfaxalone, diazepam, immobilization, pig, premedication, sedation, swine.

Introduction

Alfaxalone is a synthetic neuroactive steroid, which activates the $GABA_A$ receptor (Lan & Gee 1994), producing anaesthesia and some muscular relaxation. A previously used preparation (Saffan) consisted of alphaxalone and alphadolone, another weakly hypnotic steroid, which increased the solubility of alphaxalone, solubilized in Cremophor EL. Intramuscular (IM) administration of Saffan has been used in pigs at a dose rate of 6 mg kg^{-1} (Hall 1972; Cox et al. 1975) and, following sedation with azaperone, given intravenously (IV) at 2 mg kg^{-1} (Cox et al. 1975).

The new formulation of alfaxalone-2-hydroxypropyl-beta-cyclodextrin, (Alfaxan) has been used IV at a dose rate of 0.7–0.9 mg kg^{-1} in pigs premedicated

with azaperone (Keates 2003). This formulation of alfaxalone has been administered successfully IM in rabbits (Marsh et al. 2009). As unsedated pigs are difficult to inject IV, for routine practice, an IM regimen would have advantages for anaesthesia of this species.

Keates (2003) described muscular twitching following the use of alfaxalone in pigs. Diazepam acts as a muscle relaxant via GABA receptor activation. Our hypothesis was that combining diazepam with alfaxalone would reduce muscular twitching observed after the use of alfaxalone alone. The objective of this study was to investigate this hypothesis and to describe the effects of IM alfaxalone given alone or in combination with diazepam to pigs prior to induction of anaesthesia.

Materials and methods

Twelve healthy 2 month-old Landrace x Large White pigs weighing (mean ± SD) 21.3 ± 2.4 kg were the subjects of the study. All animals were handled according to the guidelines set in the 'Guide for the Care and Use of Laboratory Animals' published by the National Institutes of Health. The institutional animal care and use committee approved the study.

Prior to the day of the study, pigs were deprived of food, but not water, overnight. Pigs were allocated randomly into two groups: group A ($n = 6$) to receive 5 mg kg^{-1} of alfaxalone (Alfaxan; Vetoquinol, Spain); and group AD ($n = 6$) to receive 5 mg kg^{-1} of alfaxalone + 0.5 mg kg^{-1} of diazepam (Valium; Roche Farma, Spain). The alfaxalone and diazepam were mixed in the same syringe, and the total volume for injection (for both groups) was standardized at 14 mL, by dilution in 0.9% sodium chloride. All drugs were administered IM by injection into the lumbar muscle. In order to assess pain on injection, the needle, attached to a line extension, was pre-placed into the muscle. After confirming the absence of any discomfort due to the needle, the administration of the drugs was carried out via the line extension over a period of 20 seconds.

Two independent evaluators unaware of the treatment, evaluated the pain on injection, the quality of induction of sedation and recumbency, and the effect of the drugs on each pig. The pain on injection was scored using a modified scale from that of Michou et al. (2012): no pain; mild pain (movement of tail and turning head towards injection side); moderate pain (attempting to remove the needle scratching the wall); severe pain (vocalization and major movement requiring manual restraint). The quality of induction of recumbency was evaluated using a scale modified from that of Covey-Crump & Murison (2008): smooth (without excitement, quick lateral recumbency and good muscle relaxation); fair (slight excitement and muscle twitching or movement of limbs); poor (marked excitement, muscle twitching, paddling of limbs and head movements); very poor (severe excitement and vocalization). The degree of sedation was assessed 10 minutes after drugs administration by scoring the pigs' apparent degree of unawareness of their surroundings using a scale modified from that of Covey-Crump & Murison (2008): no effect; mild sedation (quiet, reluctant to move, possibly slightly ataxic but able to walk); moderate sedation (unable to walk but react to noisy stimulus); deep sedation (central depression accompanied by drowsiness and possibly not react to noisy stimulus).

The time to lateral recumbency was recorded and mandibular, palpebral and corneal reflexes were evaluated at five and ten minutes after drug injection. Pulse rate (PR) and oxygen saturation of haemoglobin (SpO_2) were monitored continuously by pulse oximetry (5250 Respiratory Gas Monitor, Ohmeda-BOC, Spain) using a probe placed on the tail once the pig became recumbent. Respiratory rate (f_R) was recorded by counting thoracic respiratory movements. These three physiological variables were recorded at five and ten minutes after drug administration.

During the study, the pigs were not stimulated other than by assessment of physiological variables, evaluation of reflexes and by assessment of the level of sedation.

Ten minutes after the injection of alfaxalone (with or without diazepam), the animals were transported to the surgery room. Anaesthesia was induced/deepened by the administration of sevoflurane by facemask. Thereafter, endotracheal intubation was performed and anaesthesia maintained with sevoflurane for an interventional radiological procedure. The ease of carrying out this procedure was not scored.

Statistical analysis of continuous data was performed using SPSS 15.0 software program (SPSS Inc, Chicago, IL, USA). Following confirmation of normal distribution (Shapiro–Wilk test), data for PR, f_R and SpO_2 were analyzed using a two way ANOVA and *post hoc* comparison using the Tukey test. Times to recumbency were analyzed using a *t*-test for