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RESEARCH PAPER

Diabetes mellitus affects the duration of action of vecuronium in dogs

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Abstract

Objective To compare the duration of action of vecuronium in diabetic dogs with a control group.

Study design Prospective clinical study.

Animals Forty client-owned diabetic (n = 20) and non-diabetic dogs.

Methods Dogs were considered free from other concurrent disease based on clinical examination and laboratory data. After pre-anaesthetic medication with acepromazine and methadone, anaesthesia was induced with intravenous (IV) propofol and maintained with isoflurane-nitrous oxide in oxygen. Neuromuscular blockade (NMB) was achieved with vecuronium, 0.1 mg kg^{-1} IV and its effects recorded by palpation (pelvic limb digital extension) and electromyography (*m. tibialis cranialis*) of responses (twitches; T) to repeated train-of-four (TOF) nerve stimulation. Time to onset of NMB was the period between vecuronium injection and loss of fourth twitch (T4) in the TOF pattern recorded by EMG and palpation. Duration of NMB was defined as the time from drug administration to return of T1 by palpation ($T1_{tactile}$) and EMG ($T1_{EMG}$). Times to return of T2-4 were also recorded. Time from induction of anaesthesia to vecuronium injection was recorded. Heart rate, non-invasive mean arterial pressure, body temperature, end-tidal isoflurane and end-tidal CO_2 concentrations were recorded at onset of NMB and when $T1_{EMG}$ returned. Loss and return of palpable and EMG responses for diabetic and non-diabetic dogs were compared using t-tests and Mann Whitney U-tests.

Results There were significant ($p < 0.05$) differences between diabetic and non-diabetic dogs for the return of all four palpable and EMG responses. Times (mean ± SD) for return of $T1_{tactile}$ were 13.2 ± 3.5 and 16.9 ± 4.2 minutes in diabetic and non-diabetic dogs respectively. There were no differences between diabetic and non-diabetic dogs in the time to onset of vecuronium with EMG or tactile monitoring.

Conclusions and clinical relevance The duration of action of vecuronium was shorter in diabetic dogs as indicated by both tactile and EMG monitoring.

Keywords diabetes mellitus, dog, muscle relaxant, neuromuscular blockade, vecuronium.

Introduction

Dogs with diabetes mellitus commonly are anaesthetized for phacoemulsification of cataracts. Neuromuscular blockade (NMB) produced by non-depolarising drugs, such as vecuronium, is desirable as part of the anaesthetic technique because it predictably produces a central, immobile eye which facilitates surgery. In human patients with type II diabetes mellitus and receiving peri-operative insulin, when compared to non-diabetic subjects the duration of action of vecuronium is prolonged, i.e.,

an increased time after injection to return of first (T1) and fourth (T4) response to 'train of four' (TOF) stimulation of a peripheral nerve. An increased current is also required for supramaximal nerve stimulation (Saitoh et al. 2003). Furthermore, antagonism of NMB with neostigmine and atropine is less effective; a significantly greater number of diabetic than non-diabetic patients have a TOF ratio of <0.9 following reversal. That is T4 remains <90% of T1, despite the administration of reversal agents. The basis of these effects is not completely understood but may result from changes in the neuromuscular junction and motor nerve conduction (Saitoh et al.2004). These altered responses to vecuronium are observed in human diabetic patients during inhalational anaesthesia with sevoflurane but not total intravenous anaesthesia (Saitoh et al. 2005).

Although the pharmacokinetics of vecuronium have been documented in the dog (Marshall et al. 1980a,b; Jones 1985a,b; Thut et al. 1994) there is no information available regarding the clinical use of the drug in diabetic dogs. The aim of this study was to record the duration of action of vecuronium in dogs with diabetes mellitus and compare it with a control population undergoing anaesthesia for the same procedure.

Methods

This prospective clinical study included 40 dogs presented to the Animal Health Trust for phacoemulsification of cataracts between January 2005 and January 2006. All animals underwent pre-operative physical examination. Routine pre-anaesthetic blood sampling was undertaken to determine packed cell volume, plasma total protein, urea, creatinine and electrolyte concentrations. A more extensive biochemical evaluation and venous blood gas analysis was performed on the basis of preliminary findings. Animals with alanine transaminase (ALT) or alkaline phosphatase (ALKP) concentrations in excess of 500 iu L^{-1} were not studied in an attempt to exclude hepatopathy as a confounding factor affecting vecuronium clearance (Feldman & Nelson 2004).

Dogs were regarded as being diabetic on the basis of a history consistent with diabetes mellitus, persistent serum hyperglycaemia, glucosuria and an appropriate response to insulin administered at the referring veterinary surgeon. Non-diabetic animals did not meet any of these criteria. Additionally, owners evaluated diabetic stability based on polyuria, polydipsia and polyphagia, and referring veterinary surgeons serially evaluated blood glucose and serum fructosamine prior to referral. No further attempt was made to evaluate the stability of diabetic cases following referral. Dogs were excluded from the study if there was a history and/or clinical signs of, or biochemical indicators of severe cardiovascular or other systemic disease, if they were <6 months of age, or temperament precluded the use of a standard anaesthetic technique. Current medications were recorded. Dogs were fasted from midnight on the day prior to surgery. Water was freely available. All dogs received topical non-steroidal anti-inflammatory drugs and appropriate mydriatic drugs before surgery.

Blood glucose was measured prior to pre-anaesthetic medication in all diabetic patients and insulin administered at the discretion of the anaesthetist. All procedures were undertaken in the morning. In all cases, pre-anaesthetic medication was methadone (0.2 mg kg^{-1}) (Physeptone; Martindale Pharmaceuticals, UK) and acepromazine (0.01 mg kg^{-1}) (ACP; Novartis Animal Health, UK) administered intramuscularly (IM) given approximately 30 minutes before aseptic placement of an over-the-needle catheter in a lateral saphenous vein.

Anaesthesia was induced with propofol (Propoflo; Abbott Animal Health, UK) administered intravenously (IV) to effect. The trachea was intubated with an appropriately sized cuffed endotracheal tube to which a heat and moisture exchange device had been attached. This was then connected to an appropriate breathing system and ventilator, and intermittent positive pressure ventilation imposed. Anaesthesia was maintained with isoflurane (end-tidal isoflurane concentration ($F_E'Iso$) 1.0–1.5%) vaporized in oxygen and nitrous oxide with an inspired oxygen concentration >0.3. Non-steroidal anti-inflammatory drugs (carprofen or meloxicam) or steroids (dexamethasone), and antibiotics (potentiated amoxycillin) were administered IV at the discretion of the surgeon.

Routine anaesthetic monitoring, applied to all dogs, consisted of capnography and inspired/end tidal agent monitoring, pulse oximetry, electrocardiography, non-invasive blood pressure (oscillometric), and rectal temperature (Kolormon 7251 plus; Kontron, UK). End tidal carbon dioxide concentration ($P_E'CO_2$) was maintained at 4.6–6.4 kPa (35–45 mmHg) and mean arterial pressure (MAP) >60 mmHg. Persistent hypotension unresponsive to a decreased inspired isoflurane concentration was grounds for exclusion from the study. In diabetic