Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2013 doi:10.1111/vaa.12047

RESEARCH PAPER

Effects of pre-operative administration of medetomidine on plasma insulin and glucose concentrations in healthy dogs and dogs with insulinoma

Alonso GP Guedes* & Elaine P Rude*

*Veterinary Clinical Sciences Department, College of Veterinary Medicine, University of Minnesota, St. Paul, MN, USA

Correspondence: Alonso GP Guedes, Department of Surgical & Radiological Sciences, School of Veterinary Medicine, University of California, 2112 Tupper Hall, One Shields Avenue, Davis, CA 95616, USA. E-mail: aguedes@ucdavis.edu.

Abstract

Objective To investigate the effect of medetomidine on plasma glucose and insulin concentrations in dogs with insulinoma and in healthy dogs undergoing anesthesia and surgery.

Animals Twenty-five dogs with insulinoma and 26 healthy dogs.

Methods In dogs with insulinoma, medetomidine (5 μg kg^{-1}) was randomly included ($n = 12$) or omitted ($n = 13$) from the pre-anesthetic medication protocol, which typically contained an opioid and an anticholinergic. Healthy dogs received medetomidine (5 μg kg^{-1}; $n = 13$) or acepromazine (0.04 mg kg^{-1}; $n = 13$) plus an opioid (morphine 0.5 mg kg^{-1}) and an anticholinergic (atropine 0.04 mg kg^{-1}) as pre-anesthetic medications. Pre-anesthetic medications were given intramuscularly. Plasma glucose and insulin concentrations were measured before (sample 1) and 30 minutes after pre-anesthetic medication (sample 2), and at the end of surgery in dogs with insulinoma or at 2 hours of anesthesia in healthy dogs (sample 3). Glucose requirement to maintain intra-operative normoglycemia in dogs with insulinoma was quantified and compared. Data were analyzed with ANOVA and Bonferroni post-test, *t*-tests or chi-square tests as appropriate with $p < 0.05$ considered significant. Data are shown as mean ± SD.

Results Medetomidine significantly decreased plasma insulin concentrations and increased plasma glucose concentrations in healthy dogs and those with insulinoma. These variables did not change significantly in the dogs not receiving medetomidine. In the dogs with insulinoma, intra-operative glucose administration rate was significantly less in the animals that received medetomidine compared to those that did not.

Conclusions Pre-anesthetic administration of medetomidine significantly suppressed insulin secretion and increased plasma glucose concentration in dogs with insulinoma and in healthy dogs undergoing anesthesia and surgery.

Clinical relevance These findings support the judicious use of medetomidine at low doses as an adjunct to the anesthetic management of dogs with insulinoma.

Keywords alpha-2 agonists, dogs, glucose, insulin, insulinoma, medetomidine.

Introduction

Insulinomas are functional tumors of pancreatic β-cells that cause hypoglycemia due to excessive and uncontrolled insulin secretion. Although relatively rare, insulinomas are the most common type of neoplasia of the endocrine pancreas and one of the most frequently diagnosed of all types of

neuroendocrine tumors in dogs and humans (Abood et al. 2009). Clinical signs include changes in behavior, weakness, muscle tremors, lethargy, vomiting, seizures and coma (Leifer et al. 1986; Lurye & Behrend 2001; Polton et al. 2007). These are caused by glucose deprivation in neurons of the central nervous system (e.g., neuroglycopenic symptoms) and by hypoglycemia-induced increase in autonomic nervous system activity (e.g., neurogenic symptoms). The best therapeutic option is surgical removal of the tumor (Meleo 1990; Polton et al. 2007; Abood et al. 2009). Correcting plasma glucose concentration in order to decrease the risk of neuroglycopenia is critical for the stabilization of the patient both prior to and during anesthesia and surgery (Abood et al. 2009). Neuroglycopenic patients are prone to hypotension during anesthesia and likely to have a delayed anesthetic recovery (Meleo 1990; Dougherty & Cronau 1998; Lurye & Behrend 2001).

Medetomidine is a highly selective α_2-adrenergic receptor (AR) agonist with strong sedative, analgesic, cardiovascular and neurohormonal properties. It is formulated as a racemic mixture of two stereoisomers, with the D-stereoisomer being the active component and the L-stereoisomer being pharmacologically inactive (Savola et al. 1986; Virtanen et al. 1988; Kuusela et al. 2000). Studies in healthy conscious (Burton et al. 1997; Ambrisko & Hikasa 2002, 2003; Ambrisko et al. 2005) and anesthetized dogs (Benson et al. 2000) showed that medetomidine reliably decreased plasma insulin concentrations even though significant changes in glucose concentrations were not always documented. Such hormonal effects might be useful during the anesthetic management of dogs with insulinoma but, to our knowledge, this has not been tested. Additionally, to our knowledge, the effects of lower and clinically pertinent (Muir et al. 1999) doses of medetomidine on blood glucose and insulin concentrations in dogs have not been published.

Reported advantages of using medetomidine as part of the anesthetic protocol include sedation and analgesia, modulation of stress responses to surgery, maintenance of better hormonal and metabolic stability and anesthetic-sparing effects (Savola et al. 1986; Muir et al. 1999; Benson et al. 2000; Ko et al. 2000; Kuusela et al. 2000; Ambrisko et al. 2005). However, there are only a small number of published clinical studies using low doses (<10 μg kg^{-1}) of medetomidine for pre-anesthetic medication in dogs. Medetomidine doses of 2 and 5 μg kg^{-1} administered intramuscularly either alone or in combination with butorphanol to systemically healthy, middle-aged to old dogs undergoing anesthesia for elective surgery produced only minor complications and no detectable anesthetic-sparing effect (Muir et al. 1999). In systemically healthy dogs, intravenous medetomidine at 1 μg kg^{-1} combined with butorphanol produced clinically satisfactory sedation with only minor adverse effects (Girard et al. 2010). Hemodynamic and respiratory undesirable effects are less pronounced at low doses (Savola et al. 1986; Pypendop & Verstegen 1998; Kuusela et al. 2000), but should still be considered when anesthetizing older and/or higher risk patients that are more prone to perianesthetic complications (Brodbelt et al. 2008).

The primary goal of this study was to determine the effects of a low dose of medetomidine included in the pre-anesthetic medication on plasma glucose and insulin concentrations in dogs with insulinoma and in healthy dogs undergoing anesthesia and surgery. The potential effect of medetomidine on basic hemodynamic, respiratory and other clinically relevant anesthetic variables in the dogs with insulinoma were also evaluated.

Material and Methods

The Institutional Animal Care and Use Committee approved the study protocols and client-signed consent forms were obtained.

Animals and pre-anesthetic preparation

Dogs with insulinoma comprised of 25 client-owned dogs of various ages, breeds and sex (Table 1) presented for surgical removal of an insulinoma at the Veterinary Medical Center of the College of Veterinary Medicine, University of Minnesota between 2002 and 2006 were compared with healthy dogs (26 adult female Beagles) that were used in a non-recovery surgical teaching laboratory for veterinary students. Animals were fasted from solids for 12 hours and from liquids for 2 hours prior to anesthesia and surgery. To facilitate drug and fluid administration and collection of blood samples, over-the-needle catheters (Cathlon, Johnson & Johnson Medical, TX, USA) were placed aseptically in one (healthy dogs) or two (dogs with insulinoma) peripheral veins (cephalic and/or saphenous) before induction of anesthesia.

