Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2016, **43**, 379–387 doi:10.1111/vaa.12319

RESEARCH PAPER

Intravenous infusion of amino acids in dogs attenuates hypothermia during anaesthesia and stimulates insulin secretion

Satoshi Takashima, Sanae Shibata, Kazuto Yamada, Mizuho Ogawa, Naohito Nishii & Hitoshi Kitagawa
Department of Veterinary Medicine, Faculty of Applied Biological Sciences, Gifu University, Gifu, Japan

Correspondence: Sanae Shibata, Department of Veterinary Medicine, Faculty of Applied Biological Sciences, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan. E-mail: shiba211@gifu-u.ac.jp

Abstract

Objective To evaluate the effect of intravenous infusion of amino acids on the prevention of hypothermia during anaesthesia in dogs.

Study design Randomized experimental trial.

Animals Seven healthy Beagle dogs.

Methods Four concentrations of amino acids were prepared with a 10% amino acid solution and an acetated Ringer's solution, and dogs were infused with each of the solutions at 1 week intervals. Dogs were infused with amino acid solution at 12 mL kg^{-1} $hour^{-1}$ for 60 minutes before and for 60 minutes after induction of anaesthesia. Acetated Ringer's solution was infused at the same rate for the remaining 60 minutes of anaesthesia. The infusion treatments were: 1) A0, nutrient-free acetated Ringer's solution; 2) A6, 0.6 g kg^{-1} $hour^{-1}$; 3) A9, 0.9 g kg^{-1} $hour^{-1}$; and 4) A12, 1.2 g kg^{-1} $hour^{-1}$. Rectal temperature (RT), heart rate (HR), mean arterial pressure (MAP), blood insulin, glucose, urea nitrogen (BUN) and creatinine concentrations, and time to extubation were measured.

Results Before anaesthesia, RT was not affected by amino acid infusion. RT decreased progressively during anaesthesia and the absolute values of RT from 30 to 120 minutes were significantly higher in A12 than in A0 ($p < 0.05$). Reductions in HR and MAP during anaesthesia were attenuated by amino acid infusion in a dose-dependent manner. Plasma insulin concentration was significantly higher in A12 than in A0 during amino acid infusion and the increase in insulin concentration was greater during than before anaesthesia. BUN increased during amino acid infusion in a dose- and time-dependent fashion. Time until extubation was shorter in A12 than in A0.

Conclusions and clinical relevance Amino acids infused at 1.2 g kg^{-1} $hour^{-1}$ in dogs attenuated the decrease in RT, HR, and MAP during anaesthesia, and induced a significant increase in plasma insulin concentration.

Keywords amino acids, anaesthesia, dog, infusion, rectal temperature.

Introduction

Intraoperative hypothermia in dogs, defined as temperature <36.7 °C (Kennedy et al. 2011), is a common complication of surgical procedures and examination techniques, such as computed tomography and magnetic resonance imaging, involving general anaesthesia. In humans, anaesthesia-induced hypothermia constitutes a clinical problem by increasing blood loss, transfusion requirements (Schmied et al. 1996), incidence of surgical wound infection and hospitalization duration (Kurz et al. 1996). Moreover, hypothermia causes postoperative

shivering, which augments oxygen consumption (Alfonsi et al. 2003). In dogs, intraoperative hypothermia prolongs recovery time from anaesthesia (Pottie et al. 2007) and time to extubation (Redondo et al. 2012). These undesirable effects emphasize the necessity of preventing perioperative hypothermia.

It has been known that administration of amino acids stimulates resting energy expenditure and hence thermogenesis (Brundin & Wahren 1994a, b), even during general anaesthesia (Selldén et al. 1996; Sessler 1997). In humans and rats, it has been shown that amino acid infusion causes nutrient-induced thermogenesis as a result of heat production in skeletal muscle and prevents reduction in metabolism and hypothermia during anaesthesia (Selldén et al. 1994, 1996; Yamaoka et al. 2006). Moreover, studies using anaesthetized rats showed that administration of amino acids increases the plasma insulin concentration and the anabolic effect of insulin on muscle (Yamaoka et al. 2006, 2009). These findings suggest that amino acids facilitate heat generation and retention in the body. The metabolic and thermogenic effects of intraoperative amino acid infusion have also been studied in dogs (Jin et al. 2012; Clark-Price et al. 2015). However, a clinically useful infusion protocol has yet to be established, because adequate dose and treatment practices for infusion of amino acids are unknown.

The present study was conducted to determine the dose of intravenous (IV) infused amino acids for the prevention of hypothermia during anaesthesia in dogs. Furthermore, plasma insulin concentrations were measured to verify the contribution of insulin to the effect of amino acid infusion on the body temperature. Our hypothesis was that amino acid infusion at an effective dose would enhance insulin secretion and prevent hypothermia during anaesthesia.

Materials and methods

Animals and preanaesthetic preparation

All procedures involving the study dogs were performed at Gifu University and were approved by the Animal Care and Use Committee for Animal Experimentation of Gifu University (no. 12001). Seven mature Beagle dogs, three intact males, one intact female and three castrated males, [mean ± standard deviation (SD)] 3.5 ± 1.5 years of age and 12.8 ± 1.6 kg body weight, underwent four infusion protocols. Each dog had a body condition score of 3 (five-point scale). Normal health status was confirmed by a general physical examination, complete blood count and biochemical profile performed before the experiment. Food was withheld from the dogs for 12 hours before experiments, but free access to water was allowed.

Infusion and anaesthetic protocol

Before the experiment, a catheter (Surflo 22 gauge 32 mm; Terumo, Tokyo, Japan) was placed aseptically into the cephalic vein of each dog. This catheter was connected via a plastic tube to a three-way stopcock, enabling the infusion and injection of drugs.

In the present study, four infusion treatments were evaluated: 1) treatment A0, amino acid infusion rate of 0 g kg^{-1} $hour^{-1}$, acetated Ringer's solution; 2) treatment A6, amino acid infusion rate of 0.6 g kg^{-1} $hour^{-1}$, 5% amino acid solution; 3) treatment A9, amino acid infusion rate of 0.9 g kg^{-1} $hour^{-1}$, 7.5% amino acid solution; and 4) treatment A12, amino acid infusion rate of 1.2 g kg^{-1} $hour^{-1}$, 10% amino acid solution. The tested solutions were prepared from nutrient-free acetated Ringer's solution (Solacet F; Terumo) and a 10% amino acid solution (Amiparen; Otuka Pharmaceutical Factory, Inc., Tokushima, Japan) containing a mixture of 18 amino acids that provided 15.65 g nitrogen L^{-1}.The dogs were administered general anaesthesia for 120 minutes and infused at 12 mL kg^{-1} $hour^{-1}$ with each tested solution for 60 minutes before induction of anaesthesia and for the first 60 minutes of anaesthesia. Subsequently, dogs were infused at the same flow rate with acetated Ringer's solution until the end of anaesthesia. The tested dogs received all four infusion treatments, and infusion and anaesthesia events were separated by a 1 week washout period. The order of the four infusion doses was randomly assigned by drawing numbered cards from a hat before the first procedure.

Anaesthesia was induced with IV injection of 6 mg kg^{-1} propofol (1% Propofol for animals; Mylan, Inc., Tokyo, Japan). After endotracheal intubation, the dogs were placed in lateral recumbency. Anaesthesia was maintained with isoflurane in >90% oxygen under intermittent positive-pressure ventilation delivered by a mechanical ventilator (KV-2N; Kimura Ikakiki Co., Tokyo, Japan) to