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RESEARCH PAPER

# Stress-related biomarkers in dogs administered regional anaesthesia or fentanyl for analgesia during stifle surgery

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## Abstract

**Objectives** To compare the effects of regional anaesthesia and opioid administration on adrenocortical and glycaemic responses, postoperative pain and recovery quality in dogs undergoing stifle surgery.

**Study design** Prospective, blinded clinical study.

**Animals** Forty-five dogs anaesthetized for tibial tuberosity advancement or tibial plateau levelling osteotomy, and 15 healthy dogs undergoing non-invasive orthopaedic diagnostic procedures.

**Methods** The baseline behaviour of each dog was classified on a descriptive scale before anaesthesia. Dogs were anaesthetized using a standard protocol. Those undergoing surgery were randomly assigned to one of three intraoperative analgesia protocols: 1) peripheral (femoral and sciatic) nerve block (bupivacaine 0.5%; 0.15 mL $kg^{-1}$ in each nerve; group PNB); 2) spinal anaesthesia (isobaric bupivacaine 0.5%; 0.05 mL $kg^{-1}$; group SPI); and 3) intravenous fentanyl variable rate infusion and postoperative methadone (0.2 mg $kg^{-1}$; group FEN). Blood samples were collected for measurement of cortisol and glucose concentrations on arrival ($T_{AR}$), at induction ($T_{IND}$), at tracheal extubation ($T_{EXT}$), and 1 hour post-extubation ($T_{PEX}$). After extubation, a researcher unaware of the dog's group assignment evaluated pain and recovery quality using the Glasgow Composite Measure Pain Scale (Short-Form) and a descriptive scale, respectively.

**Results** Median recovery quality was significantly worse in group FEN ($p < 0.0001$) compared with all other groups. Postoperative pain scores were lower in group PNB compared with groups SPI and FEN. Cortisol and glucose concentrations increased significantly from $T_{AR}$ at $T_{EXT}$ and $T_{PEX}$ ($p < 0.0001$) in group FEN, and were unchanged from $T_{AR}$ in the other groups.

**Conclusions and clinical relevance** Analgesia with a peripheral nerve block or spinal anaesthesia prevented the glycaemic and cortisol responses to surgery, promoted better recovery quality, and decreased postoperative pain scores compared with FEN. In the present study, the regional anaesthesia techniques used were found to be excellent alternatives to fentanyl administration.

*Keywords* dog, peripheral nerve block, regional anaesthesia, spinal anaesthesia, stress.

## Introduction

Trauma and surgery are potent triggers of a neurohumoral stress response in all animals (Kehlet 1989). This response developed in nature to allow injured animals to survive by catabolizing their own stored body fuels. However, it has been argued that

the stress response may be unnecessary and even harmful in patients undergoing surgery (Desborough 2000). In fact, studies in humans have shown that a perioperative stress response has adverse effects on immune function, which may increase postoperative susceptibility to infections. Moreover, stress can predispose to prolonged ileus and hypercoagulability, increase the risk for ischaemia–reperfusion injury and determine systemic inflammatory responses (Liu et al. 1995; Wolf 2012).

Fentanyl is commonly used to provide perioperative analgesia in dogs (Pascoe 2000; Lamont & Mathews 2007). However, this drug is associated with several side effects that include bradycardia, hypotension, hypoventilation, ileus, nausea, vomiting and dysphoria (Lamont & Mathews 2007; Becker et al. 2012; Keating et al. 2013).

A large number of studies have shown that neuraxial anaesthesia can prevent the endocrine and metabolic response to surgery (Wolf et al. 1993; Liu et al. 1995; Meissner et al. 1997; Sibanda et al. 2006). Spinal (intrathecal) anaesthesia provides a profound degree of blockade of both afferent impulses from the surgical site and efferent autonomic pathways to the liver and the adrenal medulla, thus abolishing the adrenocortical and glycaemic responses to surgery (Wolf et al. 1998; Wolf 2012). A recent meta-analysis suggests that regional anaesthesia in humans may improve postoperative outcomes by reducing morbidity after surgery, especially in critically ill patients (Kettner et al. 2011).

In humans, severe regional anaesthesia-related complications are rare (Auroy et al. 1997), but higher incidences of complications, including nerve damage and hypotension, are associated with spinal anaesthesia. A prospective survey in children revealed that overall complication rates were six times higher after central than after peripheral nerve blocks (Ecoffey et al. 2010). Urinary retention, pruritus, respiratory depression and nausea are associated with the intrathecal administration of opioids as adjuvant analgesics (Auroy et al. 1997; Sarotti et al. 2011).

Peripheral nerve blocks (PNB) and spinal anaesthesia are techniques that reliably provide effective regional anaesthesia and analgesia during pelvic limb surgical procedures in dogs (Campoy et al. 2012; Sarotti et al. 2012; Portela et al. 2013; Vettorato et al. 2013).

No studies have been performed to assess the effects of PNB on the adrenocortical and glycaemic responses after orthopaedic surgery in dogs. The aim of the present study was to compare the effects of three analgesic techniques (PNB, spinal anaesthesia and opioid administration) on adrenocortical and glycaemic responses in dogs undergoing stifle surgery in a clinical setting to test the hypothesis that PNB and spinal anaesthesia would reduce the adrenocortical and glycaemic responses to surgery in the selected population compared with opioid administration.

## Materials and methods

### Animals

This prospective, blinded clinical study was conducted in accordance with national legislation on the protection of animals used for scientific purposes and was approved by the Institutional Animal Care and Use Committee of the University of Pisa (protocol no. 1397).

Forty-five dogs admitted to the Clinica Veterinaria Apuana (CVA) for tibial tuberosity advancement (TTA) or tibial plateau levelling osteotomy (TPLO) and 15 healthy dogs undergoing planned non-invasive orthopaedic diagnostic procedures (computed tomography or radiography) under general anaesthesia were included in this study after written informed consent had been obtained from their owners. Physical, haematological and biochemical evaluations were used to assess the health status of each animal; dogs classified as having American Society of Anesthesiologists (ASA) physical status of class I or II were enrolled in the study. Animals weighing <6 kg or >40 kg, aged <1 year or >10 years, assigned a pre-anaesthetic behaviour score of 4, receiving concurrent medications, with clotting, neuromuscular or neurological disorders, with skin infections, or with an ASA physical status of class III or higher were excluded from the study.

Fifteen healthy dogs with no sign of pain or lameness undergoing official hip and elbow dysplasia diagnostic procedures were included as a control group (group CTR). Forty-five dogs scheduled for surgery were randomly assigned into three groups of 15 dogs each by withdrawing pieces of paper with group identifications from a bag. The three groups, respectively, were to be administered the following analgesic protocols: 1) PNB of the femoral and sciatic nerves (group PNB); 2) spinal (intrathecal) analgesia (group SPI); and 3) fentanyl variable rate intravenous (IV) infusion (group FEN).

  