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Case Report

Anaesthetic Management of a 1-Month-Old Puppy Undergoing Lateral Thoracotomy for Vascular Ring Anomaly Correction

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A 1-month-old male flat-coated retriever was anaesthetized for correction of oesophageal constriction caused by a vascular ring anomaly. Anaesthesia was uneventfully induced with intravenous fentanyl, diazepam, and propofol and maintained with isoflurane in oxygen and air. An intercostal block with bupivacaine and lidocaine was performed, and additional analgesia with an infusion of fentanyl was provided. Fluid therapy consisted in 5% glucose in lactated Ringer's solution and hetastarch 6%, which proved adequate to maintain normoglycemia and normovolemia. A lateral thoracotomy was performed, and the ligamentum arteriosum was ligated. Intraoperatively, heart rate (HR) varied between 120 and 180 beats min^{-1} without accompanying changes in blood pressure. No arrhythmias were observed or bleeding occurred. The dog recovered uneventfully. Postoperative analgesia consisted in fentanyl infusion adjusted to the patient's requirement and metamizol. This paper describes for the first time the use of balanced anaesthesia and multimodal analgesia in a paediatric dog undergoing thoracotomy.

1. Introduction

Literature about paediatric patients in veterinary medicine does not provide concise data regarding the development of physiological important parameters for anaesthesia. Dogs until 12 weeks old are considered paediatric patients and are characterized by organ immaturity thus having a unique physiology and pharmacology [1]. In these patients, the gluconeogenesis and glycogenolysis are only partially activated, and the glucose storage capacity of the liver is less for body weight than in adults [2]. Thus, plasma glucose levels in puppies should be closely monitored during anaesthesia [1, 2].

Nonshivering thermogenesis and thermal vasoconstriction are active in paediatric patients; however, heat loss is enhanced by the low subcutaneous fat reserves and the increased surface area/weight ratio [3, 4]. These active thermoregulatory responses are inhibited by anaesthetic agents [4]. Thus, puppies undergoing anaesthesia should be actively warmed to minimize temperature losses [3].

The sympathetic and parasympathetic systems in dogs become fully functional by about 7 weeks of age [5]. It has been seen in rats that positive inotropic responses to sympathetic nerve stimulation first develop between 2 and 3 weeks of age [6]. As cardiac innervations are not functionally mature in neonates, puppies may react only moderately to sympathetic stimulation [6].

The hepatorenal system of neonatal dogs continues to develop until 3 to 6 weeks of age [7], the hepatic enzymes responsible for biotransformation are immature, and the glomerular filtration rate is decreased [8]. The composition of water in paediatric patients is higher than that in adults, and the concentration of plasma proteins to bind drugs is reduced [8]. Thus, clearance, metabolism, and excretion of many drugs may be reduced and the dosing and dosing intervals may be altered [7].

To correct vascular ring anomalies in veterinary medicine, thoracotomy is performed [9–12]. To avoid lung atelectasis during these procedures, control of the ventilation is necessary. In paediatric patients, lung protective mechanisms should be used; the chest wall is highly compliant and presents minimal elastic recoil, which can end in airway collapse while in normal tidal breathing during anaesthesia, and, therefore, ventilation needs to be assisted [13]. Moreover, thoracotomy-related pain is considered in adults to be the most intense possible [13]. In infants, transduction from

polymodal nociceptors is functional, and central nociceptive processing develops gradually after birth [8, 14]. Thus, adequate pain management should be provided in paediatric patients [15].

In this paper, we describe for the first time the use of balanced anaesthesia to preserve physiological stability while providing adequate analgesia in a paediatric dog undergoing thoracotomy for vascular ring anomaly correction.

2. Case Description

A 1-month-old male flat-coated retriever weighing 4.6 kg was presented with retching and swallowing problems. The dog was alert and showed normal quiet and calm behaviour. Haematology and serum biochemical analysis were within normal limits. A radiologic examination of the thoracic and abdominal cavity was carried out including esophagography. A presumptive diagnosis was made as persistent right aortic arch (PRAA) on the basis of the anamnesis, clinical signs, radiographic examination, and the esophagography. The diagnosis was confirmed surgically as PRAA with left ligamentum arteriosum (LA) and an aberrant left subclavian artery (SA).

Preanaesthetic examination revealed a heart rate (HR) of 180 beats min^{-1}, respiratory rate (RR) of 40 breaths min^{-1}, pink mucous membranes, capillary filling time of 2 seconds, and temperature of 38.4 degrees. The dog was deprived of food for 6 hours without water restriction. The right cephalic vein of the dog was catheterized using a 22-gauge-over-needle peripheral catheter (Surflo catheter, Terumo, Leuven, Belgium). Preoxygenation was performed with a mask during 5 minutes. Coinduction of anaesthesia consisted on the intravenous administration of fentanyl (Sintenyl, Sintetica AG, Mendrisio, Switzerland) (5 mcg kg^{-1}), diazepam (Valium, Roche Pharma, Reinach, Switzerland) (0.1 mg kg^{-1}), and propofol (Propofol, Fresenius kabi AG, Stans, Switzerland) to effect. After intubation of the trachea, the cuffed endotracheal tube (Athlone, Hi-contour, Mallinckrodt, Ireland) (6 mm ID) was connected to an anaesthesia machine (Megamed 700, Megamed AG, Cham, Switzerland) using a small circle system (Intersurgical, United Kingdom) with a heat and moisture exchanger (Hygrobaby, Mallinckrodt dar, Tyco, Mirandola, Italy).

Anaesthesia was maintained with isoflurane (Isoflo, Provet, Lyssach, Switzerland) in oxygen (0.2 L min^{-1}) and air (0.2 L min^{-1}) resulting in an inspiratory fraction of oxygen (FiO_2) of 0.6. The dog was mechanically ventilated (20 breaths min^{-1}) using intermittent positive pressure ventilation (IPPV) volume controlled (tidal volume (V_T) = 10 mL kg^{-1}), pressure limited (peak inspiratory pressure (PIP) = 12 mmHg) with a respiratory rate setting to maintain normocapnia (end-tidal carbon dioxide ($EtCO_2$) = 6 kPa (45 mmHg)). Positive end expiratory pressure (PEEP = 3 mmHg) was applied when the thoracic cavity was open. The isoflurane concentration (end-tidal concentration (ETiso) 1.1 to 1.4%) was adjusted to maintain an appropriate anaesthesia depth judged by the position of the ocular globe, evaluation of the palpebral reflex, and the breathing pattern.

Intraoperative pain management consisted of a fentanyl infusion (10 mcg kg^{-1} h^{-1}) and desensitising the third to the fifth intercostal nerves with 0.5 mg kg^{-1} bupivacaine (Carbostesin 0.5%, Astra Zeneca, Zug, Switzerland) and 1 mg kg^{-1} lidocaine (Lidocaine 2%, Kantonsapotheke, Zurich, Switzerland) as described by Gaynor and Mama [16].

Fluid therapy consisted of 5% glucose (Glucose 50%, Kantonsapotheke, Zurich, Switzerland) in lactated Ringer's solution (Ringer Laktat, Fresenius kabi AG, Stans, Switzerland) (8 mL kg^{-1} h^{-1}) and hetastarch 6% (Haes 6%, Fresenius kabi AG, Stans, Switzerland) (2 mL kg^{-1} h^{-1}). Glucose plasma levels were measured every 30 minutes, and supplementation aimed at glucose blood values between 5 and 9 mmol L^{-1} (Table 1).

Heat loss was prevented with the help of an active air warming device (Bair Hugger, Carbamed, Zurich, Switzerland), a heating blanket (Solis, Zug, Switzerland), and a heat and moisture exchanger.

Monitoring of cardiovascular function consisted of the evaluation of a constantly displayed ECG and oscillometric measurements of indirect arterial blood pressures over an antebrachial artery. The FiO_2, RR, Etiso, and $EtCO_2$ were permanently obtained using a sidestream probe connected at the Y-piece of the breathing system. The haemoglobin oxygen saturation (SpO_2) was evaluated by placing a pulse oximeter probe on the tongue, and body temperature was monitored using a thermometer placed in the oesophagus. All above-mentioned parameters were obtained with a multiparameter monitor (Cardiocap, Datex Ohmeda, Helsinki, Finland) and recorded every 5 minutes.

A total of 6 mg kg^{-1} IV propofol were necessary to induce anaesthesia. No regurgitation occurred. The surgical approach consisted in a left lateral thoracotomy at the level of the 4th intercostal space. Intraoperative antibiotherapy consisted of cefazolin (Kefzol, Teva Pharma AG, Aesch, Switzerland) (22 mg kg^{-1} IV) and metronidazole (Metronidazole, B.Braun, Sepmbach, Switzerland) (10 mg kg^{-1} IV).

Cardiovascular parameters are represented in Figure 1. Mean arterial blood pressure ranged from 58 to 70 mmHg during maintenance of anaesthesia. Heart rate decreased from 180 beats min^{-1} to 120 beats min^{-1} in the first hour. Following opening of the thoracic cavity, during the following 110 minutes, HR varied between 120 and 180 beats min^{-1}. When the thorax closure started, heart rate decreased and remained between 100 and 140 beats min^{-1} until the end of anaesthesia. No arrhythmias were observed. The capillary refill time was always 2 seconds, and the mucous membranes were pink. The SpO_2 during maintenance of anaesthesia was 96–99%. Temperature increased over time from 36.2 to 38.1 degrees centigrade. During surgery, the LA was ligated and transected without manipulation of the aberrant left SA. The oesophagus did not present any macroscopic lesions. A tube gastrostomy was also performed. Total anaesthesia time was 3 hours and 30 minutes.

For recovery of anaesthesia, isoflurane was discontinued, the trachea was extubated, and the dog was transferred to a warm and padded cage at the intensive care unit. Continuous ECG was monitored during the following 24 hours, and no

Table 1: Glucose values from a dog during anaesthesia for ring anomaly correction. The samples were obtained every 30 minutes corresponding to beginning of maintenance of anaesthesia (T0 h), minute 30 (T0.5 h), 60 (T1 h), 90 (T1.5 h), 120 (T2 h), 150 (T2.5 h), 180 (T3 h), and 210 (T3.5 h).

	T0 h	T0.5 h	T1 h	T1.5 h	T2 h	T2.5 h	T3 h	T3.5 h
Glucose (mmol L^{-1})	5.4	5.4	5.8	6.4	7.6	8.8	8.9	9.1

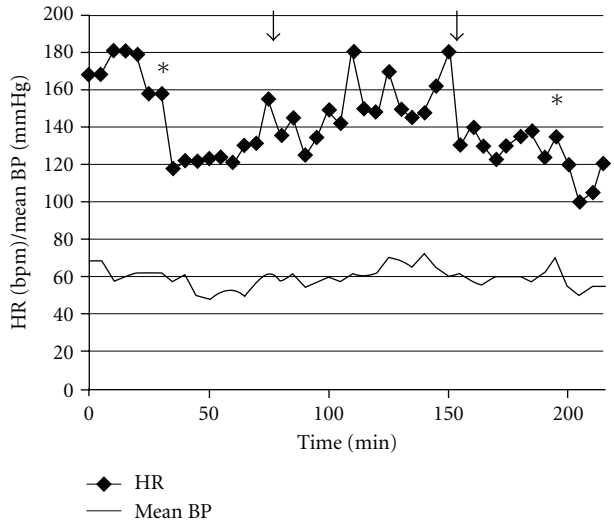

Figure 1: Noninvasive mean arterial blood pressure (mean BP, mmHg) and heart rate (HR, beats min^{-1}) during maintenance of anaesthesia of a dog undergoing surgery for vascular ring anomaly correction. The beginning and the end of surgery are marked with an asterisk (*). The beginning and the end of the intraoperative period during which the heart was manipulated are marked with arrows.

arrhythmias were observed. Fluid therapy consisted in 5% glucose in lactated Ringer's solution (2 mL kg^{-1} h^{-1}) and was given for five days after surgery. During this period, postoperative analgesia was provided with 2–10 mcg kg^{-1} h^{-1} fentanyl IV. The fentanyl dose was adjusted to the patient requirements. On day 6, fentanyl was discontinued, and metamizol (Novalgin, Veterinaria AG, Pfäffikon, Switzerland) (30 mg kg^{-1} IV tid) was administered for a week. Further antibiotherapy with cefazolin (22 mg kg^{-1} IV tid) was administered during 2 weeks. The gastrostomy tube was removed 2 weeks after surgery, and the patient was discharged from the hospital.

3. Discussion

To the author's knowledge, there is scarce information regarding anaesthetic techniques for thoracotomy in puppies, and this is the first paper in which a balanced anaesthetic technique and a multimodal analgesic approach are described in a 1-month-old dog undergoing thoracotomy for vascular ring anomaly correction.

One main concern during induction of anaesthesia was the risk of aspiration pneumonia after regurgitation secondary to megaesophagus [1]. Propofol, a fast-acting induction agent, was chosen because it abolishes quickly the swallowing reflex and intubation of the trachea can be rapidly performed [17]. However, propofol impairs cardiovascular function in a dose-dependent manner and a reduction of the dose is desirable. Therefore, fentanyl and diazepam were coadministered as it has been shown in adult dogs to reduce the requirements of propofol necessary for induction of anaesthesia [18]. As fentanyl, diazepam, and the soya-oil-based propofol used are lipid soluble, the higher body water content of the puppy was expected to minimally influence the distribution of the drug; for this reason we decided to use dosing described for adult dogs [7]. Extrapolating from human data, clearance of these drugs was not expected to be delayed in this puppy. Indeed, the major metabolic pathway of fentanyl and propofol, glucuronidation, reaches adult rates by the first year of life. In addition, hepatic hydroxylation in neonates is active and fully contributes to a rapid drug clearance [19]. There is also evidence that the CYP3A4 enzyme, responsible for the hepatic metabolism of diazepam, appears during the first week of life [20]. Propylene glycol, the excipient of the commercially available formulation of diazepam, is only partially metabolized in the liver and excreted up to 45% unchanged in the urine [21]. It could be speculated that elimination of propylene glycol may have been delayed as glomerular filtration rate is reduced in puppies [8] and a formulation of a benzodiazepine without propylene glycol such as midazolam could be a better option; however, the LD_{50} of this adjuvant has been reported to be at volumes of 9 mL kg^{-1}, a volume 100 times above the one administered to this puppy [22].

Severe pain is accompanying thoracotomies [23]. Although information in puppies is missing, human data showed that nociception in the neonate is facilitated as both A and C fibers activate spinal pathways. Central nociceptive pathways, including spinothalamic and cortical fibers, are functional, and the descending inhibitory pathways are delayed although responsive [7, 15, 24]. Hence, it was decided to combine lidocaine and bupivacaine to provide local analgesia at the surgical side in combination with a fentanyl CRI. This multimodal approach has been proven to provide adequate analgesia during and following thoracotomy in dogs [25, 26]. These amino amide local anaesthetic agents are metabolized in the hepatic microsomes via dealkylation, hydrolyzed, and excreted in the urine [8]. As dealkylation activity in neonates is close to the adult pattern [27], it was speculated that their elimination would be appropriate.

Fentanyl was chosen as part of the multimodal approach in this puppy as it is a potent analgesic recommended for severe pain relief in dogs [7]. Opioid receptors have been found in humans and laboratory animals to be present since birth, suffering reorganisation over time [24]. Advantageously, fentanyl has an increased volume of distribution in

children [19]. This may contribute to the reduced degree of respiratory depression seen in neonates after administration of 10 mcg kg^{-1} IV fentanyl [28]. However, neonates are more sensitive to the depressant effects of opioids because the blood-brain barrier is immature [19]. This puppy received fentanyl infusion intra- and postoperatively, and side effects described in children due to opioids administration such as respiratory depression, apathy, nausea, ileus, urinary retention, or itching were not observed [8]. A prolonged effect of fentanyl due to reduced clearance of the drug may have occurred in our puppy [19]; six days following thoracotomy, the pain management of the puppy was reduced to metamizol. As opioid tolerance can occur in children [29], the fentanyl dose rate administered postoperatively to our puppy was decreased according to the patient requirements.

In this puppy, variations in HR were observed during intrathoracic surgical manipulations. This was considered a compensatory mechanism to reduced venous return secondary to compression of the vena cava or other thoracic vessels. As puppies have a highly compliant chest wall, it might be easier to compress the organs in the thoracic cavity [13]. However, maturation of the baroreflex in dogs occurs with growth from 1 week to 6 months [30]. Therefore, this reflex may have been immature in this 4-week-old puppy [1, 6]. Changes in mean blood pressure did not accompany increases in HR. This could be explained by a slower maturation of alpha adrenergic receptors in the vascular smooth muscle, which regulate and maintain vascular tone [31].

Increases in HR could also be interpreted as inadequate analgesia provision or even awareness. It is possible that the intercostal blocks failed because the technique was not performed adequately or because mixing lidocaine (with fast onset and intermediate duration, 1-2 hs) and bupivacaine (with long onset and duration of action, 3–10 hs) provides unpredictable analgesic effects due to changes in baricity and pH [32].

Adjunctive analgesia, such as the continuous administration of lidocaine, would probably have allowed a reduction in the dose of fentanyl and isoflurane as well as the concurrent prevention of ventricular arrhythmia-associated direct manipulation around the heart. Lidocaine decreases automaticity of the heart by blocking sodium channels, and this effect in a paediatric patient could have resulted in a decreased cardiac output [6, 33]. Therefore, the use of intravenous lidocaine in this paediatric patient was disregarded because a potential decrease in its metabolic clearance would have resulted in drug accumulation. In addition, the reduced concentration of the plasma α1-acid glycoproteins observed in paediatric patients would hypothetically lead to potential toxic concentrations of unbound lidocaine that could cause seizures and cardiac depression [8].

Multimodal analgesia could have been improved with nonsteroidal anti-inflammatory drugs (NSAIDs). The cyclooxygenase (COX) enzyme oxidizes arachidonic acid to eicosanoids, including prostaglandins, which are synthesized at constant rate (not stored) and facilitate physiological functions such as generation of the mucosal defences, correct platelet function, leukocyte adherence, and renal protection, and maturation [34]. The NSAIDs inhibit the COX enzymes, and their use is restricted to well-hydrated and normotensive patients older than 6 weeks [35]. For this reason, NSAIDs were not administered in this puppy.

This patient received for postoperative pain management metamizol instead. Metamizol has been classified by some authors as antipyretic drug that provides smooth muscle relaxation and spasmolysis [36]. Metamizol, however, could have been deleterious in this patient as it may cause neutropenia, leukopenia, agranulocytosis, and aplastic anemia, all of which have been described in children [37–39]. However, evidence in dogs demonstrating these side effects is missing, and no side effects were observed in this puppy.

"Low stretch" ventilation strategies were used in this puppy aiming at providing lung protection [40]. The PIP was limited to 12 mmHg and the V_T was lower (10 mL kg^{-1}) than that reported for adult dogs (V_T = 16 mL kg^{-1} [41]). This strategy may be advantageous in children as it decreases the work of breathing [13]. Children have a lower proportion of diaphragm fatigue-resistant fibers, and the functional residual capacity is near to the alveolar closing volume [8]. The situation is worsened when intercostal muscle tone is decreased by induction of anaesthesia [13]. The PEEP used in this puppy was the lowest to avoid visible lung collapse.

Hepatic glucose production and storage are immature in paediatric patients, gluconeogenic enzymes to convert amino acids to glucose are inefficient, and hepatic glucose release is decreased as the glycogen phosphorylase and the glucose-6 phosphatase enzymes are not fully active [2].

Transient hypoglycaemia has been associated with neurologic injury in neonates, while hyperglycaemia can induce osmotic diuresis and, consequently, dehydration and electrolyte disturbances [42]. Lactated Ringer's solution was supplemented with 5% glucose because it has been shown in human paediatric anaesthesia patients to decrease the incidence of hypoglycaemia, without significantly affecting the incidence of hyperglycemia [42]. In dogs, a 5% glucose infusion has been suggested to maintain normoglycemia during anaesthesia [43].

Severe complications can result from hypothermia such as impaired coagulation and platelet function, reduced immune function, and prolonged recovery [44]. Strategies to actively warm the puppy were applied during anaesthesia because, in addition to low subcutaneous reserves, the vasodilation caused by isoflurane would facilitate further heat loss [45]. The body surface was maintained warm using a heating pad and a forced hot air device, while the heat losses due to humidifying and heating inspiratory gases were minimized using a heat and moisture exchanger. These strategies proved to be effective because, despite temperature decreased during preparation of the surgical field, it increased over time.

The combination of PRAA with left LA and aberrant left SA is a rare vascular ring anomaly, which causes oesophageal stenosis and needs surgical correction [46]. Luckily, the major complications reported during surgery, namely, acute bleeding or life-threatening arrhythmias secondary to manipulations, did not occur in this puppy.

4. Conclusion

This paper describes a multimodal anaesthetic and analgesic approach using intercostal blocks and a fentanyl infusion to minimize intraoperative nociception in a paediatric dog undergoing thoracotomy.

Disclosure

The authors do not have a direct financial relation with the commercial identities mentioned in the paper that might lead to a conflict of interest for any of the authors.

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