Opioid-free anaesthesia for the surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome in five dogs

Opioid-free anaesthesia is currently becoming more popular in human medicine, as it provides multimodal analgesia, affecting multiple nociceptive pathways without the use of opioids, in order to minimise opioid-related side effects. This article presents the cases of five dogs undergoing surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome , all of whom received opioid-free anaesthesia for surgery. All dogs received a bilateral maxillary nerve block with bupivacaine 0.5% and a combination of non-opioid analgesic drugs. Buprenorphine was allowed during the postoperative period, based on pain assessment. Three out of five dogs received buprenorphine 6–7 hours after the nerve block was performed. Opioid-free anaesthesia provided adequate conditions for surgery and no adverse effects were reported. Prospective controlled studies comparing opioid-free anaesthesia with opioid-based techniques are required to elucidate whether or not opioid-free anaesthesia confers objective advantages.

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Opioids are effective analgesic drugs often used to control pain or nociception and contribute to sedation in small animals (Epstein et al, 2015). However, they are not exempt from adverse effects. Some of the reported unwanted side effects, reported in both humans and dogs, include respiratory depression, ileus, nausea, vomiting, dysphoria, hyperalgesia and immunomodulatory effects (Lefebvre et al, 1981; Chu et al, 2008; De Boer et al, 2017; Bini et al, 2018).

Opioid-free anaesthesia has been receiving increased attention in recent years because of the opioid abuse crisis in the USA. As a result, there is now a better understanding of their unwanted side effects (Gupta et al, 2020). The aim of opioid-free anaesthesia is to modulate intraoperative nociceptive stimuli, effectively combining regional anaesthetic techniques with non-opioid analgesics (Frauenknecht et al, 2019). Scarce reports in veterinary medicine describe the use of this technique in dogs with good outcomes (White et al, 2017; Zannin et al, 2020).

Brachycephalic dogs are prone to develop perianaesthetic complications, including regurgitation or vomiting, leading to possible aspiration pneumonia, respiratory distress and death (Lorison et al, 1997; Poncet et al, 2005; 2006; Davies et al, 2015; Tarricone et al, 2019). Some opioids have also been linked to increased incidences of vomiting, gastroesophageal reflux and regurgitation in dogs (Poncet et al, 2005; Wilson et al, 2007). Panting and sedation induced by opioids can also contribute to upper airway obstruction (Monteiro et al, 2008; Menegheti et al, 2014). A recent study showed that administration of methadone, regardless of pain score, after orthopaedic procedures significantly increased the risk of vomiting, dysphoria and reduced food intake in dogs (Bini et al, 2018). Therefore, it is possible that reducing or avoiding administration of opioids could curtail their unwanted effects and ameliorate anaesthetic recovery in the specific setting of surgery for brachycephalic obstructive airway syndrome.

This retrospective case series describes five separate cases of dogs undergoing surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome, while being successfully anaesthetised with opioid-free anaesthesia.

Case histories

All animals had a preoperative examination, venous blood gas analysis, airway examination and radiographs (two orthogonal views) prior to surgery. Case details including the opioid-free anaesthesia protocols are presented in *Table 1*.

Method

Using anatomical landmarks, a bilateral extraoral maxillary nerve block with bupivacaine (MarcainPolyamp, AstraZeneca) 0.5% was performed in all cases. After skin preparation and disinfection, a needle was introduced percutaneously ventral to the downwards curvature of the zygomatic arch in a direction perpendicular to the long axis of the head. The needle was advanced until it made contact with bone (pterygopalatine fossa), then slightly withdrawn to inject the bupivacaine into the fat pad found in this area (Castejón-González and Reiter, 2019).

Intraoperative nociception was considered when at least two of the following variables, heart rate, respiratory rate and non-invasive blood pressure increased more than 20% from the previous measurement (Hernandez-Avalos et al, 2019). Only in case 3 was an event of intraoperative nociception detected and treated with an intravenous bolus of medetomidine 1 µg/kg.

Postoperative pain was assessed using the Glasgow Composite Measure Pain Scale. Buprenorphine (Vetergesic, Ceva) 20 µg/kg IV was administered as postoperative rescue analgesia when the pain score was ≥5/20 or 6/24. Three out of five cases (case 1, 3 and 4) required buprenorphine 6–7 hours after the bilateral

Table 1. Opioid-free anaesthestic protocols used in five brachycephalic dogs undergoing surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome

Protocol	Case 1	Case 2	Case 3	Case 4	Case 5
	2-year-old French Bulldog, female neutered, 12.45 kg, BCS 5/9* and ASA III†	3-year-old Pug, female, 8.1 kg, BCS 8/9*, ASA III†	1-year-old French Bulldog, female, 7.85 kg, BCS 5/9*, ASA III†	3-year-old French Bulldog, male, 15.9 kg, BCS 6/9*, ASA III†	1-year-old French Bulldog, male, 11.6 kg, BCS 5/9*, ASA III†
Clinical signs on presentation	Inspiratory stridor	Episodes of respiratory distress, snoring and inspiratory stridor	Episodes of respiratory distress with cyanosis, snoring and inspiratory stridor	Snoring, inspiratory stridor and regurgitation episodes	Respiratory distress with cyanosis, snoring, inspiratory stridor and regurgitation
Current medication	Omeprazole (Omeprazole, Star) 10 mg/kg per os	Pexion (idiopathic epilepsy)	N/A	N/A	N/A
Premedication	Medetomidine (Sedator, Dechra) 5 µg/kg IV	Medetomidine 3 µg/kg IV	Medetomidine 10 µg/kg IM	Dexmedetomidine (Dexdomitor, Orion) 3µg/kg IV	Medetomidine 10 µg/kg IM
Induction	Propofol (PropoFlo Plus, Zoetis) 1.5 mg/kg IV	Alfaxalone (Alfaxan Multidose) 0.5 mg/kg IV	Propofol 2.5 mg/kg IV	Propofol 2 mg/kg IV	Alfaxalone 1.5mg/kg
Maintenance	Isoflurane (IsoFlo, Zoetis) in 100% oxygen	Isoflurane in 100% oxygen	Isoflurane in 100% oxygen	Isoflurane in 100% oxygen	Isoflurane in 100% oxygen
Loco-regional anaesthesia	Bilateral MNB with 1 ml each side of bupivacaine (MarcainPolyamp 0.5%, AstraZeneca) 0.5%.	Bilateral MNB with 1 ml each side of bupivacaine 0.5%	Bilateral MNB with 1 ml each side of bupivacaine 0.5% and splash of lidocaine (Hameln 2%) of 2% of 1 ml on nostrils	Bilateral MNB with 1 ml each side of bupivacaine 0.5% and intratesticular bupivacaine injection	Bilateral MNB with 1 ml each side of bupivacaine 0.5% splash of lidocaine of 2% of 1 ml on soft palate
Fluid therapy	Hartmann´s (Vetivex11 Solution for Infusion, Dechra) 4 ml/kg/h	Hartmann´s 4ml/kg/h	Hartmann´s 4ml/kg/h	Hartmann´s 4 ml/kg/h	Hartmann´s 4 ml/kg/h

Table 1. (Continued)

Drugs administered immediately after induction	Medetomidine CRI 1 mcg/kg/h, Paracetamol (Paracetamol Injection, Braun) 10 mg/kg, maropitant (Prevomax, Dechra) 1 mg/kg and metoclopramide (Emeprid, Ceva) 1 mg/kg/24h CRI IV.	Medetomidine CRI 1 mcg/kg/h, Paracetamol 10 mg/kg IV	Omeprazole 1 mg/kg over 15 min, Paracetamol 10 mg/kg, maropitant 1mg/kg and metoclopramide 1 mg/kg/24h CRI IV	Paracetamol 10 mg/kg, Omeprazole 1 mg/kg and dexamethasone (Colvasone 0.2%, Norbrook) 0.2 mg/kg IV	Paracetamol 10 mg/kg, dexamethasone 0.2 mg/kg, maropitant 1 mg/kg, omeprazole 1 g/kg and CRI of metoclopramide 1 mg/kg/24h IV
Monitoring equipment	ECG, capnography, pulse oximetry, NIBP, temperature, spirometry.	ECG, capnography, pulse oximetry, NIBP, temperature, spirometry.	ECG, capnography, pulse oximetry, NIBP, temperature, spirometry.	ECG, capnography, pulse oximetry, NIBP, temperature, spirometry.	ECG, capnography, pulse oximetry, NIBP, temperature, spirometry.
Surgical procedure	Rhinoplasty, folded flap palatoplasty and laryngeal saccule resection	Rhinoplasty, folded flap palatoplasty and laryngeal saccule resection	A folded flap palatoplasty, alar fold resection and lateral wedge alarplasty	A folded flap palatoplasty, alar fold resection and lateral wedge alarplasty, castration	A folded flap palatoplasty, alar fold resection and lateral wedge alarplasty
IV medication 24 hours postoperatively	Meloxicam (Metacam, Boehringer Ingelheim), omeprazole, Buprenorphine (Vetergesic, Ceva) (1 dose)	Meloxicam, omeprazole, Imepitoin (Pexion, Boehringer Ingelheim), medetomidine CRI 1 µg/kg/h IV	Omeprazole, paracetamol, meloxicam, buprenorphine (2 doses)	Omeprazole, paracetamol and buprenorphine (3 doses).	Omeprazole and paracetamol

ASA American Society of Anaesthesiologists; BCS Body condition score; N/A Not applicable; CRI Constant rate infusion; ECG Electrocardiogram; GA General anaesthesia; IM Intramuscular; IV Intravenous; MNB Maxillary nerve block; NIBP Non-invasive blood pressure.

**1 Emaciated, 2 Very thin, 3 Thin, 4 Underweight, 5 Ideal, 6 Overweight, 7 Heavy, 8 Obese, 9 Severely obese*

†I Patient is a completely healthy fit patient; II Patient has mild systemic disease; III Patient has severe systemic disease that is not incapacitating; IV Patient has incapacitating disease that is a constant threat to life; V Moribund patient who is not expected to live 24 hours with or without surgery.

extraoral maxillary nerve block was performed. There were no postanaesthetic complications (dysphoria, respiratory distress, stress, regurgitation, vomiting) reported, with the exception of case 2 where postoperative sedation with medetomidine was required because of stress (*Table 1*). All dogs were discharged from the hospital within 36 hours of the procedure.

Results

The cardio-respiratory variables are shown in *Table 2*.

Discussion

This case series shows opioid-free anaesthesia provided adequate conditions for surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome in five dogs. The multimodal approach used to manage intra-operative nociception permitted the avoidance of opioids until the effect of the maxillary nerve block wore off.

In every case, the alpha-2 agonists medetomidine (Sedator, Dechra) or dexmedetomidine (Dexdomitor, Orion) were administered as premedication (two dogs also received an intraoperative constant rate infusion) to produce dose dependant sedation, analgesia and reduction of sympathetic tone that could extend into the recovery period (Murrell and Hellebrekers, 2005). Dexmedetomidine 1 µg/kg/h provides analgesia comparable to that of morphine 0.1 mg/kg/h in dogs (Valtolina et al, 2009). In case 3, a bolus of medetomidine 1 µg/kg was used to successfully attenuate the sympathetic and nociceptive response.

The maxillary nerve block desensitises the palate, oral mucosa, nasal mucosa and skin, making this block a good option to provide analgesia for the surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome. The lack of sensory input following an effective block provides unsurpassed analgesia extending into the postoperative period and has pronounced anaesthetic and opioid sparing effects. Perineural injections of local anaesthetics at the correct dose are devoid of respiratory and gastrointestinal side effects. However, complications such as retrobulbar haematoma and exophthalmia have been reported following a maxillary nerve block in dogs (Loughran et al, 2016; Grubb and Lobprise, 2020). The expected duration of bupivacaine is reported to be 3–6 hours (Castejón-González and Reiter, 2019). Postoperative buprenorphine was prescribed if required according to pain score.

Table 2. Cardio-respiratory variables measured during the anaesthetic period in five brachycephalic dogs undergoing surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome

	Case 1	Case 2	Case 3	Case 4	Case 5
Heart rate (beats per minute)	88±24.4	82±14	65±6.6	85±5.6	76±8.4
Respiratory rate (breaths per minute)	12.3±3.5	21.6±3.5	23.9±5	7±3	27.9±7.1
Systolic arterial blood pressure (mmHg)	99.3±9.9	92.1±9.8	103.3±4.3	114.7±19.7	91.3±5.7
Mean arterial blood pressure (mmHg)	68.3±6.9	69.8±8.4	64.9±5.7	88±18.5	66±7.8
Diastolic arterial blood pressure (mmHg)	43.6±7.1	54.2±4.2	38±4.2	54.6±17.6	47.3±13.8

Data are presented as mean ± standard deviation. Blood pressure was taken with a non-invasive cuff (size 2 and 3) located on the metatarsal region (Veterinary Cardell, 9401 Midmark Animal Health).

Paracetamol (Paracetamol injection, Braun), maropitant (Prevomax, Dechra), dexamethasone (Colvasone 0.2%, Norbrook) or meloxicam (Metacam, Boehringer Ingelheim) were administered perioperatively. Paracetamol and meloxicam provide analgesia (Murrell, 2018; Hernández-Avalos et al, 2020; Pacheco et al, 2020). Maropitant's main action is antiemetic, a favourable effect in this scenario, but it also has anaesthetic sparing effect (Zubrzycka and Janecka, 2000; Marquez et al, 2015; Hay Kraus, 2017; Swallow et al, 2017). Dexamethasone is a potent anti-inflammatory, devoid of analgesic properties (Liu et al, 2013). The authors consider that the multimodal analgesia goal during the intraoperative period was achieved. Only in case 3, a bolus of medetomidine 1 µg/kg was used successfully to attenuate the sympathetic and nociceptive response.

There are limited reports of opioid-free anaesthesia in veterinary literature. In one study, opioid-free anaesthesia was performed successfully in three dogs undergoing ovariohysterectomy using a multimodal approach including medetomidine, ketamine (Ceva Ketamine, Ceva Animal Health Pty Ltd), carprofen (Carprieve, Norbrook Laboratories Australia Ltd), paracetamol and a bilateral transverse abdominis block with bupivacaine (White et al, 2017). Other authors demonstrated the suitability of opioid-free anaesthesia in a dog undergoing dorsal hemilaminectomy using an intraoperative multimodal approach with dexmedetomidine, dextroketamine (Ketamin; Cristália) and an ultrasound-guided erector spinae block with bupivacaine (Zannin et al, 2020).

Opioids, specifically mu-opioid agonists, delay the gastric emptying and potentiate the risk of vomiting, regurgitation and gastro-oesophageal reflux in dogs (Wilson et al, 2005, 2007; Downing and Gibson, 2018). Brachycephalic dogs present with upper airway anatomical features, such as stenotic nares, an elongated soft palate, redundant pharyngeal folds, and a hypoplastic trachea, leading to a continuous increased inspiratory effort and high negative intrathoracic pressure. This is thought to increase the risk of gastro-oesophageal reflux, regurgitation and vomiting (Costa et al, 2020). Providing adequate analgesia in the absence of opioids will allow a dog to be more alert and less stressed in the postoperative period. This is likely to reduce the risk of airway obstruction, regurgitation, vomiting and aspiration pneumonia.

These findings suggest opioid-free anaesthesia, including a bilateral maxillary nerve block, is a suitable technique for dogs undergoing surgical correction of abnormalities associated with brachycephalic obstructive airway syndrome. Future prospective randomised controlled studies comparing opioid-free anaesthesia protocols to the current standards of practice should be encouraged to elucidate whether opioid-free anaesthesia provides better outcomes.

Conflict of interest

The authors declare no conflicts of interest.

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