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Title page

‘A comparison of the effect of propofol and alfaxalone on laryngeal motion in non-brachycephalic and brachycephalic dogs’

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1 **Word count: 3003**

2

3 **A comparison of the effect of propofol and alfaxalone on laryngeal motion in non-**
4 **brachycephalic and brachycephalic dogs**

5

6

7 **Abstract**

8 **Objective** To compare the effect of propofol and alfaxalone on laryngeal motion under
9 a light plane of anaesthesia in non-brachycephalic and brachycephalic dogs
10 anaesthetized for non-emergency procedures.

11 **Study design** Prospective, randomized clinical trial.

12 **Animals** A total of 48 client-owned dogs (24 non-brachycephalic and 24
13 brachycephalic).

14 **Methods** A standardized premedication of methadone (0.2 mg kg^{-1}) and acepromazine
15 (0.01 mg kg^{-1}) was administered intramuscularly. Dogs were randomly assigned to be
16 induced with increments of propofol ($1 - 4 \text{ mg kg}^{-1}$) or alfaxalone ($0.5 - 2 \text{ mg kg}^{-1}$).

17 Laryngeal assessment was performed under a light plane of anaesthesia by a surgeon
18 (GTH) who was unaware of the induction protocol. Laryngeal movement was assessed
19 as either being present when abduction of the laryngeal cartilages upon inspiration was
20 identified or absent when abduction was not recognized. Simultaneously, a 60-second
21 video was recorded. The same surgeon (GTH) and an additional surgeon (NK) re-
22 evaluated the videos one month later. Categorical comparisons were studied using Chi
23 squared and Fisher's Exact tests where appropriate. Pair-wise evaluation of agreement
24 between scorers was undertaken with the kappa statistic (κ).

25 **Results** There were no significant differences ($p > 0.05$) identified between the
26 presence or absence of laryngeal motion between dogs administered propofol or
27 alfaxalone, as well as when analysing non-brachycephalic and brachycephalic dogs
28 separately. The majority of dogs (>75%) maintained some degree of laryngeal motion
29 with both protocols. Agreement between assessors was excellent ($\kappa = 0.822$).

30 **Conclusions** Alfaxalone maintained laryngeal motion similarly to propofol in non-
31 brachycephalic and brachycephalic dogs.

32 **Clinical relevance** Both agents would appear appropriate for allowing assessment of
33 laryngeal motion in non-brachycephalic and brachycephalic dogs. The assessment
34 technique of subjective evaluation of laryngeal motion via per oral laryngoscopy under
35 a light plane of anaesthesia produced consistent results amongst assessors, regardless of
36 the induction agent used.

37 **Keywords** alfaxalone, dog, propofol, laryngeal paralysis, laryngoscopy

38

39 **Introduction**

40 Normal laryngeal motion, which is used as an indicator for laryngeal function, is
41 demonstrated by the abduction of the arytenoid cartilages during inhalation and passive
42 relaxation during exhalation (Gross et al. 2002). Peroral laryngoscopy under a light
43 plane of anaesthesia is the most widely used clinical method for interpretation of
44 laryngeal motion in dogs with 95% interobserver agreement (Broome et al. 2000;
45 Radlinsky et al. 2009; Smith 2000). The ideal anaesthetic protocol should provide
46 relaxation of the jaw muscles, maintenance of laryngeal reflexes and minimal
47 respiratory depression (McKeirnan et al. 2014).

48

49 A previous study by Jackson et al. (2004) concluded that intravenous thiopental given to
50 effect was the best choice for assessing laryngeal motion in dogs. Significantly greater
51 arytenoid motion was demonstrated after thiopental administration when compared with
52 other anaesthetic protocols (propofol, ketamine, diazepam and acepromazine). Although
53 thiopental remains a useful agent in veterinary anaesthesia, it is no longer licensed in
54 veterinary species and has therefore been largely replaced by propofol (Clarke et al.
55 2014).

56
57 Alfaxalone is a synthetic neurosteroid that at high concentrations acts as a direct agonist
58 of the GABA_A receptor (Berry 2015). It is used in veterinary practice as an induction
59 agent for anaesthesia. Minimal studies regarding this drug's effect on laryngeal motion
60 and function have been published up until now, especially in a clinical setting. A paper
61 by Smalle et al. (2017) concluded that there was no significant difference in the total
62 number of arytenoid motions after administration of thiopental, propofol or alfaxalone
63 in six research dogs. Nelissen et al. (2012a) also identified no significant difference in
64 arytenoid cartilage motion evaluating healthy cats using video laryngoscopy after
65 administration of alfaxalone, propofol or midazolam/ketamine. On the other hand, a
66 paper looking at the efficacy and safety of alfaxalone in humans (Monagle et al. 2015)
67 identified significantly less airway obstruction and therefore better airway patency after
68 alfaxalone administration compared to propofol.

69
70 Laryngeal paralysis is a common airway disorder in large breed dogs (Holt & Brockman
71 1994; Burbridge 1994) that is diagnosed via subjective airway assessment. It is vital to
72 use an induction agent that maintains laryngeal motion in suspect cases to increase
73 objectivity and accuracy of the assessment method. Moreover, an anaesthetic agent that

74 maintains laryngeal motion will provide a patent rima glottidis during induction
75 allowing persistent oxygen flow. This may prove safer, especially in breeds where
76 difficult intubation is more likely to occur. Brachycephalic breeds often have congenital
77 defects such as narrowed nares, an overlong soft palate, tracheal hypoplasia and
78 excessive laryngeal tissue (De Lorenzi et al. 2009)]. These defects impose a much
79 higher risk of airway occlusion and secondary hypoxia especially during induction of
80 anaesthesia, before successful intubation has occurred.

81

82 The main aim of this study was to assess whether laryngeal motion was present or
83 absent under a light plane of anaesthesia after injecting either alfaxalone or propofol.
84 This was evaluated in a cohort of non-brachycephalic and brachycephalic dogs, prior to
85 routine surgical procedures performed in a university referral hospital. The second aim
86 of this study was to evaluate the degree of inter-observer variability when using peroral
87 laryngoscopy for assessment of laryngeal motion.

88

89 **Methods and Materials**

90 **Animals**

91 The study was approved by the Ethics and Welfare Committee of the Royal Veterinary
92 College (URN 2016 1603) and informed owner consent was obtained. A total of 48
93 client-owned dogs were included (24 non-brachycephalic and 24 brachycephalic dogs)
94 all of which were admitted to the Queen Mother Hospital requiring general anaesthesia
95 for non-emergency procedures. This sample size was chosen as it was deemed an
96 achievable number of dogs to enrol onto the study within the time frame that it could be
97 performed. The time frame was pre-determined by the ethical committee and surgeon
98 availability. On the basis of a full physical examination and the medical history, all non-

99 brachycephalic dogs were considered to be American Society of Anaesthesiologists
100 (ASA) grade I – II and all the brachycephalic dogs were considered to be ASA grade \leq
101 III (Tranquilli and Grimm 2015). Dogs were excluded from the study if they were
102 classified as ASA grade \geq III (non-brachycephalic) or \geq IV (brachycephalic), or if they
103 presented with a problem that may impact the nerves relating to the function of the
104 larynx, such as laryngeal paralysis. The dogs were randomly allocated to one of two
105 groups by blindly drawing a number out of an envelope. Anaesthesia was induced with
106 propofol in group P ($n = 24$: 12 non-brachycephalic, 12 brachycephalic) and with
107 alfaxalone in group A ($n = 24$: 12 non-brachycephalic, 12 brachycephalic).

108 Protocol

109 Premedication consisted of acepromazine (ACP injection; Novartis, UK) 0.01 mg kg^{-1}
110 and methadone (Comfortan; Dechra, UK) 0.2 mg kg^{-1} injected intramuscularly (IM) into
111 the cervical epaxial musculature 30 minutes prior to induction. The premedication was
112 administered in a quiet preparation room. Immediately prior to induction, an
113 intravenous (IV) catheter was placed in a peripheral vein and a sedation score using a
114 simple descriptive scale ranging from 0 (no change from pre-sedation behaviour) to 3
115 (very heavily sedated, unable to walk) (Table 1) was assigned.

116 The maximum dose of each induction agent (propofol 4 mg kg^{-1} or alfaxalone
117 2 mg kg^{-1}) were calculated for each animal, drawn up and kept hidden. Each drug's
118 dose was chosen following the data sheets' recommendation in premedicated dogs.

119 Estimated lean body weight was used in severely overweight dogs. Prior to the arrival
120 of the assessor, a drape was placed over the IV catheter site to allow the induction agent
121 to be concealed from everyone in the room apart from the injector.

122 Propofol (Propoflo; Abbott Animal Health, UK) or alfaxalone (Alfaxan; Jurox,
123 Australia) were administered in quarterly increments IV until a light plane of

124 anaesthesia was achieved; characterized by easy visual access to the larynx, persistence
125 of breathing and the maintenance of a gag reflex. Each increment was administered by
126 hand over 10 seconds with a 20-second pause before the next increment was injected.
127 An experienced board certified small animal specialist surgeon (GTH) was present at
128 each induction and assessed the airway using peroral laryngoscopy. The laryngeal exam
129 was performed by placing the dog in sternal recumbency, holding open the upper jaw to
130 expose the oral cavity, pulling the tongue forward and depressing the base of the tongue
131 just below the epiglottis (epiglottic vallecular) using a laryngoscope. If the plane of
132 anaesthesia was deemed too deep by the surgeon (GTH) for immediate laryngeal
133 assessment, the dog's oral cavity was closed and flow by oxygen was provided whilst
134 being under constant observation from the anaesthetist and surgeon. As soon as the
135 respiration rate increased, the surgeon (GTH) would attempt another laryngeal exam
136 ensuring the return of the gag reflex before beginning the assessment. In each dog
137 laryngeal motion was simply assessed as being either present or absent. This was
138 determined by the degree of arytenoid abduction during inspiration and the amount of
139 rima glottidis observed (Table 2).

140 During the assessment, a short (30 – 60 second) video was also made of the larynx
141 using an iPhone 6s over at least 4 respiratory cycles, which was to be used later for re-
142 evaluation of laryngeal motion. Following this, the dog was given more induction agent
143 to allow intubation and was no longer followed for the purposes of the study. The
144 dosages of induction agent administered to allow laryngeal assessment and intubation
145 were recorded as well as any complication that occurred.

146

147 One month after the last assessment, all the videos were reassessed for the presence or
148 absence of laryngeal motion by the same surgeon (GTH) as well as another board

149 certified small animal surgery specialist (NK). During reassessment of the videos, a
150 third intermediate answer category (presence of minimal laryngeal motion) (Table 2)
151 was added. This third category was added to refine the grading system and potentially
152 detect more subtle differences between induction agents as during the data collection
153 process varying degrees of laryngeal movement were detected. The videos were
154 evaluated separately by each surgeon. A random number shown at the beginning of
155 each video was used to identify each dog. Following this, a final collaborative
156 assessment was made between the two surgeons who agreed on one assessment
157 category for each dog.

158

159 **Statistical analysis**

160 Data were analysed using commercial software (SPSS for Mac 2015 version 23; IBM,
161 United States). Normality of the interval variables (weight, age, dose of induction agent
162 required for laryngeal assessment and dose of induction agent required for intubation)
163 was assessed graphically and by using the Shapiro-Wilk test. None of the data were
164 normally distributed and therefore results were reported as median (range). Categorical
165 comparisons (presence or absence of laryngeal motion) were studied using Chi square
166 and Fishers Exact tests as appropriate. Pair-wise evaluation of agreement between
167 scorers in the evaluation of laryngeal motion using the scale with categories was
168 undertaken with the kappa statistic. Results were considered significant when $p \leq 0.05$.

169

170 **Results**

171 A total of 48 dogs (24 non-brachycephalic; 24 brachycephalic) were recruited for this
172 project. All animals completed the study (Fig. 1). The demographic data of the animals
173 did not differ significantly between the two groups (Table 3). The dose of injectable

174 anaesthetic that allowed laryngeal assessment in all dogs was 1.9 (0.9 – 5.1) mg kg⁻¹ for
175 group P and 0.5 (0.2 – 1.9) mg kg⁻¹ for group A. The dose of injectable anaesthetic
176 agent to allow intubation in all dogs was 3.0 (1.1 – 6.9) mg kg⁻¹ for group P and 2.0 (0.5
177 – 3.0) mg kg⁻¹ for group A.

178

179 Overall the maintenance of some degree of laryngeal motion was identified in a large
180 majority of cases regardless of the induction agent used or whether the dog was non-
181 brachycephalic or brachycephalic. During the initial assessment (Fig. 2), 75% of dogs
182 were evaluated as having laryngeal motion present. During the collaborative assessment
183 (Fig. 3) after the addition of the third scoring category, 87.5% of dogs were assessed as
184 having some degree of laryngeal motion.

185

186 There were no significant differences identified between the presence or absence of
187 laryngeal motion in all dogs collectively after either propofol or alfaxalone was
188 administered, as well as when analysing non-brachycephalic and brachycephalic dogs
189 separately, in any of the assessments carried out. *P values* calculated for the initial
190 assessment made by the first surgeon (GTH) - *All dogs: p = 0.63, non-brachycephalic:*
191 *p = 0.5, brachycephalic: p = 0.653. P values* calculated for the reassessment made by
192 the first surgeon (GTH) – *All dogs: p = 0.571, non-brachycephalic: p = 0.879,*
193 *brachycephalic: p = 0.325. P values* calculated for the reassessment made by the
194 second surgeon (NK) - *All dogs: p = 0.607, non-brachycephalic: p = 0.717,*
195 *brachycephalic: p = 0.154.* There were no statistical differences found between group P
196 and group A in respect to the presence or absence of laryngeal motion in the final
197 collaborative assessment made between the two surgeons (GTH, NK) (*All dogs: p =*
198 *0.371, non-brachycephalic: p = 0.879, brachycephalic: p = 0.593*).

199

200 Agreement between the surgeons for assessment of laryngeal motion using the scale
201 with three categories was rated as excellent [κ statistic (κ) = 0.822] displaying very
202 good inter-rater reliability for the assessment method.

203

204 In total, three complications were noted during the study. One occurred in group P
205 which involved pain on injection of the induction agent. Two occurred in group A in
206 which excitation was experienced during injection of the induction agent in both dogs.
207 These complications were considered mild and the experiment was continued in all of
208 these dogs without any intervention implemented.

209 **Discussion**

210 There was no significant difference found between the use of either propofol or
211 alfaxalone on the maintenance of laryngeal motion in any of the assessments carried
212 out. This result is consistent with the results of Smalle et al. (2017). On the contrary,
213 Monagle et al. (2015) found that airway patency was maintained better with alfaxalone
214 compared to propofol in humans. The explanation given for the difference in airway
215 patency is attributed to the distribution of GABA_A subunits, targeted by alfaxalone and
216 propofol. Previous work has shown that there is a relative lack of GABA subunits
217 targeted by neurosteroids in the human brainstem compared with the cerebral cortex
218 (Persohn et al. 1992; Wegner et al. 2007) and therefore alfaxalone has little activity in
219 the brainstem (Thornton et al. 1986). The vagus nerve originates from the brainstem and
220 is ultimately responsible for the control of the intrinsic muscles of the larynx via the
221 recurrent and caudal laryngeal nerve (Hermanson & Evans 1993). However,
222 information regarding the distribution of specific GABA subunits in other species

223 including dogs is limited and therefore explaining the difference in the results between
224 the two studies can only be done by speculation.

225

226 Other factors that may have affected laryngeal motion in this study include the
227 premedication given and the speed of administration of the injectable anaesthetic agent.

228 The use of acepromazine as part of the anaesthetic protocol when assessing laryngeal
229 motion has both been advocated and advised against. Jackson et al. (2004) identified
230 that arytenoid motion was significantly less with thiopental and acepromazine than with
231 thiopental alone, suggesting that ACP depresses arytenoid motion. However, the doses
232 used (0.05 mg kg^{-1}) were five times higher than those used in the current study.

233 Moreover, numerous sources actually suggest the inclusion of low dose ACP in the
234 premedication before laryngeal assessment because of its anxiolytic effect (Dugdale
235 2010; Murrell 2016); which decreases stress and therefore the risk of airway occlusion.
236 This was deemed particularly important for the brachycephalic cohort in this study.

237

238 Achieving the optimum level of anaesthesia for laryngeal assessment can be difficult,
239 with the speed of administration of the injectable anaesthetic agent contributing heavily
240 to this. The preservation of the respiratory cycle is necessary to determine accurate
241 arytenoid motion. Rapid IV injection (less than 5 seconds) of propofol and alfaxalone
242 commonly resulted in post-induction apnoea (Amengual et al. 2013). In this study, the
243 anaesthetic agent was given slowly to effect in incremental doses. Another possible
244 method of administration would have been via a constant rate infusion using a syringe
245 driver. This method, in theory, should titrate the injectable anaesthetic agent more
246 precisely allowing the desired level of anaesthesia for laryngeal assessment to be
247 captured instantly. However, when this method was used in cats receiving different

248 anaesthetic agents for assessing laryngeal motion (Nelissen et al. 2012a), assessment
249 and intubation doses in all the cats were the same suggesting that the appropriate point
250 at which to assess had already been surpassed. From a practical point of view, the
251 method of administration performed in this study required less equipment and is more
252 reflective of common clinical practice.

253

254 Both the use of ACP as part of the premedication and the incremental injection of the
255 chosen anaesthetic agent in this study, are factors that in theory would reduce laryngeal
256 motion. Therefore, it would be expected to identify more dogs with the absence of
257 laryngeal motion than truly present. However, despite these factors the majority of dogs
258 (>75%) maintained some degree of laryngeal motion in both the propofol and
259 alfaxalone group, suggesting that they had minimal impact. Moreover, this result
260 supports the use of either injectable anaesthetic agent for laryngeal assessment.

261

262 A potential limitation in this study was the use of a scoring system with minimal
263 categories. Smalle et al. (2017) used a much more extensive scoring system comprising
264 of four categories each with two subcategories. Although not validated, the scoring
265 system utilized in this study was adopted from previous studies and adjusted using the
266 grading system for laryngeal function in non-sedated horses (Gross et al. 2002;
267 Robinson 2004; McKeirnan et al. 2014). While no significant difference was found in
268 that study between thiopentone, propofol and alfaxalone, with the much larger subject
269 numbers used in the current study, a potential difference between anaesthetic agents and
270 laryngeal motion may have been detected.

271

272 The third intermediate category (minimal laryngeal movement) for the reassessment of
273 the airways was not part of the original study protocol. However, after the initial data
274 collection it was apparent that some dogs had very obvious laryngeal motion and some
275 had minimal. The justification to implement this additional category was to potentially
276 identify a significant difference between obvious and subtle laryngeal motion and
277 whether this could be attributed to either anaesthetic agent, possibly providing some
278 clinical benefit. Due to this alteration, intra-observer variability could not be
279 determined.

280

281 Another limitation of the study was that thiopental was not used as a comparative
282 induction agent. Thiopental has historically been considered the best choice for the
283 assessment of laryngeal motion (Jackson et al. 2004) and therefore novel induction
284 agents should be compared to it. However, no licenced thiopental product is available
285 for veterinary patients in the EU or UK, therefore its use could not be justified in
286 clinical patients. Moreover, the fact that thiopental is no longer available gives more
287 reason to find a comparable, accessible alternative for laryngeal assessment.

288

289 To the knowledge of the authors, this is the first study to assess the effect of different
290 anaesthetic agents on laryngeal motion in brachycephalic as well as non-brachycephalic
291 dogs. Therefore, an appropriate assessment technique for evaluating laryngeal motion in
292 a cohort of dogs with such a grossly altered respiratory anatomy has not been described
293 before and there may be other factors that should be taken into account when trying to
294 make an accurate assessment. For example, we know that a majority of brachycephalic
295 dogs present with some degree of laryngeal collapse (Monet and Tobias 2012). The
296 effect of laryngeal collapse on laryngeal motion has not been reported although the

297 incident of both pathologies co-occurring has been described (Nelissen and White
298 2012b). The degree of laryngeal collapse was not recorded in this study; therefore, it is
299 difficult to determine whether this variable had any impact on the results obtained.
300 Future studies could focus on specific laryngeal assessment in the brachycephalic
301 population, the impact of laryngeal collapse on laryngeal motion and if our current
302 assessment measures for laryngeal motion are even applicable to brachycephalic dogs as
303 they have so many airway malformations.

304

305 **Conclusion** Alfaxalone maintains laryngeal motion similarly when compared to
306 propofol in non-brachycephalic and brachycephalic dogs. Agreement between assessors
307 was excellent.

308

309

310

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393 **Table and figure legends:**

394

395 **Table 1** Description of scoring categories used to assess degree of sedation after

396 premedication with acepromazine 0.01 mg kg^{-1} and methadone 0.2 mg kg^{-1}

397 intramuscularly in 48 dogs.

398

399 **Table 2** Descriptors used for assessing laryngeal motion.

400

401 **Table 3** Demographic and other data of all dogs included in this study. Anaesthesia was

402 induced with either propofol ($0.9 - 6.9 \text{ mg kg}^{-1}$) (group P all dogs, $n = 24$; group P non-

403 brachycephalic dogs, $n = 12$; group P brachycephalic dogs, $n = 12$) or alfaxalone ($0.2 -$

404 3.0 mg kg^{-1}) (group A all dogs, $n = 24$; group A non-brachycephalic dogs, $n = 12$;

405 group A brachycephalic dogs, $n = 12$).

406

407 **Figure 1** CONSORT flow diagram for this study. Dogs were randomly divided into two

408 groups: group P, in which laryngeal motion was evaluated after the administration of

409 propofol; and group A, in which laryngeal motion was evaluated after the

410 administration of alfaxalone.

411

412 **Figure 2** Number of dogs in each scoring category (x axis) during the initial assessment

413 of laryngeal motion after receiving either propofol or alfaxalone (y axis). A 'Present'

414 assessment equates to the maintenance of laryngeal motion and an 'absent' assessment

415 equates to the absence of laryngeal motion.

416

417 **Figure 3** Number of dogs in each scoring category (x axis) during the collaborative re-

418 assessment of laryngeal motion after receiving either propofol or alfaxalone (y axis). A

419 'present' assessment equates to the obvious maintenance of laryngeal motion, a
420 'Minimal' assessment equates to marginal laryngeal motion and an 'absent' assessment
421 equates to the absence of laryngeal motion.

422

423

ACCEPTED MANUSCRIPT

Tables**Table 1** Description of scoring categories for degree of sedation after premedication with acepromazine 0.01 mg kg⁻¹ and methadone 0.2 mg kg⁻¹ intramuscularly in 48 dogs.

| Category | Description |
|----------|--|
| 0 | No change from pre-sedation behaviour |
| 1 | Mild sedation (with head slightly lowered) |
| 2 | Moderate sedation (with head lowered and ataxia) |
| 3 | Very heavily sedated, unable to walk |

Table 2 Descriptors used for assessing laryngeal motion.

| Assessment answer | Description |
|----------------------------------|---|
| Obvious laryngeal motion present | Clear abduction of the arytenoid cartilages during inspiration. Maximal rima glottidis observed. Maintenance of laryngeal motion. |
| Absence of laryngeal motion | No obvious arytenoid abduction during inspiration. Minimal rima glottidis observed. Laryngeal motion not maintained. |
| Minimal laryngeal motion present | Mild to moderate degree of abduction of the arytenoid cartilages during |

| | |
|--|--|
| | <p>inspiration. Moderate rima glottidis observed. Maintenance of laryngeal motion.</p> |
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Table 3 Demographic and other data of all the dogs in this study. Anaesthesia was induced with either propofol (0.9 – 6.9 mg kg⁻¹) (group P all dogs, *n* = 24; group P non-brachycephalic dogs, *n* = 12; group P brachycephalic dogs, *n* = 12) or alfaxalone (0.2 – 3.0 mg kg⁻¹) (group A all dogs, *n* = 24; group A non-brachycephalic dogs, *n* = 12; group A brachycephalic dogs, *n* = 12).

| | Dogs | Group P | Group A |
|-----------------------|---------------------------|-------------------|-------------------|
| Sex | <i>Female</i> | 10 | 8 |
| | <i>Male</i> | 14 | 16 |
| Age (months) | <i>All</i> | 52.5 (11 – 167) | 51.5 (7 – 165) |
| | <i>Non-brachycephalic</i> | 69.5 (11 – 167) | 51.5 (7 – 104) |
| | <i>Brachycephalic</i> | 38.5 (12 – 119) | 46 (11 – 165) |
| Weight (kg) | <i>All</i> | 11.1 (5.8 – 34.7) | 11.4 (2.2 – 46.0) |
| | <i>Non-brachycephalic</i> | 16.5 (5.8 – 34.7) | 26.8 (5.0 – 46.0) |
| | <i>Brachycephalic</i> | 9.0 (6.2 – 18.8) | 10.2 (2.2 – 22.0) |
| Sedation score | <i>All</i> | 1 (0 – 3) | 2 (0 – 3) |
| | <i>Non-brachycephalic</i> | 1 (0 – 3) | 2 (1 – 3) |

| | | | |
|--|---------------------------|-----------------|-----------------|
| | <i>Brachycephalic</i> | 1(0 – 3) | 2 (1 – 3) |
| Dose of drug to allow laryngeal assessment (mg kg⁻¹) | <i>All</i> | 1.9 (0.9 – 5.1) | 0.5 (0.2 – 1.9) |
| | <i>Non-brachycephalic</i> | 1.9 (0.9 – 5.0) | 0.5 (0.4 – 1.0) |
| | <i>Brachycephalic</i> | 1.9(0.9 – 5.1) | 0.5 (0.2 – 1.9) |
| Dose of drug to allow intubation (mg kg⁻¹) | <i>All</i> | 3.0 (1.1 – 6.9) | 2.0 (0.5 – 3.0) |
| | <i>Non-brachycephalic</i> | 3.0(1.1 – 6.9) | 1.0 (0.7 – 3.0) |
| | <i>Brachycephalic</i> | 3.0 (1.1 – 5.1) | 1.0 (0.5 – 1.9) |
| Number of complications | <i>All</i> | 1 | 2 |
| | <i>Non-brachycephalic</i> | 1 | 1 |
| | <i>Brachycephalic</i> | 0 | 1 |





