Preliminary assessment of the AAI Index® during isoflurane anaesthesia in dogs undergoing clinical procedures

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ABSTRACT

The auditory evoked potential (AEP) is correlated to anaesthetic depth. The AEP has been used in rats, pigs, dogs and humans to assess anaesthetic depth. This study was undertaken to determine whether the AAI Index® derived from the AEP correlated with changes in end tidal isoflurane concentration in dogs. The average AAI Index was 21.8 ± 10.5 and isoflurane concentration was 1.7 ± 0.4 %. Data were divided into 0.5 % intervals of end tidal anaesthetic agent concentration (ETAA). When ETAA values were higher than 2.5 % the AAI values were 2.1–2.5 %, 1.6–2.0 % and 1.1–1.5 % higher than AAI values although not statistically different. The 2.1–2.5 % interval was statistically different from the 1.1–1.5 % and <1.1 % interval. The 1.6–2.0 % interval was statistically different from the 1.1–1.5 % and the <1.1 % intervals. The 1.1–1.5 % interval was statistically different from the <1.1 % interval. The correlation between the AAI Index and isoflurane was –0.176 and was statistically significant ($P = 0.0009$). A linear regression between the AAI Index and isoflurane revealed the following relationship: AAI = 29.074 – (4.2755 × isoflurane) with a power of 0.913. The polynomial regression relationship was AAI = 53.334 – (35.715 × isoflurane) + (10.322 × isoflurane^2) – (0.43646 × isoflurane^3) with a power of 0.999. The AAI Index was found to correlate with changes in isoflurane concentration.

Keywords: AAI Index®, anaesthetic depth, auditory evoked potentials, canine.

Joubert K E **Preliminary assessment of the AAI Index® during isoflurane anaesthesia in dogs undergoing clinical procedures**. *Journal of the South African Veterinary Association* (2009) 80(3): 185–187 (En.). Department of Para-Clinical Studies, University of Pretoria, Onderstepoort, 0110 South Africa.

INTRODUCTION

The auditory evoked potential (AEP) has been described as a method to control the delivery of isoflurane[13]. An artificial neural network was used to analyse the AEP and adjust the isoflurane concentration delivered to the patient[13]. Satisfactory levels of anaesthesia were maintained.

The AEP has been used for assessment of anaesthetic depth in rats[1,2,8], pigs[10] and dogs[9,13,15]. It consists of a set of electrical impulses (brain waves) that are formed when a sound is delivered at the external auditory meatus. The electrical impulses generated travel from the cochlea through the brainstem and mid-brain to the cognitive centres of the brain. The first 7 waves represent the responses of the brain stem (brain stem auditory evoked response, BAER)[12,17,20]. As the electrical impulses move from the brain stem to the cortical structures, an early and late cortical response can be seen[17]. The early cortical response occurs within 10–80 ms of the stimulus and is referred to as the middle latency component (MAER). Anaesthesia has been shown to have a reliable effect of altering the brain waves of the middle latency component[15,17,20]. The late cortical response occurs more than 80 ms after the stimulus and is a result of frontal cortex processing of the signal[17]. The AEP can be analysed by measurement of the amplitude and latencies of waves recorded 10–100ms after auditory stimulation[4]. A regression model with exogenous input (ARX model) is used to analyse these amplitudes and latencies to derive a dimensionless number between 0 and 100 known as the A-line ARX-Index (AAI Index®)[7]. The AAI Index has been shown to differentiate between awake and sleep states in dogs[9].

The auditory evoked response has been found to have a predictable and consistent dose-dependent response with various anaesthetic agents[5,6,14,16,19]. Volatile anaesthetic agents have been shown to exert similar effects on the auditory evoked response based on comparison of minimum alveolar concentration multiples in humans[6]. Monitoring of anaesthetic depth is particularly difficult in paralysed patients as the normal reflexes are abolished. This study was undertaken to determine whether the AAI Index has a predictable dose-response curve under isoflurane anaesthesia in dogs.

MATERIALS AND METHODS

Sample size was determined by a power analysis. The data were analysed for every 5 dogs with a power of 0.9 and a statistical significance of 0.05. A sample of size of 344 paired points of AAI and isoflurane percentage was required.

A total of 353 points collected from 27 dogs undergoing both soft tissue and orthopaedic procedures was used in this study. Informed consent was obtained from the owners. All dogs were subjected to full clinical evaluation and any additional tests as required. If systemic disease was found the dog was excluded from the study and an additional dog was enrolled. The breed, age, weight and procedure were recorded for each patient. The anaesthetic protocol used was: premedication–acetylpromazine 0.01 mg/kg or diazepam 0.2 mg/kg, morphine 0.5 mg/kg, carprofen 4 mg/kg, induction – either thiopentone 10 mg/kg or propofol 6 mg/kg and maintenance with isoflurane in 100 % oxygen. Following induction of anaesthesia the patient was prepared for surgery and placed on the operating table. The A-line ARX-Index (AAI Index) (AEP Monitor, version 1.6, Danmeter A/S, Copenhagen) was recorded after delivering a click to both ears with intensity controlled automatically[18]. Electrodes (0.35 × 25 mm solid needles, Hwato, Stockholm) for the recording of AEP were positioned as follows: the reference electrode was placed 1 cm rostral to the auditory meatus, the ground electrode on the tragus (lateral-caudal cartilage of the ear forming part of the lateral wall of the vertical ear canal) and an active recording electrode on the vertex (midline between the ears over the *crista sagittalis externa*)[12]. Earphones (Monitor Earphones, Danmeter) were placed into the external auditory meatus. End-tidal anaesthetic agent was monitored (Drager Vamos, Drager Medical, Fourways) at the end of the endotracheal tube. The anaesthetic agent analyser was calibrated daily following the manufac-

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Received: September 3008. Accepted: August 2009.

ture's instructions. Blood pressure, pulse oximetry, capnography, electrocardiography and temperature were monitored with a multi- parameter monitor (Dash 4000, GE, Medhold Medical, Kempton Park).

Anaesthetic depth was adjusted according to the requirements of surgery to ensure that the patient did not respond to surgical stimulus. The AAI Index and anaesthetic agent concentration were recorded every 5 minutes for the duration of the procedure. Physiological data were recorded on the anaesthetic monitoring form and monitored for patient safety.

Physiological data were not analysed, as there was no intention to determine any correlation between physiological data and the AAI Index or anaesthetic depth. Descriptive statistics were calculated. Statistical significance was set at $P < 0.05$. The AAI data were sorted by ETAA values into the following intervals: >2.5, 2.1–2.5, 1.6–2.0, 1.1–1.5 and <1.1. The Mann-Whitney rank sum was used to analyse interval data. A Pearson's product moment correlation, linear regression and a polynomial regression was used to determine the relationship between the AAI Index and isoflurane concentration and was run on raw data.

RESULTS

A total of 15 breeds were represented with no particular breed dominating (German shepherd dog 4, Labrador retriever 3, Daschund 3, Rottweiler 2, Cross breed 2, Great Dane 2, Ridgeback 2, Yorkshire terrier 2, Spaniel 1, Fox terrier 1, Boerboel 1, Scottish terrier 1, Chihuahua 1, Sharpei 1; Bulldog 1). The sex distribution was as follows: female sterilised 8, female 7, male 6 and male sterilised 6. The average age was 3.9 ± 3.1 years with an average weight of 20.7 ± 20.7 kg. Thirteen different procedures were performed (ovariohysterectomy 5, cruciate surgery 4, fracture repair 4, castration 2, ceiliotomy 2, arthroscopy 2, spinal surgery 2, femoral head excision 1, leg amputation 1, mast cell tumour 1, perineal hernia 1, scrotal ablation 1 and tibial crest transplantation 1).

The relationship between AAI and ETAA for one of the patients is shown in Fig. 1. The average AAI Index was 21.8 ± 10.5 and the isoflurane concentration was 1.7 ± 0.4 %. Data were divided into 0.5 % intervals of ETAA. When ETAA values were higher than 2.5 % the AAI values were 2.1–2.5 %, 1.6–2.0 % and 1.1–1.5 % higher than the AAI values, although not statistically different. The 2.1–2.5 % interval was statistically different from the 1.1–1.5 % and <1.1 % interval. The 1.6–2.0 % interval was statistically different to the 1.1–1.5 % and <1.1 % intervals. The 1.1–1.5 % interval was statistically different from the <1.1 % interval. The ETAA interval data are given in Table 1.

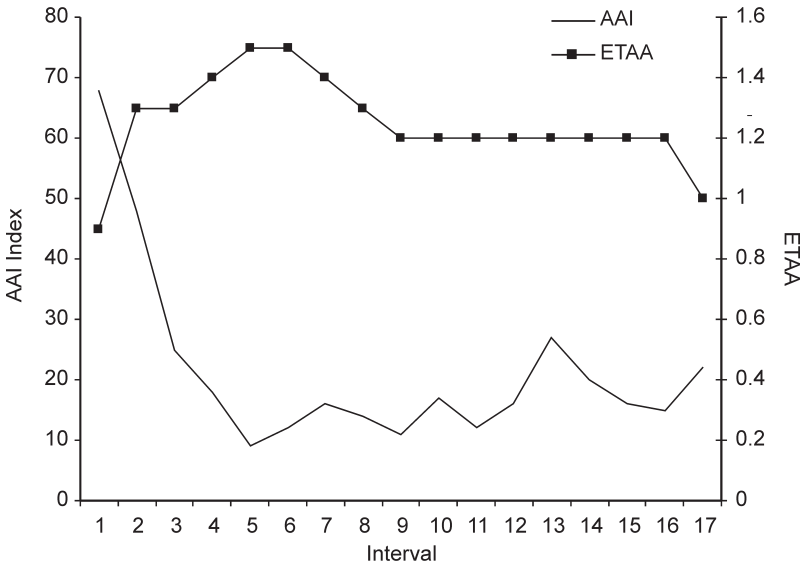

Fig. 1: **AAI and ETAA of Patient 5.** AAI = anaesthetic index, ETAA = end tidal anaesthetic agent concentration. This graph shows that as the ETAA increases the AAI decreases.

The correlation between AAI Index and isoflurane was –0.176 and was statistically significant ($P = 0.0009$). A linear regression between AAI Index and isoflurane revealed the following relationship AAI = 29.074 – (4.2755 × isoflurane) with a power of 0.913. The polynomial regression relationship was AAI = 53.334 – (35.715 × isoflurane) + (10.322 × isoflurane^2) – (0.43646 × isoflurane^3) with a power of 0.999.

DISCUSSION

This study showed that the isoflurane concentration is correlated with the AAI Index. The polynomial regression provided a better fit than the linear regression, indicating that relationship is non-linear. These data support those of the 6 dogs that were studied with artificial neural network *via* AEP to control the delivery of isoflurane to maintain anaesthesia[13]. Similar data collected from humans have shown the AEP to have a predictable and consistent dose-dependent response with various anaesthetic agents[5,6,14,16,19].

The >2.5 % interval data did not achieve statistical significance due to the small number of sample points in this group. This group represents patients who were under light anaesthesia and the anaesthetic agent was increased to deepen anaesthetic depth, hence the AAI was still higher while ETAA values had increased but brain equalisation of isoflurane had not taken place. A recent study by van Soens *et al.* has shown high variability in AAI data, making interpretation of data more difficult[21]. Visual inspection of the data from this study shows variability and this may have played a role. AEP has been used to calculate the effect site concentration of propofol[22]. The effect site concentration of isoflurane in dogs is unknown at present. This shows that the AAI Index is able to some extent to discriminate between different levels in ETAA values of isoflurane.

A potential weakness of this study is that the procedure and the premedication agents and induction agents were not standardised. This was owing to the practicalities of clinical practice and the fact that for an anaesthetic depth monitor to be useful it has to operate under a variety of conditions. Closed-loop anaesthesia has recently been discussed in veterinary medicine and in order for this to be implemented, reliable assessment of hypnosis

Table 1: **ETAA interval data presented as mean and standard deviation (SD) as well as the number of samples per group (*n*).**

ETAA interval	AAI		
	(Mean)	(SD)	*n*
>2.5	27.50	14.59	12
2–2.5	19.72	9.97	47
1.5–2	20.05	8.70	169
1–1.5	23.38	11.33	99
<1	28.69	12.63	26

and analgesia are required[3]. The validity of middle latency AEPs under sevoflurane anaesthesia has recently been questioned[11]. This seems to indicate that robust monitoring of anaesthetic depth has to be valid under a variety of clinical anaesthetic conditions.

This study was performed on clinical cases. Although it represents the day-to-day use of such a monitor, anaesthetic depth was varied according to the patient's requirements, and equilibration time between exhaled, blood and brain concentrations of isoflurane was not allowed for. This may have resulted in errors. It would be important to allow for equilibration of anaesthetic agent concentration before measurements are made. Measurements were made at set intervals throughout the anaesthetic period and not after predetermined intervals after a change in anaesthetic agent or after a set period at a constant end tidal anaesthetic agent concentration. It would be ideal to repeat the experiment using groups of animals in which the anaesthetic agent concentration is varied and time is allowed for equilibration.

Physiological variables were not kept constant throughout the anaesthetic period although they were maintained at clinically acceptable values. Physiological variables known to influence the AAI are $PaCO_2$ value[18] and a decrease in body temperature[17]. Ideally in an experimental model these values should be controlled. In a clinical context it is difficult to control all of these variables.

Van Soens *et al.* showed that a poor correlation exists between acepromazine-methadone-propofol and medetomidine-propofol anaesthesia and the AAI Index[21]. A better correlation was shown for acepromazine-methodone-etomidate and medetomidine-etomidate anaesthesia[21].

Despite the limitations in methodology in the present study, a reasonable correlation was achieved and this demonstrates that the monitor may be useful to determine anaesthetic depth in clinical cases. Further work is required to validate the AAI Index as a suitable anaesthetic depth monitor in dogs.

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