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Comparison of Neurologic Responses to the Use of Medetomidine as a Sole Agent or Preanesthetic in Laboratory Beagles

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Short, C. E, J. E. Räihä, M. P. Räihä and K. Otto; Comparison of neurologic responses to the use of medetomidine as a sole agent or preanesthetic in laboratory beagles. Acta vet. scand. 1992, 33, 77-88. – Different dose regimens of medetomidine (a potent α_2-adrenergic agonist), adding up to a combined dose of 80 μg/kg, were administered to laboratory beagles to determine physiologic responses including neurologic. The study was intended to determine EEG responses where sufficient sedative and analgesic effects are reached with medetomidine and in contrast its effects when used with ketamine or halothane.

Cardiopulmonary responses were very similar in each dose regimen, showing the characteristic properties of single doses of 80 μg/kg of medetomidine. Effective sedative and analgesic duration seemed to be a function of when the largest dose was administered. Adequate additional sedative and analgesic could be gained from injections at doses of half of the initial one.

The potent sedative and analgesic effects of medetomidine confirmed by neurologic evaluation supports its potential use as a premedication to general anesthesia in dogs. In this study, 2 different doses of medetomidine were also tested as premedication to both ketamine HCI and halothane anesthesia. Neorologic responses were determined at the same time cardiopulmonary parameters, anesthetic quality, and dose requirements were recorded.

Medetomidine was found to have favorable qualities in conjunction with these anesthetics. Cardiopulmonary parameters remained satisfactory in both groups as preanesthetic medication prior to halothane, but no additional benefits could be seen from doses of 40 μg/kg medetomidine compared to 20 μg/kg, except a significant 30% reduction in halothane requirement.

The positive chronotropic and inotropic properties of ketamine restored the medetomidine-induced bradycardia and produced a short anesthetic period of 15 to 30 min depending on the dose of medetomidine. The quality of anesthesia was better when 40 μg/kg medetomidine was used, but recorvery was quicker with 20 μg/kg medetomidine.

Medetomidine significantly reduced cerebral activity as demonstrated by recordings of total amplitude and frequency evaluation of the EEG with compressed spectral analysis. This analytical method was effective in confirming clinical signs of sedation, analgesia, and anesthesia in canine subjects.

a_2-adrenergic agonist; sedation; analgesia; cardiopulmonary parameters; external stimuli; EEGs; compressed spectral analysis.

Introduction

Medetomidine (Domitor,® Farmos group Ltd., Finland), 4[(2,3-dimethylphenyl)ethyl]-1H-imidazole, a highly specific and potent α_2-adrenergic agonist *(Bergström* 1988, *Savola et al.* 1986), is a new sedative and analgesic for dogs and cats. The basic properties and effects of a single IM or IV injection on various physiological parameters in cats and dogs are well documented *(Vainio et al.* 1986). Its reversal by the antagonist atipamezole has been confirmed *(Vainio et al.* 1990).

The classical signs and stages of anesthesia which have been described *(Guedel* 1920-1921, 1951) for the human subject and were modified for domestic animals *(Campbell & Lawson* 1958, *Hall & Clarke* 1983), are still of major importance for the evaluation of anesthetic depth *(Hall & Clarke* 1983). These are not adequate to determine levels of sedation and/or analgesia in animals.

Earlier investigations *(Derbyshire et al.* 1937, *Prynn et al.* 1968, *Garner et al.* 1972, *Auer et al.* 1979, *Brechner et al.* 1962) have shown, that dose-dependent reversible depression in central nervous function *(Guedel* 1920-1921, *Guedel* 1951) produced by anesthetic agents are accompanied by an alteration in the cerebrocortical electrical activity that can be recorded by electroencephalography (EEG). Comparison of Guedel's classification of anesthetic depth with electroencephalographic recordings during anesthesia *(Prynn et al.* 1968, *Pichlmayr et al.* 1983, *Pichlmayr et al.* 1980) demonstrated, the degree of central nervous depression can be evaluated more accurately by alteration in the EEG pattern than by clinical signs *(Pichlmayr et al.* 1983). By using surgically-implanted stainless-steel screw electrodes, which were in contact with the dura mater (electrocorticogram) *(Garner et al.* 1972), thin wires advances to the periost of the forehead *(Schneider et al.* 1981), or silverchloride disc electrodes *(Auer et al.* 1979, *Purohit et al.* 1981, *Mysinger et al.* 1985), electroencephalography in the equine species has previously been performed for recording changes in the cerebrocortical activity associated with the administration of sedatives, tranquilizers, and anesthetic agents.

Previous investigation also used the conventional EEG technique *(Walter* 1987). The goal objective of this study was to evaluate the applicability of a computerized EEG technique (Power Spectrum Analysis) *(Levy et al.* 1980) to detect changes in the brain activity during α_2 adrenergic analgesia and sedatives and the combination of α_2 agents with anesthetics. The application of this technique in experimental dogs had not been previously reported.

The 2nd objective of this study was to evaluate the applicability of EEG power spectrum analysis as a guide to depth of sedation, analgesia, and anesthesia in experimental dogs by comparing simultaneously recorded EEG data, clinical signs, and laboratory analysis.

Materials and methods

Trial 1

Mature female laboratory beagles (10 months to 2 years,6 to 10 kg) in excellent health with no congenital or acquired abnormalities on physical examination were included in this study. Three different dose regimens were used and each regimen was tested once with each dog.

Group 1 (increasing doses). Four dogs receiving an initial dose of 11.5 μg/kg of medetomidine IM, followed 20 min later by 23.0 μg/kg (twice the initial dose), followed after an additional 20 min by 45.5 μg/kg (twice the previous dose) for a cumulative dose of 80.0 μg/kg.

Group 2 (decreasing doses). Four dogs receiving an initial dose of 45.5μg/kg of med-

etomidine IM, followed 20 min later by 23.0 μg/kg (half the initial dose), followed after an additional 20 min by 11.5 μg/kg (half the previous dose) for a cumulative dose of 80 μg/kg.

Group 3 (two equal doses). Four dogs receiving an initial dose of 40.0 μg/kg of medetomidine IM, followed 20 min later by an additional 40.0 μg/kg for a cumulative dose of 80.0 μg/kg.

A minimum clearance time of 1 week between trials was allowed for appropriate removal of drug in each dog.

Heart rates, reactions to external stimuli (sound, tail clamping, and testing for palpebral reflexes) and postures were recorded prior to medetomidine and at 10 min intervals during drug effect. Dropping metal hemostats from a height of 0.5 m on a metal table 1 m away from the head of the dog was used as a standard sound stimulus throughout the study. Clamping the base of the tail with metal hemostats for 15 sec was used as a nociceptive stimulus.

Continuous ECGs were recorded utilizing a Datascope 721 A Recorder (Datascope Corporation, New Jersey, USA) monitoring recording system. EEGs were determined at 10 min intervals using a Biologics Systems Corporation Traveler (Mundelein, Illinois USA) compressed spectral analyzing systems.

The frontomastoid *(Rampil et al.* 1983, *Rampil et al.* 1987, *Spackman et al* 1987, *Long et al* 1989, *White et al.* 1989) and frontooccipital *(Rampil et al.* 1980) electrode configuration reported for computerized EEG analysis in man was duplicated, using 4 EEG needle electrodes placed bilaterally over the frontal bone and cranial portion of the atlantooccipital area. In addition, a reference electrode was placed in the midline of the nasofrontal area.

EEG signals from both hemispheres were processed using EEG power spectrum analysis performed with the biologic® Traveler LT. Prior to analog/digital conversion, the electrical signals were filtered with low and high frequency cutoffs of 1.0 Hz and 30 Hz, respectively *(Rampil et al.* 1983, *Rampil et al.* 1987, *Spackman et al.* 1987) and with a supplemental 60 Hz notch filter *(Kaieda et al.* 1989). This filter design was employed to minimize electrical interference associated with the power supply from the electrical outlet and persisting muscle activity *(Pichlmayr et al.* 1983).

After the raw EEG signal was segmented into epochs of 2.2 sec *(Levy et al.* 1980, *Cooper et al.* 1984), 80% of spectral edge frequency (SEF-80) as the frequency point below which 80% of the total amplitude were located in the current spectrum*(White et al.* 1989), and the distribution of the total amplitude into the Δ (0.03 to 3.9 Hz), Θ (4.0 to 7.9 Hz), α (8.0 to 12.9 Hz), and ß (13.0 to 32.0 Hz) frequency bands (fractional amplitudes, FA) was determined. The EEG variables were calculated as an average of 10 epochs and displayed in the compressed spectral arry format (CSA) in the range of 0.0 Hz to 32.0 Hz *(Rampil et al.* 1983) with a full-scale pen deflection at 90 μ V as well as in a numeric plot format.

The numeric data were used for off-line calculation of the percentage of distribution of the total electrical amplitude into single frequency bands.

The statistical analysis of EEG data was performed by calculation of the frequency distribution for the total amplitude (TA) and the 80% spectral edge frequency (SEF-80). Mean values, standard error, and 95% confidence limits were calculated for the percentage distribution of the total amplitude into single frequency bands. Statistical analysis

was performed with a Minitab program using the Students t-test.

Systolic, diastolic, and mean arterial blood pressures were determined using a Dinamap TM 1846 SX (Criticon, Florida, USA) noninvasive system with a cuff placed on 1 of the hind legs for measurements over the dorsal metatarsal artery.

Respiratory rates and end-tidal carbon dioxide partial pressures were recorded using a Hewlett Packard 47210 A Capnometer (HP, Maine; USA), which was connected to a specially designed plastic mask.

Oxygen saturation of arterial hemoglobin was determined using pulse oximetry (Oxygen Saturation Monitor 501+m, Criticare Systems, Inc., Wisconsin, USA) with a detector clamped on the dog's tongue.

All parameters were recorded at 10 min intervals as soon as and as long as dogs would tolerate the devices.

Trial 2

Nine mature laboratory beagles in excellent health with no congenital or acquired abnormalities on physical examination and meeting the standards of the Laboratory Animal Science Program were included in this study. No dog was used in more than 2 trials within the study.

Four different trial groups were tested.

Group 1. Four dogs receiving 40 μg/kg IM of medetomidine followed after 30 min by an IV ketamine (Ketaset, Bristol Laboratories, New York, USA) infusion until general anesthesia was achieved.

Group 2. As group 1, but with 20 μg/kg IM of medetomidine.

Group 3. Four dogs receiving 0.02 mg/kg IM of atropine (Atropine sulfate, Anpro Pharmaceutical, California, USA) 10 min prior to 40 μg/kg IM of medetomidine followed after 30 min by mask induction with a vaporizer setting of 3% halothane (Halothane USP, Halocarbon Laboratories, Inc., New Jersey, USA) in oxygen to produce general anesthesia. After induction, dogs were intubated and maintained on halothane and an oxygen flow of 2 l/min.

Group 4. As group 3, but with 20 μg/kg IM of medetomidine.

Eight dogs for groups 1 and 2 in the medetomidine-ketamine trials and 8 dogs for groups 3 and 4 in the medetomidine-halothane trials were randomly selected by picking envelopes representing each of the 9 dogs available.

Dogs that were represented in both trials were allowed a minimum clearance time of 1 week between trials for appropriate removal of drugs.

Reaction to external stimuli (toe clamping and testing for perineal and palpebral reflexes) and the posture of each dog were recorded prior to injection of medetomidine, prior to induction with ketamine or halothane, and at 10 min intervals during general anesthesia. Toe clamping was performed by clamping the middle phalanx of a toe with metal hemostats for 15 sec to produce deep pain. Perineal reflexes were tested by lightly pinching the anal region with metal hemostats.

Heart rates, ECGs, systolic, mean arterial blood pressures, respiratory rates, end-tidal carbon dioxide partial pressures, and oxygen saturations of arterial hemoglobin were recorded as described *(Räihä et al.* 1989).

All these parameters were recorded just prior to induction with ketamine or halothane and at 10 min intervals during general anesthesia. EEG analysis was as described in trial 1 of this study.

Ketamine trials

The following infusion pattern was followed as closely as pssible. An initial dose of

4mg/kg was administered IV. After that, boluses of 1 mg/kg were given at 1½ min intervals. Following each bolus, 60 sec was allowed to pass after which the dog was checked for adequate anesthesia. A new bolus was added until no response to tail clamping was detected.

Halothane trials

Halothane anesthesia was maintained using a Narkovet 2 anesthetic unit (North American Dräger, Pennsylvania, USA), with a semi-closed circuit and an oxygen flow of 2 l/min. Dogs were allowed to breathe spontaneously. End-tidal halothane concentrations were determined using a Puritan Bennet Anesthetic Agent Monitor 222 (Puritan Bennet Corporation, Boston, Massachusetts, USA) with a detector placed between the endotracheal tube and the connection to the capnometer. Based on these readings, MAC (minimum alveolar concentration) values for halothane were calculated.

MAC (Minimum Alveolar Concentration) determination

Halothane MAC values were determined in a standardized manner *(Quasha et al.* 1980, *Tranquilli et al.* 1984).

Following induction, the vaporizer setting was decreased to 1.5%. An equilibrium period of at least 20 min was allowed and after that, reactions to toe clamping were tested at this concentration. Even the slightest muscle twitch or jerking of the limb in which a toe was being clamped was interpreted as a positive reaction to toe clamping. If no response was noted, a 10 to 20% reduction in the inspired halothane concentration was made, followed by a 10 min equilibrium period. The dog was tested again for reactions to toe clamping. This pattern was repeated in a step-wise fashion until a response was seen. When a positive reaction was noted, a step-by-step increase in the inspired concentration of halothane was made followed by a 10 min equilibrium period and a retest for reactions. This was done until all response to toe clamping had disappeared. MAC for halothane was calculated as the average of the average of the lowest end-tidal concentration where no respone to toe clamping could be seen and the highest concentration with a positive response *(Quasha et al.* 1980, *Tranquilli et al.* 1984).

Results

Trial 1.

All dogs in each group showed signs of sedation after the initial dose. Dogs in group 2 (decreasing doses) and group 3 (equal doses) were more sedated than dogs in group 1 (increasind doses) and were not able to stand 20 min after the initial dose (45.5 µg/kg and 40.0 µg/kg). Dogs in group 1 remained standing or in sternal recumbency still 20 min after the initial dose (11.5µg/kg), thus in some cases not allowing attachment of equipment for proper readings until after their second dose of medetomidine. Group 1 was thus the last broup to become laterally recumbent, but also the last group to show righting reflexes (ability to maintain sternal recumbency) at recovery *(Räihä et al. 1989).* The time interval between administration of the largest dose of medetomidine and appearance of righting reflexes is the same in groups 1 and 2 and close to the time in group 3.

Analgesia occurred earlier in groups 2 and 3 than in group 1, but at 60 min (20 min after the last injection) the analgesic response was equal in all groups *(Räihä et al.* 1989).

Reactions to sound stimulus and palpebral reflexes were also lost earlier in groups 2 and 3 than in group 1, but at 60 to 80 min all groups showed only very slight palpebral

reflexes or response to sound stimulus *(Räihä et al. 1989).*

Effects on cardiovascular and respiratory systems. Medetomidine induced bradycardia and profound sinus arrhythmia in each of the groups studied. The decrease in heart rate from initial resting values prior to medetomidine administration to stable valves during bradycardia at 40 min was 67% in group 1, 71% in group 2, and 64% in group 3. At 10 min after the initial dose of medetomidine, peripheral blood pressure readings in all groups were within normal limits. Initial hypertension *(Savola* 1989) was not recorded since in most cases dogs would not alows cuffs of pressure readings immediately after the first injection. Oxygen saturation of arterial hemoglobin remained above 80% in all groups throughout the study. Respiratory rates remained constant in all groups with average values of 10 to 30 breaths/min after onset of full drug effect. End-tidal CO_2 partial pressures followed the respiratory rates in a predictable manner and no CO_2 accumulation was found in any group *(Räihä et al.* 1989).

Trial 2

All dogs were in lateral recumbency 30 min post-medetomidine administration at induction with either ketamine or halothane. All dogs in groups 1 and 3 (40 µg/kg medetomidine) were fully relaxed, except 1 which showed some alertness at 30 min. All dogs in groups 2 and 4 (20 µg/kg medetomidine), however, showed marked alertness, head lifting, or unsuccessful attempts to gain sternal position at the beginning of induction of anesthesia.

Medetomidine as a preanesthetic to Ketamine IV infusion. Group 1 required less ketamine to produce a nonresponsive level of anesthesia (mean 8.0 mg/kg) than did group 2 (mean 9.2 mg/kg). In group 2, a shorter duration of nonresponsive anesthesia could be seen (mean 19 min) than in group 1 (mean 29 min) and the time from initiation of ketamine anesthesia to voluntary walking was shorter in group 2 (mean 44 min) than in group 1 (Mean 64 min), $p = 0.015$.

Dog A in group 2 experienced 30 sec of seizure-like activity 8 min into ketamine infusion. Excessive salivation was noticed in 1 dog in each group and increased tear production was seen in 1 dog in each group during anesthesia. Slight lateral nystagmus was also found in 1 dog in each group.

A profound bradycardia and sinus arrhythmia of approximately 50 beats/min was recorded in both groups during the effect of medetomidine alone. Ketamine infusion, however, at this point restored heart rates to 77% of resting values in group 1 and up to 98% in group 2. As the positive chronotropic effect of ketamine gradually subsided, heart rates declined, but never reached the levels prior to ketamine infusion.

The respiratory rate of the dogs remained stable throughout the anesthetic period. No CO_2 accumulation could be seen in either group, although a slight increase in end-tidal CO_2, occurred in group 1 during ketamine infusion.

Medetomidine as a preanesthetic to Halothane anesthesia. Intubation was completed in all dogs within 10 min and all dogs had a 20-min stable end-tidal halothane period. MAC values were calculated and averaged for each group, with a mean of 0.7% for group 3 and 1.0% for group 4. The difference was significant, $p = 0.019$. The pre-induction heart rate values in groups 3 and 4 were of the same magnitude as correspond-

ing resting rate values. No bradycardia or sinus arrhythmia could be seen in these groups, which received atropine prior to medetomidine. After a peak at 20 min after medetomidine administration, peripheral mean arterial blood pressure gradually dropped in both groups 3 and 4 and leveled out at 60 min at about 100mm Hg in group 3 and about 70 mm Hg in group 4 with a significant difference of $p = 0.02$.

O_2 saturation of arterial hemoglobin was initially between 80% and 90%, but rose to over 90% at 30 min, when oxygen was supplied with the halothane *(Räihä et al.* 1989).

Neurologic Responses

In these studies to determine neurologic responses to medetomidine as a sole agent, all dogs showed reduction in total amplitude of the EEG and a shift from high frequencies to slow. The responses to an accumulative dosage of 80 µg/kg IM medetomidine were similar in each trial. The principle differences were in the rapidity of changes and duration. The dogs receiving the largest dosage (45µg/kg) as the final injection had the longest duration of total amplitude depression (Fig. 1).

The spectral edge analysis showed the earliest shift to slow frequencies when the dogs were started on high dosages with a latent shift downward when the highest dosage was given last (Fig. 2).

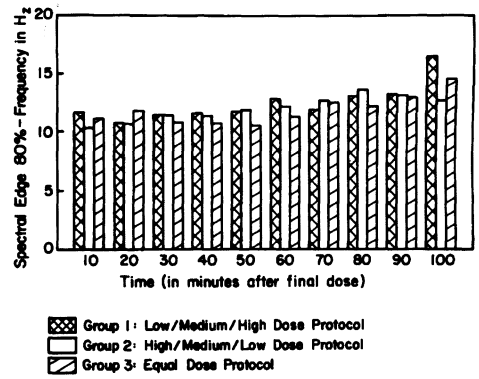

Figure 2: Spectral edge analysis (80%) (H_2) demonstrates the shift from high frequency bands to lower frequencies. Not only is there reduction in total electrical activity, but also frequency shifts correspond to clinical signs of CNS depression.

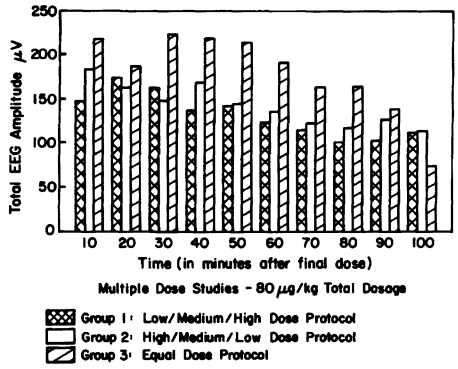

Figure 1: Total amplitude (µV) of cerebral electrical activity is depressed in dogs receiving medetomidine by varying dosage techniques.

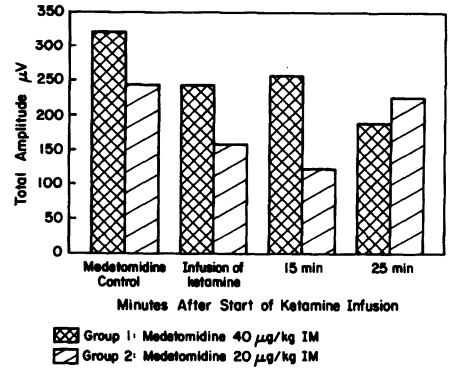

Figure 3: Comparison of cerebral responses to medetomidine and ketamine reflect depression of total amplitude (µV) with combinations of either 20 or 40 µg/kg medetomidine. Note difference in duration of CNS depression is dose dependent.

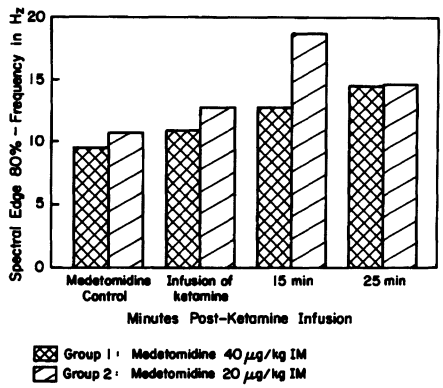

Figure 4: Compressed spectral analysis indicated a shift toward higher frequency bands with the addition of ketamine. Seizure-like neurologic activity is controlled with 40 µg/kg medetomidine and less effectively with 20 µg/kg. This is demonstrated by higher mean frequency in 20 µg/kg medetomodine treated dogs.

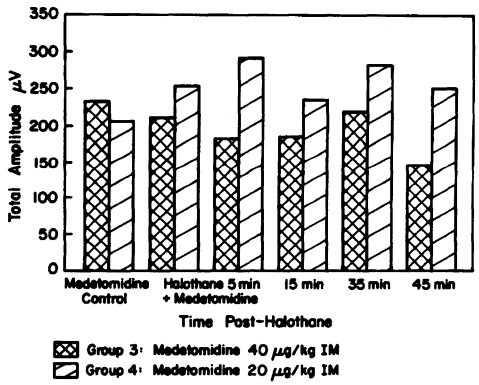

Figure 5: Total amplitude of cerebral responses of 40 µg/kg medetomidine with halothane demonstrate the need to reduce halothane MAC to avoid further CNS depression. Amplitude increases as the CNS recovers from effects of 20 µg/kg medetomidine.

Greater variation in neurologic responses were observed when medetomidine was used as a preanesthetic. The addition of ketamine to 20 µg/kg medetomidine treated dogs resulted in a drop in total amplitude of short duration compared to 40 µg/kg medetomi-

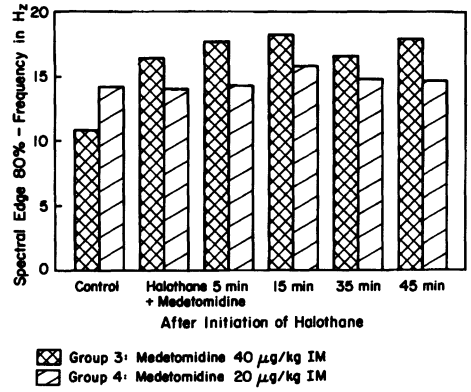

Figure 6: Spectral analysis of 20 µg/kg medetomidine and low concentrations of halothane in oxygen results in a balancing effect on the frequency responses of the CNS. In contrast, since the additive effect of 40 µg/kg medetomidine and low level halothane, addition of oxygen shows an increase in the frequency response of the EEG.

dine (Fig. 3). Ketamine caused a mild shift to high frequency spectral edge 80% in 40 µg/kg medetomidine treated dogs but a significant increase in 20 µg/kg medetomidine treatments (Fig. 4). Seizure-like activity in 1 dog at this dosage level was observed.

The addition of halothane in 40 µg/kg medetomidine treated dogs resulted in further depression of total amplitude (Fig. 5). In contrast, total amplitude increased in 20 µg/kg medetomidine dogs with the addition of halothane. The spectral edge did not change in dogs receiving 20 µg/kg medetomidine and halothane whereas there was a shift toward higher frequencies when halothane was added to the 40 µg/kg medetomidine treatment group (Fig. 6).

Discussion

Cardiopulmonary responses to medetomidine dosage regimens and medetomidine as a preanesthetic followed predictable patterns as reported *(Räihä et al.* 1989). During non-medicated evaluations, EEG responses are

active at all frequencies. Slow frequencies may increase with muscle activity but high frequencies are more likely effected by alertness or excitement. During anesthesia or potent analgesia, EEG activity is not only depressed but shifts from fast to slow frequency bands. CNS depression confirms the capability of pharmaceutical agents to cause major depression of activity. In these studies there were both depression of amplitude and shift of cerebral frequencies. This serves to confirm the development of sedation and analgesia with multiple dosage technique of α_2 agonist. The level of CNS depression was similar once a minimum of 40 µg/kg medetomidine was reached with variation in the total duration of accumulative 80 µg/kg medetomidine dosage. The rapidity of which the accumulative dose was reached was directly related to the duration of CNS depression. In clinical studies, relaxation and reduction in activity is judged to be indicative of sedation and analgesia. Only through evaluation of EEGs can one be assured of cerebral depression including a lack of responsiveness. Noise, motion, and other factors in the environment would be expected to increase total amplitude and shift the EEG to higher spectral edge were not medetomidine effective in depressing CNS responses to stimuli.

Ketamine as a sole agent can cause CNS stimulation in the dog. At 20 µg/kg of medetomidine, ketamine produced further depression of the total amplitude (more total response of the CNS) but the 20 µg/kg medetomidine was inadequate to prevent a shift to higher frequencies. This indicates although the dogs did not move or convulse with ketamine, true anesthesia was not produced. For profound anesthesia, the 80% spectral edge should be shifted to the left (slower frequency response). Medetomidine (40 µg/kg) was effective in preventing shifts to higher frequencies and indicated a physiologically-acceptable analgesia/anesthesia state. At this α_2 level more acceptable medetomidine/ketamine anesthesia is present since the medetomidine is preventing cerebral stimulation from ketamine.

The total amplitude of the EEG increased when halothane was added to 20 µg/kg medetomidine treated dogs versus a reduction in 40 µg/kg medetomidine. This reflects the shorter duration of the most effective period of the medetomidine to reduce total cerebral activity. At 20 µg/kg medetomidine, partial recovery would occur during the experiment and the values are more reflective of halothane anesthesia. Spectral analysis shows an upward shift in 40 µg/kg of medetomidine-treated animals. This is probably due to the increase in cerebral oxygen levels in dogs following the addition of halothane and oxygen administation. In contrast to the medetomidine/ketamine trial without supplemental oxygen, oxygen saturation is improved with the halothane/oxygen combination.

The results of these studies to evaluate EEG activty as an index to cerebral depression indicates medetomidine has profound depression of the CNS demonstrated by both reduction in total activity and shift to slower frequencies. At 40 µg/kg IM medetomidine, it was effective in preventing an increase in high frequency EEG activity from ketamine, which confirms its potential role to prevent CNS seizure-like activity. This would confirm that medetomidine could at least be considered for treatment of CNS seizures from other causes.

Care must be exercised when adding halothane to high concentrations of medetomidine in dogs to avoid excess depression. Both medications are capable of reducing the electrical activity of the brain and cause a

dose-related shift to slow frequencies. This study further confirms the MAC reducing properties of medetomidine. Minimum levels of halothane are needed in medetomidine-treated dogs to accomplish surgical plane anesthesia with reduction of 40 to 90% halothane concentrations expected. The addition of oxygen in severely-depressed CNS from combinations of medetomidine and halothane was benefical in increasing cerebral function. It has long been recognized in respiratory depression, that the supplementation with higher inspired oxygen concentrations is indicated. Both medetomidine and halothane reduces certain cardiac functions and can reduce respiratory capability. In addition to the direct effect of the cardiopulmonary system is the depressionn of anesthetic and analgesics on neurologic control. In these studies we are able to confirm the neurologic responses to both α_2 agonists and either injectable or inhalant anesthesia. In the dog, ketamine alone increases cerebral activity whereas halothane decreases.

The degree of CNS depression is recorded with frequency change (high to low frequency shifts) resulting in lower spectral edge and reduction in total cerebral activity as measured by electroencephalogram was consistent with increasing levels of medetomidine with the addition of halothane. Ketamine does not produce true dissociative anesthesia in the dog. Therefore, it was necessary to use some pharmaceutical agent producing adequate CNS depression to counter the CNS stimulating properties of ketamine. In part, this was accomplished with low concentrations of medetomidine but only at high doses was there significant shift of freqency responses to be confident of the α_2 agonist-dissociative anesthetic combination to assure adequate anesthesia without CNS responses to pain or distress.

Conclusion

The use of compressed spectral analysis has provided insight into the alterations in cerebral function by medetomodine as a sole agent for sedation/analgesia or as a preanesthetic. These results were determined in dogs with concurrent cardiopulmonary measurements to assure the neurologic results were an accurate representation of typical α_2 adrenergic agonist responses in dogs.

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Sammandrag

Jämförelse av neurologiska responser vid användning av medetomidin för sedering och preanestesering av försöks beaglar.

Medetomidin (en effektiv α_2- adrenergisk agonist) doserades enligt olika program, alla med en sammanlagd kombinerad dos av 80 µg/kg, åt försöks beaglar för att fastslå fysilogisk, inkluderande neurologisk, respons. Syftet med experimentet var att fastslå EEG-respons då tillräcklig sedativ och analgetisk effekt nås med medetomidin allena samt dess effekt i samband med ketamin eller halotan.

Verkningarna på cirkulations- och andningsorganen var liknande i alla 3 programmen, uppvisande samma karakteristiska egenskaper, som kunde förväntas vid en enda dos på 80 µg/kg medetomidin. Längden på den effektiva sedativa och analgetiska verkningen tycktes vara i förhållande till när den största dosen gavs. Tillräcklig ytterligare sedativ och analgetisk effekt kunde uppnås med doser hälften mindre än den ursprungliga.

Den starka sedativa och analgetiska effekten av medetomidin, bekräftad via den neurologiska värderingen, ger indikation för dess användning hos hundar som premedisinering före allmän anestesi. I detta arbete uppskattades även effekten av 2 olika doser av medetomidin som premedisinering till både ketamin HCL och halotan anestesi. Den neurologiska värderingen gjordes samtidigt som cirkulations- och respirationsparametrar, anestetisk kvalitet och doseringsbehov antecknades.

Det konstaterades att medetomidin har fördelaktiga egenskaper i kombination med dessa anestetikum. Cirkulations- och respirationsparametrarna förblev på tillfredsställande nivå i bägge grupper av premedisinering före halotan anestesi, men ytterligare fördelar av en förhöjd dos om 40 µg/kg framom en dos på 20µg/kg kunde ej uptäckas, förutom en signifikant 30% nedgång i mängden förbrukat halotan.

Ketaminets positiva kronotropiska och inotropiska egenskaper normaliserade den medetomidinförorsakade bradykardin och framkallade en kort 15 till 30 min period av anestesi, beroende på dosen medetomidine. Den anestetiska kvaliteten var bättre med 40 µg/kg medetomidine, men uppvakningsperioden var kortare med 20 µg/kg.

Registrering av EEG - totalamplituder och frekvenser med komprimerad spektral analys visade en signifikant medetomidinorsakad nedgång i hjärnaktiviteten. Denna analysmetod visade sig effektivt bekräfta kliniska tecken på sedering, analgesi och anestesi hos hundar.

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