Comparison of medetomidine and dexmedetomidine as premedicants in dogs undergoing propofol-isoflurane anesthesia

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Objective—To compare 3 dose levels of medetomidine and dexmedetomidine for use as premedicants in dogs undergoing propofol-isoflurane anesthesia.

Animals—6 healthy Beagles.

Procedure—Dogs received medetomidine or dexmedetomidine intravenously at the following dose levels: 0.4 µg of medetomidine or 0.2 µg of dexmedetomidine/kg of body weight (M0.4/D0.2), 4.0 µg of medetomidine or 2.0 µg of dexmedetomidine/kg (M4/D2), and 40 µg of medetomidine or 20 µg of dexmedetomidine/kg (M40/D20). Sedation and analgesia were scored before induction. Anesthesia was induced with propofol and maintained with isoflurane. End-tidal isoflurane concentration, heart rate, and arterial blood pressures and gases were measured.

Results—Degrees of sedation and analgesia were significantly affected by dose level but not drug. Combined mean end-tidal isoflurane concentration for all dose levels was higher in dogs that received medetomidine, compared with dexmedetomidine. Recovery time was significantly prolonged in dogs treated at the M40/D20 dose level, compared with the other dose levels. After induction, blood pressure decreased below reference range and heart rate increased in dogs treated at the M0.4/D0.2 dose level, whereas blood pressure was preserved in dogs treated at the M40/D20 dose level. However, dogs in these latter groups developed profound bradycardia and mild metabolic acidosis during anesthesia. Treatment at the M4/D2 dose level resulted in more stable cardiovascular effects, compared with the other dose levels. In addition, $Paco_2$ was similar among dose levels.

Conclusions and Clinical Relevance—Dexmedetomidine is at least as safe and effective as medetomidine for use as a premedicant in dogs undergoing propofol-isoflurane anesthesia. (*Am J Vet Res* 2001;62:1073–1080)

Medetomidine is an α_2-adrenoceptor agonist that induces dose-dependent sedation in dogs.[1] Potent analgesia, muscle relaxation, and anxiolysis are well-recognized desirable effects of medetomidine. Bradycardia, initial hypertension with later hypotension, and a substantial decrease in cardiac output are generally considered to be the most important adverse effects of α_2-adrenoceptor agonists, including medetomidine.[2,3]

Propofol is a short-acting nonbarbiturate hypnotic with cardiorespiratory depressant effects similar to that of thiopental. Recovery from propofol, however, is more rapid.[4] Propofol is a safe and effective induction agent in dogs,[5] and it is known to be useful in dogs premedicated with medetomidine.[6-9] Isoflurane is an inhalation agent that depresses cardiorespiratory function in a dose-dependent manner.[10] Administration of medetomidine as a premedicant reduces the anesthetic requirements of propofol[6-9] and isoflurane in dogs.[11,12]

Dexmedetomidine is the active enantiomer of the racemate medetomidine and, when administered at half the dose, induces similar effects as medetomidine.[13-15] However, in an earlier study of dogs anesthetized with halothane,[16] administration of 3 doses of medetomidine (1, 3, and 10 µg/kg of body weight, IV) resulted in a similar reduction in the **minimal alveolar concentration (MAC)** of halothane as did the same doses of dexmedetomidine; the levo-enantiomer was without effect. Results of our previous studies[15,17] imply that dexmedetomidine offers some sedative and analgesic benefits over racemic medetomidine in dogs.

The primary purpose of the study reported here was to compare the clinical effects of medetomidine and dexmedetomidine administered as premedicants prior to induction and maintenance of anesthesia with propofol and isoflurane, respectively, in dogs. A secondary purpose was to determine the most appropriate premedicant dose level. We hypothesized that dexmedetomidine would have a more potent anesthetic sparing effect than medetomidine.

Materials and Methods

Animals—Six (3 sexually intact females, 3 castrated males) clinically normal adult Beagles[a] were used in this study. Dogs were between 1 and 2 years old and weighed between 14 and 18 kg. They were housed together in a pen and received outdoor exercise in a yard for several hours daily. Commercial dog food was given once daily, and water was freely available. Procedures were performed during the daytime, and on study days, dogs were fed only after procedures were completed. Dogs were trained and accustomed to handling, instrumentation, the study room, and the researchers. The faculty's animal care and use committee approved these experiments.

Study design—A randomized Latin square design was

Received Jun 7, 2000.
Accepted Aug 29, 2000.
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The authors thank Juhani Tuominen, Sami Hokkanen, and Ilona Pylvänäinen for statistical assistance. Dexmedetomidine and medetomidine were gifts of Orion Pharma, Turku, Finland. Propofol was a gift of Leiras, Helsinki, Finland.

applied. The researcher (EK) who evaluated degree of sedation, analgesia, and anesthesia was not aware of which drug the dogs received but was not blinded to the dose level. The same trained person always performed evaluations.

Treatment groups—Dogs received medetomidine or dexmedetomidine at 3 dose levels, with at least 2 weeks between treatments. The dose levels used were as follows: 0.4 µg of medetomidine[b]/kg (group M0.4) and 0.2 µg of dexmedetomidine[c]/kg (group D0.2; M0.4/D0.2 dose level); 4.0 µg of medetomidine/kg (group M4) and 2.0 µg of dexmedetomidine/kg (group D2; M4/D2 dose level); and 40 µg of medetomidine/kg (group M40) and 20 µg of dexmedetomidine/kg (group D20; M40/D20 dose level). Dexmedetomidine doses were anticipated to be equipotent to those of racemic medetomidine. The drugs were prepared in syringes. Each dose was diluted with saline (0.9% NaCl) solution to the same volume and administered as an IV bolus.

Study procedure—Before sedation, a catheter[d] was inserted percutaneously (Seldinger method) in a femoral artery, and a cannula[e] was placed in a cephalic vein. During instrumentation, dogs were held with minimal restraint, and lidocaine was infiltrated locally to avoid pain and discomfort. Dogs were then placed standing on a table. Heart rate and blood pressure were allowed to stabilize before baseline measurements were obtained. The premedicant was injected, and 10 minutes later dogs were positioned in lateral recumbency for induction. Propofol[f] was administered IV in small increments over 1 minute until dogs could be intubated. Anesthesia was maintained with isoflurane[g] in oxygen delivered via a semiclosed circle rebreathing system[h] with an out-of-circle vaporizer. Flow was set and maintained between 0.3 and 2 L/min to optimize the level of anesthesia. Breathing was spontaneous. Warm Ringer's solution[i] (5 ml/kg/h) was infused during the procedure. Rectal temperature was maintained at > 37 C. The vaporizer was closed after 45 minutes (end of anesthesia), and dogs were allowed to breath oxygen at a flow rate of 2 L/min for 5 minutes or until extubated.

Monitoring—Sedation and analgesia were evaluated subjectively once after premedication but before induction. Evaluation methods were modified from those described in earlier studies of medetomidine in dogs.[1,15,17,18] Posture (scores, 0 to 4), palpebral reflex (0 to 3), eye position (0 or 2), jaw and tongue relaxation (0 to 4), resistance to positioning in lateral recumbency (0 to 3), and general appearance (0 to 4) were scored. Summing these variables gave the total sedation score (0 to 20) for each dog. Analgesic effect (score, 0 to 3) was tested by pinching the interdigital skin of a hind foot while it was being stretched.[4,18,19] To avoid unnecessary pain, pinching was initiated lightly with the fingernails and stopped immediately after a pedal reflex was induced. A score of 0 was assigned when a normal pedal reflex was induced, 1 when the reflex was slow, 2 when the foot was withdrawn only after pinching with increased intensity for 3 seconds, and 3 when pinching elicited no response. The same trained person (EK) always scored analgesic effect to obtain consistency with the stimulus intensity.[20]

The amount of propofol needed for induction was recorded, and the quality of induction was assessed as smooth, cyanosis, muscle stiffness, excitation, or apnea > 1 minute. Dogs were kept at a light plane of anesthesia, which was characterized by lack of purposeful movement in response to application of a noxious stimulus for 3 seconds, moderate relaxation of the jaws, eye rotation, and palpebral reflex. During anesthesia, noxious stimulation was applied every 5 minutes after all other measurements were made as described for evaluation of analgesic effect. If there was no hemodynamic or respiratory response to pinching, concentration of isoflurane was slightly decreased. If the dog flexed its leg or moved its head or tongue, concentration of isoflurane was slightly increased. End-tidal isoflurane was measured, using a monitor,[j] and registered every 5 minutes after induction. Adverse effects during recovery (eg, excitation, shivering, and nausea) were observed and recorded. Times from the end of anesthesia to extubation, sternal recumbency, and walking were recorded.

The arterial catheter was connected to a transducer[k] on a monitor[l] for continuous measurement of **systolic arterial pressure (SAP)**, **diastolic arterial pressure (DAP)**, **mean arterial pressure (MAP)**, and **heart rate (HR)**. The pressure transducer was adjusted to the level of the dog's right atrium. Recordings were made before premedication, before induction, and every 5 minutes during anesthesia. One-minute lead-II ECG recordings were obtained before premedication, before induction, 5 minutes after induction, and every 15 minutes thereafter until the end of anesthesia. Electrocardiograms were later evaluated for arrhythmias.

Arterial blood samples for determination of Pa_{CO_2}, Pa_{O_2}, pHa, and bicarbonate concentration were collected before premedication, before induction, 5 minutes after induction, and every 15 minutes thereafter until the end of anesthesia. A waste sample was first collected prior to collecting the sample for analysis, and the arterial catheter was flushed with 3 ml of saline solution after blood withdrawal. Samples were collected into heparinized syringes, set on ice, analyzed immediately in duplicate,[m] and mean values were calculated. Values were automatically corrected to rectal temperature measured at the same time. End-tidal and inspired P_{CO_2} and **respiratory rate (RR)** were measured every 5 minutes during anesthesia, using the same monitor[l] used for determination of end-tidal isoflurane concentration. An end-tidal P_{CO_2} of 60 mm Hg was considered the maximal acceptable value. If end-tidal P_{CO_2} was > 60 mm Hg, dogs were manually ventilated with a pressure of 20 cm H_2O every 15 seconds as needed. Before induction, RR was measured by observing thoracic movements. **Arterial hemoglobin saturation (SpO_2)** was estimated every 5 minutes during anesthesia, using a pulse oximeter[n] with the probe attached to the dog's tongue.

Statistical analyses—Numerical variables were analyzed by use of an overall ANOVA for repeated measures with 3 within factors: time, drug (medetomidine or dexmedetomidine), and dose level (M0.4/D0.2, M4/D2, or M40/D20). When significant interactions were found, separate ANOVA were performed for each time point. Categorical variables were analyzed by use of a nonparametric Friedman 2-way ANOVA at each time point. Significance was set at $P < 0.05$. Data were expressed as mean ± SD.

Results

Effects of premedicants on anesthesia—The effects of each drug administered at a given dose level on sedation and analgesia were similar before induction, but degree of sedation and analgesia were significantly affected by dose level. Dogs that were given the highest dose of medetomidine or dexmedetomidine (ie, the M40/D20 dose level) were deeply sedated (M40 total sedation score, 15 ± 2.7; D20 total sedation score, 15 ± 1.3). Degree of analgesia was also deep in these groups (M40 score, 2.8 ± 0.4; D20 score, 2.8 ± 0.4). Dogs that were treated at the M4/D2 dose level were moderately sedated (M4 score, 10 ± 3.6; D2 score, 11 ± 2.6). Analgesic effect was considered light in these

groups (M4 score, 0.5 ± 0.5; D2 score, 1 ± 0.6). Dogs that were treated at the M0.4/D0.2 dose level were only slightly sedated, as evidenced by head drooping in some dogs (M0.4 score, 0.2 ± 0.4; D0.2 score, 0.5 ± 0.8). However, no analgesic effect was apparent for either group.

Amount of propofol required for induction was significantly affected by dose level of premedicant but not by drug. Doses of propofol administered to each group were as follows: M0.4, 5.8 ± 1.0 mg/kg; D0.2, 6.0 ± 1.1 mg/kg; M4, 2.7 ± 0.3 mg/kg; D2, 2.7 ± 0.5 mg/kg; M40, 0.9 ± 0.3 mg/kg; and D20, 0.8 ± 0.2 mg/kg. Except at 55 minutes, dose level had a significant effect on the end-tidal isoflurane concentration needed to maintain an equivalent plane of anesthesia (**Fig 1**). The combined mean end-tidal isoflurane concentration (ie, the average of end-tidal concentrations for all dose levels) was higher at 35 ($P = 0.023$), 40 ($P = 0.008$), and 45 ($P = 0.015$) minutes of anesthesia in dogs that received medetomidine, compared with

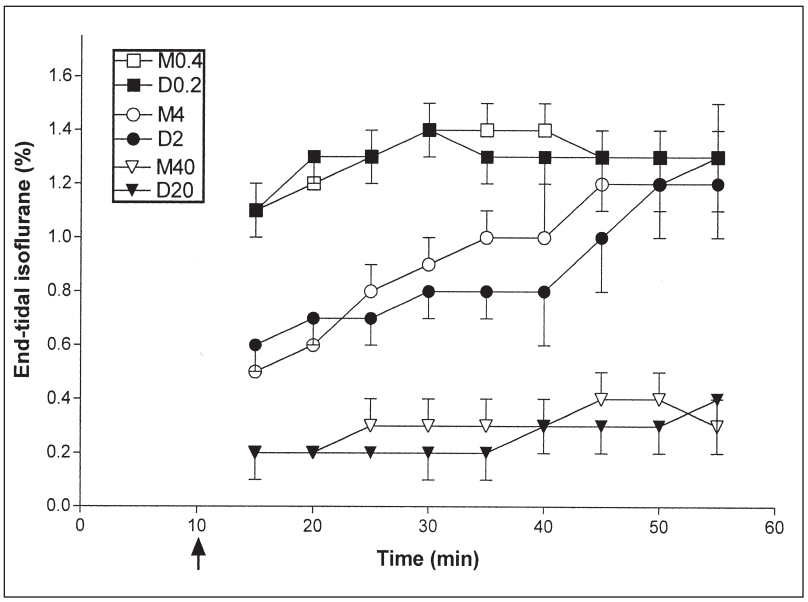

Figure 1—Mean (± SD) end-tidal isoflurane concentration in 6 healthy adult Beagles premedicated at time 0 with 3 dose levels of medetomidine (0.4 µg/kg of body weight [M0.4], 4.0 µg/kg [M4], and 40 µg/kg [M40]) or dexmedetomidine (0.2 µg/kg [D0.2], 2.0 µg/kg [D2], and 20 µg/kg [D20]). Dogs received each treatment, with at least 2 weeks between treatments. Anesthesia was induced at 10 minutes (arrow) with propofol administered to effect and maintained with isoflurane.

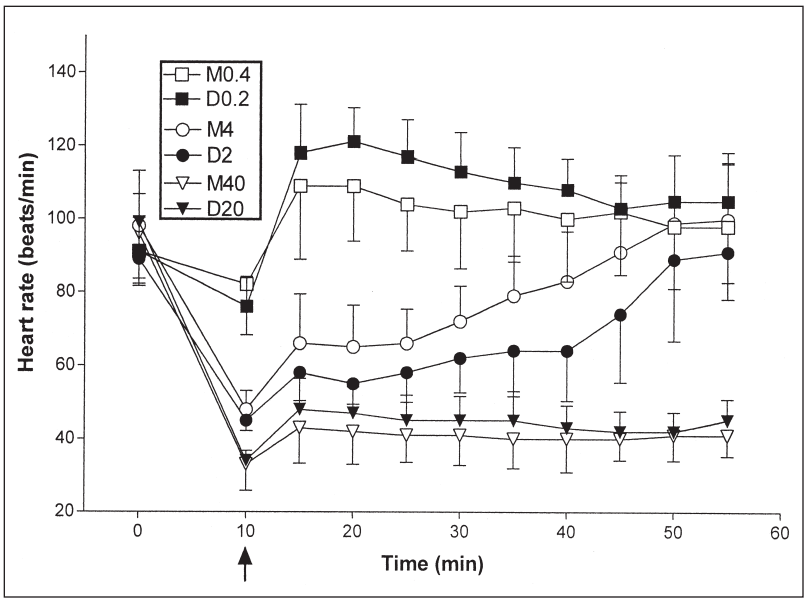

Figure 2—Mean (± SD) heart rate in 6 healthy adult Beagles premedicated at time 0 with 3 dose levels of medetomidine or dexmedetomidine. Dogs received each treatment, with at least 2 weeks between treatments. Anesthesia was induced at 10 minutes (arrow) with propofol administered to effect and maintained with isoflurane.

those that received dexmedetomidine. However, end-tidal isoflurane concentration determined at each dose level was not significantly affected by drug. At 35 minutes, mean isoflurane concentrations in the M0.4 and D0.2 groups were 79 and 85% higher than in the M40 and D20 groups, respectively, whereas isoflurane concentrations in the M0.4 and D0.2 groups were 29 and 39% higher than in the M4 and D2 groups, respectively.

All dogs were extubated within 10 minutes after the end of anesthesia. Premedicant used did not affect time to extubation, but dogs premedicated at the M40/D20 dose level were extubated significantly later than those at the M0.4/D0.2 (P = 0.044) or M4/D2 (P = 0.022) levels. Times to sternal recumbency and walking were significantly prolonged in dogs treated at the M40/D20 dose level, compared with the 2 lower dose levels. All dogs in groups M4 and D2 and most (5/6) dogs in groups M0.4 and D0.2 walked without ataxia within 10 minutes after the end of anesthesia. However, in groups M40 and D20, mean time to walking was 20 minutes (range, 6 to 40 minutes), and at this time, dogs still appeared tired and were ataxic.

Apnea after induction that lasted for 1 to 2 minutes was detected in 1 dog each in groups M0.4, M2, D2, and D20. One dog in group D2 vomited after injection of dexmedetomidine. During the same treatment, which was the first of 6 anesthetic episodes, this same dog was also startled during induction and after extubation, as evidenced by responding to a sudden sound, but was readily reassured. Shortly after extubation, leg paddling was observed in 1 dog in group M4 and 2 dogs in group D0.2. Panting was also observed in 1 dog in group D0.2 at this same time, whereas slight shivering was observed in 1 dog each in groups M4 and M0.4. Otherwise, no adverse effects were noticed during induction or recovery.

Cardiovascular effects of premedicants—Heart rate in all groups decreased significantly after administration of premedicants and increased significantly after induction (**Fig 2**). At the M0.4/D0.2 dose level, HR after induction was significantly greater than baseline, whereas at the M4/D2 and M40/D20 dose levels, HR after induction was significantly less than baseline. After premedication and until 50 minutes of anesthesia, HR differed significantly among dose levels. At 50 and 55 minutes, HR was similar between the M0.4/D0.2 and M4/D2 dose levels. Overall HR (ie, area under the HR versus time curve) was significantly less (P = 0.025) in group D2, compared with group M4. One dog in group M40 had frequent episodes of second degree **atrioventricular (A-V)** block after premedication and 5 minutes after induction; bradycardia (HR, 27 beats/min) was severe at both times. Occasional episodes of second degree A-V block were also detected after premedication in 1 dog in group D2. First degree A-V block was frequently detected after premedication and during anesthesia in dogs treated at the M40/D20 and M4/D2 dose levels and occasionally detected after premedication in dogs treated at the M0.4/D0.2 dose level. Accentuated sinus arrhythmia was detected after premedication and during anesthesia in all dogs treated at the M40/D20 dose level and after premedication in dogs treated at the M4/D2 dose level.

Mean arterial pressure increased significantly after premedication in groups M40 and D20 and decreased significantly after induction with all treatments (**Fig 3**). During anesthesia (15 to 55 minutes), MAP slowly and significantly decreased in dogs treated at the M40/D20 and M4/D2 dose levels but was stable in dogs treated at the M0.4/D0.2 dose level. Dose level had a significant effect on MAP at most times, but at 40, 50, and 55 minutes, MAP was simi-

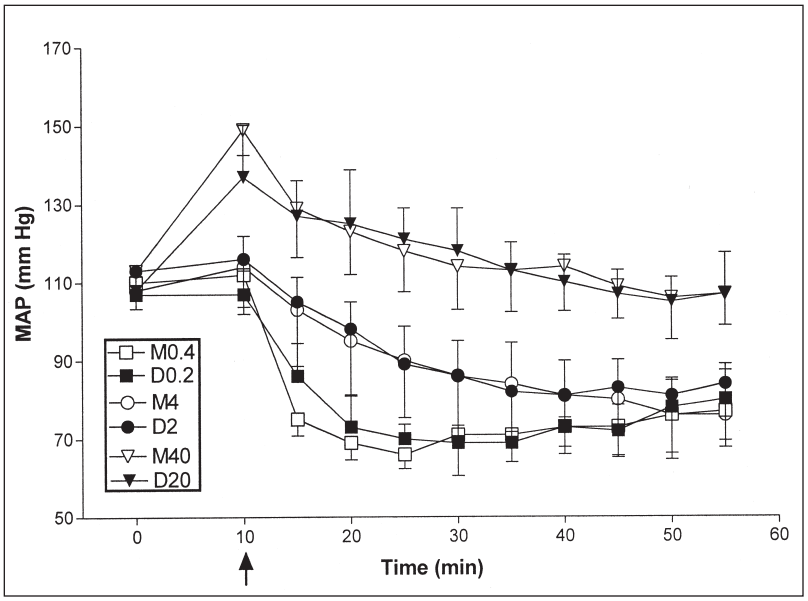

Figure 3—Mean (± SD) mean arterial blood pressure (MAP) in 6 healthy adult Beagles premedicated at time 0 with 3 dose levels of medetomidine or dexmedetomidine. Dogs received each treatment, with at least 2 weeks between treatments. Anesthesia was induced at 10 minutes (arrow) with propofol administered to effect and maintained with isoflurane.

lar between the M0.4/D0.2 and M4/D2 dose levels. At the end of anesthesia, MAP was similar to baseline values in groups D20 and M40 but significantly less than baseline values in the other groups. In general, differences in SAP and DAP among groups were similar to those in MAP.

Respiratory effects—Before induction, Pa_{O_2} and Pa_{CO_2} were not significantly affected by treatment group. During anesthesia, Pa_{O_2} remained > 400 mm Hg in all groups. However, Pa_{O_2} was slightly but significantly less in dogs treated at the M40/D20 dose level, compared with the other dose levels. No dog required manual ventilation. In all groups, Pa_{CO_2} increased significantly to 48.4 ± 3.9 mm Hg after induction and then gradually decreased significantly to 44.1 ± 4.8 mm Hg at the end of anesthesia. Correlation between end-tidal P_{CO_2} and Pa_{CO_2} was good (r = 0.83). However, end-tidal P_{CO_2} was significantly less in dogs treated at the M4/D2 dose level,

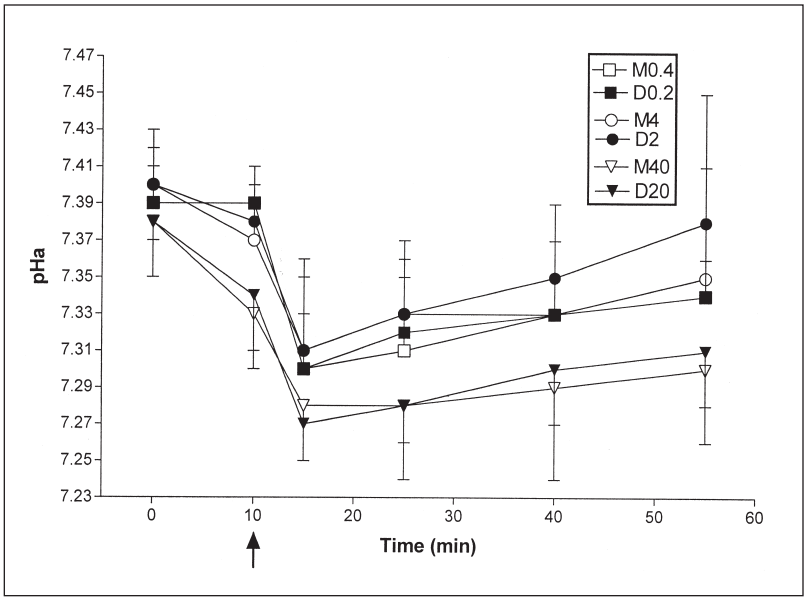

Figure 4—Mean (± SD) arterial pH in 6 healthy adult Beagles premedicated at time 0 with 3 dose levels of medetomidine or dexmedetomidine. Dogs received each treatment, with at least 2 weeks between treatments. Anesthesia was induced at 10 minutes (arrow) with propofol administered to effect and maintained with isoflurane.

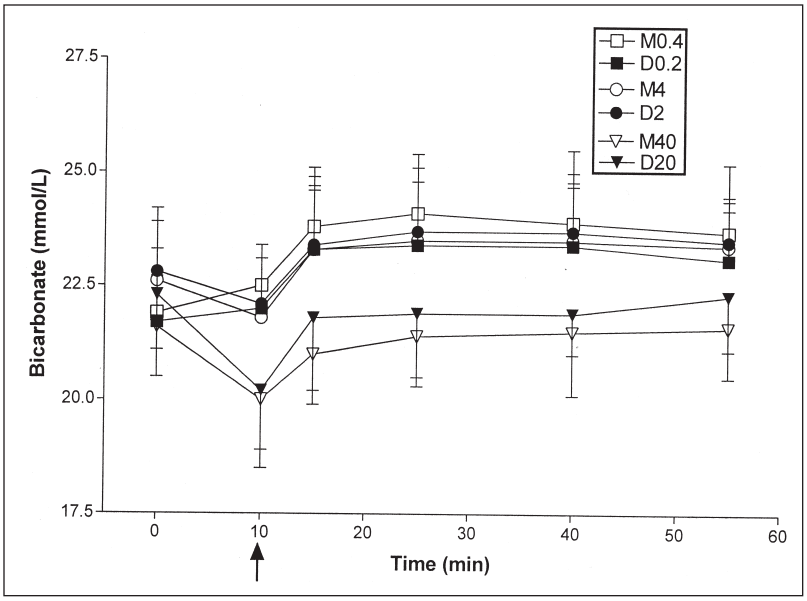

Figure 5—Mean (± SD) arterial blood bicarbonate concentrations in 6 healthy adult Beagles premedicated at time 0 with 3 dose levels of medetomidine or dexmedetomidine. Dogs received each treatment, with at least 2 weeks between treatments. Anesthesia was induced at 10 minutes (arrow) with propofol administered to effect and maintained with isoflurane.

compared with the M0.4/D0.2 ($P = 0.03$) or M40/D20 ($P = 0.014$) dose levels. Inspired CO_2 remained < 3 mm Hg at all times, confirming that no substantial rebreathing took place. Arterial pH **(Fig 4)** and bicarbonate concentration **(Fig 5)** decreased significantly after premedication at the M4/D2 and M40/D20 dose levels. After induction, pHa decreased and bicarbonate concentration increased significantly in all groups. Values for these 2 variables were significantly less at all time points after premedication in dogs treated at the M40/D20 dose level, compared with the other dose levels. In addition, pHa was significantly higher at the end of anesthesia in dogs treated at the M4/D2 dose level, compared with the other dose levels. Respiratory rate did not change significantly after premedication. After induction, RR decreased slightly but significantly in dogs treated at the M4/D2 and M40/D20 dose levels, compared with rates at 10 minutes. Significant differences in SpO_2 were not detected among treatment groups, nor did SpO_2 change significantly during anesthesia; mean SpO_2 varied between 97 and 100%.

Discussion

Effects of the corresponding doses of medetomidine and dexmedetomidine on sedation and analgesia before induction and on propofol requirements were similar, but dose level had a significant effect on these variables. The combined mean end-tidal isoflurane concentration (ie, average of end-tidal concentrations for all dose levels) was higher in dogs treated with medetomidine than with dexmedetomidine, implying that the analgesic effect of dexmedetomidine was prolonged. At the M40/D20 dose level, dogs recovered from anesthesia more slowly, compared with the other dose levels. After induction, MAP decreased below reference range and HR increased in dogs treated at the M0.4/D0.2 dose level. Treatment at the M40/D20 dose level preserved blood pressure, but bradycardia was profound, and mild metabolic acidosis was induced during anesthesia. Dexmedetomidine had a more potent anesthetic sparing effect than medetomidine, although this effect was not detected at the separate dose levels. Administration of these α_2-adrenoceptor agonists at the M4/D2 dose level resulted in more stable cardiovascular effects during propofol-isoflurane anesthesia, compared with the other dose levels, but the effect was short-term.

A light plane of anesthesia was selected to ease the effort to maintain all dogs at a similar plane regardless of premedication. The anesthetic sparing effect of an injectable drug is usually studied by determining the MAC of the inhalant anesthetic. We wanted to compare the effects of the different dose levels of the α_2-adrenoceptor agonists in the same way in which these drugs are used clinically. Thus, common clinical methods for determining depth of anesthesia were applied. The end-tidal isoflurane concentrations that we detected in dogs treated at the M0.4/D0.2 dose level were similar to a MAC of 1 for isoflurane in dogs.[10]

Medetomidine and dexmedetomidine have analgesic and muscle-relaxant effects that can be extended by increasing the dose administered.[1,14] Dogs in groups M40 and D20 had relaxed eyelids and a brisk palpebral reflex. In addition, eye position sometimes changed and depth or frequency of breathing mildly increased in these dogs in response to noxious stimulus (ie, toe-web pinching). Even though hemodynamic changes were rarely seen in dogs treated at the highest dose level, decreasing the concentration of isoflurane was usually not possible. Dogs in groups M0.4 and D0.2 tended to close their eyelids, which made evaluation of the palpebral reflex difficult. Distinct but transient increases in HR, blood pressure, and RR were seen in response to noxious stimulus. Initially, quality of anesthesia for dogs in groups M4 and D2 was similar to that for groups M40 and D20, whereas at later times, it was similar to that for groups M0.4 and D0.2. A stable plane of anesthesia was most difficult to maintain in dogs treated at the M4/D2 dose level, compared with the other dose levels; concentration of isoflurane administered had to be gradually increased in the former groups as the effects of premedication and propofol waned.

Administration of the higher premedicant dose levels resulted in distinct reductions in propofol and isoflurane requirements, compared with the lowest dose level (ie, M0.4/D0.2). Doses of propofol required for induction were similar to those described in a previous report.[7] Results of an earlier study in dogs[16] revealed that medetomidine (10 µg/kg, IV) could reduce the MAC of halothane by 90%. In addition, the MAC of isoflurane was reduced by 89% after dexmedetomidine (20 µg/kg, IV)[11] administration and 47% after medetomidine (30 µg/kg, IV) administration.[12] In the present study, propofol requirements were similar after premedication with medetomidine or dexmedetomidine, but the combined mean end-tidal isoflurane concentration was transiently lower after administration of dexmedetomidine. This finding could be attributable to the prolonged analgesic effect of dexmedetomidine.[15] However, the difference in end-tidal isoflurane concentration was too short-lived to be clinically important and should be verified by further studies with proper MAC determinations.

The dogs used in the present study, which were acclimated to handling, had smooth recoveries even when the dose level of premedicant used resulted in no significant sedative effects. However, violent recoveries after isoflurane anesthesia are sometimes seen in dogs, and some residual sedation without excessive cardiorespiratory depression would be less stressful for the dog.

Isoflurane increases HR and decreases arterial blood pressure.[21,22] The decrease in blood pressure results almost entirely from a decrease in systemic vascular resistance while maintaining cardiac output.[21] Propofol moderately decreases arterial blood pressure with variable effects on HR.[23,24,25] The cardiovascular effects we detected in dogs treated at the M40/D20 dose level were comparable to those achieved by sedation with 40 µg of medetomidine/kg.[15] With these high doses of α_2-adrenoceptor agonists, peripheral vasoconstrictive effects predominate, and the low doses of propofol and isoflurane administered seem to have only minimal cardiovascular effects.[11] Heart rate increased after induction in all groups and above the baseline in groups M0.4 and D0.2. Dogs in groups

M40 and D20 developed prominent bradycardia; mean HR was < 50 beats/min throughout each experiment. Heart rate was higher in group M4, compared with D2. This was probably attributable to an isoflurane-induced increase in HR, because dogs with low HR also had low end-tidal isoflurane concentrations.

Mean arterial pressure decreased to less than reference range in dogs treated at the M0.4/D0.2 dose level. This decrease was greater than that usually seen in dogs under a light plane of isoflurane anesthesia.[22,26] The combined effects of propofol and isoflurane may partially explain this finding, because in an earlier study,[24] the hypotensive effect of a bolus dose of propofol (6.5 mg/kg) in dogs lasted at least 30 minutes. Additionally, at these low doses of α_2-adrenoceptor agonists, central hypotensive effects may predominate over peripheral vasoconstrictive effects.[27] A placebo-controlled study may resolve this question. In groups M40 and D20, MAP remained close to baseline values during anesthesia, and in groups M4 and D2, the decrease in MAP was delayed, but the effect was short-lived.

Results of previous studies[28,29] in dogs revealed that isoflurane anesthesia at a MAC of 1 resulted in more respiratory depression, compared with a combination of isoflurane and medetomidine or dexmedetomidine at a similar level of anesthesia. In our study, degree of hypercapnia was similar among treatment groups despite significantly lower end-tidal P_{CO_2} in groups M4 and D2. This finding implies that, although dexmedetomidine and medetomidine do not induce profound respiratory depression,[1,29] administration of high doses of these drugs offers no respiratory benefits even though the isoflurane concentration can be reduced. Additionally, the combination of a high dose of medetomidine or dexmedetomidine (ie, 40 µg/kg or 20 µg/kg, respectively), propofol, and isoflurane induced mild metabolic acidosis despite a compensatory increase in arterial bicarbonate concentration. Impaired tissue perfusion may explain this finding, although arterial hemoglobin was well saturated. Cardiac output is reduced by approximately 70% in dogs premedicated with 20 µg of dexmedetomidine/kg and anesthetized with isoflurane,[11] and venous oxygen content has been shown to decrease soon after administration of an equipotent dose of medetomidine despite adequate arterial oxygenation.[30] The decrease in pHa (lowest value, 7.27) seen in our study in dogs treated at the M40/D20 dose level was not, however, considered to be clinically important. Taken together, then, our results indicate that dexmedetomidine, the active component of the racemate medetomidine, is at least as safe and effective as medetomidine when administered at an equipotent dose (ie, half the medetomidine dose) prior to induction and maintenance of anesthesia with propofol and isoflurane, respectively, in healthy dogs.

[a]Harlan, Zeist, The Netherlands.
[b]Domitor, Orion Pharma, Turku, Finland.
[c]Orion Pharma, Turku, Finland.
[d]LeaderCath 115.12 18G, Vygon, Ecouen, France.
[e]Optiva2 20G, Ethicon, Pomezia, Italy.
[f]Recofol, Leiras, Helsinki, Finland.
[g]Forene, Abbott, Espoo, Finland.
[h]CDS 2000 small animal anesthesia unit, Anesco, Georgetown, Ky.
[i]Ringersteril, Orion Pharma, Turku, Finland.
[j]Capnomac Ultima, Datex Engström, Helsinki, Finland.
[k]Ohmeda DTX, Singapore.
[l]Life Scope 6, Model OEC-6102J/K/L, Nihon, Kohden, Japan.
[m]ABL 300 acid-base laboratory, Radiometer, Copenhagen, Denmark.
[n]Model 8500V, Nonin Medical Inc, Plymouth, Minn.

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