# Onset and quality of sedation after intramuscular administration of dexmedetomidine and hydromorphone in various muscle groups in dogs

Jennifer E. Carter, DVM, DACVAA; Crace Lewis; Thierry Beths, DVM, PhD

**Objective**—To compare onset time and quality of sedation achieved by IM injection of hydromorphone and dexmedetomidine into either the semimembranosus, cervical, gluteal, or lumbar muscle groups in dogs.

**Design**—Prospective, randomized, crossover study.

**Animals**—7 dogs.

**Procedures**—Each dog was assigned to receive each treatment in random order, and at least 1 week elapsed between treatments. Dogs were sedated with dexmedetomidine and hydromorphone combined and injected IM into the assigned muscle group. An observer unaware of group assignments assessed physiologic variables every 5 minutes for 30 minutes, and a videographic recording was obtained. Recordings were evaluated by 16 individuals who were unaware of group assignments; these reviewers assessed time to onset of sedation and assigned a sedation score to each dog every 5 minutes.

**Results**—Resting pulse and respiratory rates did not differ among injection site groups. The semimembranosus site had a significantly higher sedation score than all other sites, and the cervical site had a significantly higher sedation score than the lumbar and gluteal sites. The semimembranosus and cervical sites had significantly shorter time to onset of sedation than did the gluteal and lumbar sites.

**Conclusions and Clinical Relevance**—When the combination of dexmedetomidine and hydromorphone was used to induce sedation in dogs, rapid and profound sedation was achieved with IM injection into the semimembranosus muscle. (*J Am Vet Med Assoc* 2013;243:1569–1572)

Delivery of drugs to achieve sedation is an important aspect of veterinary practice. Sedative drugs are administered for diagnostic procedures, preanesthetic sedation, postsurgical sedation, and many other reasons. In veterinary medicine, sedative drugs are most commonly administered IM, SC, or IV.

Dexmedetomidine is an $\alpha_2$-adrenoceptor agonist sedative with analgesic properties. It can be administered by several routes and provides moderate to profound sedation in dogs over a dose range of 125 to 375 $\mu g/m^2$.[1] Hydromorphone is a pure μ-opioid analgesic used to treat moderate to severe pain that, when administered to a dog, induces both analgesia and mild to moderate sedation. When $\alpha_2$-adrenoreceptor agonists and opioid drugs are administered simultaneously, they have an additive effect providing greater sedation and analgesia.[2]

Intravenous drug administration is not always practical because of patient temperament, small vein diameter, potential scarring of the peripheral veins, and potential tissue damage. Intramuscular injection provides rapid drug absorption; however, several veterinary studies[3–9] have detected differences in drug bioavailability, speed of absorption, and clinical efficacy among different sites of absorption including the cervical, biceps, triceps, lumbar epaxial, gluteal, and semitendinosus muscles. A study[10] in humans revealed that drug absorption is more rapid from the deltoideus muscle than from the vastus lateralis muscle or the gluteus muscles and identified differences in blood supply as a potential cause. However, a study[11] comparing use of acepromazine and morphine at multiple injection sites in dogs failed to detect a difference in degree of sedation. In addition, injection of a drug into a muscle belly may not result in IM deposition of the entire dose, and some may be deposited into fascial planes. In a small study[12] of injection of a radiopaque dye into several muscle groups in dogs, IM injections occurred when the material was injected into the cervical musculature or caudal aspect of the thigh.

The purpose of the study reported here was to investigate the association between site of IM injection (in semimembranosus, cervical, gluteal, and lumbar muscle groups) of hydromorphone and dexmedetomidine and onset and quality of sedation in dogs. On the basis of our clinical impressions, the hypothesis was that injection into the cervical muscles would result in faster and more profound sedation in dogs than with other commonly used muscle groups.

## Materials and Methods

**Animals**—This study was approved by the Ross University School of Veterinary Medicine Institutional

From the Department of Clinical Sciences, School of Veterinary Medicine, Ross University, Basseterre, Saint Kitts, West Indies. Drs. Carter and Beths' present address is Faculty of Veterinary Science, University of Melbourne, Werribee, VIC 3030, Australia.

Supported by an internal research grant from Ross University School of Veterinary Medicine.

The authors thank Crispin Worrell and Shakima Connor for contributions to the study.

Address correspondence to Dr. Carter (jennifer.carter@unimelb.edu.au).

Animal Care and Use Committee. Seven neutered dogs (5 male and 2 female) between 8 months and 5 years of age were studied. Dogs were deemed healthy on the basis of results of physical examination, routine blood analyses (CBC and serum biochemical profile) performed quarterly, and fecal examination. All dogs had a body condition score < 5 on a scale from 1 to 5. The dogs were isolated and not used for any other procedure during the study. The dogs were kept in individual concrete kennels that were adequately ventilated. Food was fed once per day and water was given ad libitum, but these were withheld during experimental procedures.

**Experimental design**—The dogs were assigned to 1 of 4 injection sites in a prospective randomized crossover design so that each dog received an injection at each site. At least 1 week elapsed between injections. Prior to the injection, each dog was placed in a quiet, climate-controlled room and allowed to rest for 15 minutes. At the end of the 15-minute acclimatization period, pulse rate and respiratory rate were recorded as the time 0 measurement. Rectal temperature was also measured to ensure that the body temperature was within the reference range at the start of the study. The dogs were then sedated with dexmedetomidine[a] at a dose of 3.5 µg/kg (1.59 µg/lb) and hydromorphone[b] at a dose of 0.1 mg/kg (0.045 mg/lb) combined in the same syringe and injected IM into the assigned muscle. The same veterinary nurse performed all injections in all dogs for the duration of the study. The injections were performed in the cervical epaxial, lumbar, gluteus medius, or semimembranosus muscles. The injections were given perpendicular to the skin into the center of the muscle mass while the dogs were standing, whenever possible. Injections into the cervical epaxial muscles were given at the approximate level of the third cervical vertebra, 2 to 3 cm to the left or right of the midline. The injections into the lumbar muscles were given at a point midway between the vertebra and the last rib. The injections into the gluteus medius muscle were given at a point midway between the greater trochanter of the femur and the wing of the ilium. The injections into the semimembranosus muscle were given at the caudolateral aspect of the muscle, with the tip of the needle directed toward the caudal aspect of the limb so that, if the dog moved, the needle would not advance toward the sciatic nerve. No preference was given to the left or right side of the dog. A 20-gauge, 1-inch needle was used to administer the drugs, and after it was confirmed that the needle had not been placed in a blood vessel, the injections were made briskly with a 3-mL syringe. After the injection, the dogs were left in a quiet room with a single observer (unaware of the site of injection) and a videography camera mounted on a tripod. Pulse rate, respiratory rate, eye position, and withdrawal reflexes, as assessed by pinching a toe on a pelvic limb, were assessed every 5 minutes for 30 minutes (7 observations including time 0). After the 30-minute recording period, the dog was allowed to recover under observation until fully ambulatory.

At the conclusion of the data collection period, videographs of the dogs that received injections were evaluated by 16 individuals who were unaware of the injection site. Each reviewer evaluated the time of onset of sedation and assigned a sedation score to the dog every 5 minutes for 30 minutes. The level of sedation was assessed on a numeric rating scale where 0 = no sedation; 1 = standing or sitting and head lower than before sedation; 2 = standing or sitting unbalanced, muscle weakness, and refusing to lie down; 3 = lying in sternal recumbency but responsive; 4 = lying in lateral recumbency but responsive; and 5 = lying in lateral recumbency and unresponsive. Any incident of vomiting was also recorded. Each reviewer evaluated the videographs independently and did not discuss their scores with the other reviewers.

**Statistical analysis**—Prevalence of vomiting was analyzed with a general linear model 2-way ANOVA accounting for the influence of the site of injection and individual dog. Sedation scores were analyzed with a general linear model 3-way ANOVA accounting for the influence of the site of injection, the observer, and individual dogs, followed by a Holm-Sidak multiple pairwise comparison post hoc test for all significant ($P < 0.05$) pairings. The time to onset of sedation was analyzed with a balanced design 3-way ANOVA accounting for the influence of the site of injection, the observer, and individual dogs, followed by a Holm-Sidak multiple pairwise comparison post hoc test for all significant ($P < 0.05$) pairings. The pulse rate and respiratory rate at time 0 were compared among dogs with a 1-way ANOVA. No statistical analysis on pulse rate or respiratory rate was performed for the remaining time points, as this was beyond the scope of the study. The analyses were performed with commercially available statistical software.[c] Values of $P < 0.05$ were considered significant in all analyses.

## Results

The mean ± SD body weight of the dogs used in the study was 19.35 ± 1.4 kg (42.57 ± 3.08 lb), with a range from 14.75 to 23.1 kg (32.45 to 50.82 lb). Mean ± SD pulse rate at time 0 was 107 ± 18 beats/min for the cervical group, 103 ± 10 beats/min for the gluteal group, 109 ± 30 beats/min for the semimembranosus group, and 99 ± 13 beats/min for the lumbar group. There were no significant differences in pulse rate among groups at time 0 ($P = 0.794$). Mean ± SD resting respiratory rate was 26 ± 6 breaths/min for the cervical group, 27 ± 2 breaths/min for the gluteal group, 31 ± 5 breaths/min for the semimembranosus group, and 25 ± 4 breaths/min for the lumbar group. Several dogs in each group were recorded as panting during the preadministration examination and were excluded from analysis for the mean; however, there were no significant differences among groups for resting respiratory rate at time 0 ($P = 0.604$). All dogs in all groups had central eye position and present and appropriate withdrawal reflexes at time 0. Mean pulse rate, respiratory rate, eye position, and withdrawal reflex changes over the course of the study were summarized (**Table 1**).

There was no significant difference in the prevalence of vomiting between the groups with 3 dogs in the cervical group, 5 dogs in the semimembranosis group, 3 dogs in the lumbar group, and 4 dogs in the gluteal group vomiting during the study ($P = 0.661$). In

Table 1—Mean values for variables measured at various time points in 7 dogs that received a combined IM injection of hydromorphone and dexmedetomidine into the semimembranosus, cervical, gluteal, or lumbar muscles in a study of the onset and quality of sedation.

| | Pulse rate (beats/min) | | | | Respiratory rate (breaths/min) | | | | Eye position | | | | Withdrawal reflex | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Time (min) | G | S | L | Ce | G | S | L | Ce | G | S | L | Ce | G | S | L | Ce |
| 0 | 103 | 109 | 99 | 107 | 27 | 31 | 25 | 26 | C | C | C | C | I | I | I | I |
| 5 | 65 | 52 | 69 | 55 | 18 | 34 | 32 | 30 | C | C | C | C | I | I | I | I |
| 10 | 59 | 43 | 59 | 48 | 20 | 34 | 19 | 31 | C | C | C | C | I | A | I | I |
| 15 | 48 | 45 | 52 | 44 | 31 | 30 | 21 | 17 | C | VM | C | VM | A | A | I | I |
| 20 | 47 | 44 | 48 | 41 | 23 | 17 | 18 | 16 | C | VM | C | V | A | A | I | A |
| 25 | 47 | 44 | 47 | 44 | 18 | 16 | 17 | 17 | C | VM | C | VM | A | A | I | A |
| 30 | 47 | 47 | 48 | 41 | 16 | 13 | 20 | 17 | C | VM | C | VM | A | A | I | A |

A = Absent. C = Central. Ce = Cervical. G = Gluteal. I = Intact. L = Lumbar. S = Semimembranosus. V = Ventral. VM = Ventromedial.

addition, there was no influence of individual dogs on the prevalence of vomiting—6 of the 7 dogs vomited at some point ($P = 0.102$).

Mean sedation score for each injection site was determined except the time 0 score, which was a score of 0 in all dogs in all groups. Mean ± SD and median (range) sedation scores were 3.34 ± 0.8 and 3 (0 to 5) for the cervical group, 2.72 ± 0.85 and 3 (0 to 5) for the gluteal group, 3.67 ± 1.03 and 4 (0 to 5) for the semimembranosus group, and 2.84 ± 0.64 and 3 (range, 0 to 5) for the lumbar group. There was a significant ($P < 0.001$) difference in sedation scores among the groups, and there was no effect of the different observers on this finding ($P = 1.000$). The semimembranosus group had a significantly ($P < 0.001$) higher sedation score than any other group. The cervical group had a significantly ($P < 0.001$) higher sedation score than the lumbar and gluteal groups . The lumbar group did not have a significantly ($P = 0.153$) different sedation score than the gluteal group.

Time to onset of sedation for each injection site was determined. Mean ± SD and median (range) times to onset of sedation were 7:30 ± 4:58 minutes and 6:37 (1:20 to 21:00) minutes for the cervical group, 10:15 ± 7:15 minutes and 8:00 (2:00 to 30:00) minutes for the gluteal group, 6:59 ± 5:50 minutes and 5:50 (1:20 to 18:18) minutes for the semimembranosus group, and 10:59 ± 7:00 minutes and 6:45 (1:20 to 30:00) minutes for the lumbar group. There was an overall significant ($P < 0.001$) difference in the time to onset of sedation among the injection sites even when allowing for the differences among dogs and among observers. However, there was no significant ($P = 0.162$) difference between the semimembranosus and cervical injection sites despite the fact that times for onset of sedation were each significantly ($P < 0.001$ for all interactions) less than for the gluteal and lumbar sites. There was also no significant ($P = 0.359$) difference in times to onset of sedation between the gluteal and lumbar sites.

## Discussion

This investigation aimed to evaluate the effect of different sites for IM injection of dexmedetomidine and hydromorphone on the onset and quality of sedation in dogs. Results indicated that the most rapid onset of sedation was achieved with injection into either the cervical or semimembranosus muscle groups, which partially supported our hypothesis. This finding was in contrast to findings in a study[13] in pigs in which the site of IM injection of azaperone and ketamine did not influence the onset of recumbency, which was the measure of sedation in that study. Another study[11] evaluating IM acepromazine and morphine in dogs did not specifically measure the onset of sedation, but it was noted that dogs in the gluteal group were significantly less sedated at 10 minutes after injection, compared with those in the cervical, quadriceps, or triceps muscle groups. One potential explanation for the rapid onset of sedation from the cervical and semimembranosus groups could be that those muscle groups have a greater blood supply than the gluteal muscles or lumbar muscles. Blood flow to a muscle group is dependent on the activity and function of the muscle, with postural muscles receiving greater blood flow than nonpostural muscles at rest.[14] This would only provide a partial explanation, however, because the cervical muscles are not postural in dogs. However, both the cervical region and the semimembranosus muscle have substantial collateral circulation, which theoretically could result in increased blood flow to the muscle bellies and therefore more rapid drug absorption.[15] Further research, possibly by use of corrosion casting, could shed additional light on the perfusion of different muscle groups in dogs. Another possible explanation might be that IM injection was more consistently performed at the cervical and semimembranosus sites. Previous studies[12,14,16] revealed that IM injection or injection into fascial planes or fat stores results in slower absorption of drugs. However, one study[16] of cervical injections in horses found that only 50% of the injections resulted in true IM deposition of drugs, and another study[12] found that among several IM injection sites in dogs, use of the lumbar muscles resulted in the most consistent successful IM injection. Although all injections were performed by the same investigator and all dogs received all injections, a final possible explanation may lie in the temperament of individual dogs and the excitement and possible pain resulting from injection at the specific sites. Pain and resulting movement of the dogs could increase blood flow to the injected area. Self et al[11] evaluated several IM injection sites in dogs and detected a substantial pain reaction on injection at the quadriceps and triceps muscles, although some study dogs reacted to injections at the cervical and gluteal sites as well. In a study[13] of IM injections in pigs, injections into the cervical region resulted in the least number of reactions suggesting pain. Unfortunately, these subjective measurements were not collected in the present study.

Results of the present study indicated that injection into the semimembranosus muscle resulted in a signifi-

cantly higher overall sedation score than did injection into the cervical, lumbar, or gluteal muscle groups. This was in direct contrast to results of a study[11] performed in dogs with acepromazine and morphine IM injections, in which there was no difference in final sedation scores among the cervical, gluteal, triceps, and quadriceps injection sites. It is possible that this difference resulted from the different sedative premedications used in each study. In a recent study,[17] the depth of sedation following premedication with buprenorphine and either acepromazine or dexmedetomidine was evaluated, and dogs receiving the dexmedetomidine premedication had significantly higher sedation scores. The doses of both drugs were larger than those used in the present study or the previous study,[11] which might have influenced the depth of sedation; however, they were paired with buprenorphine, which lacks substantial sedative qualities in dogs, as opposed to the pure μ-opioid agonists used by Self et al[11] and in the present investigation. Two other similar studies[18,19] failed to detect a significant difference in sedation scores between dogs receiving buprenorphine combined with acepromazine and those receiving buprenorphine combined with dexmedetomidine or medetomidine. It is important to note that the cervical musculature was used for injection in both of those studies,[18,19] whereas the site of injection was not specified in the study by Herbert et al.[17] Lastly, the factors regarding the influence on perfusion and blood flow to different muscle groups that were discussed regarding the onset of sedation would likely apply to the overall quality of sedation as well because better absorption from a muscle group would result in greater bioavailability of the drug and, likely, greater effect.

Results of the present study suggested that when the combination of dexmedetomidine and hydromorphone is used at doses and under conditions similar to those reported here to achieve sedation or premedication in dogs, IM injections should be made into the semimembranosus muscle group to achieve both rapid and profound sedation.

a. Dexdomitor, Pfizer Animal Health, New York, NY.
b. Hydromorphone, West Ward, Eatontown, NJ.
c. Sigma Stat, version 3.5, Systat Software Inc, San Jose, Calif.

## References


1. Dexdomitor [package insert]. Espoo, Finland: Orion Corp, 2007.
2. Ossipov MH, Harris S, Lloyd P, et al. Antinociceptive interaction between opioids and medetomidine: systemic additivity and spinal synergy. *Anesthesiology* 1990;73:1227–1235.
3. Firth EC, Nouws JFM, Driessens F, et al. Effect of the injection site on the pharmacokinetics of procaine penicillin G in horses. *Am J Vet Res* 1986;47:2380–2384.
4. Marshall AB, Palmer GH. Injection sites and drug bioavailability. In: Van Miert ASJPAM, Frens J, Vander Kreek FW, eds. *Trends in veterinary pharmacology and toxicology*. Amsterdam: Elsevier Scientific Publishing Co, 1980;54–60.
5. Baxter JS, Evans JM. Intramuscular injection in the cat. *J Small Anim Pract* 1973;14:297–302.
6. Hartman EG. Influence of the injection site on the depot-effect of procaine penicillin in dogs. In: Van Miert ASJPAM, Bogaert MG, Debackere M, eds. *Comparative veterinary pharmacology, toxicology, and therapy*. Lancaster, Lancashire, England: MTP Press Ltd, 1987;85–91.
7. Nouws JF, Vree TB. Effect of injection site on the bioavailability of an oxytetracycline formation in ruminant calves. *Vet Q* 1983;5:165–170.
8. Wilson RC, Duran SH, Horton CR Jr, et al. Bioavailability of gentamicin in dogs after intramuscular or subcutaneous injections. *Am J Vet Res* 1989;50:1748–1750.
9. Oukessou M. Influence of injection site on the absorption of benzylpenicillin sodium in the dromedary. *Zentralbl Veterinarmed A* 1995;42:431–434.
10. Greenblatt DJ, Koch-Weser J. Intramuscular injection of drugs. *N Engl J Med* 1976;295:542–546.
11. Self IA, Hughes JML, Kenney DA, et al. Effect of muscle injection site on preanaesthetic sedation in dogs. *Vet Rec* 2009;164:323–326.
12. Autefage A, Fayolle P, Toutain PL. Distribution of material injected intramuscularly in dogs. *Am J Vet Res* 1990;51:901–904.
13. Clutton RE, Bracken J, Ritchie M. Effect of muscle injection site and drug temperature on pre-anaesthetic sedation in pigs. *Vet Rec* 1998;142:718–721.
14. Benet LZ, Kroetz DL, Sheiner LB. Pharmacokinetics: the dynamics of drug absorption, distribution, and elimination. In: *Goodman and Gilman's the pharmacological basis of therapeutics*. 9th ed. New York: McGraw-Hill, 1996;3–27.
15. Evans HE. The heart and arteries. In: *Miller's anatomy of the dog*. 3rd ed. Philadelphia: Saunders, 1993;587–681.
16. Boyd JS. Selection of sites for intramuscular injection in the neck of the horse. *Vet Rec* 1987;121:197–200.
17. Herbert GL, Bowlt KL, Fort-Fennah V, et al. Alfaxalone for total intravenous anaesthesia in dogs undergoing ovariohysterectomy: a comparison of premedication with acepromazine or dexmedetomidine. *Vet Anaesth Analg* 2013;40:124–133.
18. Bell AM, Auckburally A, Pawson P, et al. Two doses of dexmedetomidine in combination with buprenorphine for premedication in dogs; a comparison with acepromazine and buprenorphine. *Vet Anaesth Analg* 2011;38:15–23.
19. Grint NJ, Alderson B, Dugdale AH. A comparison of acepromazine-buprenorphine and medetomidine-buprenorphine for preanesthetic medication of dogs. *J Am Vet Med Assoc* 2010;237:1431–1437.