

A Chronic Model for Investigation of Experimental Spinal Anesthesia in the Dog

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A chronic model for investigation of spinal anesthesia in the dog is described. This model incorporates the use of a chronically implanted catheter in the lumbar subarachnoid space. An 18-gauge thin-walled Crawford needle is passed percutaneously into the subarachnoid space. An 18-gauge epidural catheter is then threaded through the needle into the subarachnoid space and the distal end attached to a special metal valve which is sutured under the skin. One-milliliter volumes of various local anesthetic solutions were injected intrathecally via the valve and catheter. Durations of the effects of the local anesthetics were evaluated. Duration of subarachnoid conduction blockade was defined as the time during which hind-limb paralysis persisted in the dog. The times to onset and durations of motor blockades were evaluated following the intrathecal injection of dibucaine, tetracaine, lidocaine, bupivacaine, chloroprocaine, and mepivacaine. Times to onset ranged from 1.1 to 2.3 min. Durations of motor blockade were longest for dibucaine and tetracaine, followed in order of decreasing duration by bupivacaine, lidocaine, chloroprocaine, and mepivacaine. The durations of subarachnoid conduction motor blockades in the dog are qualitatively similar to reported values for spinal anesthesia in man. Therefore, the technique described may provide a useful model to evaluate factors that may influence spinal anesthesia. (Key words: Anesthetic techniques, spinal. Anesthetics, local: bupivacaine; chloroprocaine; dibucaine; lidocaine; mepivacaine; tetracaine.)

THE FIRST REPORTED INSTANCE of spinal anesthesia occurred in 1885, when Corning accidentally performed a spinal block in a dog with cocaine.¹ Since that time, spinal anesthesia has become probably the most commonly used regional anesthetic technique in modern anesthesia. Although much has been written concerning spinal anesthesia, few well-controlled studies have been carried out, particularly in animals, where it should be possible to maintain standardized experimental conditions. Experimental methods of spinal and epidural anesthesia using surgically implanted catheters in the cat, dog, and rat have been described.²⁻⁴ In addition, some nonsurgical tech-

niques for spinal and epidural anesthesia in the sheep and dog have been reported.⁵⁻¹⁰ However, to date, no information about the comparative effects of standard local anesthetics in these animal models relative to man has been available.

The present report describes a chronic model for investigation of spinal anesthesia in the dog, in which the animal can be subjected to administration of various drugs on different occasions and thus serve as its own control for a comparative study of different local anesthetic drugs. The report describes the technique of catheter implantation and data obtained regarding durations of anesthesia with lidocaine, tetracaine, bupivacaine, dibucaine, mepivacaine, and chloroprocaine. A comparison of the values obtained in the dog with published values for these agents in man indicates a reasonable correlation between the two species.

Materials and Methods

Twenty-five adult dogs of either sex, ranging in weight from 10 to 20 kg, were used. Each was anesthetized with pentobarbital sodium, 30 mg/kg, iv. The dog was placed on an operating table in the prone position. The hind limbs were extended cranially alongside the abdomen in an effort to separate the lumbar intervertebral spaces maximally. The lumbosacral region of the back was shaved and cleaned with a surgical preparation scrub. Using a sterile technique, an 18-gauge thin-walled Crawford epidural needle was introduced percutaneously at the L3-L4, L4-L5, or L5-L6 interspace by means of a median or paramedian approach. An 18-gauge epidural catheter (Portex) was inserted through the Crawford needle and advanced so the tip lay approximately 4-8 cm beyond the needle tip.

Placement of the tip of the needle in the subarachnoid space was verified by one or more of the following signs: 1) There can often be felt two distinct "pops" as the needle penetrates the ligamentum flavum and subsequently the dura. There is also occasionally a distinct twitch of the hind limb. The latter sign is not definitive, as hind-limb twitch could be caused by mechanical stimulation of the spinal nerve roots in the epidural space. 2) Cerebrospinal fluid (CSF) is withdrawn or flows spontaneously through the spinal needle. 3) Spontaneous flow of CSF through

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the implanted catheter is seen, or it is possible to withdraw CSF through the catheter.

The spinal needle was removed, leaving the tip of the implanted catheter in the subarachnoid space. The catheter was cut to a length sufficient to allow 5–7 cm to be looped subcutaneously before being connected to a metal valve. This allowed some play in the catheter to accommodate movement under the relatively loose skin of the dog.

A Schraeder-type valve was fabricated of stainless steel (fig. 1). The valve operates on the same principle as an automobile tire valve. An adaptor that screws onto the valve opens the valve and allows for the free injection of test drug into the catheter.¹¹ The adaptor is fitted with a plastic tube to which a Luer Lock connection is attached. A Luer Lock syringe can then be connected to the adaptor for injection of the anesthetic solution. When the adaptor is removed the valve is closed by an internal spring and gasket. While each dog was anesthetized an incision was made in the skin overlying the lumbar spinal area and the valve implanted subcutaneously. The incision was sutured with 2-0 silk and the animal returned to the kennel for recovery. On the morning following catheter implantation the dog was evaluated for signs of sensory or motor deficit indicative of mechanical damage to the cord or nerve roots. When no neurologic deficit was apparent, the animal was utilized for the study. Antibiotics were not given to these animals.

TEST PROCEDURE

All animals were evaluated prior to administration of test drugs for sensory and motor responses. Test drugs were all commercially available local anesthetic solutions. A 1-ml volume of anesthetic solution was injected into the subarachnoid space via the implanted catheter and valve with the animal in a standing or prone position. Immediately after injection the animal was released and allowed freedom of movement in the room. In the first five dogs, lidocaine was administered and the duration of motor blockade determined. Subsequently, the remaining 20 dogs received either lidocaine or tetracaine and one of the other four agents evaluated, *i.e.*, mepivacaine, chlorprocaine, dibucaine, or bupivacaine. Each dog received two injections separated by 48 hours. The order of injection was randomized.

Evaluation of sensory blockade was attempted by observing the response to pinching the toes with Allis tissue forceps. Failure of the dog to vocalize or attempt to withdraw its hind leg was taken as indication of sensory analgesia. It soon was apparent that the animals became rapidly conditioned to the testing procedure for sensory analgesia. Therefore, further at-

tempts to evaluate the presence or absence of sensory analgesia were abandoned.

Motor blockade was evaluated by observations of gait and ability to stand on the hind limbs. The presence of an ataxic gait was defined as partial motor blockade. Inability to stand on the hind limbs was defined as complete motor blockade. Time to onset of complete motor blockade was defined as the time from injection of drug to the time the animal was unable to stand erect on its hind limbs. Duration of complete motor blockade was calculated as the time from onset of motor blockade to the time the animal was able to stand on its hind limbs without assistance. Time to complete recovery from motor blockade was defined as the time from onset of complete motor blockade to the time when the animal was able to walk without signs of ataxia. The animals were observed continuously from time of injection to time of complete recovery. At 5–10-min intervals manual attempts were made to stand the dogs on their hind limbs. Failure to stand unassisted on hind limbs was taken as an indication of the presence of complete motor blockade.



TABLE 1. Average Durations of Motor Blockades Following Subarachnoid Administration of Various Local Anesthetic Agents in the Dog

	Average Time to Onset of Complete Motor Blockade (Min \pm SE)	Average Duration of Complete Motor Blockade (Min \pm SE)	Average Time to Complete Recovery (Min \pm SE)	N
1) Dibucaine, 0.25 per cent	2.30 \pm 1.06	155.90 \pm 14.99*	206.20 \pm 12.91*	5
2) Tetracaine, 0.5 per cent	1.98 \pm 0.27	148.15 \pm 9.87*	175.05 \pm 8.82*	10
3) Bupivacaine, 0.75 per cent	1.50 \pm 0.44	92.10 \pm 10.00†	129.80 \pm 14.42†	5
4) Lidocaine, 5.0 per cent	1.55 \pm 0.23	57.40 \pm 4.21	70.00 \pm 6.14	15
5) Chloroprocaine, 3.0 per cent	1.10 \pm 0.29	44.20 \pm 5.56	44.25 \pm 4.51	5
6) Mepivacaine, 2.0 per cent	1.35 \pm 0.22	29.60 \pm 2.37‡	60.70 \pm 9.67‡	5

* Significant difference vs. solutions 3-6, $P < 0.01$.† Significant difference vs. solutions 1, 2, 4-6, $P < 0.01$.‡ Significant difference vs. solutions 1-5, $P < 0.05-0.01$.

Two per cent lidocaine, 0.25 per cent dibucaine, 0.5 per cent tetracaine, 0.75 per cent bupivacaine, and 3 per cent chloroprocaine were used in this study, since these concentrations are similar to those commonly employed for spinal anesthesia in man. Two and 4 per cent mepivacaine have been used for subarachnoid block in man. Since the 4 per cent concentration of mepivacaine is not available in the United States, only 2 per cent mepivacaine was used. Hyperbaric solutions of tetracaine, dibucaine, and lidocaine were used, since hyperbaric solutions are administered most often for spinal anesthesia in man. Bupivacaine, chloroprocaine, and mepivacaine were administered as isobaric solutions, since it was impossible to formulate hyperbaric solutions of these agents without diluting the anesthetic strength.

The variation in durations of motor blockade following repetitive administrations of a local anesthetic agent was evaluated in two dogs. These animals received either lidocaine or tetracaine at two- to seven-day intervals for periods of 21-28 days. The possibility of neural irritation due to chronic catheter implantation was examined in these two dogs, in which the catheters remained in the subarachnoid space for 30 days. The animals were killed by overdoses of pentobarbital and the spinal cords removed and placed in formalin. Sections of the cords at various levels were taken and slides prepared for histologic examination. Microscopic examinations of the spinal cord sections were made by a pathologist.

Statistical analysis was performed by analysis of variance, followed by multiple Student's *t* tests for paired data or group mean data as appropriate for the comparative group. The times to onset of complete motor blockade and the durations of complete motor blockade and partial motor blockade were evaluated statistically.

Results

Times to onset of motor blockade, *i.e.*, the times from injection to when the animals could no longer stand on their hind limbs, were relatively short with

all agents tested, and no significant difference existed among the agents (table 1).

Durations of complete motor blockade ranged from 156 \pm 33.7 min for dibucaine to 30 \pm 5.3 min for mepivacaine (table 1). Dibucaine and tetracaine produced significantly longer durations of motor blockade than did all other agents ($P < 0.01$). The duration of blockade with 0.75 per cent bupivacaine was significantly shorter than those of blockades with tetracaine and dibucaine, but significantly longer than those of blockades with all other agents. Lidocaine and chloroprocaine produced similar durations of motor blockade. The duration of motor blockade with 2 per cent mepivacaine was significantly shorter than those produced by all other agents.

Time to complete recovery was the time from onset of complete motor blockade to the time when an animal could walk without any sign of ataxia. Approximately 30-40 min usually elapsed between the time that an animal could stand and the time ataxia was no longer noticeable. The only exception was in those animals treated with chloroprocaine. The duration of complete motor blockade and the time to complete recovery in the chloroprocaine-treated animals were almost identical (table 1).

Of the two dogs given repetitive intrathecal injections of lidocaine or tetracaine the durations of lidocaine-induced blockade ranged from 30 to 61 min in the first and from 50 to 75 min in the second (table 2). The durations of tetracaine induced-blockade ranged from 137 to 194 min in the first dog and from 124 to 160 min in the second dog. These two animals, in which the catheters remained in the subarachnoid space for 30 days, were then examined by necropsy. No gross abnormality of the spinal cord was observed. Histologic examination of the cords failed to reveal any sign of neural irritation. A slight inflammatory arachnoiditis was seen in both cases.

Discussion

A method for spinal anesthesia in dogs using a chronically implanted catheter is described. Although

some difficulty was encountered initially, due to lack of experience in identifying the subarachnoid space, it is possible to pass a needle percutaneously into the subarachnoid space of the dog. The present technique offers the advantages of minimal surgical manipulation and the ability to use each animal as its own control. In the current study, catheters remained patent and usable for 14 to 60 days. The major cause of failure was the fact that, with time, the catheters in some animals had a tendency to curl up subcutaneously and thus dislodge from the subarachnoid space.

With regard to the results obtained with the various local anesthetic agents, table 3 compares the values from this study in dogs with reported values in man for the agents tested. As can be seen, a qualitative correlation appears to exist between the durations of motor blockade observed in our chronic dog model and the durations of motor blockade reported to occur in man with the various drugs.

Dibucaine and tetracaine produced the longest durations of subarachnoid blockade in both man and dog. Bupivacaine appears to produce blockade of somewhat shorter duration than those produced by tetracaine and dibucaine. Lidocaine and chlorprocaine provide relatively short durations of subarachnoid blockade in man and dog. The concentrations of dibucaine, tetracaine, bupivacaine, lidocaine, and chlorprocaine employed in this study are similar to those used for spinal anesthesia in man. The volumes and total doses in milligrams do vary, depending upon the specific agent. For example, tetracaine is frequently employed in volumes ranging from 1 to 4 ml and in total doses of approximately 10 to 20 mg in man. One milliliter containing 5 mg of tetracaine was used in the dog. Lidocaine is frequently employed in volumes of 1 to 2 ml containing 50 to 100 mg in man. One milliliter containing 50 mg of lidocaine was used in the dog. In terms of a mg/kg dose regimen, the dog received a larger dose of local anesthetic compared with man.

Mepivacaine showed the greatest discrepancy between durations of blockades in dog and in man. This was probably related to the use of a 2 per cent solution in our dog studies, while most human studies were conducted with a 4 per cent mepivacaine solution.

TABLE 2. Durations of Motor Blockades (Min) in Two Dogs Following Repetitive Intrathecal Injections of Lidocaine or Tetracaine at Two- to Seven-day Intervals for 21-28 Days

	Dog 1		Dog 2	
	Lidocaine	Tetracaine	Lidocaine	Tetracaine
Day 1	30	—	—	160
Day 3	—	187	50	—
Day 5	—	137	—	150
Day 7	49	—	75	—
Day 11	—	194	—	137
Day 14	61	—	77	—
Day 21	57	—	—	124
Day 28	—	—	65	—

Since 4 per cent mepivacaine is not available in the United States, it was not possible to use this concentration in our studies. However, Lipton, Sinnott and Batt used a 2 per cent solution of mepivacaine for a study of spinal anesthesia in obstetrics, and reported a mean duration of motor blockade of 55 min.¹² This is similar to the value of 60.7 ± 9.67 min needed for complete motor recovery in our dogs following subarachnoid administration of 2 per cent mepivacaine.

The time differentials between durations of complete motor blockade and durations of partial motor blockade were similar with all local anesthetic solutions except chlorprocaine. These time differences ranged from 12 to 50 min for all of the agents except chlorprocaine. No difference was found between the duration of complete motor blockade and the duration of partial motor blockade in those animals that received chlorprocaine. The reason for this phenomenon with chlorprocaine is not clear. However, the rapid regression of anesthesia following neural blockade with chlorprocaine has been observed in man.

Tetracaine, dibucaine, and lidocaine were administered as hyperbaric solutions to mimic the situation commonly existing in man. It was not possible to use hyperbaric solutions of the other agents without diluting the concentrations or altering the volumes of solution administered. The effect of baricity of tetracaine solutions has been studied in man.¹³ Motor blockades of significantly longer duration were found following the use of isobaric solutions of tetracaine,

TABLE 3. Comparative Durations of Motor Blockades in Dog and Man (Mean \pm SE)

	Duration of Complete Motor Blockade in the Dog (Min)	Time to Complete Recovery in the Dog (Min)	Duration of Motor Blockade in Man (Min)
Dibucaine	155.90 \pm 14.99	206.20 \pm 13.91	120-300 ¹⁴
Tetracaine	147.15 \pm 9.87	175.05 \pm 8.82	142 \pm 14, ¹⁵ 157 \pm 14.6 ¹⁶
Bupivacaine	92.10 \pm 10.00	129.80 \pm 14.42	121 \pm 13 ¹⁵
Lidocaine	57.40 \pm 4.21	70.00 \pm 6.14	76 \pm 10.3, ¹⁷ 90 \pm 5 ¹⁸
Chlorprocaine	44.20 \pm 5.56	44.25 \pm 4.51	70 \pm 2.2 ¹⁹
Mepivacaine	29.60 \pm 2.37	60.70 \pm 9.67	55, ¹² 131.7 ²⁰

compared with the hyperbaric solution. Therefore, the variation in baricity of the solutions used in this study may have influenced the differences in durations of motor blockade observed with the various agents. For example, the durations of motor blockades produced by dibucaine, tetracaine, and lidocaine might have been longer had these agents been administered in isobaric rather than hyperbaric solutions.

Differences clearly exist between man and dog in terms of anatomy of the subarachnoid space, methods of performing spinal anesthesia, and dosages and volumes of anesthetic solutions. Despite these differences, it would appear that the present model is capable of predicting qualitatively relative durations of spinal anesthesia that are comparable to those observed in man. Thus, it should be possible with the current model to examine, in a controlled fashion, the influences of various factors on the duration of spinal anesthesia. For example, the optimal concentration of epinephrine for prolonging spinal anesthesia with either lidocaine or tetracaine has not been studied in a controlled fashion. Such studies could be conducted under standardized conditions utilizing the dog with a chronically implanted catheter for spinal anesthesia, as described in this report.

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