Effects of Concentration and Volume of 2-Chloroprocaine on Epidural Anesthesia in Volunteers

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Background: Effect of local anesthetic concentration and volume on the spread and density of epidural anesthesia is unclear. This study was performed to delineate effects of a threefold difference in concentration and volume of 2-chloroprocaine on epidural anesthesia.

Methods: Twelve healthy volunteers underwent lumbar epidural anesthesia with 300 mg of 2-chloroprocaine as a 3% (10 ml) and a 1% (30 ml) solution in a randomized, double-blind, balanced, crossover fashion. Sensory block was assessed with pinprick, touch (calibrated plastic filament), cold, and electrical stimulation. Motor block was assessed at the quadriceps and gastrocnemius muscles with isometric force dynamometry. Differences between solutions were assessed with repeated measures analysis of variance followed by post hoc testing.

Results: The number of dermatomes blocked to pinprick, touch, and cold was significantly greater with the 1% concentration (2 dermatomes greater than the 3% concentration on average, P < 0.05). Similar intensity of sensory block to electrical stimulation developed at the hip and knee and was unaffected by concentration of 2-chloroprocaine. Similar intensity of motor block developed at the quadriceps with both concentrations.

Conclusions: Intensity of sensory and motor block from epidural anesthesia with 2-chloroprocaine appears to depend primarily on total milligram dose. (Key words: Anesthetic techniques; epidural. Anesthesics local; 2-chloroprocaine. Differential nerve block. Tetanic stimulation.)

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There will be no reprints provided for this paper.

EFFECTS of altering concentration and volume of local anesthetic solution on development of epidural anesthesia are unclear. Standard anesthesia textbooks typically state that increasing concentrations of local anesthetic are needed to provide denser sensory and especially motor block with minimal consideration of total milligram dose.1,2 However, animal studies suggest that total dose of local anesthetic is the primary determinant of intensity of epidural anesthesia.3 Results from human clinical studies have been inconsistent.4-6 Methodologies used in previous studies may have contributed to conflicting findings. For example, some studies did not use a consistent milligram dose of local anesthetic,5 whereas other studies used poorly quantitative measures of sensory (pinprick) and motor block (Bromage scale).7,8 Difficulties in detecting concentration-dependent differences may have been increased by interindividual variability in development of epidural anesthesia.7 Such interindividual variability is consistent with the recently documented interindividual variability in lumbar cerebrospinal fluid volume9 and thoracolumbar nerve root diameters.10 We have previously used a crossover protocol with quantitative measures of sensory and motor function to study spinal anesthesia.11 Such a design would minimize the previously mentioned limitations. This study was performed to delineate effects of a threefold difference in concentration and volume of 2-chloroprocaine on sensory and motor block during epidural anesthesia in a crossover fashion.

Methods

After institutional review board approval and informed consent were acquired, 12 healthy volunteers (6 male and 6 female) were enrolled in the study. Subjects were not per os for 6 hours. Lactated Ringer’s solution was administered as a bolus of 6 ml/kg over 15 min before initiation of epidural anesthesia, followed by 8 ml · kg⁻¹ · h⁻¹ for the first hour, and then mainte-
nance infusion at a rate of 2 ml·kg\(^{-1}\)·h\(^{-1}\). With the subject in the seated position, the epidural space was identified at the L2–L3 level via a midline approach with loss of resistance technique. An epidural catheter was then inserted approximately 3 cm into the epidural space. No sedatives were administered during placement of the epidural catheter or throughout the study period. The subject was then placed in the supine position for the duration of the study period. Each subject received two epidural anesthetics via the indwelling epidural catheter. Each injection contained 300 mg of 2-chloroprocaine given as a 1\% (30 ml) or 3\% (10 ml) solution in a randomized, double-blind, balanced, crossover manner. Epidural injections were performed over 5 min, and the investigator performing the injection had no further contact with the subject. To minimize potential movement of the epidural catheter, the two epidural anesthetics were performed during a single study period with the second anesthetic initiated 30 min after complete resolution of the first epidural anesthetic (return of sensation to pinprick in all dermatomes cephalad and caudal to the L2–L3 dermatome and return of motor function of the quadriceps and gastrocnemius muscles > 90\% of baseline values).

Dermatomal levels of sensory block to pinprick (18-gauge needle), cold (iced test tube), and touch (calibrated plastic filament, Stoelting Company, Wood Dale, IL) were measured every 5 min after injection of epidural solution until resolution of anesthesia. Subjects were given a reference sensation of pinprick and cold at the C5–C6 dermatome before each measurement. A dermatome was considered free of sensory block to pinprick and cold if sensation was reported to be the same as the reference sensation. A plastic filament was calibrated for each subject for each epidural anesthetic in the following fashion. Using the L2 dermatome as a reference, plastic filaments were applied in descending diameter until the subject could not detect the filament. The previous diameter filament was then applied, and a bracketing process was used such that the smallest detectable plastic filament was selected. A dermatome was considered free of sensory block if the selected plastic filament could be detected. Dermatomes were assessed bilaterally for sensory block in a systematic order moving from blocked to unblocked dermatomes and in the order of pinprick, followed by cold, followed by touch. Sensory block to pinprick, cold, and touch was recorded as number of dermatomes cephalad to L3 that were blocked to sensation (dermatomal level, L2 = 1 and C4 = 19).

Tolerance to transcutaneous electrical nerve stimulation (TENS) was assessed as previously described.\(^6\) TENS leads (Red Dot electrocardiogram pads, 3-M, Minneapolis, MN) were placed bilaterally at T12 (apex of iliac crest), L3 (8 cm cephalad to medial prominence of tibial plateau), and S1 (immediately cephalad to medial malleolus of the ankle). Tolerance to electrical stimulation was assessed before and 4 min after injection of epidural solution and measured every 10 min thereafter by testing with 5\,s of 50-Hz tetanus initially at 10 mA and then increasing in 10-mA increments (Model NS252, Fisher & Paykel, Auckland, New Zealand). Sixty mA of current was used as a cutoff because previous studies have determined this intensity of stimulation to be equivalent to surgical incision.\(^11,12\) Each TENS location was tested in a systematic order moving from distal to proximal sites.

Motor block was assessed at the quadriceps and gastrocnemius muscles with isometric force dynamometry as previously described.\(^10\) A commercially available isometric force dynamometer (Micro FET, Hoggan Health Industries, Draper, UT) was used to assess 5\,s isometric maximal force contraction of bilateral quadriceps and gastrocnemius muscles. Measurements were performed before and every 10 min after epidural injection until return to > 90\% of baseline strength. Return of > 90\% of baseline motor function is necessary for ability to ambulate.\(^13\) Measurements were performed in triplicate and then averaged bilaterally for each measurement period.

Statistical Analysis

Pilot data were initially obtained from four subjects. A power analysis based on these data indicated that 12 subjects were sufficient to detect a 20\% difference (alpha = 0.05; beta = 0.8) in sensory block to TENS at the knee and to motor block at the quadriceps with a crossover design.\(^11\) Repeated measures analysis of variance (ANOVA) followed by post hoc testing with Fisher's protected least significant difference was used to determine differences between the 1\% and 3\% solutions in number of dermatomes blocked to pinprick, cold, and touch over time. Repeated measures ANOVA followed by post hoc testing with Fisher's protected least significant difference was also used to determine differences between the 1\% and 3\% solutions in intensity of sensory block to TENS.
Fig. 1. A. Time course of sensory block to cold. Boxplot displays median and tenth, twenty-fifth, seventy-fifth, and ninetieth percentiles for values. * = Significant block over time (P < 0.001) with 1% solution differing from 3% solution (P < 0.05). B. Time course of sensory block to pinprick. Boxplot displays median and tenth, twenty-fifth, seventy-fifth, and ninetieth percentiles for values. * = Significant block over time (P < 0.001) with 1% solution differing from 3% solution (P < 0.05). C. Time course of sensory block to touch. Boxplot displays median and tenth, twenty-fifth, seventy-fifth, and ninetieth percentiles for values. * = Significant block over time (P < 0.001) with 1% solution differing from 3% solution (P < 0.05).

and in motor block over time. A P < 0.05 was considered significant.

**Results**

The average subject’s age was 31 ± 4 yr (mean ± SD); height was 155 ± 7 cm, and weight was 70 ± 15 kg. Number of dermatomes blocked to pinprick, cold, and touch was significantly greater with the 1% solution (fig. 1A–C). Sensory block to TENS was similar with either the 1% or 3% solution at the T12 and L2 sites (fig. 2A–C). No significant block to TENS developed at the S1 site in either group. Motor block at the quadriceps was similar with either the 1% or 3% solution (fig. 3A–B). No significant motor block at the gastrocnemius was detected with either the 1% or 3% solution.

**Discussion**

Our data suggest that a low concentration–high volume solution of local anesthetic is as effective as a high concentration–low volume solution for block of electrical stimulation (TENS) and motor function. There are clinical implications for these findings. Previous studies
have determined that TENS is a more intense stimulus than pinprick\textsuperscript{15} and can be equivalent to surgical incision.\textsuperscript{11,12} Our data suggest that epidural anesthesia intended to block surgical stimuli and motor function, such as for operative anesthesia, would primarily depend on total drug mass of local anesthetic. This finding may be contrary to common assumptions, but it is consistent with previous studies examining mechanisms of action of epidural anesthesia.

Previous studies indicate that local anesthetics administered in the epidural space readily cross the dura\textsuperscript{16} and exert their primary effects on spinal roots and spinal cord tracts.\textsuperscript{3,17} Consistent with this concept is the previous finding that concentrations of local anesthetic in the cerebrospinal fluid during epidural anesthesia are similar to concentrations found during spinal anesthesia.\textsuperscript{18} We speculate that dilution and distribution of epidurally administered local anesthetic in the cerebrospinal fluid led to similar intensity of sensory and motor block from the 1% and 3% solutions. Previous studies of spinal anesthesia support this speculation, as 20-fold variations in concentration and volume of local anesthetic solutions for spinal anesthesia have little effect on development of sensory and motor block.\textsuperscript{19} Thus, the
would be exposed to the higher volume of the 1% solution. Thus, greater cephalad spread of the low concentration–high volume 1% solution may explain the greater extent of sensory block to pinprick, cold, and touch.

Neither solution of 2-chloroprocaine was effective at blocking sensory and motor function in the sacral dermatomes. Clinical difficulties in blocking sacral dermatomes with epidural anesthesia have been previously reported. The sacral nerve roots have the largest diameter of spinal nerve roots, and our solutions probably lacked sufficient drug mass to adequately block these roots.

There are limitations to the clinical implications from our data. 2-Chloroprocaine has different physicochemical properties (higher pKa and lower lipid solubility) than other commonly used local anesthetics. These properties may affect mechanism and development of epidural anesthesia when compared with other local anesthetics. We used a single dose of 2-chloroprocaine that did not result in complete sensory block to TENS or complete motor block in some subjects. Use of a different dosage could produce different results. We used a bolus injection of 2-chloroprocaine in a lumbar epidural catheter. Different effects may occur with an infusion of local anesthetic or with a thoracic epidural catheter.

In summary, concentration and volume of 2-chloroprocaine solution did not affect intensity of sensory block of electrical stimulation or intensity of motor block. These data suggest that epidural anesthesia intended to block surgical stimuli and motor function, such as for operative anesthesia, would primarily depend on total drug mass of local anesthetic.

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