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Hyperbaric Dye Solution Distribution Characteristics after Pencil-point Needle Injection in a Spinal Cord Model

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Background: **The flow-rate limiting and directional characteristics of caudally directed microcatheters, which lead to intrathecal maldistribution of hyperbaric 5% lidocaine, are believed to have contributed to at least 11 cases of cauda equina syndrome. The authors investigated the distribution characteristics of hyperbaric dye solutions *via* caudally directed side-port needles at various rates of injection in a spinal cord model to determine the potential for maldistribution.**

Methods: **Using a digital video image processing technique, we injected a hyperbaric solution of phthalocyanine blue dye through caudally directed side-port needles into a supinely oriented transparent spinal canal model filled with simulated cerebrospinal fluid. Injections *via* commonly used spinal needles (24-gauge and 25-gauge Sprotte, and 25-gauge and 27-gauge Whitacre) were recorded using five injection rates (2, 4, 6, 8, and 16 ml/min).**

Results: **For all needles tested, injection rate had a significant effect on the peak dye concentration ($P < 0.0001$). Injection rates ≥ 6 ml/min (2 ml/20 s) resulted in peak dye concentrations of less than 168 mg/l (extrapolated concentration of 1% lidocaine). Injection *via* the 24-gauge Sprotte needle, which has a larger orifice area and internal diameter, resulted in significantly lower peak dye concentrations than *via* the smaller Whitacre needles tested ($P < 0.05$).**

Conclusions: **Sacral maldistribution could be minimized by using injection rates ≥ 6 ml/min (2 ml/20 s), for all of the side-port spinal needles used in this model study. When very slow injection rates (2 ml/min) are used, peak dye concentrations varied inversely and significantly with needle internal diameter and orifice area. (Key words: Anesthetic techniques, spinal: pencil point needles. Anesthetics, local: lidocaine. Complications, neurological: maldistribution.)**

MALDISTRIBUTION of hyperbaric local anesthetics is thought to be associated with neurological injury, predominately in conjunction with continuous spinal anesthesia.[1-4] Five percent lidocaine in 7.5% dextrose, a drug previously considered to have little potential for neurotoxicity,[5-8] is associated with most of these complications. Reports of back pain, tingling, perineal hypesthesia, or all three occurring transiently after a single dose of hyperbaric spinal lidocaine[9-12] have implicated it as a causal agent in the syndrome "transient radicular irritation."[13] Hampl *et al.*[10] defined transient radicular irritation as pain, dysesthesia, or both after recovery from a spinal anesthetic, that resolves within 72 h. One common feature in two of these reports was the use of pencil-point spinal needles.[9,12]

We reported two cases of transient and mild neurological deficits after subarachnoid injections of hyperbaric 5% lidocaine using Whitacre needles.[12] These cases raised questions about what role the side-port plays in sacral maldistribution of intrathecal local anesthetics. After our initial work we concluded that sacral bevel orientation of Whitacre needles contributed to maldistribution at slow rates of injection (2 ml/min).[12]

Because a rate of 2 ml/min is far slower than "normal" injection rates previously determined,[14] the purpose of this study was to closely examine the quantitative relation between injection rate and peak dye concentration across a clinically relevant range of rates for several commonly used pencil-point (side-port) spinal needles when directed caudally. A further goal was to determine the minimum injection rate required to produce an

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equivalent peak dye concentration of 1% of less lidocaine, with the side port directed caudally. One percent lidocaine was chosen as our threshold based on an *in vitro* functional study of toxicity with spinal local anesthetic.[15] Finally, we analyzed the peak concentrations resulting from the different sizes of Sprotte and Whitacre needle types at various injection rates.

Materials and Methods

In Vitro *Model of the Subarachnoid Space*

Details of the methodology have been described previously.[12,16] Briefly, a model of the subarachnoid space was constructed from clear acrylic tubing (inner diameter, 1.8 cm; outside diameter, 2.5 cm; Thermoplastic Processes, Newark, NJ) based on magnetic resonance imaging measurements of adult male spines.[14] The model was 66 cm long; the distal 5 cm was machined from acrylic plastic to approximate the human sacral taper. The cauda equina was simulated with ten pairs of 2-mm outside diameter, 20-cm-long polyethylene tubes anchored at T12 and freely floating in the model subarachnoid space. The model was filled with lactated Ringer's solution (measured density of 1.005 g/ml at 22°C, comparable to human cerebrospinal fluid [CSF]). All trials were performed with the model at room temperature (22°C) with the spinal model in the supine position, as performed in previous *in vitro* modeling studies.[12,14,16]

Dye Injections

The injected solution contained 7.5% (weight/volume) dextrose and 0.84% (weight/volume) phthalocyanine blue dye (Aldridge Chemical, Milwaukee, WI), with a density of 1.042 g/ml, measured using a DMA 35 digital densitometer (Anton Paar, Graz, Austria). This density was chosen for our model to simulate the calculated maximum *in vivo* density difference between CSF and 5% hyperbaric lidocaine, approximately 4%.[16] (Commercially available 5% hyperbaric lidocaine has a maximum specific gravity of 1.037 at 20°C,[17] calculated density = 1.0348 g/ml at 22°C, specific gravity = density of lidocaine at 22°C ÷ density of water at 22°C.[18]) Injections were performed using a programmable syringe pump (model 2304; Harvard Apparatus, Boston, MA). After each trial, the model was drained, refilled with fresh Ringer's solution, and repositioned for the next injection.

Video Recording and Analysis

To view the injection process, the model was backlit with a fluorescent light box. Video recording began 1 min before injection and continued for 4–6 min after its completion. Video images of the model were recorded and digitally analyzed. Preinjection images were subtracted from the postinjection images (captured after the apparent cessation of dye spread, or approximately 4–5 min after injection) to determine distribution of the dye. Dye concentration was calibrated by comparing the pixel intensity levels in the model with those in calibration samples of standard dye dilutions. Peak dye concentrations in the sacral tip were calculated directly from the subtracted images and extrapolated to lidocaine concentrations using other data.[14,16,19]

Experimental Protocol

Four commonly used spinal needles (24-gauge and 25-gauge; 9-cm Sprotte ([Pajunk Medizintechnologie GmbH, Geisingen, Germany], and 25-gauge and 27-gauge, 9-cm Whitacre [Becton-Dickinson, Franklin Lakes, NJ]) were used for triplicate injections at five rates (2, 4, 6, 8, and 16 ml/min). Measurements of orifice size and internal diameter were made for each needle using a light microscope (model OPMI 1; Carl Zeiss, Thornwood, NY). Digitized images were used to measure exit angles for each needle with a protractor and corrected for diffraction effects. An injectate volume of 2 ml was used. The spinal needles were inserted perpendicular to the model's long axis, simulating midline placement. All needles were inserted into the model with side ports directed sacrally. This represented the worst-case scenario for maldistribution.[12] Of the 60 injections performed, 57 injections (29 Whitacre, 28 Sprotte) were analyzed. Recordings from three injections were technically unusable.

Data Analysis

Analysis of Variance. The 57 sacrally directed trials were evaluated by analysis of variance using peak concentration as the dependent variable, and the needle type and injection rate as independent variables. Multiple pairwise comparisons were performed using the Student-Newman-Keuls method, to identify differences.

Regression Analysis. Linear regression was used to evaluate the effects of needle orifice area and diameter on the peak concentration. However, the effect of injection rate on peak concentration for each needle was highly nonlinear. This behavior was analyzed by fitting an exponential model to the peak concentration *versus*

injection rate data from each needle. The following two-parameter exponential model was used:

$$C_{pd} = a/(1 - \exp(bR_i)) \quad (1)$$

where C_{pd} = peak dye concentration for one of the four needles, R_i = injection rate, and a and b are the two fitted parameters. Parameter a represents the amplitude of the peak dye concentration, whereas parameter b sets the curvature of the nonlinear relation. Equation 1 was fit to the data using a Levenberg-Marquardt nonlinear curve-fitting routine. The coefficient of determination, R^2, a measure of the closeness of fit, and probability values of the two parameters were analyzed to gain a better understanding of the relation between injection rate and peak concentration.

Probability values less than 0.05 were considered significant. The analysis of variance, paired comparisons, and nonlinear regression tests were performed with SigmaStat for Windows, version 1.0 (Jandel Scientific Software, San Rafael, CA) on a personal computer.

Equivalent lidocaine concentration was determined by comparing the peak pixel intensity in the subtracted image with the calibration samples in the image. This value is directly related to a corresponding concentration (previously validated) and is calculated as percentage of lidocaine = $(C_{pd}/840) \times 5\%$, where C_{pd} = measured peak dye concentration (mg/l) in the sacral tip.[12]

Results

Direct Observations

Dye injected *via* all needles at rates of 2 and 4 ml/min exited the orifices very smoothly, forming an expanding fan-shaped stream that flowed caudally and upward toward the ventral surface of the model. Minimal change in the flow pattern occurred when the upper surface of the model deflected the dye, with most of the injectate continuing to flow caudally. At 6 ml/min, a less-distinct, fan-shaped stream hit the ventral model wall, deflecting dye downward in both sacral and cephalad directions, with enhanced mixing. At 8 and 16 ml/min, the exiting dye stream formed a cloud immediately on hitting the top of the model, showing highly vortical flow and thorough mixing of the dye with the artificial CSF.

Qualitative Dye Distribution Histogram

The effect of injection rate on the dye distribution along the model is shown in histogram form in figure 1 for a sample set of injections *via* a 25-gauge Whitacre needle. The faster injection rate results in a reduction in dye concentration in the sacral tip by a factor of 2. The other needles showed similar results (reduced dye concentration) at faster injection rates.

Needle Size and Jet Angle Measurements

Table 1 summarizes the internal diameters, orifice size measurements, and calculated orifice areas for each needle. Differences in measured jet angles were attributed to the design of the exit orifice and to the way the jet impinges on the orifice surface before exiting the needle. The flat annulus (perpendicular to the needle axis) of the Whitacre needle orifice resulted in a more sacrally directed jet (55 degrees from the horizontal), whereas the slightly angled annulus of the Sprotte needle had a more vertically oriented jet (65 degrees from the horizontal).

Effects of Injection Rate

For all needles, the peak dye concentration was found by analysis of variance to depend significantly on injection rate ($P < 0.0001$). The lowest injection rates had the highest peak concentrations. When multiple pairwise comparisons were done, in each case only the 6 *versus* 8 ml/min, the 6 *versus* 16 ml/min, and the 8 *versus* 16 ml/min injection rates were not different from each other (see table 2). All other pairs of injection rates were significantly different ($P < 0.05$). No further decrease in peak concentration was found when the injection rate was increased from 6 ml/min.

For each of the four needles, equation 1 fit the data well (by nonlinear regression (fig. 2), with R^2 values ≥ 0.77, or R (correlation coefficient) ≥ 0.87, and $P < 0.0001$ in all cases. This supports the conclusion that peak dye concentration depends significantly on injection rate. Parameter a was significant at $P < 0.0001$. Parameter b was also significant at $P < 0.0001$, showing that the highly curved shape of the injection rate dependence can be adequately described by an exponential function.

Effects of Needle Type

Needle type also had a significant effect on the peak concentration (by analysis of variance, $P = 0.0006$). However, pairwise multiple comparisons showed that only two pairs of needle type were significantly different from each other at the $P < 0.05$ level of significance (table 2): 24-gauge Sprotte *versus* 27-gauge Whitacre needles, and 24-gauge Sprotte *versus* 25-gauge Whita-

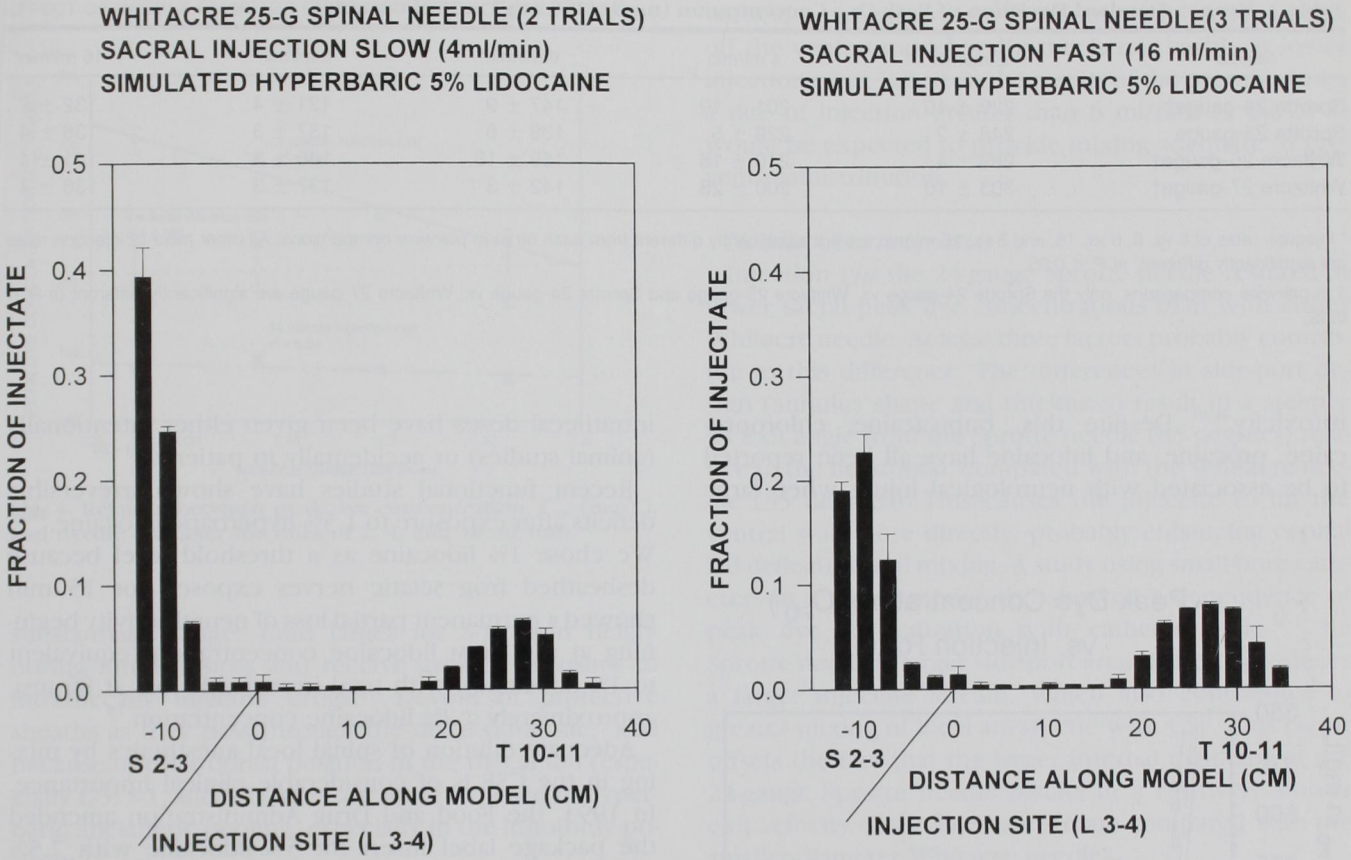

Fig. 1. Dye distribution histograms with a 25-gauge Whitacre needle directed caudally at slow (left plot, two trials) and fast (right plot, three trials) injection rates. The abscissa is the distance along the model measured in centimeters. The injection site is zero (equivalent to the L3/L4 interspace), negative direction is caudal, and positive direction is cephalad. The ordinate is the mean fraction of the injectate.

cre needles, and only at the slowest injection rate of 2 ml/min. All other pairs were not significantly different. Thus significant differences were demonstrated only when needles had a difference in orifice area equal to or greater than 7 mm^2, or a difference in needle diameter equal to or greater than 0.05 mm.

In addition, there was a significant interaction between injection rate and needle type (analysis of variance, $P = 0.0007$). Linear regression analysis showed that peak dye concentration varied linearly with orifice area and needle diameter only at the slowest injection rate, 2 ml/min (figs. 3 and 4). At higher injection rates, the very low correlation coefficients (R^2) indicated that a linear relation was not probable. The 24-gauge Sprotte (largest orifice area/inner diameter tested) had significantly lower peak dye concentrations than did the Whitacre needles, particularly at the lower injection rates (table 2). For all needles, a minimum injection rate of 6 ml/min or more was required to ensure that peak equivalent lidocaine concentrations were less than 1%.

Table 1. Measured Needle Dimensions

Needle	Gauge	Orifice (l.a.)	Orifice (s.a.)	Orifice Area (mm^2)	I.D. (mm)
Sprotte	24-g	7.25 mm	1.25 mm	9.1	0.305
Sprotte	25-g	3.75 mm	0.75 mm	2.8	0.279
Whitacre	25-g	2.75 mm	0.75 mm	2.1	0.254
Whitacre	27-g	2.0 mm	0.5 mm	1.0	0.229

l.a. = long axis; s.a. short axis.

Discussion

Subarachnoid injection of local anesthetics has long been regarded as safe, with minimal clinical risk of neu-

Table 2. Mean ± Standard Deviation of Peak Dye Concentration (mg/l) (168 mg/l ~ 1% lidocaine)

Needle	2 ml/min	4 ml/min	6 ml/min*	8 ml/min*	16 ml/min*
Sprotte 24-gauge†	229 ± 10	201 ± 19	147 ± 9	131 ± 4	132 ± 7
Sprotte 25-gauge	248 ± 2	228 ± 5	138 ± 8	137 ± 3	136 ± 4
Whitacre 25-gauge†	289 ± 4	210 ± 16	159 ± 18	145 ± 3	141 ± 4
Whitacre 27-gauge†	303 ± 10	200 ± 28	142 ± 3	137 ± 3	136 ± 4

* Injection rates of 6 *vs.* 8, 6 *vs.* 16, and 8 *vs.* 16 ml/min are not significantly different from each other in pairwise comparisons. All other pairs of injection rates are significantly different, at $P < 0.05$.

† In pairwise comparisons, only the Sprotte 24-gauge *vs.* Whitacre 25-gauge and Sprotte 24-gauge *vs.* Whitacre 27-gauge are significantly different at $P < 0.05$.

rotoxicity.[8,20] Despite this, bupivacaine, chloroprocaine, procaine, and lidocaine have all been reported to be associated with neurological injury when large intrathecal doses have been given either intentionally (animal studies) or accidentally in patients.[21-26]

Recent functional studies have shown irreversible deficits after exposure to 1.5% hyperbaric lidocaine.[27,28] We chose 1% lidocaine as a threshold level because desheathed frog sciatic nerves exposed for 15 min showed a permanent partial loss of neural activity beginning at a 40 mM lidocaine concentration (equivalent to 1% lidocaine), with total irreversible loss at 80 mM, approximately a 2% lidocaine concentration.[15]

Adequate dilution of spinal local anesthetics by mixing in the CSF is of considerable clinical importance. In 1994, the Food and Drug Administration amended the package label insert for 5% lidocaine with 7.5% dextrose to cite references indicating that a twofold dilution with CSF may reduce the chances of causing neural toxicity. Local anesthetic toxicity is most likely in the cauda equina, where the sacral root sleeves are

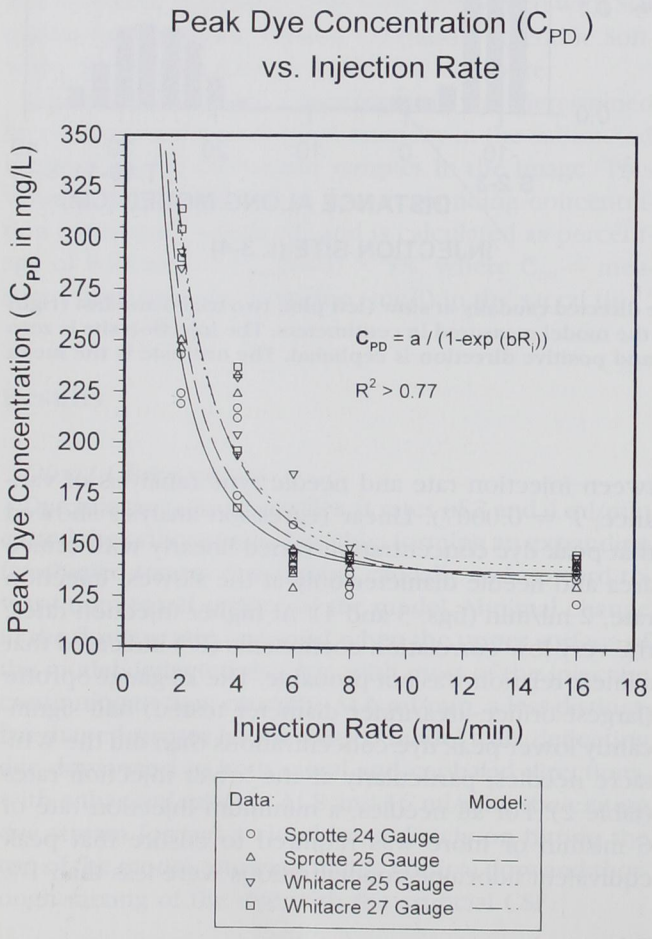

Fig. 2. Relation between peak dye concentration, C_{pd} (mg/l), and injection rate (ml/min) for caudally directed injections through 24-gauge Sprotte (○), 25-gauge Sprotte (△), 25-gauge Whitacre (▽), and 27-gauge Whitacre (□).

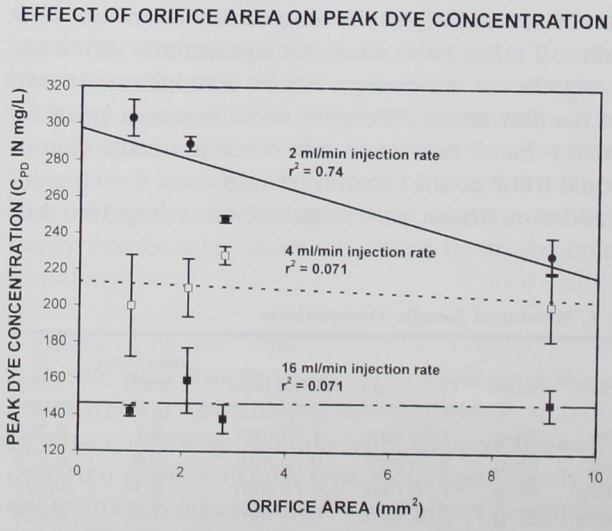

Fig. 3. Relation between peak dye concentration, C_{pd} (mg/l), and orifice area for rates of 2, 4, and 16 ml/min.

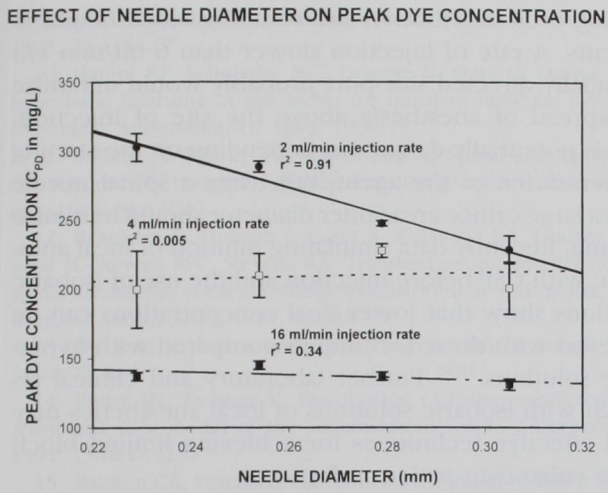

Fig. 4. Relation between peak dye concentration, C_{pd} (mg/L), and needle diameter for rates of 2, 4, and 16 ml/min.

substantially longer (and larger for S-1) than neighboring lumbar roots and receive greater exposure to intrathecally injected drugs.[19] Devoid of protective sheaths as they pass through the distal dural sac,[1] and because of their dorsal position in the thecal sac (especially L-5, S-1, and S-2), they are more exposed to hyperbaric anesthetic pooling, especially in the lithotomy position.[9]

Injection Rate

Our previous investigation established that maldistribution of dye occurs after injection with sacrally directed, pencil-point needles at 2 ml/min.[12] The results of the present study show that, for both Whitacre and Sprotte needles, injection rate had a significant effect on the peak dye concentration and could be modeled empirically by an exponential function. Injection rates of 4 ml/min or less resulted in peak dye concentrations corresponding to a lidocaine concentration greater than 1%, whereas rates of 6 ml/min and greater produced levels less than 1%. The lower concentrations seen at the faster injection rates are probably due in part to the presence of turbulence at these higher flow rates. Direct observation of the injections clearly supports this conclusion, even though the calculated Reynolds numbers for the jets are not technically turbulent. Transition from a laminar to a more turbulent-appearing flow occurs at 6 ml/min, whereas injections at 2 and 4 ml/min display minimal tumbling and mixing of the dye. Impact with the ventral wall of the model has minimal effect on this flow. At rates greater than 6 ml/min, far more vortical mixing is evident (particularly in jet separation off the ventral model wall); this is not visible at lower injection rates. Based on the results of the present study, a rate of injection greater than 6 ml/min (2 ml/20 s) would be expected to provide mixing adequate to prevent maldistribution.

Needle Characteristics

Injection *via* the 24-gauge Sprotte needle resulted in lower sacral peak dye concentrations than with either Whitacre needle. At least three factors probably contribute to this difference. The differences in side-port design (annulus shape and thickness) result in a steeper jet exit angle from the Sprotte needle (65 degrees) relative to the horizontal, compared with the Whitacre needle (55 degrees). This causes the injectate to hit the ventral wall more directly, probably enhancing cephalad deflection and mixing. A study using small-bore catheters in a spinal model also showed a dependence of peak dye concentration with catheter angle.[16] The Sprotte needles' larger side-port area (table 1) produces a larger injectate stream, which also contributes to greater mixing of local anesthetic with CSF. This factor offsets the fact that the larger internal diameter of the 24-gauge Sprotte needle results in a relatively slower exit velocity of the injectate stream compared with the smaller-diameter Whitacre needles.

Data analysis at each injection rate greater than 2 ml/min showed no correlation of dye concentration with orifice area or inner diameter. We suspect this results from the interaction between the contributing effects of these two characteristics. As the rate of injection increases, the effect of stream velocity becomes more significant compared with stream size, resulting in equivalent mixing among all needles tested, and no significant differences in peak concentration. It is difficult to precisely differentiate between the effect on the peak dye concentration by the orifice area *versus* the needle diameter. However, based on fluid mechanics, for a given flow rate, the orifice characteristics (area, shape, and thickness of annulus) would seem to be the most important parameters, because they determine the width and velocity of the anesthetic jet.

Although we cannot say which factor is most important, small differences in needle design and dimensions appear to have little effect on final concentration at normal clinical rates of injection. Of the six paired comparisons, only the combination of large side-port area differences coupled with 0.051 and 0.076 mm internal diameter differences seen in 24-gauge Sprotte

versus the 25-gauge and 27-gauge Whitacre needles, respectively, were significant. The 24-gauge Sprotte needle's orifice area is 4.3 and 9.1 times greater than the 25-gauge and 27-gauge Whitacre needle areas, respectively. In contrast, for 25-gauge Sprotte *versus* 27-gauge Whitacre needles, peak concentrations were not significantly different despite the fact that the 25-gauge Sprotte needle has an internal diameter 0.05 mm larger and an orifice area 2.8 times greater than the 27-gauge Whitacre needle.

Study Limitations

Our model, like any other, had several potential limitations. First, a syringe pump was used to achieve reproducible injections and to define the injection rate; however, manual injections are less uniform, which probably results in improved mixing and lower peak concentrations. Second, dye density (directly related to baricity) adjustments were necessary for our room-temperature (22°C) model and simulated solutions. The density difference of 4% between the simulated hyperbaric lidocaine, 1.042 g/ml, and the simulated CSF, 1.005 g/ml, simulates the worst-case difference between the lowest normal density for CSF (0.9944 g/ml at 37°C)[18] and the highest reported density of commercially available 5% lidocaine (1.0348 g/ml calculated at 22°C). As demonstrated by Sosis *et al.*,[29] the distribution of hyperbaric spinal anesthetics is directly related to the solution's baricity (greater baricity leads to higher final concentration). Third, our model orientation was always equivalent to the horizontal supine position, unlike clinical practice. When patients are moved to this position from a sitting or lateral decubitus position after subarachnoid injection, there is some opportunity for further mixing of CSF and local anesthetic. Recently Ross *et al.*[30] reported lower sacral concentrations with injections done in a vertically oriented spinal model, suggesting increased mixing of CSF and hyperbaric lidocaine over that in a horizontal supine model. The significance of this is unclear given the demonstration in a supine model that as long as 4 min in the vertical position after injection has little effect on final hyperbaric bupivacaine distribution.[31] However, we believe none of these limitations alter the conclusions of our study.

Conclusions

The effect of injection rate on the distribution of hyperbaric subarachnoid agents has implications for controlling drug distribution and resulting block height in patients. A rate of injection slower than 6 ml/min *via* a caudally directed side-port probably would minimize the spread of anesthesia above the site of injection. This is potentially dangerous depending on the starting concentration of the agent, but using a spinal needle with a large orifice area/inner diameter should minimize pooling. Recently data simulating dilution of local anesthetic with CSF before injection and the use of isobaric solutions show that lower final concentrations can be achieved with these techniques compared with hyperbaric solutions.[32,33] Further laboratory and clinical research with isobaric solutions of local anesthetics may yield effective techniques for achieving limited block while enhancing patient safety.

At clinically relevant rates of injection, needle characteristics minimally affect solution distribution. However, results from our spinal model studies suggest that injection rates greater than 6 ml/min (2 ml/20 s) may be advantageous when injecting intrathecal hyperbaric local anesthetic solutions to avoid local anesthetic maldistribution in the event a side-port needle is directed caudally. At very slow rates of injection, a large side-port needle (≥24 gauge) with large orifice area will minimize maldistribution.

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