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Pressures of Injection in a Cadaver Model of Peripheral Nerve Blockade

Scott Ross[1], Kelly Edwards[2], Kathryn McFadden[3], Paul E Bigeleisein[4] and Steven L Orebaugh[1]*

[1]Department of Anesthesiology, University of Pittsburgh School of Medicine, USA
[2]Biomedical Engineering Student, University of Pittsburgh, USA
[3]Department of Pathology, University of Pittsburgh School of Medicine, USA
[4]Department of Anesthesiology, University of Maryland School of Medicine, USA

Abstract

Objective: Pressure monitoring during injection has been suggested to help detect intrafascicle needle placement. We performed injections, guided by ultrasound, into the cervical nerve roots, peripheral nerves of the extremities, and perineural soft tissues of an unpreserved cadaver. We hypothesized that needle tip placement into these three sites would yield significantly different injection pressures, and that histologic analysis would allow comparison of intrafascicle vs. extrafascicle pressures of injection.

Methods: Injections of 5 ml ropivacaine 0.5% were conducted at cervical roots (n=4), peripheral nerves of the extremities (n=10) and perineural soft tissues (n=9), at constant rate while monitoring pressure. Dye was instilled at the termination of the injection for histologic determination of needle position. Peak pressures and time to peak pressures, were compared for these three sets of injections. After microscopic examination, all intrafascicular and extrafascicular pressures were grouped together and compared.

Results: Mean peak injection pressures for the three groups were found to be significantly different, (p=0.0002). At histological examination, four of 10 peripheral nerve injections resulted in deposition of dye within fascicles, while six of 10 did not. Mean peak intrafascicle injection pressures were significantly higher than those for injections outside of fascicles (p<0.0001). Time to peak injection pressure was not different for these two groups.

Discussion: Comparison of intrafascicle versus extrafascicle injections showed a clear delineation of peak pressures into two ranges. This adds to prior evidence, from both human cadavers and live animals, showing that intrafascicle injections generate high pressures, whether conducted in nerve roots or peripherally.

Keywords: Intraneural; Injection; Ultrasound; Pressures; Nerve; Fascicles; Nerve block

Introduction

Inadvertent injections of local anesthetic into nerve may occur during peripheral nerve blocks, even with ultrasound guidance [1,2], and if the needle is placed within a nerve fascicle, some experimental data suggest that high injection pressure and axonal injury may result [3,4]. However, the pressure resulting from a subepineural injection may be high or low, depending upon the actual location of the needle tip: with injection between the fascicles in animal models, pressures are not elevated, and nerve injury appears not to result [3,5]. Clinical data in humans also suggests that subepineurial injection does not result in a high incidence of nerve injury [6-8].

While it has been suggested to use pressure monitoring during injection to help detect intrafascicle needle placement in the clinical realm [9], the relationship between pressures of injection for intrafascicle injections and subepineurial (but not intrafascicle) injections in humans has not been well studied. In this investigation we performed deliberate nerve injections, guided by ultrasound, into the fascicular tissue of the cervical nerve roots of a cadaver specimen, and into peripheral nerves of the extremities, as well as into perineural soft tissues, to evaluate the relationship between pressures generated in these locations. We hypothesized that needle tip placement into these three sites would yield significantly different injection pressures, with the highest at the cervical root level and lowest at the peri-neural site, with intermediate pressures at the intraneural sites, reflecting a likely mix of both intra-fascicle and non-fascicle injections within the substance of the nerve. Secondarily, we determined needle tip position for the peripheral nerve injections, based on histologic analysis of dye deposition, for categorization into intra-fascicle versus extra-fascicle injection, and re-analyzed pressures generated at these sites.

Methods

This study was evaluated and approved by the Committee on Research Involving the Dead at the University of Pittsburgh School of Medicine. One non-preserved human cadaver was utilized for a total of 22 planned injections. Four injections were performed at the C5 and C6 cervical nerve roots, separately on each side (intended to be intrafascicular). Ten were placed peripherally, with deliberate placement of the needle tip into the musculocutaneous and ulnar nerves at the axilla, the radial nerve in the supracondylar region and into the median nerve in the mid-forearm (bilaterally). In addition, one injection was conducted at each femoral nerve, at the level of the femoral crease. Eight perineural injections were performed by placing the needle tip into the soft tissue adjacent to the median nerve in the proximal and distal forearm bilaterally.

A SonoSite S-Nerve Unit (Sono-Site, Bothell, WA), with a 6-13 MHz transducer was utilized to locate and visualize nerve structures identified at the above locations. A short axis view was obtained of the

***Corresponding author:** Steven L Orebaugh, Department of Anesthesiology, University of Pittsburgh School of Medicine, UPMC-Southside/Mercy Anesthesia; 2000 Mary Street Pittsburgh PA 15203, USA, Tel: 412-488-5799; Fax: 412-488-5796; E-mail: orebaughsl@anes.upmc.edu

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brachial plexus and peripheral nerves at the interscalene, axillary, distal arm and mid-forearm levels, as well as at the femoral crease.

A 50 mm, 22 gauge blunt-tipped stimulating block needle (Stimuplex, B-Braun, Bethlehem, PA) was guided with real-time imaging toward the identified nerve using an in-plane technique. With the needle held firmly in place during injection, five ml of 0.5% Ropivacaine was injected, from a 20 mL syringe, at a rate of 5 ml/15 secs using an automated pump (Fusion 2000, Chemyx, Inc., Stafford, TX). We chose this five ml volume as it is a clinically relevant dose and volume (particularly for single, small peripheral nerves in the upper extremity or for individual cervical roots), and is consistent with prior studies evaluating pressures of intra-neural injection [3,5,10]. An in-line pressure monitor (PV 350, Fluke Corporation, Everett, WA) was utilized to measure and record injection pressures. The nerve was visualized throughout the injection process to confirm fixed placement of the needle tip and observe nerve expansion upon injection.

Immediately following injection of Ropivacaine, 0.1 mL of India ink was injected through the block needle to help identify the location of needle tip during injections. The specimen was then immediately dissected in the interscalene, axillary, upper and lower arm, and femoral regions. A 2 cm section of the target nerve was excised, with the area of most intense dye staining located in the mid portion of this segment. Resected nerve elements, comprising the C-5 and C-6 nerve roots, and the segments of the above listed peripheral nerves, were fixed in 10% buffered formalin. The specimens were then serially sectioned at 0.5 centimeter intervals and those sections that were seen to be grossly ink-stained were paraffin-embedded and sectioned by microtome at 4 microns. Routine hematoxylin and eosin-stained sections were examined by light microscopy in order to evaluate for evidence of dye deposition within the epineurium between fascicles (extrafascicle injection), or dye entry into the fascicles (intrafascicle).

The following outcome variables were recorded: peak injection pressure, pressure-time curves, and the presence of nerve expansion on ultrasound imaging during the injection. Peak pressures at the three different sites of injection (cervical nerve root, peripheral nerve, perineural) were compared using the analysis of variance, with post hoc test using pairwise differences with a Bonferroni correction. The level of significance was set at $p<0.05$. Statistical analysis was performed using GraphPad Prism [6]. Time-to-peak pressures were similarly compared. After histological confirmation of the needle tip position (into or outside of fascicles) during the peripheral nerve injections, the injections were re-classified as intrafascicle vs. extra-fascicle, and compared using a two-tailed t-test.

Results

When the three locations of injection (cervical nerve root, peripheral nerve, and perineural) were compared, mean peak injection pressures were found to be significantly different, as shown in Table 1 ($p=0.0002$). A statistically significant difference was evident when comparisons amongst the groups were performed for both cervical root vs. peripheral ($p=0.0028$) and cervical root vs. perineural ($p=0.0001$), but not when comparing peripheral nerve injection pressures to perineural. There was no significant difference between groups for time to peak injection pressure.

Nerve swelling was evident during cervical root injections, for all peripheral nerve injections as shown in Figure 1, except for the two femoral nerve injections, which remained essentially unchanged in size (however, both nerves were clearly stained internally with ink, confirming intraneural injection). One peripheral nerve injection in the arm resulted in the nerve immediately being pushed away from the needle, with no evidence of nerve swelling. The remaining volume of Ropivacaine solution was clearly deposited in the perineural tissue, so this injection was considered to be perineural, resulting in 9 total perineural injections.

	Peak Pressure of Injection (PSI)	Time to Peak Pressure (sec)
Cervical Root	60.2 (17.3)	12.1 (3.2)
Peripheral Nerve	32.6 (14)	8.1 (3.3)
Perineural	21.5 (8.6)*	9.5 (2.5)
*Peak pressures of injection for three groups significantly different, ANOVA ($p=0.0002$)		

Table 1: Mean Peak Injection Pressures and Time to Peak Pressures for Injections at Cervical Roots, Peripheral Nerve and Perineural Tissues.

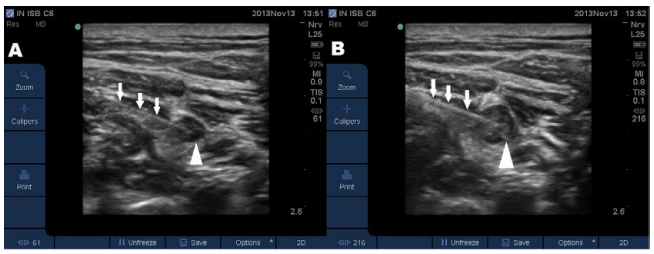

Figure 1: Intra-root placement of needle before (A) and after (B) injection of local anesthetic solution, showing swelling of nerve root. Small arrows delineate the needle; large arrowhead indicates the nerve root.

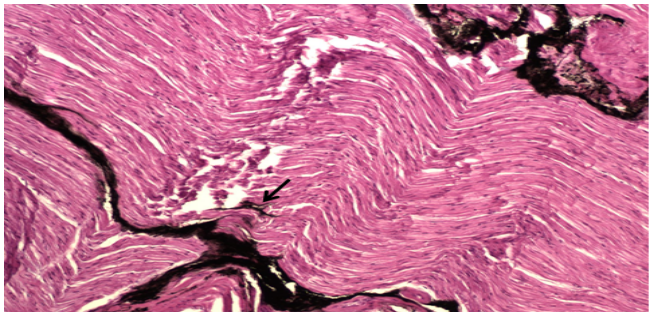

Figure 2: Histological section of nerve with intra-fascicle injection, showing particulate dye within the fascicle (arrow) as well as disruption of the fascicular elements.

Grossly, all of the intended intraneural injections resulted in obvious dye staining of the target nerve. Histologic analysis identified dye within the fascicles of all 4 cervical root injections (Figure 2) and revealed that four of 10 peripheral nerve injections resulted in deposition of dye within fascicles, while six of 10 did not enter fascicles (Figure 3). The peak injection pressures for all cervical root injections were combined with the four histologically confirmed intrafascicular injection at the peripheral nerves to create a group identified as intrafascicle (IF) injections. The remaining six peripheral injections, histologically confirmed to be extrafascicular, were combined with the perineural injections and grouped as extrafasicular (EF). The mean peak injection pressure for the IF group was found to be significantly higher than those of the EF group, as shown in Table 2, and Figures 4A and 4B. Mean time to peak injection pressure was not different between the two groups.

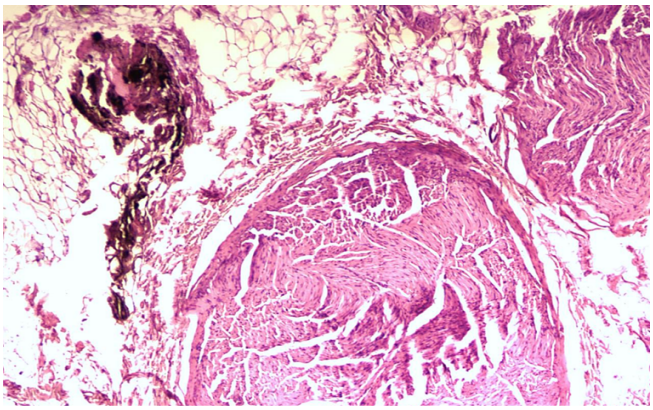

Figure 3: Histologic section of nerve with subepineurial injection, which resulted in extra-fascicular collection of particulate dye, but no dye within fascicles.

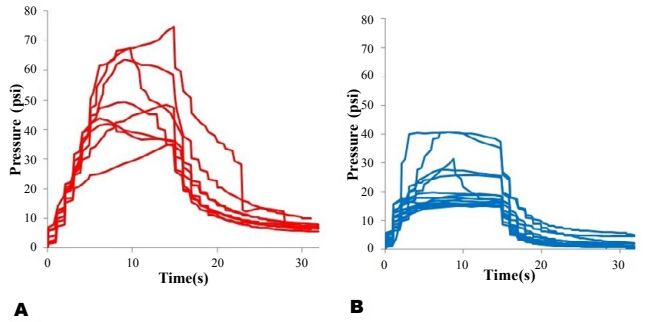

Figure 4: Pressure-time curves for (A) Intra-fascicle injections (including injections into roots and peripheral nerves) and (B) Extra-fascicle injections (including perineural injections and those into peripheral nerve which proved on histologic exam to be outside of fascicles.

	Peak Pressure of Injection (PSI)	Time to Peak Pressure (sec)
Intrafascicle Group (n=8)	52.9 (13.9)	10.6 (3.5)
Extrafascicle Group (n=15)	22.4 (8.8)	8.6 (2.9)
P value	<0.0001	NS

Table 2: Mean Peak Injection pressures and Time to Peak Pressure, intrafascicle versus extrafascicle Injections.

Discussion

In this non-preserved cadaver model of neural (and extra-neural) injection, we determined that mean pressures were highest with US-guided injection into the ample fascicular tissue that comprises the majority of the cervical nerve root; lowest for injections placed in a perineural location, and intermediate for injections placed within peripheral nerves. Although it was not clear during the experiment whether injections into peripheral nerves were placed within or between fascicles, subsequent microscopic examination of nerve samples allowed this determination. Intrafascicle injections resulted in pressures considerably higher than those of subepineurial injections between fascicles, which generated relatively low pressures similar to those of peri-neural injections. Thus, these peripheral nerve injections yielded, on average, pressures that were intermediate, prior to identifying whether the needle tip was placed within a fascicle or between fascicles. These intermediate mean pressures were not significantly different from those of perineural injections, until further categorized, with the use of histologic examination, into IF or EF injections. Subsequent comparison of these two groups of injections (IF versus EF) showed a clear delineation of peak pressures into two ranges, and this more precise categorization of data resulted in a statistical difference between the IF and the EF groups. This adds to prior evidence, from both human cadavers and live animals, showing that IF injections generate high pressures, whether conducted in nerve roots or peripherally [3-5,10].

When nerve injury occurs in the wake of peripheral nerve blockade, it may be difficult to ascertain the exact pathophysiologic cause of the injury. Indeed, many authors note that an insult to a nerve in the perioperative period is most likely multifactorial, with needle penetration into the nerve's fascicles contributing one of the possible adverse effects [11,12]. Use of US likely reduces the possibility of injection into the nerve, but imaging is not always optimal, and some investigators have found a substantial incidence of injection into nerves when viewing offline video images after the blocks were performed [1,2]. Several case reports also provide evidence of this occurrence during US guidance, with significant consequences for patients [13,14]. It is in these situations, when needle tip position may not be clear to the anesthesiologist, that pressure monitoring may be of most use-high pressures are likely to represent placement into a fascicle, whereas low pressures indicate an extra-fascicle position, either next to the nerve or even within it. Since nerve damage is likely when fascicles are disrupted, but not when local anesthetic is deposited between fascicles or outside of a nerve, it is the distinction between intra-fascicle and extra-fascicle that is most important to make. As such, it is likely that any reliable indicator of needle tip placement into a fascicle may offer protection against nerve injury.

Multiple monitoring techniques for PNB have been suggested, including nerve stimulation threshold [15], US imaging to detect nerve swelling [16], and measurement of electrical impedence [17]. Pressure monitoring is another possible modality to help determine needle tip placement, and is recommended by some authors [9], though clinical data is very limited, and animal studies have yielded variable results [3,5,18,19]. A recent clinical study of interscalene block with pressure monitoring suggests that high opening injection pressure may consistently detect contact of the needle tip with the nerve root, which may allow prevention of injection when the tip is inadvertently advanced into the nerve [20].

The results of this study help to substantiate the utility of pressure monitoring for situations in which the needle tip is not well-visualized. However, while mean pressures differed substantially, some overlap exists between pressures generated by injection into different tissues. While we chose to evaluate multiple injections, at a variety of sites, in a single specimen, such overlap might be more pronounced if multiple specimens were evaluated. Other limitations of the study include the use of dye injectate as a marker to differentiate needle tip placement within the nerve, since dye deposition and spread may be influenced by local factors and histologic preparations. Cadaveric tissue is a reasonable approximation of human nerves, but stripped of vitality, some membranes may not provide barriers to spread as effectively as in a living organism. Another consideration is that pressures of injection determined during actual fluid infusion do not accurately represent the static intra-nerve pressure, since fluid movement against the resistance of the system will elevate pressures, and different volumes and rates of injection may yield differing pressures. Nonetheless, pressure detection as injection is occurring represents a more practical clinical correlation

than determination of steady-state, post-injection pressures.

A final limitation is that there is a short period of time after injection is initiated before peak pressures occur, so that a small volume of injectate is likely to be instilled into the nerve before pressures considered to be dangerous are evident. Our peak pressures occurred at about 8-12 seconds after initiation of injection, consistent with prior studies which utilized a similar rate of injection [3,10], and probably reflecting initial swelling of the nerve structure, with eventual rupture, causing a decline in pressures thereafter. Thus, the anesthesiologist should be aware of rapidly rising pressures during the initial part of the injection. This suggests that pressure monitoring is open to a critique sometimes leveled against US imaging as an indicator of injection into the nerve: an effect on the nerve may inevitably occur before the operator can actually detect the perilous situation. Although both pressure monitoring and US imaging allow rapid withdrawal of the needle tip to abort this process, it is uncertain if a degree of damage may already have been done when the misplaced injection is recognized.

In conclusion, this cadaver model of nerve injection supports prior studies which show that IF injection produces significantly higher pressures than injections conducted outside the nerve, or between fascicles within a nerve. While it is not yet clear that pressure monitoring aids in prevention of nerve injury, further research, particularly in the clinical realm, may help to further define the role of this monitoring modality in contributing to patient safety during PNB.

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