Best Practice & Research Clinical Anaesthesiology 33 (2019) 47–56

Contents lists available at ScienceDirect

Best Practice & Research Clinical Anaesthesiology

journal homepage: www.elsevier.com/locate/bean

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Pressure monitoring: The evidence so far

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Keywords:
nerve block
peripheral nerve injury
anesthesia, conduction
injection pressure
patient monitoring

Nerve injury is a relatively rare but devastating complication of peripheral nerve blockade (PNB). Monitoring injection pressure during PNB is one method advocated to prevent injury by detecting needle tip placement in a noncompliant position (intraneural or abutting the epineurium). Animal studies show that gross neural damage and clinical injury are associated with injection pressures exceeding 15–20 psi. In contrast, pressures <15 psi are associated with an extraneural needle tip position and no histologic or clinical injury. Injection pressure monitoring has been shown to prevent injection against the brachial plexus roots or femoral nerve during peripheral nerve block. Multiple methods are available to monitor injection pressure, and most of them are inexpensive and easy to use. Large-scale registry database or pragmatic trials are indicated to show that injection pressure monitoring reduces injury in a patient setting.

Monitoring for injury during peripheral nerve blockade: an unmet need

Despite the safety of peripheral nerve blockade, postoperative neurologic injury resulting in long-term or permanent disability remains one of the most feared complications of regional anesthesia practice. Estimated incidence of neuropathy after peripheral nerve blockade is as high as 3%, and reported rate of long-term injury has remained in the range of 2–4 per 10,000 peripheral blocks for the past several decades [1,2]. Nerve injury after regional anesthesia may occur as a result of many factors

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https://doi.org/10.1016/j.bpa.2019.03.001
1521-6896/

including needle-related trauma and local anesthetic-induced direct neurotoxicity [3]. Violation of any of the connective tissue layers of the nerve by the needle increases the risk of axonal injury and functional deficits [3–5]. Injection within the fascicle is particularly hazardous, resulting in direct mechanical injury to nerve fibers and capillaries, edema formation, and local ischemia due to increased intrafascicular pressure [6–8]. As such, clinical guidelines from the American Society of Regional Anesthesia conclude that anesthesiologists should not pursue intentional needle–nerve contact or intraneural injection [2]. For the purposes of this review, "intraneural" refers to injection that is subepineurial (i.e., deep to the outermost covering of the nerve) and intraneural injections will be discussed as either intrafascicular or extrafascicular when applicable. Fig. 1 shows a peripheral nerve and the three layers of interest to the clinician.

There is a lack of consensus on methods to avoid intraneural needle placement and injection. Despite advances afforded by ultrasound-guided nerve blockade, the incidence of nerve damage compared to nonultrasound techniques appears to be unchanged [2]. Difficult or inadequate needle visualization of needle tip position during ultrasound imaging may result in unintentional needle–nerve contact or nerve trauma. Visualization of the needle tip does not necessarily ensure the absence of needle–nerve contact or intraneural injection. In one interscalene simulation study in cadavers, participants were asked to place a needle adjacent to the hypoechoic cervical nerve roots but performed unintentional intraneural injections in 50% of attempts [9]. Several post-hoc studies of ultrasound images reveal an unintentional intraneural injection rate of up to 17% in both brachial plexus and sciatic block models [10–12].

Electrical nerve stimulation provides some additional information, especially if the evoked motor response is present at a very low (e.g., <0.2 mA) current intensity, a threshold associated with intimate needle–nerve contact [13,14]. However, nerve stimulation is insensitive (i.e., the needle may be inside the nerve, and yet there is no motor response) [15]. It may be most useful as an adjunct to ultrasound imaging. While both ultrasound and nerve stimulation are helpful monitors, both are imperfect, and a case can be made for additional complementary monitors of needle–nerve contact.

Injection pressure monitoring: the background

Excessive injection pressure during nerve blockade has long been associated with adverse neurologic sequelae in animals [4,8]. High injection pressures may represent a needle tip position that is in a noncompliant fascicle, a structure that is vulnerable to mechanical stress [16,17]. As such, monitoring of injection pressure during nerve blockade has evolved as another method to avoid unintentional nerve contact or intraneural injection. The physics of injection pressure are important for the anesthesiologist to understand. During injection through a syringe-tubing-needle system, pressure can be thought of as occurring in two phases. The first phase is the opening injection pressure (OIP). This pressure must be reached within the syringe/tubing/needle circuit to overcome frictional resistance and initiate flow. According to Pascal's law, the pressure during this phase (the static phase, where no fluid is moving) is

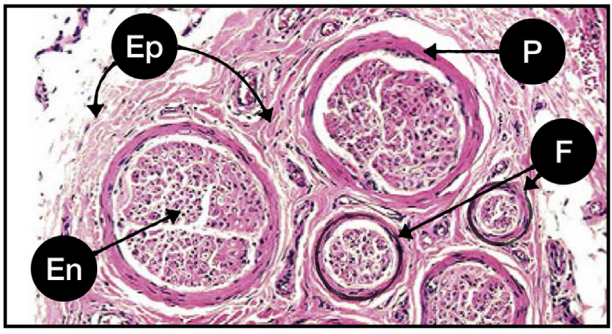

Fig. 1. Histology of the peripheral nerve. Fascicles (F) are ensheathed by the tough, laminar perineurium (P), which protects the delicate endoneurium (En) inside. The fascicles are supported and surrounded by the epineurium (Ep), which is a loose, areolar tissue that condenses at the periphery of the nerve to form a slightly tougher "shell" or "rind."

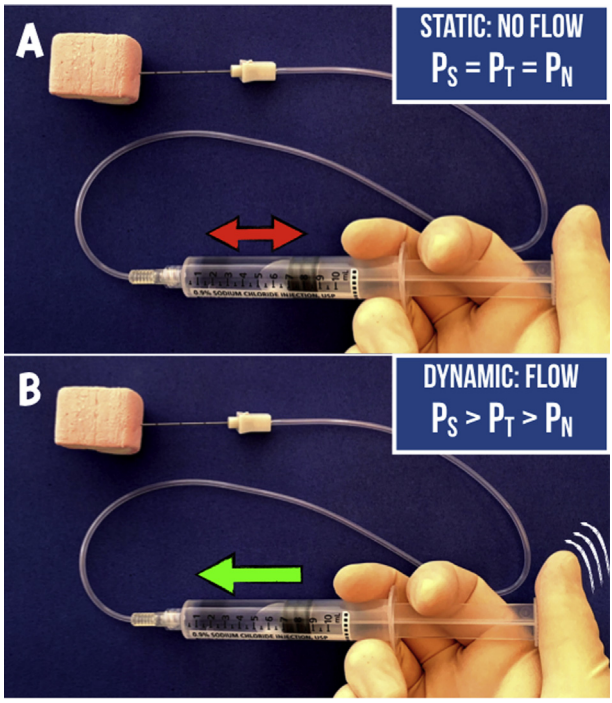

Fig. 2. Static versus dynamic phases of injection. Panel A shows static phase, where slight pressure is applied to the plunger, but frictional resistance has not yet been overcome and no flow is occurring. Pressure is equal in all parts of the system. In Panel B (dynamic phase), the frictional resistance has been overcome, and flow has commenced. The pressure in the syringe (PS) is greater than the pressure in the tubing (PT), which is greater than the pressure at the needle tip (PN).

equal throughout the closed system, regardless of the internal diameter of the needle, the length of the tubing or needle, or the viscosity of the solution (Fig. 2). Practically, this is important because limiting the pressure applied to the syringe plunger at the exact moment when flow begins will ensure that the pressure at the tip of the needle is, at most, no higher than the OIP.

The second pressure of interest is the dynamic injection pressure, which occurs after flow begins. The dynamic injection pressure in the syringe is influenced by the rate of injection, diameter and length of the syringe/tubing/needle components, and the viscosity of the solution (Bernoulli's principle). This dynamic pressure–flow relationship follows a predictable, directly correlated linear course for commonly used 25G, 22G, and 21G needles [18] and is controlled for in many studies by a fixed rate of injection. From a practical point of view, it is important to remember that for flow to occur, the pressure in the tissue (i.e., the needle tip) is always lower than that in the syringe or tubing. Even though dynamic pressure is more complex due to the multiple variables, observing the injection pressure throughout the course of injection allows the clinician to estimate the maximum pressure being applied to the tissue at any given time. To minimize the effect of needle resistance on the measured dynamic injection pressures (i.e., in order to avoid false-positive high readings), it has been recommended that injections are performed at a rate of no greater than 15 ml min^{-1} [18].

Injection pressure monitoring: preclinical studies

Hadzic et al. described both histological and functional nerve injury as a result of intentional intraneural injection in a canine sciatic nerve model [4]. Needles (25 gauge) were placed either inside a sciatic nerve fascicle (intrafascicular) or within the nerve at an extra-fascicular position. Following this, injection pressures were recorded after 2% lidocaine with 4 $mcg.ml^{-1}$ of epinephrine was injected at a rate of 4 ml min^{-1}. Four of seven intrafascicular injections were associated with

high opening injection pressures (≥25 psi, range, 25–45 psi) as well as persistent motor deficits and evidence of neural destruction on histologic exam. All of the extrafascicular injections and 3 of the intrafascicular injections demonstrated low (<12 psi) injection pressures, and all 10 of these animals exhibited normal motor recovery and histology, confirming an association between high injection pressures and injury. These conclusions were supported by another similar canine sciatic nerve study where 4 ml of 2% lidocaine was administered at 4 ml min^{-1} either intraneurally or extraneurally [19]. All of the extraneural injections and 60% of the intraneural injections were associated with both low (<12 psi) injection pressure along with complete functional recovery and normal histology. In the remaining 8 of 20 intraneural injections, OIP ranged from 20 to 38 psi, and in each of these animals, the investigators observed neurologic deficits and, upon histologic examination, axonolysis and cellular infiltration. Together, these animal data suggest that intraneural injection does not always result in injury; however, those injections associated with high opening pressures are likely to cause serious neurologic injury, suggesting that injecting when there is resistance during nerve blockade should be avoided.

Krol et al. used low-volume (1 mL), slow-rate (0.1 mL s^{-1}) injections to assess intraneural and extraneural pressures in the medial, radial, and ulnar nerves of soft-preserved human cadavers [20]. Needles placed intraneurally produced higher opening injection pressure, defined as pressure peak following initiation of injection, across all three nerves (29.4 vs. 7.2 psi at median nerve, 27.3 vs. 8.3 psi at radial nerve, 17.9 vs. 6.7 psi at ulnar nerve). The ulnar nerve was noted to have generally lower intraneural injection pressure, with 60% of intraneural injections performed at <20 psi. All extraneural injections resulted in pressures of <12 psi. Ultrasonography was used to determine needle position, and the resolution of the images did not permit a distinction between intrafascicular versus extrafascicular needle placement. However, this supports the high sensitivity of pressure monitoring, as all extraneural injection pressures were <12 psi.

In a similar study of lower limb nerve blocks in fresh cadavers, OIP was significantly higher for intraneural than for extraneural injections, ranging from 21.5 psi to 25.8 psi for intraneural injections and from 3.8 psi to 6.1 psi for extraneural injections [21]. Furthermore, the rate of increase of OIP was found to be 3–6 times higher during the intraneural condition than that during the extraneural condition. In other words, the time to reach peak pressure was significantly reduced during intraneural injection. The authors suggest that, rather than waiting to detect a specific high target OIP (i.e., 15 psi) to halt injection, the *rate of increase* of injection pressure may indicate a hazardous needle tip position sooner and allow the clinician to avoid reaching that threshold altogether.

The anatomic location of the nerve may influence OIP during unintentional needle entry during blockade. Compared to extraneural injection, intraneural injection within the C6 and C7 nerve roots in unembalmed cadaver models led to markedly elevated OIP (mean 48.9 psi) in addition to decreased time to peak pressure compared to extraneural injection [22]. The pressures in this study were also significantly higher than those observed in the cadaveric studies of forearm and lower limb blocks. Ross et al. performed a direct comparison of intrafascicular versus extrafascicular injections at the level of the cervical root, peripheral nerves, and extraneural soft tissues on an unembalmed cadaver model [23]. Mean peak injection pressures were significantly higher in the cervical root versus peripheral nerve specimens and in the cervical root versus extraneural specimens.

The relationship between anatomic location and intraneural pressure may be explained by the relative amounts of connective tissue and the number and size of nerve fascicles. As a general rule, the proportion of neural tissue is highest at proximal sites (i.e., nerve root or interscalene) and decreases distally (i.e., axillary or forearm) [24,25]. Cervical nerve roots are essentially monofascicles, and therefore, injection into a root is virtually always an intrafascicular injection. In contrast, an intraneural injection into the median nerve in the forearm may or may not violate the perineurium of the fascicle, as there is a greater proportion of supporting fatty epineurium. In fact, some investigators argue that it is relatively difficult to pierce a fascicle in such peripheral nerves such as the sciatic, as the needle tends to pass between or glance off of fascicles [26]. Blocks performed at nerves typically made up of either one (e.g., interscalene) or two (e.g., common peroneal nerve at the popliteal fossa) fascicles do indeed have the highest rates of postoperative neurologic symptoms [27].

Injection pressure monitoring: the clinical studies

While it is clear that puncturing the perineurium and damaging a fascicle should be avoided, a monitor that alerts only the clinician after this event may have limited utility. Just as ultrasound and nerve stimulation can guide the anesthesiologist as to when the needle is nearby (but not within) the nerve, injection pressure monitoring may be able to warn of needle–nerve *contact* prior to a potentially injurious nerve puncture. To investigate this relationship, Gadsden and colleagues [16] measured OIP in patients scheduled for shoulder surgery under interscalene block, hypothesizing that the presence of high (≥15 psi) opening pressure would reliably detect needle–nerve contact. Pressure measurements were taken with the needle tip placed against the nerve root with the minimum force required to displace or indent the nerve slightly. Needle–nerve contact resulted in the generation of pressures ≥15 psi in 97% of cases, signaling a blinded observer of pressure to stop the injection before flow occurred. Attempted injection with the needle positioned 1 mm from the nerve root resulted in significantly lower opening pressure and the ability to commence the injection of local anesthetic. Interestingly, OIP was significantly more sensitive at detecting needle–nerve contact than either evoked motor response at 0.5 mA or the presence of paresthesia. While needle–nerve contact itself can result in inflammation [5], it is primarily the mechanical insult of the needle and the flow of injectate *within* the perineurium that provokes long-term injury. Monitoring OIP appears to be useful in preventing excessively forceful flow of injectate at or into a nerve root under these conditions.

Pressure monitoring also assists with needle positioning during nerve blocks that require detection of specific fascial planes, including femoral blockade. Gadsden et al. described the incidence of high opening pressure during needle–nerve contact and needle–fascia contact during femoral blockade [28]. OIP of 15 psi or greater was detected in 90% of patients during needle contact with the femoral nerve and in 100% of patients when the needle indented the fascia iliaca. All injections away from the nerve (1 mm distance) or deep into the fascia iliaca resulted in low opening pressures (≤15 psi), with the latter facilitating correct placement of 20 mL of local anesthetic for the nerve block. This further supports the observation that low OIP provides a high negative predictive value for avoiding injection into a low compliance tissue structure or incorrect tissue plane.

High-pressure injections have also been associated with broader safety concerns, including unwanted spread of injectate during peripheral nerve blockade. A study of 80 patients undergoing knee arthroscopy randomized adult subjects to receive either low-pressure (<15 psi) or high-pressure (>20 psi) injection during lumbar plexus blockade using 35 ml of local anesthetic [29]. The study was terminated early after interim analysis revealed that high injection pressures resulted in bilateral femoral nerve blockade in 60% of patients, and bilateral neuraxial blockade to T11 or above in 50% of patients, including sensory block extending to the T4 level in one patient. None of the low-pressure injections resulted in bilateral blockade, suggesting that spread to the neuraxis (and hence the contralateral lumbar plexus roots) may be largely a function of pressure, rather than volume, as the injectate moves medially along fascial planes in the psoas compartment toward the intervertebral foramina.

How can injection pressure be measured in the clinical setting?

Anesthesiologists often depend on subjective “syringe feel” as an indicator of abnormal resistance to injection. Although perception of change in force required to inject may be appreciated by some experienced injectors, this method is inconsistent, and there is a wide variation in the perception of appropriate force and rate of injection. In a simulated and blinded injection model of anesthesiologists asked to inject with their “usual” force and rate, Claudio and colleagues [30] noted that initial injection pressure exceeded 20 psi in 70% of those studied and exceeded 25 psi in over half. Anesthesiologists are also poor at identifying the type of tissue where the needle tip is located in by evaluation of the resistance alone and cannot reliably detect intraneural injection [31]. These data suggest that an objective, quantifiable means of monitoring injection pressure would be useful.

Several objective methods exist to monitor injection pressure. The compressed air injection technique (CAIT) involves drawing a fixed volume of air into the same syringe as the injectate solution and observing the compression of that air bubble while force is applied to the plunger [32]. This method takes advantage of Boyle's law, which states that for an ideal gas in a closed system, pressure and

volume are inversely proportional [33]. For example, if the volume of a bubble of air in a syringe is decreased by 50%, and no flow has occurred, the pressure in the system is doubled. Assuming that the starting pressure in the syringe, needle, and tissue is atmospheric (14.7 psi at sea level), the doubling of that pressure adds another 14.7 psi to the system. Ensuring that the bubble never reaches half of its original size would mean that the tissue is never exposed to pressures as high as 14.7 psi. Conveniently, 15–20 psi is the pressure threshold below which injection is thought to be safe based on the animal and cadaver data [4,19,20,22].

While simple and inexpensive, this method poses some practical limitations such as needing to maintain the syringe upright, the possibility of a gas embolism, and variability among users, especially trainees. Also, while the bubble size is relatively easy to estimate in the static phase of injection (prior to flow), once the syringe plunger starts to move it can be more difficult to accurately judge changes in the amount of air in a moving column. In order to circumvent some of these limitations, Patil et al. [34] devised an improvised pressure gauge using an extended 1 mL syringe and three-way stopcock. At rest, the fluid meniscus in the barrel of the 1 ml syringe is at the zero mark (Fig. 3). As pressure increases in the system, the meniscus climbs proportionately. This method demonstrated good agreement between calculated and measured pressures, with changes in the meniscus level corresponding reliably to injection pressure changes as force applied to a 20 mL syringe pushed fluid into the 1 mL syringe. When the meniscus reached the 0.5 ml mark, the line pressure was found to be approximately 10 psi, a useful low threshold for safe injection. The main limitation of this method relates to intermittent aspiration during injection; negative pressure from the injectate syringe will aspirate air from the improvised pressure gauge into the mainline tubing, unless the clinician incorporates an additional step of turning the stopcock to exclude the 1 mL syringe during aspiration.

Currently, there are two commercially available, single-use pressure monitors available for clinical use. The B. Braun BSmart™ injection pressure manometer (B. Braun Medical Inc., Bethlehem, PA) is an in-line device that uses simple fluid mechanics and a small flexible diaphragm within the device to push a small piston up as the line pressure increases (Fig. 4a). Markings on the piston indicate when pressures are in the <15 psi, 15–20 psi, or >20 psi ranges during injection. Color coding of these ranges (beige, orange, and red, respectively) may further enhance the ability to detect potentially hazardous injection pressures. The BSmart™ has been validated in a cadaver model of nerve blocks against an electronic transducer over a range of clinically relevant pressures (0–40 psi) [35].

The NerveGuard™ device (Pajunk Medical Systems, Geisingen, Germany) is another disposable in-line device, but it functions in a manner different from that of the BSmart™. Rather than being a

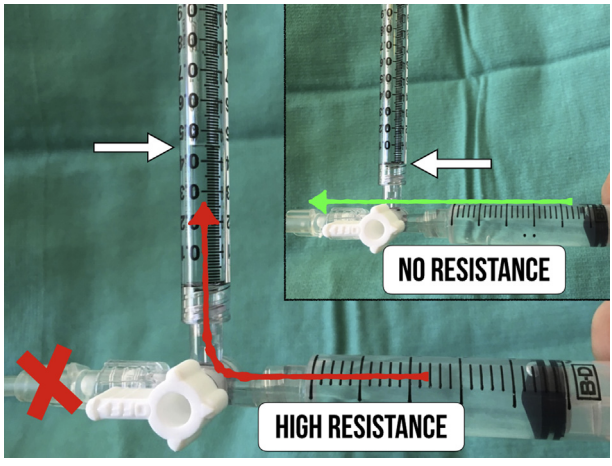

Fig. 3. An improvised pressure gauge using a stopcock and an air-filled 1 ml syringe with the plunger pulled out to its stop. In the absence of resistance, flow occurs into to the needle tubing. If resistance is encountered, the pressure upstream forces the injectate into the 1 ml syringe, causing the meniscus to rise (white arrows). The mensiscus at the 0.5 ml mark corresponds to a line pressure of approximately 10 psi.

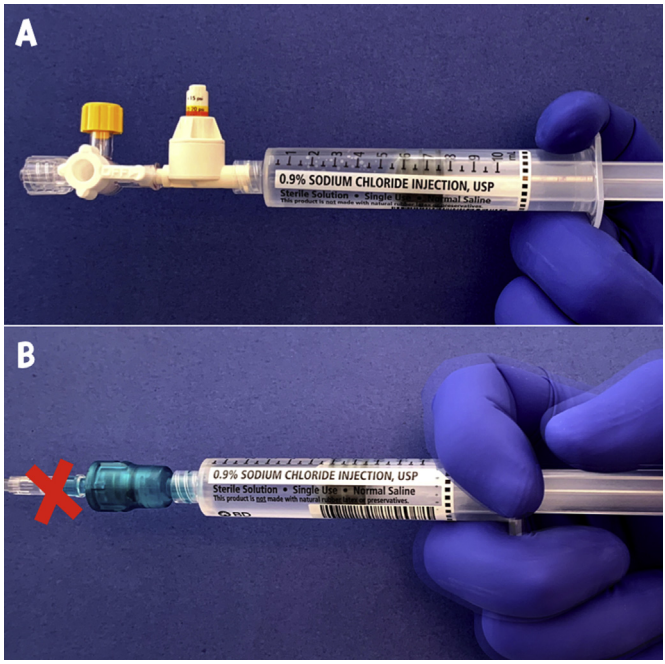

Fig. 4. Two commercially available in-line pressure devices. The BSmart™ (A) incorporates a piston that rises with increasing downstream resistance, indicating three pressure ranges by color. The NerveGuard™ (B) is a pressure limiter, closing off when pressures exceed 15 psi and preventing further flow.

quantifiable monitor of injection pressure, the NerveGuard™ functions as a pressure limiter. If injection pressure exceeds 15 psi, a flow-limiting valve within this device automatically stops the injection (Fig. 4b), prompting the anesthesiologist to release the force applied on the plunger to start again. This carries the advantage of not requiring constant vigilance in watching the monitor (e.g., bubble, meniscus, or piston), while attention is focused on the ultrasound screen or patient.

Recent studies have investigated the utility of monitoring injection pressure directly at the needle tip. Quadri and colleagues argued that the pressure measured at the syringe or tubing does not accurately reflect the pressure at the needle tip when fluid is moving, as the line pressure is influenced by rate of injection; size and length of the needle; and the size, length and compliance of the injection tubing [36]. This group has developed a novel system of directly measuring needle tip pressure (LightSens Medical SA, Bellinzona, Switzerland). The system consists of a Fabry-Pérot optical cavity bonded to the tip of an optical fiber that is inserted within the shaft of a standard block needle. Alterations in pressure at the needle tip deform a membrane on the optical cavity, changing its length; these changes are detected using a white-light interferometer, and a tip pressure is inferred with a resolution of 0.0014 psi and an accuracy of 0.14 psi [36]. A connection to a control unit permits real-time continuous recording of the pressure profile at the needle tip. Saporito et al. tested this system in a silicone gel model at various injection rates and found that peak pressures measured at the syringe tubing (line pressure) increased proportionately with the rate of injection; however, independent of injection rates, pressure at the needle tip remained both constant and substantially lower than line pressure, especially at higher flow rates [37]. The same group has demonstrated the feasibility of this system in a cadaveric sciatic nerve model, where the sensing needle was able to discriminate extraneural or intraneural placement of the needle tip at various sites along the sciatic nerve during injection of 5 ml of saline over 30 s (10 ml min^{-1}) [38]. Mean (SD) peak pressures were 2.0 (0.9) and 19.0 (8.1), respectively, for extra-versus intraneural injections. The authors suggest that continuous monitoring at the needle tip may be useful in reducing the incidence of false-positive measurements, as may be encountered with overly rapid (>15 ml min^{-1}) injection speeds.

What DON'T we know regarding injection pressure monitoring?

The biggest unanswered question relates to the efficacy of monitoring and limiting injection pressures in reducing neural injury. No study to date has demonstrated in a rigorous fashion that the use of such monitors leads to better outcomes. This is primarily due to the (fortunately) low incidence of nerve injury following peripheral nerve block. With the current estimated rates of injury, it would require a comparative study of tens of thousands of patients to show a difference, making a randomized controlled trial unwieldy and unlikely to be done. A pragmatic trial comparing the results of several institutions—some that use monitoring and some that do not—might be a good "best alternative." Registry databases exist, but it is unclear whether these include data on the use of injection pressure monitoring.

Injection pressure may influence other outcomes related to peripheral nerve block. Just as high pressures were demonstrated to result in contralateral spread during lumbar plexus block [29], the effect of high versus low injection pressures on fluid dynamics at other block sites—and the consequences of such—is another unexplored area. Similarly, the effect of injection pressure on the pharmacokinetics of local anesthetics (e.g. does high-pressure injection lead to elevated plasma levels) has yet to be explored and is an area worth addressing.

Summary

Injection pressure monitoring, while a relatively recent concept, is increasingly being recognized as a potential safeguard against intraneural injection during peripheral nerve blockade, as evidenced in a number of studies and by clinical measurement techniques that have been developed. Animal and cadaveric data suggest that injection pressure is consistently higher during intrafascicular injection than extrafascicular injection and that high pressure (>20–25 psi) predicts subsequent histologic and functional nerve damage. While nonspecific (high pressure may have many causes such as a needle tip lodged in tendon or a clotted needle), injection pressure monitoring seems to be highly sensitive: if the OIP is <15–20 psi, the needle tip is not in a dangerously noncompliant space such as a fascicle.

While early studies focused on the role of OIP, it seems prudent to objectively monitor injection pressure throughout the course of injection, especially as peak pressures may increase over time. Various methods of quantifying injection pressure exist, but the key principle is to limit the pressure at any given time to a safe threshold; according to the available evidence, that threshold is approximately 15 psi. Most of the methods currently available rely on the operator recognizing a visual cue, such as the size or position of an air bubble or meniscus, an LED readout, or the position of a labeled piston on an inline device. The development of auditory or haptic cues warning of resistance to injection may further improve the utility of such monitors, and research should be directed to this area. Alternatively, the use of a pressure-*limiting* device reduces the need for the clinician to pay attention to sensory cues. Research validating the use of this device in a clinical setting is also indicated. Future studies are required to better understand the clinical implications of the advances in and growing evidence for injection pressure monitoring as a tool to improve both patient safety and nerve block efficacy.

Practice points

- Injection pressure monitoring is nonspecific, but it is very sensitive for detecting potentially injurious needle tip position during peripheral nerve blockade
- Limiting pressure to <15 psi appears to provide safe conditions for peripheral nerve blockade
- During the dynamic phase of injection (when flow is occurring), pressure at the needle tip is always lower than that in the syringe/tubing assembly. Maintaining a line pressure of 15 psi or less ensures that the tissue adjacent to the needle tip is not exposed to harmful pressure.
- Injection pressure can be measured or limited in various ways. There are pros and cons to each, but in general, these are inexpensive and easy to incorporate into regional anesthetic practice.

Research agenda

- Large-scale, registry database studies or pragmatic studies across institutions with different practice patterns are needed to be able to characterize a more definitive relationship between the use of these monitors and any protective effect
- The development of other sensory cues (e.g. auditory or haptic) to indicate high resistance to injection should be investigated and compared to the current visual cue systems
- The rate of increase of injection pressure may provide an earlier warning of hazardous conditions than the achievement of a single pressure threshold of 15 psi; further research in other block sites and in a clinical setting is indicated
- Research is warranted on the effect of controlling injection pressure on outcomes distinct from neural injury, namely, fluid dynamics within tissues and subsequent block effects as well as local anesthetic kinetics

Conflicts of interest

None.

Funding source

None.

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