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Current Understanding

Block Efficacy Above The Clavicle : Volume Of Local Anaesthetic Agents

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Introduction

The regional anaesthesiologist's primary goal is to deposit adequate local anaesthetic (LA) in the vicinity of nerves for the desired effect without complications. Our inability to visualise nerves, during landmark and peripheral nerve stimulation techniques, was the biggest obstacle against accurate deposition. Ultrasound (US) guidance enables accurate deposition of local anaesthetics due to objective and consistent visualisation of target nerves [1]. However, the minimum effective local anaesthetic volume (MELAV) varies among clinicians. Stephan Kapral in 1994 described the first ultrasound-guided supraclavicular brachial plexus block [2]. However, the image quality and the injection technique similar to our present-day practice appeared in 2003, where Vincent Chan et al injected 40 ml of local anaesthetic (LA) volume to achieve a 95% success rate [3]. This article reviews the studies that explored the MELAV for US-guided brachial plexus blocks (BPB) above the clavicle and explores the possible reasons for variations reported by authors and to direct future research for identification of safe and effective local anaesthetic volume for the BPB above the clavicle.

Minimum Alveolar Concentration (MAC) versus MELAV

In 1965 Eger et al introduced the concept of MAC for quantification of inhalational agent required for effective general anaesthesia [4]. To identify the MAC, a known concentration of agent (percentage of gas mixture) was administered through the lungs and a single objective response i.e. movement, was observed to a standard stimulus i.e skin incision. The minimum concentration that inhibits movement in 50% of individuals was labelled MAC of that particular agent. In regional anaesthesia, MELAV is used to express the minimum amount of local anaesthetic required for an effective peripheral nerve block. However, the determination of MELAV is more complex than MAC for the following reasons:

1. The partial pressure of the agent determines the clinical outcome, and since it is directly proportional to concentration, manipulating the concentration of the administered agent linearly affects the outcome. However to achieve successful nerve conduction blockade, both LA volume and concentration influence outcomes. Literature states that conduction blockade across a nerve fibre requires involvement of more than 70% of sodium channels over three consecutive nodes of Ranvier and considering that internodal distances range from 0.2 to 2 mm [5, 6] a minimum 6 mm length of nerve would need to be exposed for blockade. The volume administered act a vehicle to carry the LA molecule across 6 mm length of nerve, at the same time concentration (number of molecules present per unit volume) should be adequate enough to occupy 70% of the receptors so that impulse conduction can be blocked.
2. Inhalational agents are administered to the lungs is via breathing circuits. Factors affecting agent delivery, such as fresh gas flow, dial setting, and minute ventilation are very much predictable and easy to standardize. Whereas during peripheral and plexus nerve blockade, the block outcomes vary significantly based on the injection technique adapted i.e single point vs. multipoint injections and the site of drug deposition (extrafacial vs subfacial).

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3. MAC assessment relied on movement in response to skin incision as the only outcome, whereas for PNB both the stimulus (soft tissue or bony procedures) and the outcome (analgesia or anaesthesia) varied across different studies, investigating the MELAV.

Methodologies evaluating the MELAV for US-guided BPB above the clavicle

Till date, to the best of our knowledge, nine articles analysed the MELAV for US-guided BPB above the clavicle (Table 1). The MELAV 95 reported ranges from as low as 5 ml to 42 ml. Three methodologies have been used, in these studies, for identifying MELAV. Dixon-Mood (DM) up-and-Down method remains the most prevalent, however few studies have used the Biased Coin Design (BCD) variant Bayesian analysis and Continual Reassessment Method (CRM). The advantage of DM up-and-down method is the requirement of smaller sample size; however it measures only to the 50th quantile (ED 50– Effective dose) and estimates the ED 90/95/99 resulting in a measurement that is weak in accuracy [7]. On the other hand, the BCD and CRM methods directly measure higher quantiles (ED 90/95/99) but require larger sample sizes. Even though the ED 50 is sufficient to measure potency and compare pharmacological agents, during peripheral nerve blockade, the dose that provides 95% success rate (ED 90/95) is clinically more relevant than ED 50. So this review focussed on studies reporting MELAV 90/95.

A single intervention with different outcomes, reflects the fact that multiple factors are responsible for the cause effect relationship, in order to define a MELAV. We discuss the influencing factors according to the degree of impact they have in every day clinical practice at the authors discretion.

Pharmacological

The number of LA molecules needed to block 70% sodium channels over three consecutive nodes of Ranvier is influenced by the LA's potency, which in turn impacts the MELAV. For example, MELAV of a local anaesthetic with low potency like lidocaine 1.5% was 32 ml [8], whereas LA with higher potency like ropivacaine 0.5% required only 15 ml [9]. Even different concentrations of the same local anaesthetic, resulted in different volumes to produce the same conduction blockade, evidenced by a study investigating the US-guided supraclavicular BPB where 0.5%, 0.375% and 0.25% concentrations of bupivacaine, required 17, 26, and 38 ml respectively, for a successful block [10]. This observation reflects the physical principle, that as concentration reduces, more volume of LA would be needed to soak the length of the nerve for effective conduction blockade [11]. Finally the role of adjuvants, that are claimed to hasten onset or prolong the duration, may influence the pharmacodynamics of LA thereby affecting the MELAV.

Technique for drug deposition

The technique for LA deposition varied, across the studies, from a single to multipoint injections or deposition around or within the brachial plexus sheath. Studies with single point injections observed the MELAV was 42 ml [12] which fell to 32 ml when a double point injection was performed (50% at corner pocket and 50% at the middle of the nerve cluster) [8] and fell further to 17 ml when multiple points injections were performed across all the nerve clusters [13]. When LA was deposited within the brachial plexus sheath (subfacial injection), the presenting authors found that the time to readiness for surgery was hastened by 13 minutes, when compared with LA deposition around the sheath(extrafacial injection) (7 ± 3 versus 20 ± 10 minutes; P=0.000) [14]. The authors also found by following a selective truncal approach, of all three trunks with an equal mixture of 2% lidocaine with adrenaline and 0.5% bupivacaine, the MELAV was 10 ml [15]. When there is so much variation in the dynamics of BPB even under direct visualisation through US guidance, the MELAV determined from these studies may not be applicable for surface landmark or PNS guided BPB techniques, and goes beyond the scope of this review.

Defining the block outcome

The spectrum of conduction blockade ranges from normal sensory-motor function to complete absence of both i.e complete conduction blockade(CCB), where analgesia and surgical anaesthesia are placed in-between. The differential blockade property of LA can result complete loss of sensory function at the dermatome, which may not necessarily correlate with a complete blockade at the myotome or osteotome, which would not be considered as CCB. So one may obtain adequate surgical anaesthesia at the forearm, however not considered as CCB, as movement of the fingers maybe intact. Hence analgesia [16], time to readiness for surgery [14], surgical anaesthesia [8] and complete conduction blockade [15] should be taken as different endpoints requiring different MELAV.

Anatomical

The number of axons exiting the spinal cord reorganise into multiple fascicles as they traverse from central neuraxis to form peripheral nerves. During their course the average number of fascicles in the BP increased from 29 at the trunks

Table 1: Studies on Minimum Effective Local Anaesthestic Volumes used for Brachial Plexus blocks above the clavicle.

Sr.No	Author year	No. of patients	Access to BPB	Site of LA injection	Outcomes Assessed for success of block	LA used & Concentration	MELAV (95% Confidence Interval)	Comments
1.	Duggan et al [12] 2009	21	Supraclavicular	Supraclavicular Single point injection Lateral to artery, cephalad to 1st rib in close proximity to the neural elements.	Sensory blockade and Surgical anaesthesia for upper limb ambulatory surgeries, (excluding shoulder) – both soft tissue and bony procedure	50:50 mixture of lignocaine 2%, Bupivacaine 0.5% and adrenaline	42 ml (19- 65 ml)	Single point injection hence distribution of LA across all elements is limited.
2.	De Q H Tran et al [8] 2011	54	Supraclavicular	Supraclavicular double point injection i Intersection between 1st rib and SCA "corner pocket" ii Redirected towards neural elements (intracluster)	Composite score - Success was defined, at 30 minutes, as a minimal score of 14 of 16 points using a composite scale encompassing sensory and motor block.	lignocaine 1.5% with adrenaline 5mic/ml	32 ml (30 - 34 ml)	Following two-point injection the distribution of LA is better than single point still soakage of all elements in given time is limited.
3.	P Gautier et al [21] 2011	20	Interscalene	Three injections for three trunks identified 2 cm above the clavicle.	Complete conduction blockade at 30 minutes or inadequate Surgical anaesthesia	0.75% Ropivacaine	5 ml (1.7ml for each trunk)	The authors misinterpreted the traffic light sign as three trunks and the complete conduction blockade of all five terminal nerves of BP was not demonstrated.
4.	L F R Falcao et al [22] 2013	25	Interscalene	Above the clavicle single point injection with LA deposited at two sites – one between upper and middle trunk, one between middle and inferior trunk	The block was considered positive when there was absence of thermal distinction and absence of pain.	0.5% bupivacaine with epinephrine (1:200 000)	0.95 ml (0.6–1.22 ml)	General Anaesthesia was administered for the surgery – cant comment on surgical anaesthesia
5.	J G Song et al [13] 2013	30	Supraclavicular	Multi-point LA deposition	Successful blockade was defined as complete sensory blockade (sensory block score = 0 in all five terminal nerve distributions) in the distribution of five terminal nerves at 30 minutes.	1.5% Mepivicaine	17 ml (13-42 ml)	Multipoint injection hence soakage of all the BP elements was ensued in the given time
6.	Pavicic Saric et al [20] 2013	44	Supraclavicular	Two point injection – One lateral to the subclavian artery and cranial to the first rib. After administering half of the determined LA volume, the needle was repositioned cranially toward the neural cluster in order to allocate the other half.	A successful block is defined as complete sensory blockade (total loss of pinprick sensation and total loss of cold sensation) in all four regions of distal nerves assessed within 30 min of LA injection.	50 : 50 mixture, 0.5% levobupivacaine and 2% lidocaine	middle-aged -23.0 ml (13.7–32.3ml) Elderly 11.9 ml, (9.3– 14.6 ml)	The cross sectional area for the BP 0.95 ±0.15 cm2 was found in the middle-aged group, whereas 0.51± 0.06 cm2 was found in the elderly group. (P < 0.001)
7.	Stephen Choi et al [23] 2017	54	Posterior approach to interscalene	Adjacent to the C5 and C6 nerve roots	To provide surgical anaesthesia for shoulder arthroscopy under propofol sedation without phrenic nerve involvement.	0.75% Ropivacaine	Study terminated due to futili ty. Between 5 to 20ml of LA volume not able to ach ieve surgical anaesthesia without phrenic nerve involvement.	
8.	Pushpender et al [9] 2018	29	Supraclavicular	Drug was injected with single injection method and confirmed as separation of plexus from subclavian artery	Overall, the ultimate maximal composite score (motor + sensory) was decided as 12 points. Minimal composite score of 10 points was considered successful block.	0.5% Ropivacaine	15 ml	Study endpoint does not target complete conduction blockade (12/12) whereas 10/12 defines success.
9.	Sivashanmugam T et al [15] 2020	21	Targets individual trunk of BP across interscalene and supraclavicular area.	Above the clavicle from interscalene to supraclavicular – multipoint injection targeting three trunks (below outermost epineurium)	Total composite score for conduction blockade of 20/20 at 30 min after block-time was considered successful. Requirement of supplementation during surgery was considered as failure	50:50 mixture of Lignocaine 2% with adrenaline and 0.5% Bupivacaine.	10.47 ml	The authors identified individual trunks and did intra truncal injection of LA. Hence complete conduction blockade of all five terminal nerves in lowest LA volume.

to 46 at the level of cords. Correspondingly volume of connective tissue has been reported to increase from 28%, 58% and 90% at the roots, trunks and terminal peripheral nerves respectively [17]. The ratio of neural to non-neural connective tissue has been reported to impact the block dynamics [18], as it may reflect the amount of resistance to the spread and distribution of LA [19]. Hence, the MELAV used for the truncal block at the supraclavicular fossa may not be applicable to blockade of the cords at the costoclavicular space or peripheral nerve block at the level of axillary crease.

Physiological

Individual patients' characteristics like age, sodium channel density, subtype, and sensitivity to local anaesthetics can affect the MELAV for the desired outcome. J. Pavicic Saric et al demonstrated that the MELAV 50% of the middle-aged (42 ± 6) patients was 23 ml (95% CI 13.7 -32.3 ml), whereas the MELAV 50 of elderly (75 ± 7) patients were 11.9 ml (95% CI 9.3 – 14.6 ml, P = 0.027) during US-guided supraclavicular BPB [20]. They associated the less MELAV to the deterioration changes in the neuronal system reflected by the smaller surface area of the BP at the first rib in elderly patients (0.51 ± 0.06 cm^2 vs 0.95 ± 0.15 cm^2). Because of this myriad of genetic and interindividual variation, at any given MELAV, some individuals may not attain the same block outcome.

Direction for future research

Since MELAV is affected by the type of drug, volume, concentration, deposition site, injection technique adapted, outcome assessed, adjuvants added and individual patient's susceptibility, studying them randomly will provide innumerable permutations of combinations, which is not only impractical but also will not provide any conclusive evidence for clinical application. Based on the ten years of experience in brachial plexus block research, the authors suggest a systematic approach to explore the MELAV for BPB above the clavicle. Among the various factors discussed, the two in clinicians' gambit are technical approach and blockade outcome assessment.

Hence clinicians embarking on MELAV studies may adopt the following steps:

1. Adopt an **injection technique** that distributes local anaesthetics across all the neural elements and provides consistent results even in difficult sonoanatomy. The injection technique and the clinician experience should be such that incomplete conduction blockade is only due to drug characteristics not due to faulty technique. (The competence of the block performer is a major bias factor to be standardized)
2. Choose commonly used **LA or LA combinations** (Be aware that intrinsic properties of LA can impact the block outcomes - for e.g. at low volumes, lignocaine may not last the surgical duration, whereas bupivacaine has a prolonged onset time to achieve surgical anaesthesia (> 30minutes) which is not viable in clinical practice – Unpublished data)
3. Choose clear **objective endpoints** in the spectrum of conduction blockade (Composite score/complete conduction blockade) to reduce inter-observer bias. (Since there is no universally accepted ideal duration of surgical anaesthesia and analgesia for a given block, the meaning of the word "effective" in the MELAV commonly represent the onset and quality of surgical anaesthesia. Hence the MELAV that satisfies the onset characteristics may not last long and may not guarantee complication-free regional anaesthesia)
4. **Reduce** the study cohort's variations, standardise the surgical stimulus (bony procedures) so that the MELAV identified in this cohort can be extrapolated to the population with minimal modifications.
5. **Avoid use of adjuvants** (Dexamethasone/Clonidine/Opioids) until pharmacodynamics of the MELAV are well defined.
6. Once the MELAV of a particular agent or combination of agents is identified, it must be prospectively observed in larger populations to describe the block dynamics (Duration of surgical anaesthesia, analgesia and complication profile) and refine the volume to suit the clinical need. Hence the MELAV has to mature into **Clinically Effective Local Anaesthetic Volume CELAV.**

Conclusion

Even after introducing ultrasound guidance in regional anaesthesia, the MELAV for BPB above the clavicle is still not established. However, the minimum safe and effective volume continues to reduce as our understanding of BP sonoanatomy improves, and consistency of targeted component blockade evolves. The authors recommend the readers to adopt a systematic approach to study and comprehend the MELAV findings.

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