Challenges to implement minimum effective volume in regional anesthesia

The incidence of providing regional anesthesia either as a sole anesthetic or combined with general anesthesia for surgical procedures has increased significantly in the past few decades.[1] Ensuring patient safety and providing quality regional blockade are the key components of a good nerve block. The success is also related to the total volume of local anesthetics administered for any given nerve block.[2] Nerve stimulator has been used to achieve better quality of nerve blockade with relatively less volume of anesthetics.[3] With significant increase in the utilization of ultrasonography for regional anesthesia, anesthesiologists are now not only able to visualize the desired anatomical structures easily but also substantially reduce the volume of local anesthetics, required to achieve the same quality of nerve blockade.[4-6]

Nerve blocks that are performed in close proximity of either major vascular structures or nerve tissues may adversely affect the physiological functions warranting usage of lesser drug volume. One such example is the interscalene block (ISB), which invariably compromises breathing by causing partial or complete phrenic nerve palsy.[7] Avoidance of phrenic blockade is vital in geriatricpatients, especially those with compromised pulmonary status. Many approaches have been proposed to minimize the phrenic nerve blockade such as using less drug volume,[8] different approaches such as periplexus[9] or intrafascial[10] or multisite injections, or completely avoiding ISB and choosing alternative blocks for shoulder surgery.[11] Among these methods, minimum effective volume (MEV) technique is widely used to minimize complications associated with nerve blockade with varying responses.[8] ED_{50}, ED_{90}, and ED_{95} are used by the investigators to calculate MEV for local anesthetics.[12-14]

In this issue, Mittal *et al.* attempted to determine the MEV_{90} for 0.5% ropivacaine for ISB to avoid untoward complications/side effects.[15] Determining MEV is paramount in clinical practice, as it balances toxicity and safety. Furthermore, miscalculation of the MEV may lead to misleading information and serious consequences in the future larger sized clinical trials.[16]

Methods to Determine MEV

Various "up-down methods" such as "3 + 3," accelerated titration, biased coin, k-in-a-row, group up-and-down, cumulative group up-and-down, nonparametric optimal, and dose selection based on isotonic regression have been described to determine MEV or maximum tolerated dose (MTD) in other clinical scenarios. Among these, isotonic regression method has shown superior performance but is more challenging to implement in clinical practice, as it selects desirable drug volume based on the isotonic estimate of toxicity probability which is undesirable for regional anesthesia. In most of the clinical scenarios, researchers choose biased coin design as it is easy to apply, and most importantly, it is very flexible. To choose MEV or MTD, by biased coin method, researchers used only outcome data of the recently used patient/subject. It has a disadvantage of having low efficiency compared with other up and down methods mainly due to not including the data from previously treated individuals. This imposes challenges for the readers in interpreting outcomes from the studies based on coin biased method.[16-18]

Mittal *et al.* highlighted the rationale for choosing MEV primarily to avoid phrenic nerve palsy by assessing the diaphragmatic function with ultrasound.[15] They choose most commonly used up-down method in spite of its limitations. Even though there are a few limitations in their study design, their observations on MEV_{90} for ropivacaine are promising. MEV (8.64 mL) reported by Mittal *et al.* is much lower in similar clinical settings[15]; however, Falco *et al.* estimated lower MEV (4.29 mL) in their study when they used bupivacaine with epinephrine.[13] The authors concluded that there was no significant change in the onset and duration of the blockade with one-third of the usual volume required to perform the ISB.[15] Studies have shown challenges in measuring MEV accurately for ISB in spite of using unique method for up down by Narayana. Narayana rule estimates volume based on the cluster dose around the effective dose. Choi *et al.* had to end their observational study for ISB prematurely, due to no influence of decreasing well-defined complications, such as phrenic nerve palsy in spite of reducing block drug volume as per Narayana rule.[19]

To conclude, the study by Mittal *et al.* contributes to the limited evidence of determining MEV in ISB.[15] Authors addressed one of the unique challenges in regional anesthetic technique; however, it still raised many questions whether one can perform block with minimum drug volume to prevent complications, but without comprising quality of blockade. Based on the literature, it is always challenging to estimate MEV for any local anesthetics as it is primarily determined by up-down method used, technique used to perform block (single versus multiple sites), and the endpoints decided by the investigators mostly for the duration of blockade. Unfortunately, there is no one single safest way to estimate MEV; however, by combining ultrasound along with nerve simulator technique, there is a possibility to administer the desired volume of local anesthetics with minimal or no untoward complications related to nerve blockade.

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References

1. Mariano ER, Marshall ZJ, Urman RD, Kaye AD. Ultrasound and its evolution in perioperative regional anesthesia and analgesia. Best Pract Res Clin Anaesthesiol 2014;28:29-39.
2. Joshi G, Gandhi K, Shah N, Gadsden J, Corman SL. Peripheral nerve blocks in the management of postoperative pain: Challenges and opportunities. J Clin Anesth 2016;35:524-9.
3. Urmey WF. Using the nerve stimulator for peripheral or plexus nerve blocks. Minerva Anestesiol 2006;72:467-71.
4. Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJ. Effect of local anaesthetic volume (20 vs 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. Br J Anaesth 2008;101:549-56.
5. Koscielniak-Nielsen ZJ. Ultrasound-guided peripheral nerve blocks: What are the benefits? Acta Anaesthesiol Scand 2008;52:727-37.
6. Marhofer P, Chan VW. Ultrasound-guided regional anesthesia: Current concepts and future trends. Anesth Analg 2007;104:1265-9.
7. Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. Anesth Analg 1991;72:498-503.
8. Lee JH, Cho SH, Kim SH, Chae WS, Jin HC, Lee JS, *et al.* Ropivacaine for ultrasound-guided interscalene block: 5 mL provides similar analgesia but less phrenic nerve paralysis than 10 mL. Can J Anaesth 2011;58:1001-6.
9. Palhais N, Brull R, Kern C, Jacot-Guillarmod A, Charmoy A, Farron A, *et al.* Extrafascial injection for interscalene brachial plexus block reduces respiratory complications compared with a conventional intrafascial injection: A randomized, controlled, double-blind trial. Br J Anaesth 2016;116:531-7.
10. Renes SH, Rettig HC, Gielen MJ, Wilder-Smith OH, van Geffen GJ. Ultrasound-guided low-dose interscalene brachial plexus block reduces the incidence of hemidiaphragmatic paresis. Reg Anesth Pain Med 2009;34:498-502.
11. Gautier P, Vandepitte C, Ramquet C, DeCoopman M, Xu D, Hadzic A. The minimum effective anesthetic volume of 0.75% ropivacaine in ultrasound-guided interscalene brachial plexus block. Anesth Analg 2011;113:951-5.
12. McNaught A, Shastri U, Carmichael N, Award IT, Columb M, Cheung J, *et al.* Ultrasound reduces the minimum effective local anaesthetic volume compared with peripheral nerve stimulation for interscalene block. Br J Anaesth 2011;106:124-30.
13. Falcão LF, Perez MV, de Castro I, Yamashita AM, Tardelli MA, Amaral JL. Minimum effective volume of 0.5% bupivacaine with epinephrine in ultrasound guided inter scalene brachial plexus block. Br J Anaesth 2013;110:450-5.
14. Di Filippo A, Falsini S, Adembri C. Minimum anesthetic volume in regional anesthesia by using ultrasound-guidance. Braz J Anesthesiol 2016;66:499-50.
15. Mittal K, Janweja S, Prateek, Sangwan P, Agarwal D, Tak H. The Estimation of Minimum Effective Volume of 0.5% Ropivacaine in Ultrasound-Guided Interscalene Brachial Plexus Nerve Block: A Clinical Trial. J Anaesthesiol Clin Pharmacol 2019;35:41-6.
16. Liu S, Cai C, Ning J. Up-and-down designs for phase I clinical trials. Contemp Clin Trials 2013;36:218-27.
17. Dixon WJ. The up-and-down method for small samples. J Am Stat Assoc 1965;60:967-78.
18. Pace NL, Stylianou MP. Advances in and limitations of up-and-down methodology: A precise of clinical use, study design and dose estimation in anaesthesia research. Anesthesiology 2007;107:144-52.
19. Choi S, Wang JJ, Awad IT, McHardy P, Safa B, McCartney CJ. The minimal effective volume (MEAV 95) for interscalene brachial plexus block for surgical anesthesia under sedation: A prospective observational dose finding study. Can J Pain 2017;1:8-13.

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/joacp.JOACP_279_18

How to cite this article: Subramani S, Garg S. Challenges to implement minimum effective volume in regional anesthesia. J Anaesthesiol Clin Pharmacol 2019;35:47-8.