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## Exploring cocktails, remixes and innovations in regional nerve blocks: The clinical research journey continues

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Ever since Halsted and Hall's sensory block of peripheral nerves using cocaine injection stunned the world in 1880, the journey of regional anaesthesia has been remarkable and today, nerve blocks are commonly performed all over the world.

A major concern in the past was a higher failure rate of the nerve blocks. Several factors are responsible for the success or failure of a peripheral nerve block- the operator's thorough knowledge of the descriptive and topography of the nerve to be blocked, his technical skills, experience, location of the needle tip in the proper plane, proper nerve location, proper needle size and correct volume and concentration of drugs. Even in the best of the hands, failures were still not uncommon and resulted in the form of total failure, an incomplete block, a patchy block, a wear-off block or a misdirected block.<sup>[1]</sup>

In due course of time, it was realised that proper nerve location was the key to success in regional anaesthesia. Morgan had stated that 'Regional anaesthesia always works – provided you put the right dose of the right drug in the right place.' Different techniques of nerve localisation gradually evolved to assist the landmark technique. It took 100 years after the introduction of the concept of nerve block, for the adoption of electro-localisation during peripheral nerve blockade in the 1990s, with Perthes developing the electrical nerve stimulator in 1912 and Pearson introducing the concept of insulated needles for nerve localisation in 1955. Ansbro first described the continuous peripheral nerve block technique in the supraclavicular area in 1946. It was the team of Ting and Sivagnanaratnam in 1989 who first used

ultrasonography (USG) to confirm needle location and visualise the spread of a local anaesthetic in the axillary sheath while performing an axillary brachial plexus block.

Peripheral nerve stimulation and ultrasound guided techniques to locate nerves soon became popular in clinical practice. Novel approaches to block peripheral nerves using advances in ultrasound technique, introduction of long acting local anaesthetics and extended release local anaesthetics have now come up. Research on automated nerve recognition and automated nerve block performance without human intervention culminated in the design of the Magellan system in 2013-the first robotic system designed specifically to perform nerve blocks.<sup>[2]</sup>

No medical stream can advance further without the assistance of research activities. Clinical research is going on since 2015 on nanocarriers like liposomes, polymersomes in extended release for local anaesthetic drug delivery and combinations of nanocarriers and hybrid-nanocarriers. Extended release local anaesthetics continuously release a safe dose of drug with single administration. Recently, there have been positive results seen in research conducted on nano-structured extended release local anaesthetics; liposomal and polymeric are prominent mainstream systems amongst these.<sup>[3]</sup>

EXPAREL (Pacira Pharmaceuticals, New Jersey, USA) is the first extended release liposomal local anaesthetic loaded with bupivacaine and approved by the American Food and Drug Administration (FDA). It was allowed legally initially in limited clinical situations

like wound infiltration in 2011 and in interscalene brachial plexus block in 2018. It can achieve prolonged release and analgesic efficacy up to 72 hours. Positive results using EXPAREL have been demonstrated in interscalene block for shoulder arthroplasty, posterior intercostals (IC) nerve block in lung resection, multilevel IC block in open thoracotomy, IC nerve rib blocks in video-assisted thoracoscopic pulmonary resection, transversus abdominis plane (TAP) block in major lower abdominal and laparoscopic hand-assisted donor nephrectomy.<sup>[3]</sup>

The wide spectrum of regional anaesthesia provides numerous choices for achieving the desired results. Regional nerve blocks for chest wall surgery like in modified radical mastectomy (MRM) include paravertebral block (PVB), pectoral nerve (PECS) block (PECS I and II or combined), serratus anterior plane (SAP) block and erector spinae plane block. Researchers have compared these blocks with each other to demonstrate superiority of one block over the other in terms of quality of analgesia, reduction in opioid consumption and better clinical benefit. This issue of the IJA has several studies and case series on the use of different nerve blocks and their combinations for the chest and chest wall.<sup>[4-6]</sup>

Regional nerve blocks like TAP block, rectus sheath block, quadratus lumborum (QL) block are being tried as a part of multimodal anaesthesia technique for a variety of abdominal surgeries like hernia repair and laparoscopic surgeries.<sup>[7]</sup> Ultrasound-guided QL block has been reported to have provided excellent postoperative analgesia with decreased opioid consumption when used in laparoscopic renal surgeries as has been observed in the study by Rajagopalan V *et al.* being published in this issue of the IJA.<sup>[8]</sup>

The SAP block can block the lateral cutaneous branches of the IC nerves and long thoracic nerves. Blanco *et al.* had described ultrasound-guided SAP block as an alternative to regional anaesthesia techniques in patients undergoing breast surgeries.<sup>[9]</sup> Since then, different techniques of SAP block have been described and compared. A recent study found that compared to local anaesthetic infiltration, ultrasound guided SAP block may provide better analgesia and decreased consumption of opioid after thoracoscopic surgery.<sup>[10]</sup>

Nerve blocks offer several advantages in that they decrease the dose of systemic anaesthetics and analgesics needed. This reduction in requirement

of systemic opioids and their associated side effects forms the basis of the popularity of nerve blocks in clinical practice; nevertheless, nerve blocks presently form an important mode of the enhanced recovery after surgery (ERAS) concept and protocol, which is gaining rapid momentum. They are used currently in various fields which include but are not limited to various surgical procedures, acute and chronic pain management and emergency medicine.<sup>[6,11,12]</sup> Nerve blocks have become an important clinical strategy of the anaesthesiologists so as to avoid the airway during the coronavirus pandemic for all the surgeries which are feasible under regional blocks. An example of this is a novel customised face mask devised specially for use in the patient during the corona virus disease (COVID) pandemic as an alternative to the usual face mask while performing facial nerve blocks for chronic pain.<sup>[13]</sup> This issue of the IJA also carries the results of a nationwide survey carried out by Sahoo RK *et al.* The survey clearly shows that Indian pain physicians adopted Telehealth modality and provided continued care against all odds during the coronavirus pandemic.<sup>[14]</sup>

Another merit of regional anaesthesia includes abolition of the surgery mediated neuro-endocrine stress response and preservation of immune function. It also attenuates immunosuppression by decreasing doses of other general anaesthetic agents and opioids. All this attenuates tumour metastasis and promotes favourable long-term outcomes when compared to general anaesthesia.<sup>[15,16]</sup> This is a hot topic for research since the last few years and evidence on this is gradually accumulating.

In breast cancer surgeries, there is conflicting evidence of regional anaesthesia including epidural and paravertebral block for survival benefit including overall survival, disease-free survival, local-regional recurrence and metastasis-free survival.<sup>[7]</sup> A novel double blind randomised controlled study by Shagun Bhatia Shah *et al.* in this issue of the IJA compares the standard general anaesthesia (GA) technique using opioids and sevoflurane with an alternative GA technique devoid of opioids and sevoflurane but supplemented by pre-emptive PECS blocks, pre-incisional intravenous (IV) ketamine and pre-incisional IV dexmedetomidine for MRM cases. They have reported practicality, simplicity, patient comfort, ERAS-protocol conformity, reduced postoperative nausea and vomiting and constipation with the alternative technique.<sup>[17]</sup> Another problematic situation can arise in geriatric patients with comorbidities and in those

with a difficult airway. In such cases, regional nerve blocks can provide better haemodynamic stability and postoperative analgesia with less perioperative complications as compared to general anaesthesia. This issue of the IJA has a randomised controlled study by Dhawan S *et al.* which emphasises that a combination of glossopharyngeal block with lignocaine gargles, superior laryngeal nerve block and recurrent laryngeal nerve block proved more beneficial and safer than general anaesthesia technique with propofol and succinylcholine for diagnostic direct laryngoscopy in American Society of Anesthesiologists (ASA) grade 3 and 4 patients with perilaryngeal lesions.<sup>[18]</sup>

Adjuvants have contributed immensely during the last few decades in popularising the nerve blocks research academics. Adjuvants like dexamethasone and dexmedetomidine have shown prolongation of block duration but the evidence on their widespread use in clinical practice is still weak. In a randomised double blind preliminary trial in MRM patients being published in this issue of the IJA, Vinod Kumar *et al.* found that the addition of 8 mg dexamethasone to 0.375% ropivacaine (0.4 ml/kg) in ultrasound guided SAP block increased the time to first rescue analgesic in the postoperative period.<sup>[19]</sup>

USG has undoubtedly made blocking nerves easier and safer. USG is a safe and excellent method of imaging peripheral nerves and guiding needles to the site of nerves; however, the use of ultrasound for nerve blocks has its own share of woes. Evidence shows that the use of ultrasound has not eliminated intraneural needle placement or the incidence of post-operative neurological symptoms after regional anaesthesia.<sup>[20]</sup>

Research on novel methods to decrease the risk of nerve injury including injection pressure monitoring, intraneural/intrafascicular local anaesthetic injection, real time 3-D visualisation by ultrasound guidance is currently underway.<sup>[21]</sup>

Technical solutions to aid USG by facilitating a clear view of the needle tip have come up. These include needle guides, alterations to needle or needle tip, three and four dimensional (3D/4D) ultrasound, electromagnetic or Global positioning system (GPS) systems, optical tracking, augmented (virtual) reality, robotic assistance and computerised needle detection. However, the evidence for these solutions is mainly from phantom studies, case reports and case series. Vibrating needle tip, needle tips with photoacoustic effect to aid

tip recognition, needle tip with sensor technology to allow needle detection at greater depth and steeper angles have been tried. 3D/4D ultrasound has been tried to monitor spread of local anaesthetic. Echogenic needles, beam steering and compound imaging have been reported to increase needle visibility.<sup>[22]</sup>

The use of ultrasound in daily clinical practice requires high precision machines and a good training of the anaesthesiologist using it. Failures and complications can occur even with the use of ultrasound for nerve blocks. Improper probe handling, advancing the needle without seeing the needle tip properly, accidental damage to structures not visible on ultrasound screen, unintentional movements leading to nerve penetration are common.<sup>[22]</sup> Experts have already predicted that, in the future, ultrasound technique will become a part of the core training of every anaesthesiologist and that ultrasound imaging will become an important component of the anaesthesia machine in the near future.<sup>[23]</sup>

Experts in radiology have voiced their concerns that if non-radiologists are not adequately trained in USG, they could leave themselves open to litigations.<sup>[24]</sup> An anaesthesiologist is a non-radiologist and even after using USG for a peripheral nerve block, if nerve injury/damage to the surrounding structures occurs, his skill in USG will certainly be questioned. Considering these medico-legal implications, it is very important, therefore, that just in the manner in which surgeons and gynaecologists have mandatory laparoscopy training, training in ultrasound techniques should be made compulsory and a part of core curriculum for all anaesthesiologists- including consultants and post-graduate students. Even under-graduate medical students in some universities in the United States get hands on training in USG in lab sessions and USG is included in the clinical exams for 3<sup>rd</sup> year students.<sup>[24]</sup> A difficult situation can arise in places wherein the ultrasound machine is not available or it is available but the anaesthesiologist is not technically confident in using it. Rajagopalan V *et al.* have come out with a novel solution for such situations. Their alternative technique of laparoscopy-guided subcostal TAP block is being published in this issue of the IJA.<sup>[25]</sup> Three cases of successful pain management by direct PEC block when USG guided PEC block was not possible due to anticoagulation problems and difficulty in appreciating the sonoanatomy have been presented in another article that adorns this issue of the IJA.<sup>[26]</sup>

Ultrasound has thus undoubtedly helped in the research, development and fast progress in newer techniques of nerve blocks. Studies on nerve blocks are a favourite topic of postgraduate dissertations nowadays. However, it is highly desirable that these studies on nerve blocks should follow all ethics correctly. Emphasising on such ethical issues, the need for testing the efficacy of a novel nerve block by comparing it with a sham (placebo) block is currently debatable.<sup>[27]</sup>

To conclude, currently, a number of novel regional nerve blocks and techniques are available; many of them form the backbone of our perioperative management; the novel local anaesthetics and adjuvants add to our flavourful regional anaesthesia cuisine. Their use makes blocking nerves certainly easy though not as easy as blocking a person on face book, WhatsApp, chats and phones, and of course the coronavirus!

Let us block all bitter memories of the year of the COVID and march ahead confidently taking all the positives of the corona pandemic into the new year which is welcoming us and whispering 'Start learning and practising novel nerve block techniques.....'

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