The Relevance of Regional Anesthesia in Orthopaedic Surgery: Advantages, disadvantages and challenges.

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Abstract: The relevance of regional anaesthesia in orthopaedic surgery cannot be overemphasized because it has aided reduction in intra-operative and postoperative pain which has always been a challenge in surgical practice. It also reduces the risk of haemorrhage and infection. Though there are complications associated with regional anaesthesia, these complications are rare and can be anticipated; thus prompt intervention measures can be instituted. The outcome of every surgical procedure takes into consideration the risks and benefit of the method, and hence, since the benefits of regional anaesthesia in orthopaedic surgery outweighs the risks, it is highly recommended. Regional anaesthesia is of great importance in orthopaedic surgery because it offers continuous but controlled analgesia. It induces hypotension which leads to a reduction in blood loss during operation. It allows early recovery and ambulation of patients, thus reducing the risks associated with prolonged bed stay, which may, in turn, affect the overall outcome of surgery. This review aims to highlight the advantages and challenges of regional anaesthesia in orthopaedic surgery. Keywords: Regional Anaesthesia, Sub-arachnoid block, Epidural Block, Orthopaedic surgery, Benefits, Challenges.

INTRODUCTION

Regional anaesthesia is a pharmacologically induced and reversible state of analgesia, loss of responsiveness, loss of skeletal reflexes, decreased stress response or all of these simultaneously affecting a large part of the body, such as a limb or lower half of the body. Regional anaesthesia is often done without interference with the patient's consciousness using a single drug or multiple drugs such as hypnotics, sedatives, paralytics and analgesics used in the correct combination (*Abenstein et al., 2004; Corning, 1884*). In some cases, regional anaesthesia can be modified to produce predominantly analgesia with minimal or moderate impairment of motor and autonomic functions, as such the term regional anaesthesia and analgesia are often used interchangeably.

ADVANTAGES

Regional anaesthesia can also be used for the treatment of conditions associated with chronic pain in orthopaedic surgery by administration of the local anaesthetic agent into the site of pain under image guidance with the aid of fluoroscopy or the c-arm. Anaesthetic agent with a long-acting, extended slow release steroid, is used for conditions like rotator cuff syndrome, plantar fasciitis and low back pain amongst other conditions associated with chronic pain (*Marx*, 1994). Regional anaesthesia allows for the early discharge of



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patients postoperatively reducing the risk of prolonged hospitalization and complications related to it such as nosocomial infections and pressure ulcers amongst other complications (Costley & Lorhan, 1972; Tessler & Kleiman, 1994; Goodwin et al., 1984; Berger & Desmonts, 1993; O' Donell & Iohom, 2008; Junger et al., 2002; Drasner, 2010).

Regional anaesthesia allows for early ambulation of patients postoperatively thus reducing the risk of atrophy of muscles and hence decreased muscle strength. Muscle strength is of utmost importance in the outcome of orthopaedics treatments. Early ambulation also reduces the risk of deep vein thrombosis, especially following major lower limb orthopaedic surgeries like total hip replacement (Junger et al., 2002).

Epidural anaesthesia allows for continuous but intermittent administration of analgesic and anaesthetic agents intra and postoperatively thus allowing for adequate management of intraoperative and postoperative pain in orthopedic surgery by continuous peripheral nerve block administered through catheter (Marx, 1994; Diz et al., 2002). Extended-release epidural anaesthesia has beneficial effects on postoperative respiratory dysfunction and reduces the rate of postoperative pneumonia (Eledjam et al., 1989). Postoperative epidural analgesia results in shorter ICU stay (Yeager et al., 1987), improved pulmonary function (Eledjam et al., 1989), less thromboembolic and cardiovascular complications (Yeager et al., 1987), earlier bowel movements and functioning (Liu et al., 1995), and shorter hospital stay (Guinard et al., 1992). The reason adduced for this is that epidural analgesia blocks stress response through pain relief and sympathetic blockade (Carvalho & Lemônica, 1998). These reasons, with active post-operative mobilization and early return to oral nutrition (Kehlet, 1997) may contribute to improved patients' evolution (Liu et al., 1995) and decreased morbidity and mortality (Kehlet, 1997), with postoperative epidural analgesia. Subarachnoid block has become an established and reliable method of providing anaesthesia. It has remained safe and effective for lower limb surgery in orthopaedics (Costley & Lorhan, 1972; Tessler & Kleiman, 1994; Goodwin et al., 1984). It also reduces the incidence of phantom limb pain post amputation (Goodwin et al., 1984).

Epidural anaesthesia which allows for adequate

postoperative management of pain reduces the exaggerated metabolic response to trauma following surgery (Milosavljevic et al., 2014). Inadequate analgesia could worsen the metabolic response to surgery leading to systemic inflammatory response syndrome (SIRS) and multiple organ failure amongst other complications (Milosavljevic et al., 2014).

The onset of action of analgesia in sub-arachnoid regional technique is about 5 mins. (Abenstein et al., 2004), hence quick onset of surgery and less waiting time. For ambulatory surgery, the anaesthesia induction time although shorter for general anaesthesia, but the recovery time from the end of operation to transfer of patient out of the operating room is shorter for regional anaesthesia when compared to regional anaesthesia (Abenstein et al., 2004; Corning, 1884). The use of regional anaesthetic technique hence reduces discharge time for day-case surgery (Berger & Desmonts, 1993). Furthermore, epidural anaesthesia is of particular relevance in orthopaedic surgery because several shots of the anaesthetic agent can be given intraoperatively taking into cognizance the patient's threshold for pain. Spinal anaesthesia also has significant neuromuscular blockade.

Most surgeries in orthopaedics usually involve significant blood loss. As a side effect, central neuraxial anaesthesia causes hypotension which is of advantage in orthopaedic surgery as it reduces blood loss (Popping et al., 2008). Central neuraxial blockade minimizes the risk of haemodynamic instability. However, blood pressure and pulse rate should be are closely monitored to prevent the risk of severe hypotension and bradycardia that may be associated with central neuraxial blockade (Marx, 1994).

Epidural and spinal anaesthesia represent safe and simple methods for surgeries of the lower limbs because of its simplicity and handiness (Neal et al., 2010). Subarachnoid and epidural nerve blocks which are regional methods of nerve block are reserved for surgeries in orthopaedics that involve the lower limb thereby reducing the risk associated with general anaesthetic technique (Abenstein et al., 2004). The orthopaedic surgeon can give instructions that may assist surgery to the patient, converse with and reassure his patient.

DISADVANTAGES

Epidural anaesthesia does not cause significant neuromuscular block unlike spinal anaesthesia unless specific local anaesthetic agent is used to block motor fibres (*Abenstein et al., 2004*). This technique may interfere with full muscle relaxation that is needed for effective manipulations in orthopaedic surgery. There is increased incidence of post-operative reactionary bleeding when blood pressure rises to its pre-operative level especially if the patient's blood pressure is allowed to remain too low during surgery. This approach therefore increases the risks of postoperative haemorrhage, with its attendant haemodynamic instability.

Spinal anaesthesia allows for only one shot of the anaesthetic agent to be injected into the subarachnoid space. Catheters are not used in spinal anaesthetic technique, hence there may be the need for re-administration of anaesthetic agents using other anaesthetic methods depending on the duration of the surgery and patients reaction to pain (*Abenstein et al., 2004*). These come with challenges and complications.

Subarachnoid nerve block and epidural nerve block carry the risk of inadvertent direct injection of the local anaesthetic agent into the nerve fibres thereby causing neurotoxicity, neurapraxia or some form of total nerve damage leading to paralysis of a limb. Thus a surgery attempted to salvage or restore an injured, or a deformed limb to its physiological state would, therefore, end up causing more damage, hence essence of the operation is defeated.

The onset of Epidural analgesia is about 30 minutes following administration (*Abenstein et al., 2004*), in contrast to intra-venous or general anaesthesia that takes just seconds. This delay in onset of action prolongs the time of surgery because most orthopaedic surgeries are long-lasting in duration hence adding more pressure in the already limited and stretched operating room availability. This can be a challenge considering the large volume of cases and limited available resources, particularly in low and middle-income countries.

There is also the risk of total spinal which is a rare but occasional complication of neuraxial anaesthesia. This complication occurs when the anaesthetic agent meant to block the sensory and motor roots of the nerves in the subarachnoid block, now ascends higher than the preferred level and end up blocking the sympathetic outflows leading to profound hypotension, haemodynamic instability and sometimes cardiac arrest. Inadvertent introduction of local anesthetics into the intracranial subarachnoid space has been reported during attempted interscalene (*Ross & Scarborough, 1973*), epidural (*De Saram, 1956*), and spinal blocks (*Gupta et al., 1994*). In some cases of total spinal anesthesia produced during neuraxial blocks, the mechanism of production was obscure (*Gupta et al., 1994*; *Leivers, 1990; Waters et al., 1994; Park et al., 1998*). If not identified early and corrected, it often results in catastrophic consequences which may include death (*Bier, 1899*).

CHALLENGES

Regional anaesthesia with all its above-outlined advantages and benefits in orthopaedic surgery also has its problems. Risk of inadvertent injection of the local anaesthetic agent directly into the nerve may lead to toxicity predisposing to neuropraxia or irreversible damage of the nerve. Hence paralysis of an affected limb and permanent loss of sensation (*Bier, 1899*).

There is a potential risk of cardiac arrest associated with regional anaesthetic techniques especially the total intravenous anaesthetic technique that makes use of two tourniquets (*Bier*, 1899). The proximal tourniquet occludes venous return to the heart while concentrating the anaesthetic agent in the peripheral veins and the tissues in the operation area. If the proximal tourniquet is not firmly applied especially in surgeries involving the arm, there could be a gradual backflow of the anaesthetic agent to the heart thus predisposing to cardiac arrest (*ASA*, 2004) and ultimately death.

Cerebral manifestations of such systemic leakage of anaesthetic agents may either be due to stimulation or selective inhibitory effects of the cortex or subcortical centers (*Corning, 1884; Bier, 1899*). Signs and symptoms may range from restlessness, tinnitus, lightheadedness, circumoral pallor where visible, hypertension to twitching and frank convulsions which could be followed by coma and depression of the central nervous system which may put the cardio-respiratory system in danger. Seizures are one of the challenges of regional anaesthesia, and it may follow sudden abnormal discharge of impulses from the brain, which could occur intra-operatively or postoperatively.

There is associated failure rate of 1-10% following regional anaesthesia (*Junger et al., 2002*), thus general anaesthesia may become necessary even when a procedure was initially not planned to be conducted under general anaesthesia. Therefore, there is the need for regional anaesthesia to be carried out in fully equipped and staffed hospitals with capacity and capability to provide safe general anaesthesia should it be needed following the failure of the regional technique.

Local Anaesthetic Systemic Toxicity (LAST) is a potentially life-threatening complication of regional anaesthesia (Goodwin et al., 1984). Some peripheral nerve blocks commonly use large doses of local anaesthetics. Local anaesthetic system toxicity can either be minor (with central nervous system features like agitation) (Neal et al., 2010; Lee et al., 2008; Drasner, 2010) or major (seizures and cardiac arrest) due to toxicity (Neal et al., 2010; Di Gregorio et al., 2010). According to the American Society of Anaesthesiologists, Closed Claims database indicates that LAST is a significant source of morbidity and mortality following peripheral nerve block, being associated with 7 of 19 claims involving death or brain damage (Vincent et al., 2007). Although life-threatening, LAST rarely occurs in the contemporary practice of peripheral nerve block. There are important risk factors, such as the site of injection, local anaesthetic type, dosage, body weight and technology used to perform the peripheral nerve block (Vincent et al., 2007).

Spinal shock, a known complication of regional anaesthesia was first defined by Whtyy in 1750 as loss of sensation accompanied by motor paralysis with an initial loss but gradual recovery of reflexes, following a spinal cord injury, most often in a complete transection. Reflexes in the spinal cord caudal to the spinal cord injury are depressed or absent while those rostral to the lesion are unaffected. Autonomic dysreflexia may occur. Vasovagal hypotension and bradyarrhythmias may also occur. Unchecked sympathetic stimulation below the injury may lead to extreme hypertension, loss of bladder/bowel control, sweating, headaches and other sympathetic effects (*Di* Gregorio et al., 2010; Barrington et al., 2009; Abrahams et al., 2009). These may all occur in some cases of spinal anaesthesia.

Post-dural puncture headache or post-spinalheadache occurs following puncture of the dura matter with loss of cerebrospinal fluid into epidural space (*Sites et al., 2012; Amata, 1994*). Such perforation may occur accidentally in sub-arachnoid spinal anaesthesia and much less so in epidural anaesthesia. There is an increased tendency of occurrence if there is excessive movement of the upper trunk or head during injection of the anaesthetic agent. It presents with a severe headache which is mostly bi-frontal or occipital and nausea that worsens when the patient assumes the upright position.

Other adverse effects of regional anaesthesia include inadvertent intravascular injection, allergic/anaphylactic reactions to the anaesthetic agent and infections following such injections. Cardiovascular complications include myocardial depression, vasodilatation, interference with the electrical conducting system of the heart, altered sympathetic innervations, and depression of cardiovascular centres (Tucker et al., 1972). Other challenges of the neuraxial blockade are related to complications of the procedure, which can result from the procedure itself or from the drugs used in the procedure. These include infective complications such as abscesses (epidural, subdural), bacterial meningitis, post-dural puncture headache, aseptic meningitis, chemical arachnoiditis. Others include cauda equina syndrome, subdural haematoma, subarachnoid spread of drug, damage to spinal needle or catheter, misplacement or migration of epidural catheter, failure of the epidural component and failure of the spinal component in cases of CSEA occasionally requiring conversion to an unwanted general anaesthesia (Arendt & Segal, 2008).

Inadvertent vascular or nerve puncture leading to haemorrage, systemic dissemination and irreversible nerve damage respectively are challenges of regional anaesthesia that can be reduced by ultrasound-guided procedures (*Tucker et al., 1972; Ismail, 2015; Mulroy & Hejtmanek, 2010*). Ultrasound-guided peripheral nerve block (*PNB*) reduces the incidence of inadvertent puncture and reduces local anaesthetic requirements when compared with nonultrasound techniques (*Tucker et al., 1972; Ismail, 2015;*

Mulroy & Hejtmanek, 2010).

Local Anaesthetic Systemic Toxicity can also be reduced by employing the ultrasound-guided nerve block. This reduction in the risk of LAST may be due to secondary delayed absorption of local anaesthetic. Ultrasound-guided PNB may be executed successfully with reduced local anaesthetic doses (Tucker et al., 1972; Ismail, 2015; Mulroy & Hejtmanek, 2010). There exists a plausible mechanism for ultrasound-guided nerve block reducing the incidence LAST from either inadvertent intravenous injection or delayed absorption of a tissue depot of local anaesthetic. However, factors unrelated to ultrasound imaging such as the site of injection, patient co-morbidities and other practice patterns may contribute to LAST (Tucker et al., 1972; Ismail, 2015; Mulroy & Hejtmanek, 2010). One recommendation for preventing local anaesthetic systemic toxicity is the use of intravascular marker such as epinephrine.

Cardiovascular complications like myocardial depression, vasodilatation, interference with the electrical conducting system of the heart, altered sympathetic innervations, and depression of cardiovascular centers are known challenges (ASA, 2004; Bier, 1899). These are challenges to the orthopaedic surgeon as this may lead to morbidity, lengthen the operation time, affect the outcome of surgery negatively and if not identified and prompt resuscitative measures are not instituted, could lead to the death of the patient secondary to anaesthetic complication and not necessarily the orthopaedic pathology. This challenge can be anticipated and prevented. Interventions are aimed at improving cardiac output by raising the legs of the patient, avoiding abrupt removal of tourniquet if applied, intravascular volume expansion by administration of intravenous fluids pre-operatively, intraoperatively and if necessary postoperatively. Injection of vasopressors, injection of atropine if there is bradycardia, administration of supplemental oxygen to improve oxygen delivery to tissues, and full cardiopulmonary resuscitation if there is evidence of cardiopulmonary arrest (ASA, 2004; Abenstein et al., 2004) are critical interventions.

Cerebral or central nervous system manifestations may either be due to stimulation or selective inhibitory effects of the cortex or subcortical centres (ASA, 2004). Convulsions should be aborted immediately with an anticonvulsant that does not affect the respiratory centres to cause respiratory depression (ASA, 2004). Drugs like thiopentone are to be used with maximal caution. Diazepam is a safer alternative. If convulsions are still difficult to control, a short-acting muscle relaxant may be given and ventilation controlled during periods of apnoea (ASA, 2004; *Bier, 1899*).

The incidence of true anaphylactic reaction to anaesthetic agents due to allergy is rare (*Bier, 1899*). An awareness of this challenge during surgery is important since it can quickly become fatal. Urticaria, angioneurotic oedema, bronchospasm, and circulatory collapse are common features of an anaphylactic reaction. The management of such reaction would include administration of corticosteroids, antihistamines, oxygen, bronchodilators, intravenous fluids, and vasopressors. However, as a preventive measure, the presence or absence of drug allergy in all patients scheduled for local anaesthesia should be sought and an intra-cutaneous test done in those with a positive history (*ASA*, 2004).

Post-anaesthesia dural puncture headaches can be prevented by making a self-closing puncture in the dura, using a simple beveled needle with a specific angle and bevel orientation (*Turnbull & Shepherd, 2003; Hatfalvi,* 1995). Treatment of post dural puncture headache, if it has already occurred, involves analgesia and bed rest but if persistent and severe, an epidural blood patch is the mainstay of treatment.

REFERENCES

Abenstein, JP; Long, KH; MCGlinch, BP; Dietz, NM. (). Is physician anesthesia cost-effective? Anesthesia and Analgesia. 2004; 98(3): 750-757.

Abrahams MS, Aziz MF, Fu RF, Horn JL. Ultrasound guidance compared with electrical neuro-stimulation for peripheral nerve block: a systematic review and metaanalysis of randomized controlled trials. Br J Anaesth. 2009; 102(3): 408-17.

Amata OA. Incidence of post-spinal headache in Africans. West Afr J Med. 1994; 13:53-5.

American Society of Anesthesiologists (ASA). Continuum of Depth of Sedation. Definition of General Anesthesia and Levels of Sedation / Analgesia. [Internet]. Washington D.C.: American Society of Anesthesiologists (ASA); October 27, 2004. Available at: http://www.asahq.org/~/ media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/continuum-of-depth-of-sedation-definition-of-general-anesthesia-and-levels-of-sedation-analgesia.pdf.

Arendt K, Segal S. Why Epidurals Do Not Always Work. Rev Obstet Gynecol. 2008; 1(2): 49–55.

Barrington MJ, Watts SA, Gledhill SR, Thomas RD, Said SA, Snyder GL, Tay VS, Jamrozik K. Preliminary results of Australasian Regional Anasthesia Collaboration: a prospective audit of more than 7000 peripheral nerve and plexus blocks for neurologic and other complications. Reg Anaesth Pain Med. 2009; 34:534-41.

Berger JL, Desmonts JM. Loco-regional anesthesia for surgery of limbs. Ann Chir. 1993; 47(5);446-50.

Bier A. Experiments on cocainization of the spinal cord. Deutsche Zeitschrift fur Chirurgie. 1899;51: 361-9.

Carvalho WA, Lemônica L. Mecanismos centrais de transmissão de modulação da dor. Atualização terapêutica. Rev Bras Anestesiol. 1998; 48:221-241.

Corning JL. A further contribution on local medication of the spinal cord, with cases. NY Med J. 1884; 40: 643-4.

Costley DO, Lorhan PH. Intravenous regional anaesthesia. Survey of Anaesthesiology. 1972; 16(4):359-60.

De Saram M. Accidental total spinal analgesia. Anaesthesia. 1956; 11(1):77-79.

Di Gregorio G, Neal JM, Rosenquist RW, Weinberg GL. Clinical presentation of local anaesthetic system toxicity: a review of published cases. 1979 to 2009. Reg Anesth Pain Med. 2010; 35(2): 181-187.

Diz J.C, Franco A, Bacon DR, Rupreht J, Alvarez J. (eds). The history of anaesthesia: proceedings of Fifth international Symposium. Amsterdam: Elsevier, 2002. 205-6.

Drasner K. Local anaesthetic systemic toxicity: a historical perspective. Reg Anaesth Pain Med. 2010; 35: 162-66.

Eledjam JJ, de la Coussaye JE, Viel E. Techniques of locoregional anesthesia of the lower limb. Phlebologie. 1989; 42(1):31-43.

Goodwin DRA, Rubenstein N, Otremski I. Intravenous anaesthesia in the upper limb; a review of 225 cases. Int Orthop. 1984;8(1): 51-4.

Guinard JP, Mavrocordatos P, Chiolero R, Carpenter RL. A randomized comparison of intravenous versus lumbar and

thoracic epidural fentanyl for analgesia after thoracotomy. Anesthesiology. 1992; 77(6):1108-1115.

Gupta A, Enlund G, Bengtsson M, Sjoberg F. Spinal anaesthesia for caesarean section following epidural analgesia in labour: A relative contraindication. Int J Obstet Anesth. 1994; 3(3):153-6.

Hatfalvi BI. "Postulated Mechanisms for Post Dural Puncture Headache: Clinical experience and Review of Laboratory Models". Reg Anesth. 1995; 20 (4): 329-36.

Ismail S. Ultrasound Guided Central Neuraxial Block. Anaesth Pain & Intensive Care. 2015; 19(3):361-365.

Junger A, Klasen J, Hartmann B, Benson M, Rohrig R, Kuhn D, Hempelmann G. Shorter discharge time after regional or intravenous anaesthesia in combination with laryngeal mask airway compared with balanced anaesthesia with endotracheal intubation. Anaesthesiol. 2002; 19(2):119.

Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997; 78(5): 606-617.

Lee LA, Posner KL, Cheney FW, Caplan RA, Domino KB. Complications associated with eye blocks and peripheral nerve blocks: an American Society of Anaesthesiologists closed claims analysis. Reg Anesth Pain Med. 2008; 33:416-422.

Leivers D. Total spinal anesthesia following early prophylactic epidural blood patch. Anesthesiology. 1990; 73:1287-9.

Liu SS, Carpenter RL, Mackey DC. Thirlby RC, Rupp SM, Shine TS, Feinglass NG, Metzger PP, Fulmer JT, Smith SL. Effects of perioperative analgesic technique on rate of recovery after colon surgery. Anesthesiology. 1995; 83(4):757-765.

Liu SS, Carpenter RL, Neal JM. Epidural anesthesia and analgesia. Their role in postoperative outcome. Anesthesiology. 1995; 82:1474-1506.

Marx GF. "The first spinal anaesthesia. Who deserves the laurels?". Reg Anesth. 1994;19 (6): 429-30.

Milosavljevic SB, Pavlovic, AP, Trpkovic SV, Ilić AN, Sekulic AD. Influence of Spinal and General Anesthesia on the Metabolic, Hormonal, and Hemodynamic Response in Elective Surgical Patients. Med Sci Monit. 2014; 20: 1833– 1840.

Mulroy MF, Hejtmanek MR. Prevention of local anaesthetic

system toxicity. Reg Anaesth Pain Med. 2010; 35: 177-80.

Neal JM, Bernards CM, Butterworth JF, Di Gregorio G, Drasner K, Hejtmanek MR, Mulroy MF, Rosenquist RW, Weinberg, GL. American Society Of Regional Anaesthesia Practice Advisory on local anaesthetic systemic toxicity. Reg Anesth Pain Med. 2010; 35:152-161.

O' Donell BD, Johom G. Regional anaesthesia technique for ambulatory orthopedic surgery. Curr Opin Anaesthesiol. 2008; 21(6): 723-8.

Park PC, Berry PD, Larson MD. Total Spinal Anesthesia following Epidural Saline Injection after Prolonged Epidural Anesthesia. Anesthesiology 11. 1998; 89: 1267-1270.

Popping DM, Zahn PK, Van Aken HK, Dasch B, Boche R, Pogatzki-Zahn EM. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. Br J Anesth. 2008;101(6): 832-40.

Ross S, Scarborough CD. Total spinal anesthesia following brachial plexus block. Anesthesiology. 1973; 39:458-60.

Sites BD, Taenzer AH, Herrick MD, Gilloon C, Antonakakis J, Richnis J, Beach ML. Incidence of local anaesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound guided nerve blocks: an analysis from a prospective clinical registry. Reg Anaesth Pain Med. 2012; 37(5):478-482.

Tessler MJ, Kleiman SJ. Spinal anaesthesia for patients with previous lower limb amputations. Anaesthesia. 1994; 49(5):439-41.

Tucker GT, Moore DC, Bridenbaugh PO, Bridenbaugh LD, Thompson GE. Systemic absorption of mepivacaine in commonly used regional block procedures. Anesthesiology. 1972; 37:277-87.

Turnbull DK, Shepherd DB. "Post dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth. 2003; 91(5): 718-29.

Vincent O, Hubler M, Kirschner S, Koch T. The value of regional anaesthesia and general anaesthesia in orthopaedic surgery. Orthopade. 2007; 36(6): 529-36.

Waters JH, Leivers D, Hullander M. Response to spinal anesthesia after inadequate epidural anesthesia (letter). Anesth Analg. 1994; 78:1033-4.

Yeager MP, Glass DD, Neff RK, Brinck-Johnsen T. Epidural

anesthesia and analgesia in high-risk surgical patients. Anesthesiology. 1987; 66(6):729-736.