



Review Article on Local and Spinal Anaesthesia

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Review Article

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Abstract

Anaesthesia is a state of controlled, temporary loss of sensation or awareness that is induced for medical purposes. It may include some or all pain relief, muscle relaxation, loss of memory and unconsciousness. Anesthesia on basis of action on body part can be divided under several heading as general, spinal and local. Spinal anesthesia is given on spine and local anesthesia is introduced locally on body part.

Keywords: Anesthesia; Local Anaesthesia; Spinal Anesthesia; Amnesia; Analgesia; Muscle Relaxant

Abbreviations: MW: Molecular Weight; PABA: Para-Amino Benzoic Acid.

Introduction

The term anesthesia, derived from the Greek term *anaesthesia* from *an*-“without” + *aesthesia*- “sensation”, meaning ‘insensibility’, is used to describe the loss of sensation to the entire or any part of the body. The term anaesthesia was first used by Oliver W. Holmes to denote the state that incorporates amnesia, analgesia, and narcosis to make painless surgery possible. Anesthesia can be classified into two main categories: general anesthesia and regional anesthesia.

Local anesthesia is any technique to induce the absence of sensation in a specific part of the body, generally for the aim of inducing local analgesia, that is, local insensitivity to pain, although other local senses may be affected as well. It allows patients to undergo surgical and dental procedures with reduced pain and distress.

Spinal anaesthesia also called spinal block, sub-arachnoid block, intradural block and intrathecal block, is a form of

neuraxial regional anaesthesia involving the injection of a local anaesthetic or opioid into the subarachnoid space [1].

Components of balanced anesthesia are:

- Amnesia
- Hypnosis
- Analgesia
- Immobilization or muscle relaxation
- Quick acting and rapid recovery
- No toxic effects - large margin of safety [2].

Methodology

A thorough search was made on Google, PubMed, Research Gate and Medical Wikipedia. Also various textbooks and published PowerPoint presentation were checked to fetch important points.

Result

Historical Background

Pain control has not always been as efficacious as it currently is. Throughout our known history, people have

attempted to manage pain using many different methods and techniques. Many of the techniques previously slowly evolved over time becoming more efficient and reproducible. Baron Larrey, Napoleon's army doctor, noted the ease and relative patient comfort when amputating limbs that were nearly frozen during Napoleon's invasion of Russia. In nineteenth century the British physician, Benjamin Ward Richardson, used the technique of spraying ether onto the surgical site, in order to desensitize it. A major breakthrough in modern local anesthesia was made in 1841 when Zophar Jayne, an American physician, created the framework for the modern hypodermic syringe. In 1860, Nieman isolated first local anaesthetic agent from leaves of Coca tree. Karl Koller published his first paper on the use of cocaine in eye surgery in 1884.

Surgeons did not quickly adopt the use of cocaine as an anesthetic. However, dentists began using it subcutaneously for tooth extraction. In 1855, Corning accidentally administered cocaine intrathecally. In 1891, Quincke made use of spinal puncture in diagnosis. In 1898 August Bier of Germany introduced the technique of spinal anesthesia and Pitkin popularized the method of introducing agent's intrathecally. In 1905, first effective and widely used synthetic local anesthetic Procaine produced by Einhorn from benzoic acid and diethyl amino ethanol. The most recent major innovation came in 1949 when the Swedish pharmaceutical company Astra introduced Lidocaine to the market. Lidocaine, also known as Xylocaine, was the first non-ester local anesthetic available. Lidocaine proved to have even fewer side effects than procaine while instilling even deeper anesthesia. There are three main types of local anesthetics that are clinically used today. Lidocaine 2% with epinephrine 1:100,000, Bupivacaine 5% with epinephrine 1:200,000 is used for longer procedures. Mepivacaine is the

most common local anesthetic, if the use of epinephrine is contraindicated. This anesthetic is used for short procedures and when vasoconstriction is less imperative. Another novel breakthrough in local anesthesia that has yet to catch on widely came in 2009, when an injectable form of phentolamine mesylate, a vasodilator that reverses local anesthesia, was introduced to the market. Currently, there is ongoing research on how to decrease the pain during the application of local anesthesia [3-5].

Local Anesthetic Agents

The clinically useful local anesthetic agents can be divided chemically into the amino-esters, e.g., procaine, chlorprocaine and tetracaine, and the amino-amides, e.g., lidocaine, mepivacaine, prilocaine, bupivacaine and etidocaine. Pharmacologically, these agents can be categorized as agents of low potency and short duration of action, e.g., procaine and chlorprocaine; agents of intermediate potency and duration of action, e.g., lidocaine, mepivacaine and prilocaine; and agents of high potency and long duration, e.g., tetracaine, bupivacaine and etidocaine [6].

Pharmacology of Local Anaesthetics

Local anaesthetic drugs are water-soluble salts of lipid-soluble alkaloids. The structure of local anaesthetics consists of three components: a lipophilic aromatic group, an intermediary link and a hydrophilic amine group Figure 1. The intermediary link categorises local anaesthetics into esters or amides Table 1 [7]. For example, increasing the length of carbon chains attached to either the aromatic ring, amide linkage or the tertiary amine offers higher lipid solubility, potency and increased duration of action.

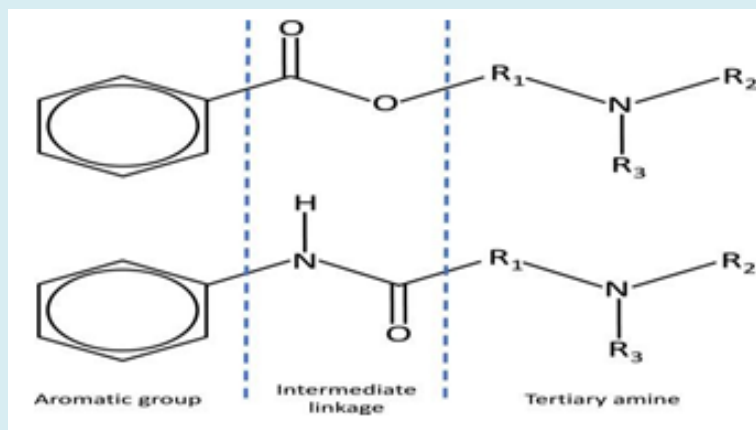


Figure 1: Structure of ester (top) and amide local anaesthetics. Each contains an aromatic group, an intermediate linkage (ester/amide), and a tertiary amine Figure 1 [8-10].

Structural classification	MW	pKa	Protein binding(%)	Partition Coefficient	Onset	Elimination half life (min)	Maximum dose without vasoconstrictor	Maximum dose with vasoconstrictor
Cocaine	Ester	311	8.6	95	-	Fast	100	-
Chloroprocaine	Ester	271	9.1	-	17	Fast	6	11
Prilocaine	Ester	220	7.7	55	50	Fast	100	6
Lidocaine	Amide	234	7.8	70	110	Fast	100	3
Mepivacaine	Amide	246	7.7	77	42	Fast	115	5
Bupivacaine	Amide	288	8.1	95	560	Moderate	210	2
Ropivacaine	Amide	274	8.1	94	230	Moderate	120	3
Levobupivacaine	Amide	288	8.1	95	-	Moderate	210	2

Table 1: Physicochemical characteristics of local anaesthetics [8-10] MW, molecular weight.

Replacement of the tertiary amine by a piperidine ring increases lipid solubility and duration of action; the addition of a butyl group in place of the amine on the benzene ring of procaine gives tetracaine (amethocaine); and the addition of a propyl or butyl group to the amine end of mepivacaine results in ropivacaine or bupivacaine, respectively. Compared to bupivacaine, ropivacaine's propyl group gives a lower lipid solubility that causes it to penetrate large myelinated motor fibres to a lesser extent, giving a more selective sensory blockade [8].

Bupivacaine exists in two enantiomers, which are mirror images of each other. Although structurally identical, enantiomers can exhibit clinical differences including potency and adverse effects. The discovery of a selective blockade of cardiac Na⁺ channels by the dextro- enantiomer of bupivacaine led to the creation and widespread use of two levo-enantiomers: levobupivacaine and ropivacaine [9]. These exhibit lower potency at myocardial Na⁺ and K⁺ channels and have less effect on myocardial electrical conduction and contractility compared to bupivacaine.

Enantiomers were historically classified according to their ability to rotate the plane of polarised light. For example, the prefix dextro indicates clockwise rotation and the prefix levoindicates anticlockwise rotation of polarised light. Alternatively, enantiomers may be classified by the order of atoms around the central carbon molecule. For example, in a rectus (*R*) configuration, atomic mass reduces in a clockwise direction whereas the opposite occurs in the sinister (*S*) configuration.

Pharmacological Properties of Local Anaesthetics

The speed of onset, potency and duration of local anaesthetics is dependant on the pKa, lipid solubility and

protein binding, respectively.

pKa

The dissociation of amphipathic local anaesthetics is determined by their pKa and the pH of the tissue into which they are injected.

The pKa is the pH at which the ionised and un- ionised forms are present in equal amounts. For bases, such as local anaesthetics, the higher the pKa, the greater the ionised fraction in solution. The ratio of the two states is described by the Henderson-Hasselbalch equation:

$$\log [A^-]/[AH] = pKa - Ph$$

where [A⁻] is the ionised form and [AH] is the non-ionised form.

As rate of diffusion across the nerve sheath and nerve membrane is related to the proportion of non-ionised drug, local anaesthetics with low pKa have a fast onset of action, and local anaesthetics with a high pKa have a slow onset of action. For example, lidocaine (pKa=7.8) has a fast onset in comparison with bupivacaine (pKa=8.1), because at pH 7.4 a greater proportion of lidocaine exists in the non-ionised form. Inflamed and infected tissue is more acidemic, and therefore more local anaesthetic exists in the ionised form, reducing the amount of un-ionised drug available to cross the nerve and provide analgesia. The pH of tissue can be affected by adjuvants, for example, some clinicians add bicarbonate to speed the onset of epidural anaesthesia.

Molecular Weight

The smaller the molecular weight, the more rapidly molecules diffuse through membranes.

Lipid Solubility

Lipid solubility and potency are closely related. The lipid solubility of local anaesthetics is expressed as the partition coefficient, which is defined as the ratio of concentrations when local anaesthetic is dissolved in a mixture of lipid and aqueous solvents. Greater lipid solubility enables more rapid diffusion through lipid membranes to reach their site of action, influencing the speed of onset, although—as outlined above—other factors are also important. In addition, greater lipid solubility gives a greater volume of distribution.

Protein Binding

Local anaesthetics with high protein binding to α_1 -acid glycoprotein have a longer duration of action and lower bioavailability. Hypoxia, hypercarbia, and acidaemia all decrease protein binding, and increase the risk of toxicity. Children younger than 6 months have less protein binding capacity.

Vasoactivity

The vasoactivity of local anaesthetics influences potency and duration of action. For example, more rapid absorption occurs after lidocaine administration compared to bupivacaine.

Levobupivacaine and ropivacaine have a bimodal vasoactive response. Both vasodilate at clinical doses and vasoconstrict at subclinical doses. Concentrations of adrenaline as low as 1:800,000 are sufficient to cause vasoconstriction in tissues in the presence of local anaesthetics.

Pharmacokinetics Absorption

The absorption of local anaesthetics is dependent on the site of injection, rate of injection, dosage and vasoactivity of the injectate. Typically, intrapleural block is associated with the highest absorption and subcutaneous infiltration with least absorption. The order of peak plasma concentration after a single dose is intrapleural > intercostal > lumbar epidural > brachial plexus > subcutaneous > sciatic > femoral.

Distribution

Esters local anaesthetic agents are less protein bound than amide local anaesthetics (Table 1). Tissue distribution tends to be proportional to the tissue/blood partition coefficient of the local anaesthetic, and the mass and perfusion of the tissue.

Metabolism and Clearance

Ester and amide local anaesthetic agents differ concerning their metabolism and allergic potential. Esters are hydrolysed rapidly in plasma by pseudocholinesterase to the metabolite para-amino benzoic acid (PABA), which can cause an allergic reaction. Plasma half-life varies from less than 1 min (chloroprocaine) to 8 min (tetracaine) and is prolonged in the presence of atypical cholinesterase. Cocaine, unlike other esters, undergoes hepatic hydrolysis followed by renal excretion [7].

In the liver, amide local anaesthetics undergo aromatic hydroxylation, amide hydrolysis and *N*-dealkylation [7]. Amide metabolism is much slower than plasma hydrolysis, and thus amide local anaesthetics are more prone to accumulation in the presence of hepatic dysfunction or reduced hepatic blood flow [7]. Prilocaine undergoes metabolism in the lungs. Amides have a very low allergic potential themselves, and an observed reaction may be caused by an additive such as the stabilising agent methylparaben. In addition, response to vasoconstrictor adjuvants may be mistaken for allergy.

Clearance values and elimination half-times for amide local anaesthetics represent mainly hepatic metabolism because renal excretion of unchanged drug is minimal. Accumulation of metabolites may occur in renal failure.

Lidocaine has a high hepatic extraction ratio: clearance is dependent on hepatic blood flow and is relatively unaltered by changes in hepatic enzyme activity. Owing to the efficiency of the drug in dissociating from plasma proteins, entering the hepatocyte, and undergoing metabolism, the rate limiting step is hepatic perfusion. This is important in critical illness, particularly in states of low cardiac output and reduced hepatic blood flow [10].

Spinal Anesthetic Agents

Lidocaine, tetracaine, and bupivacaine are the local anesthetic agents most commonly employed for spinal anesthesia. Lidocaine provides a short duration of anesthesia and is primarily useful for surgical and obstetrical procedures lasting less than one hour. Tetracaine and bupivacaine are used for procedures lasting 2 to 5 hours. Bupivacaine may be better than tetracaine for use in orthopedic surgical procedures since it appears to be associated with a lower incidence of tourniquet pain [11].

Ideal Characteristics of Local and Spinal Anesthetics

- Its actions must be reversible.

- It should be non-irritating to the tissues.
- It should not produce any local reactions.
- It should be rapid in action
- It should have a low degree of systemic toxicity.
- It should have sufficient potency to provide complete local anaesthesia.
- It should be of sufficient duration to be advantageous.
- It should have sufficient penetrating properties.
- It should not produce allergic reactions.
- It should be stable in solution and undergo bio transformation readily within the body.
- It should be either sterile or capable of being sterilized by heat without deterioration.
- It should be stable in light.
- It should be liquid and vaporizable at room temperature.
- It should have long shelf life.
- It should not produce any permanent damage.
- It should be non-addictive.
- It should be combined with other agents.
- It should have high therapeutic ratio.

Mechanism of Action of Local Anaesthesia

Topical anesthetics reversibly block nerve conduction near their site of administration, thereby producing temporary loss of sensation in a limited area. Local anesthetics inhibit depolarization of the nerve membrane by interfering with both Na^+ and K^+ currents. The action potential is not propagated because the threshold level is never attained.

Although the exact mechanism by which local anesthetics retard the influx of sodium ions into the cell is unknown, 2 theories have been proposed. The membrane expansion theory postulates that the local anesthetic is absorbed into the cell membrane, expanding the membrane and leading to narrowing of the sodium channels. This hypothesis has largely given way to the specific receptor theory. This theory proposes that the local anesthetic diffuses across the cell membrane and binds to a specific receptor at the opening of the voltage-gated sodium channel. The local anesthetic affinity to the voltage-gated Na^+ channel increases markedly with the excitation rate of the neuron. This binding leads to alterations in the structure or function of the channel and inhibits sodium ion movement. Blockade of leak K^+ currents by local anesthetics is now also believed to contribute to conduction block by reducing the ability of the channels to set the membrane potential [12].

Mechanism of Action of Spinal Anaesthesia

Spinal anesthesia blocks small, unmyelinated sympathetic fibers first, after which it blocks myelinated (sensory and motor) fibers. The sympathetic block can exceed motor/sensory by two dermatomes [13].

Indication of Local Anaesthesia

- Incision and drainage of incised abscess.
- Removal of cysts, residual infection areas, hydrophilic groups and neoplastic growths, ranula and salivary calculi.
- In treatment of tic douloureux by producing prolonged anesthetic with the combination of a local anesthetic agent and alcohol injection.
- In dentistry- extraction of teeth and fractured roots, odontectomy, treatment of alveolgia, alveolectomy, apicoectomy.

Contraindications of Local Anaesthesia

History of allergy to local anesthetic agent or history of allergy to any of the constituent of local anesthetic solution:

- Fear and apprehension.
- Presence of acute inflammation or suppurative infection at the site of insertion of the needle
- Infants or small children.
- Mentally retarded patients.
- Epilepsy
- Hemodynamic instability
- Presence of methaemoglobinemia
- Presence of typical plasma cholinesterase [14].

Indication of Spinal Anaesthesia

It is most commonly used for surgeries below the umbilicus, however recently its uses have extended to some surgeries above the umbilicus as well as for postoperative analgesia. Procedures which use spinal anesthesia include:

- Orthopaedic surgery on.
- the pelvis, hip, femur, knee, tibia, and ankle, including arthroplasty and joint replacement.
- Vascular surgery on the legs.
- Endovascular aortic aneurysm repair.
- Hernia (inguinal or epigastric)
- Haemorrhoidectomy.
- Nephrectomy and cystectomy in combination with general anaesthesia.
- Transurethral resection of the prostate and transurethral resection of bladder tumours.
- Hysterectomy in different techniques used.
- Caesarean sections
- Pain management during vaginal birth and delivery.
- Urology cases.
- Examinations under anaesthesia.
- Spinal anaesthesia is the technique of choice for Caesarean section.

Contraindications of Spinal Anaesthesia

Prior to receiving spinal anesthesia, it is important to provide a thorough medical evaluation to ensure there are no absolute contraindications and to minimize risks and complications. Although contraindications are rare, below are some of them:

- Patient refusal
- Local infection or sepsis at the site of injection.
- Bleeding disorders, thrombocytopaenia, or systemic anticoagulation (secondary to an increased risk of a spinal epidural hematoma).
- Severe aortic stenosis
- Increased intracranial pressure.
- Space occupying lesions of the brain.
- Anatomical disorders of the spine such as scoliosis (although where pulmonary function is also impaired, spinal anaesthesia may be favored).
- Hypovolaemia e.g. following massive haemorrhage, including in obstetric patients.
- Allergy
- Relative Contraindication
- Ehlers Danlos Syndrome, or other disorders causing resistance to local anesthesia [15].

Risk and Complication of Local Anaesthesia

Various complications of local anesthetics can be evaluated systemically and locally. Common systemic reactions due to local anesthesia are reported as psychogenic reactions, systemic toxicity, allergy, and methemoglobinemia. Common local complications associated with local anesthesia are given as pain at injection, needle fracture, prolongation of anesthesia and various sensory disorders, lack of effects, trismus, infection, edema, hematoma, gingival lesions, soft tissue injury, and ophthalmologic complications [16].

Risk and Complication of Spinal Anaesthesia

Complications of spinal anesthesia can result from the physiologic effects on the nervous system and can also be related to placement technique. Most of the common side effects are minor and are self-resolving or easily treatable while major complications can result in more serious and permanent neurological damage and rarely death. These symptoms can occur immediately after administration of the anesthetic or be delayed.

Common and minor complications include:

- Mild hypotension
- Bradycardia
- Nausea and vomiting.
- Transient neurological symptoms (lower back pain with pain in the legs).

- Post-dural-puncture headache or post-spinal headache.

Serious and permanent complications are rare but are usually related to physiologic effects on the cardiovascular system and neurological system or when the injection has been unintentionally at the wrong site. The following are some major complications:

- Nerve injuries: Cauda equina syndrome, radiculopathy.
- Cardiac arrest.
- Severe hypotension.
- Spinal epidural hematoma, with or without subsequent neurological sequelae due to compression of the spinal nerves.
- Epidural abscess.
- Infection (e.g. meningitis) [17].

Discussion

Local and spinal anesthesia is one of the biggest achievements in the history of medicine which have made surgical procedure more convenient. They both serve the purpose of providing pain relief during surgical procedures but they differ in their mechanism of actions, applications and potential complications. Local anesthesia is primarily utilized for superficial procedures, providing targeted pain relief with minimal systemic effects. In contrast, spinal anesthesia offers excellent surgical anesthesia and prolonged postoperative pain control for specific surgical procedures. The choice between the two techniques depends on the surgical requirements, patient characteristics and the expertise of the anesthesiologist. Understanding the unique features of local and spinal anesthesia enables healthcare professionals to optimize patient care and ensure safe and effective pain management during surgical interventions.

The objective of modern anesthesia is to rapidly induce anesthesia, maintain the state and rapid recovery. For which balanced anesthesia has been devised this comprises of combination of several anesthetic agents in appropriate doses along with detailed pre-anesthetic assessment, premedication and better cardiorespiratory monitoring. General anesthesia despite being critical in surgery and invasive procedures, its exact mechanism of action is still unclear. However, action of different anesthetics on different level of receptors is being studied to know the mechanism of local and spinal anesthesia. This indicates need of further more researches on this topic.

Anesthesia is a huge and a vague topic that requires lots of studies and researches to be done to devise best anesthetics and technique to reduce any possible adverse effects or pre or postoperative complications.

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