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Intrathecal spinal anesthesia for Cesarean Section: Possible role of Dexmedetomidine as Adjuvant to Hyperbaric Prilocaine (2%) or Bupivacaine (0.5%)

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Abstract: Various local anesthetics have been explored for spinal anesthesia, falling into two primary categories: esters and amides. Initial investigations focused on esters like cocaine and amylocaine. However, amylocaine is no longer used in clinical practice. Procaine, known as Novocain, was synthesized and saw research into its intrathecal use. Procaine gained popularity due to its presumed systemic effects and concerns over the neurotoxicity of spinal cocaine administration. Notably, procaine's side effects often include nausea, vasomotor paralysis, and an elevated risk of anaphylaxis due to its metabolite para-aminobenzoic acid (PABA). Subsequently, bupivacaine, an intermediate to long-acting amide local anesthetic, was discovered, synthesized, and widely applied clinically. Concerns about potential toxicity led to research on two (S)-enantiomers of bupivacaine for spinal anesthesia. Initial studies on spinal ropivacaine (the S-enantiomer of bupivacaine) were conducted. Further investigations into the other pure (S)-enantiomer of bupivacaine, levobupivacaine, began. Intrathecal administration of both levobupivacaine and ropivacaine continues to be explored. After chloroprocaine's approval, mepivacaine and prilocaine were introduced for spinal anesthesia. Both of these medications, also xylidine derivatives, displayed similar potency to lidocaine. However, due to concerns about transient neurologic symptoms associated with intrathecal lidocaine administration, mepivacaine and prilocaine are being further investigated as alternatives for ambulatory or short to moderate duration surgeries

Keywords: *Intrathecal spinal anesthesia, Cesarean Section, Dexmedetomidine, Adjuvant, Hyperbaric Prilocaine, Bupivacaine*

Introduction

A fundamental knowledge of vertebral anatomy and its relationship to associated neurological and vascular structures is essential to the successful and safe placement of an Intrathecal spinal anesthesia [1].

The Bony Anatomy

The spinal column consists of 24 true vertebrae and two sets of fused vertebrae (total of 33 vertebrae) stacked upon one another from the cranium to the tip of the coccyx. This column forms the bony enclosure of the spinal cord and supports the weight of the body while allowing mobility in multiple spatial planes. The vertebrae are classified according to their location and structure. The first 7 extend from the base of the cranium through the neck and are called cervical vertebrae. Of these, the first and second vertebrae, referred to as the atlas and axis, respectively, are atypical. Their unique articulations allow for a wider range of movement than can occur in other areas of the axial skeleton. Attached to the ribs, the thoracic vertebrae comprise the next 12 segments followed inferiorly by 5 lumbar vertebrae. The most caudal portion of the vertebral column consists of 5 fused sacral vertebrae and 4 small rudimentary coccygeal vertebrae [2].

Although vertebrae differ in their structure and function depending on their location, most of the articulating vertebrae are comprised of a body, an arch, and seven processes (Fig. 1). The vertebral body is the largest and most anterior structure, providing strength to the vertebral column. The intervertebral discs, which function as shock absorbers to the axial skeleton, separate the vertebral bodies. Pedicles arise from the vertebral body and project posterior to join paired, adjoining laminae. Together, these form the vertebral arch that provides the bony protection of the spinal column [3].

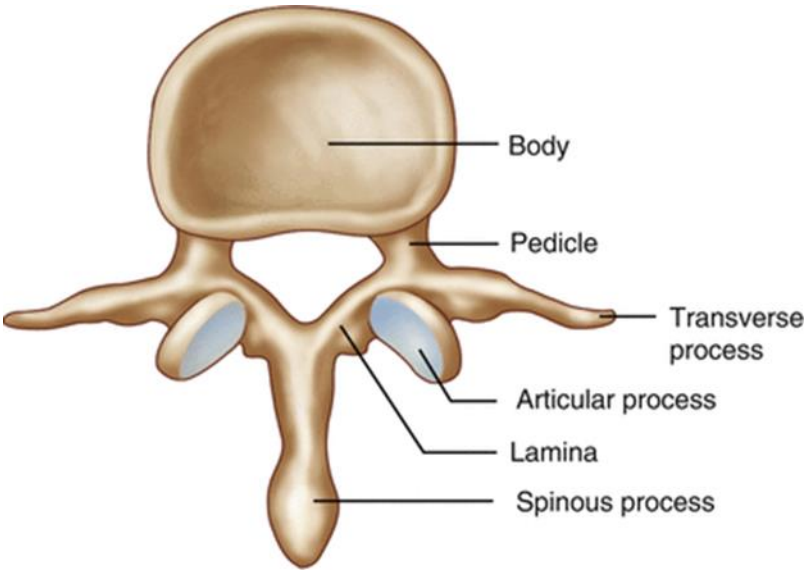

Fig (1): Structure of a vertebra [4]

Seven processes arise from the vertebral arch. At the junction of the right and left laminae, the spinous process projects posteriorly. A spinous process overlaps the process below it with progressively steeper projections from the lumbar to the thoracic regions. This often makes placement of an epidural via the midline approach challenging in the mid- to upper thoracic region. Transverse processes arise from the vertebral arch at the junction of the lamina and pedicle and project posterolaterally. Superior and inferior articular processes project from the junction of the lamina and pedicle. Each articular process has an associated articular facet, enabling extension and flexion of the spine. The spinous and transverse processes allow for the attachment of the deep back muscles, while the articular process restricts movement in particular directions [5].

The vertebral column has four normal curvatures—cervical, thoracic, lumbar, and sacral. The thoracic and sacral curvatures are concave anteriorly, while the cervical and lumbar are concave posteriorly. This importance becomes apparent when considering the baricity of anesthetic solutions and their distribution in

the intrathecal space depending on the position of the patient immediately following intrathecal injection of an anesthetic [6].

Ligaments

Multiple ligaments link the bony components of the spinal column. They provide a path through which the epidural or intrathecal space may be accessed by a traversing needle. The most posterior of these ligaments and, therefore, the first encountered is the strong supraspinous ligament. The weaker interspinous ligament immediately follows. Together, these ligaments unite adjacent spinous processes in a vertical fashion. Encountered next, the ligamentum flavum (Fig. 2) links adjacent lamina and is the final ligament encountered prior to entering the epidural space. It is the strongest and most elastic of the ligaments, often described as having a hard, rubber-like feel as the needle transverses its strong fibers. The posterior longitudinal ligament is anterior to the epidural space and the dural sac, but posterior to the vertebral bodies, so it is not traversed in placement of neuraxial anesthesia. Finally, the anterior longitudinal ligament is anterior to the vertebral bodies [7].

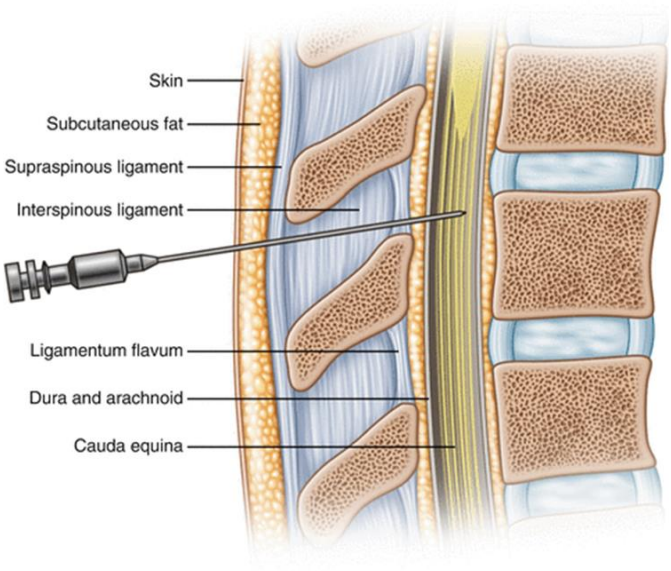

Fig (2): Spinal ligaments [4]

Spinal Cord

The spinal cord originates from the medulla oblongata in the brainstem and extends to the lumbar region of the spinal canal. It serves as a major neural conduction pathway between the body and the brain, as well as a

major reflexive center. In newborns, the cord terminates between the L2 and L3 vertebrae, while in adults it usually extends only to the disc space between L1 and L2. However, as evidenced by MRI scans, the spinal cord extends to L3 in approximately 2 % of adults [8].

Spinal Nerves

Thirty one (31) pairs of spinal nerves (C1–8, T1–12, L1–5, S1–5, and one coccygeal nerve) emerge from the spinal cord and exit the spinal canal via the intervertebral foramina, except for the coccygeal nerve that exits through the sacral hiatus. Each spinal nerve is comprised of an anterior and posterior nerve root. These are formed by the convergence of anterior and posterior rootlets that arise from the surface of the spinal cord. The part of the spinal cord from which rootlets emerge to form nerve roots comprises a segment of the spinal cord and forms the basis of dermatomal distribution of sensation. Although the spinal cord terminates at L2 in most adults, vertebral discs below this level have corresponding spinal nerves. These nerves emerge as the cauda equina from the inferior aspect of the spinal cord, called the lumbosacral enlargement. The fibers of the cauda equina travel in the lumbar cistern (subarachnoid space), bathed in CSF, until they emerge from the spinal canal at the corresponding vertebral level [9].

Blood Supply

Not surprisingly, the spinal cord is dependent on a rich blood supply. One anterior and two posterior longitudinal spinal arteries feed the anterior and posterior aspects of the spinal column, respectively. Rather than forming a continuous longitudinal blood supply to the spinal cord, interruption of the anterior spinal artery occurs with segmental blood supply provided by penetrating medullary arteries that arise from the aorta and transit through the intervertebral foramina. In general, three large and discrete areas of distribution along the anterior spinal cord exist, the cervicothoracic area, the mid-thoracic area, and the thoracolumbar area. In addition, these arteries provide blood supply to the posterior and anterior roots of the spinal nerves and their coverings. The largest anterior radicular artery, also known as the artery of Adamkiewicz or anterior radicularis magna, arises from T9 to T12 in 75 % of individuals but may originate as high as T5 or as low as L2. Spinal veins form plexuses that run longitudinally inside and outside the vertebral canal and can often be engorged during pregnancy [10].

Intrathecal Spinal Anesthesia

Drugs of Intrathecal Spinal Anesthesia

Various local anesthetics have been explored for spinal anesthesia, falling into two primary categories: esters and amides. Initial investigations focused on esters like cocaine and amylocaine. However, amylocaine is no longer used in clinical practice. Procaine, known as Novocain, was synthesized and saw research into its intrathecal use. Procaine gained popularity due to its presumed systemic effects and concerns over the neurotoxicity of spinal cocaine administration. Notably, procaine's side effects often include nausea, vasomotor paralysis, and an elevated risk of anaphylaxis due to its metabolite para-aminobenzoic acid (PABA) [11].

In a subsequent era, longer-acting local anesthetics such as dibucaine and tetracaine were discovered and used intrathecally. Dibucaine showed promise due to its shorter duration of action compared to procaine, a more favorable ratio of sensory to motor fiber blockade, less sympathetic blockade, and less perceived toxicity. Lidocaine, originally called Xylocaine, was first administered as a spinal anesthetic. Its pharmacologic profile made it ideal for short to moderate duration surgical procedures. Chloroprocaine, synthesized from procaine, was approved for spinal anesthesia and became the preferred choice for rapid onset and resolution of spinal

blockade due to rapid ester hydrolysis. Its improved safety profile allowed for nearly twice the dosage compared to procaine without toxicity. These three local anesthetics chloroprocaine, lidocaine, and tetracaine found widespread use in various operative procedures [12].

After chloroprocaine's approval, mepivacaine and prilocaine were introduced for spinal anesthesia. Both of these medications, also xylidine derivatives, displayed similar potency to lidocaine. However, due to concerns about transient neurologic symptoms associated with intrathecal lidocaine administration, mepivacaine and prilocaine are being further investigated as alternatives for ambulatory or short to moderate duration surgeries [13].

Mechanism of action of local anesthetics:

Delivery of local anesthetic into the subarachnoid space induces a rapid and dense blockade of sensory, motor, and autonomic neural transmission. The intrathecal distribution of local anesthetic implicate a number of potential sites of action. Not surprisingly, high concentrations of local anesthetics can be found in the posterior nerve roots as they exit the dura. Local anesthetics also diffuse through the pia mater and into the spinal cord, with higher concentrations noted in the posterior and lateral columns, as well as the gray matter of the spinal cord [14, 15].

Anatomic differences among nerve fibers, including size and myelination, account for their differing sensitivities to blockade by local anesthetics. Blockade of unmyelinated, small diameter sympathetic fibers precedes blockade of the larger, myelinated sensory and motor fibers. The sympathetic block usually exceeds the somatic and motor block by two dermatomal levels, but sometimes by as many as six. This may help to explain the hypotension that accompanies even low sensory blockades. As for the sensory nerve fibers, the C-fibers, which are sensitive to temperature, are blocked first and remain blocked the longest (Fig. 3). A-delta fibers, which are responsible for pinprick sensation, are blocked next but are faster to recover than the C-fibers. The fibers that give sensation to touch, the A-beta fibers, are blocked last and recover the fastest. The length of blockade of the A-beta fibers correlates with the length of surgical anesthesia. Finally, the motor fibers are the least sensitive to blockade and typically are blocked two to four levels below the sensory blockade [16].

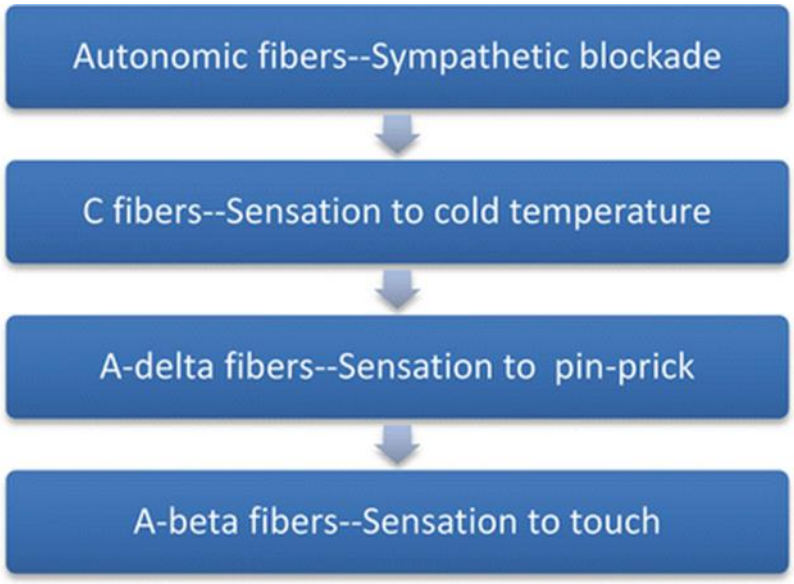

Fig (3): Progression of blockade during spinal anesthesia [4]

Besides the dose of local anesthetic injected, there are a number of factors that may influence intrathecal anaesthetic spread, including the contents of the injected solutions, clinical procedures, patient variables. An individual's volume of cerebrospinal fluid as determined by MRI estimation appears to be the most important factor in determining extent of anesthetic dermatomal distribution. This proves to have little clinical utility as a patient's volume of CSF is neither routinely measured nor easily predicted based on a patient's characteristics. However, it may help to explain why higher peak sensory levels often occur in patients who are older, obese, or pregnant. In these patients CSF volume is often, although not always, diminished compared to younger, leaner patients [17].

Elimination of local anesthetic from the intrathecal space depends on vascular absorption of the anesthetic solution. Intrathecal metabolism does not occur. Blocks covering wider dermatomal areas regress faster than blocks covering fewer dermatomes when the same anesthetic dose is used. The increased surface area allows for faster absorption of the anesthetic by the blood vessels of the pia mater. Toxic blood levels of local anesthetics do not occur because of the relatively small doses required for spinal anesthesia [14].

Physiologic effects of intrathecal anesthesia:

Cardiovascular effects

Undoubtedly, the spinal administration of local anesthesia can result in hypotension. This is largely believed to be secondary to a sympathetic nervous system blockade in the region of the pre-ganglionic neuron prior to its synapse on the sympathetic chain ganglion. This blockade results in vascular dilation, which produces a decrease in systemic vascular resistance (SVR) (venous > arterial) [18]. This decrease in SVR, and the associated decrease in preload, may stimulate a reflexive baroreceptor response increasing the heart rate to maintain cardiac output. However, it has been well reported that patients may also experience a different type of cardiac reflex known as the Reverse Bainbridge (atrial), or Bezold-Jarisch reflex (ventricular). These reflexes stem from the recognition of a decreased preload to either the atria or ventricle, which results in reflexive bradycardia to slow the heart and allow for increased filling time. This ultimately results in a lower cardiac output [19].

Additionally, the distribution of local anesthetic can block cardiac accelerator fibers which stem from thoracic sympathetic ganglia T1-T4, further preventing the reflexive cardiac baroreceptor response. Due to the complexity of these interacting variables, changes to cardiac output with spinal anesthesia are also variable. Ultimately, spinal anesthesia often results in a decrease in mean arterial pressure (MAP), though this is not necessarily true for pre-eclamptic patients with non-sympathetically mediated elevations in blood pressure. When untreated, depressed cardiovascular effects may result in decreased cerebral perfusion, nausea/vomiting, and cardiovascular collapse [20].

Respiratory effects

[21] investigated the effects of spinal lidocaine and bupivacaine on resting pulmonary function in eleven volunteers. They identified a slight decrease in end-tidal CO2 (34 mmHg - 31 mmHg) with an inverse age correlation (i.e., younger patients had a greater drop in end-tidal CO2). They reported the absence of significant change in tidal volume, respiratory rate, and minute ventilation, hypothesizing instead an increase in dead space ventilation associated with spinal administration. They further comment on the paralysis of abdominal musculature leading to an increase in chest wall compliance and a decrease in mechanical work of breathing. It is interesting to note their comments regarding increased chest wall compliance and increased respiratory frequency variation. Of note, they also allude to spinal level deafferentation of the chest wall receptors, but make no specific reference to intercostal involvement.

Renal effects

It is well recognized that the kidney receives direct sympathetic innervation from renal sympathetic nerve fibers derived from the sympathetic chain ganglia. In addition, the kidney auto-regulates its blood flow utilizing humoral/endocrine factors released as a result of changes sensed in the macula densa. It is believed that this mechanism functions both interdependently and independently from sympathetic function, enabling the preservation of renal blood flow in the absence of sympathetic directive [22]. As originally described by [23], "It is possible to assume that the renal vascular bed acquires autonomy de novo only as a consequence of denervation, but in view of the rapidity and smoothness of anesthetic denervation any such assumption seems quite superfluous." It is now understood that there is little effect on overall renal function as a result of spinal or epidural sympathetic blockade from local anesthetic administration. Glomerular filtration and renal blood flow are recognized to only decrease slightly in direct relation to decreases in mean arterial pressure associated with the sympathetic blockade.

Digestive effects

Sympathetic nervous system blockade as a consequence of spinal local anesthetic administration leads to unimpeded parasympathetic nervous system activity and gastrointestinal hyperactivity. Hypotension encountered as a result of spinal local anesthesia may lead to gastrointestinal ischemia and the release of emetogenic substances such as serotonin. Furthermore, hypotension may lead to hypoperfusion of the area postrema of the medulla (brain stem—known chemoreceptor trigger zone for vomiting) resulting in increased serotonin release. The combination of these factors may contribute to intraoperative/postoperative nausea and vomiting. It is also important to recognize that hypotension associated with spinal local anesthetic administration may result in hypoperfusion of the liver. Because hepatic blood flow is not auto-regulated, this low perfusion pressure may result in impairment of metabolic functions to include subsequent drug metabolism [24].

Immunological effects

Regarding the anti-inflammatory and immunomodulatory effects of local anesthetics, [25] wrote that it is well recognized that the innate and adaptive immune systems contribute to the destruction of foreign substances and tissue repair following injury. The immune cells involved in these processes include neutrophils, macrophages, monocytes, mast cells, T-cells, and B-cells. These cells must undergo chemotactic targeting to the area of injury, adhere to blood vessel walls, traverse the blood vessel wall into the tissue, engulf the offending agent, and destroy it. Local anesthetics have been thought to interfere with every step of this process. They inhibit leukocyte adherence to the vascular endothelium by possibly interrupting interactions between leukocyte cell membrane integrins and their receptors (cellular adhesion molecules—CAMs) expressed on the vascular endothelium. Similarly, they inhibit the trans-endothelial migration and motility of leukocytes and may interfere with the "priming" of leukocytes, preventing their full pathogen-destroying capability by decreasing their free radical production. It has been suggested that local anesthetics further interrupt the normal cellular actomyosin filament activity resulting in disruption of the ability of the leukocyte to modulate the cell membrane to engulf the offending agent for lysosomal destruction. Furthermore, local anesthetics are responsible for a dose-dependent decrease in the release of lysosomal enzymes [26].

Of additional interest are the anti-inflammatory properties of local anesthetics that are believed to stem from their inhibition of arachidonic acid derivative synthesis, their release of histamine, and their attenuation of cytokine release (i.e., IL-1, IL-6, IL-8, TNF-alpha, etc.). Inhibition of phospholipase A2 synthesis prevents arachidonic acid cleavage; inhibition of prostaglandin E1/E2 synthesis has been attributed to a potential reduction in inflammatory pain; inhibition of thromboxane A2 synthesis results in decreased platelet aggregation; and inhibition of leukotriene B4 synthesis has been implicated in the reduction of capillary hyper-permeability, resulting in decreased edema formation due to inflammatory plasma extravasation. Based on this aggregate model of cell membrane interference (i.e., ion channel inhibition, cell membrane protein cleavage, cell membrane receptor binding and inhibition, cell membrane actomyosin function disruption, etc.) researchers have targeted investigation of specific local anesthetics for their antibacterial and antiviral effects [27].

Factors Which Affect Intrathecal Spread

Several factors are considered relevant to the intrathecal spread of local anesthetic. These factors may be divided into three categories: factors specific to the local anesthetic solution, factors specific to the patient, and factors specific to the procedure itself. All of these have been described in an article by Hocking and Wildsmith [28].

With regard to the local anesthetic solution, the degree of intrathecal spread is related to the baricity, temperature, viscosity, and dosage of local anesthetic administered. Baricity is the ratio of substance density to CSF density. As such, there are hyperbaric, hypobaric or isobaric (i.e., denser than cerebrospinal fluid, less dense than cerebrospinal fluid, or similar density to cerebrospinal fluid) formulations of local anesthetic solution. Upon injection, baricity affects the caudal versus cephalad spread of solution within the CSF. Baricity, in combination with patient positioning, will ultimately determine the spread and distribution of local anesthetic within the thecal sac. Temperature also affects the density of a local anesthetic solution such that a refrigerated or warmed solution may possess a baricity different from its manufactured specification [12]. Investigations evaluating the additional effect of local anesthetic solution viscosity on intrathecal spread suggest that increased viscosity is associated with increased local anesthetic distribution within the intrathecal space. Finally, there is a relationship between dosage, volume, and concentration. Recognizably, changes in any of these variables influence the others as they pertain to the specific mixture of a local anesthetic solution

prepared for administration. Though several studies have been performed to evaluate these factors, dosage seems to have the most significant impact on the intrathecal spread of local anesthetic [29, 30].

In discussing patient factors, patient height, position, and age all contribute to the spread of intrathecal local anesthetic. Though it may affect spread, gross height is not a reliable characteristic for determination of local anesthetic dosing. Regarding thecal sac characteristics, it is recognized that the vertebral column curvatures (and thus variations in thecal sac positioning) influence the intrathecal spread of local anesthetic. The interplay between lumbar lordosis, thoracic kyphosis, and baricity helps to explain the largely "dependent" thoracic distribution of hyperbaric local anesthetic solutions after intrathecal injection and positioning of a patient in the supine position. With regard to baricity, it was demonstrated that the density of CSF varies between patients [31].

Intrinsic characteristics of cerebrospinal fluid may play a role in the effects of a subarachnoid block, as the CSF serves as the solvent in which the anesthetic must act. The density of CSF is not constant among patients and varies with characteristics commonly encountered in patients during spinal anesthesia, including age, pregnancy, and illness. Even small changes in the density of CSF affect the baricity of the anesthetic solution—defined as the relative density of the anesthetic solution in relation to its solvent. This may help to explain the observed clinical differences among these patient populations in the extent of anesthetic spread [32]. CSF in women is less dense than in men. It is less dense in pregnant women than in non-pregnant women and is less dense in pre-menopausal women than in post-menopausal women. It has been further demonstrated that extremes of age can impact the spread of intrathecal local anesthetic. Increasing length of time required for the maximum upper level of analgesia is seen with advancing age. This was associated with an inverse onset of motor blockade relationship such that a faster onset of motor blockade was seen with advancing age. Furthermore, the time to peak plasma concentration of local anesthetic was increased, and the total plasma clearance decreased with advancing age [12].

Finally, procedural components may have an impact on the distribution of local anesthetic. It is known that the initial pressure generated by the injection of local anesthetic creates waves within the CSF. It was previously believed that generation of additional fluid waves, via a technique known as barbotage, would facilitate greater spread. Several investigations have demonstrated that barbotage does not affect the ultimate height of the sensory blockade. It may, however, slightly decrease the time to achieve maximum sensory and motor blockade, though this may be of limited clinical value. Regarding injection speed and pressure itself, studies have been mixed. It would seem that utilizing increasing speed, and pressure of injection potentially facilitates a greater spread of isobaric local anesthetic with diminishing effects seen with hyperbaric local anesthetic [33].

Lastly, the needle orientation and approach (midline versus paramedian) to the neuraxis may alter local anesthetic distribution. [34] demonstrated a faster onset of T4 block when the Sprotte needle was inserted with the side eye facing cephalad. [35] also reported a higher dermatomal distribution when the side aperture of the needle was oriented in a cephalad manner. To the contrary, [36] reported that the orientation of the aperture of the Whitacre needle did not influence the cephalad spread of hyperbaric bupivacaine in parturients. [37] demonstrated that a paramedian approach with steep angle (70–100 degrees from level) was also associated with a greater cephalad sensory blockade.

Complications of Spinal Anesthesia

Hemodynamic Collapse

Spinal anesthesia has been associated with cardiac arrest in otherwise healthy patients. Premonitory symptoms often do not precede many of these events. It is believed the sudden sympathectomy causes a sudden decrease in the afterload without a compensatory tachycardiac response due to inhibition of the cardioaccelerator fibers. Although unexplained cardiac arrest is more common in younger, healthy patients, survivability following the event appears to be inversely proportional to age and ASA classification [38].

High Spinal Anesthesia

Complications of spinal anesthesia may encompass the occurrence of high spinal anesthesia which is a condition where the level of sensory and motor block extends higher than intended. This unintended extension can lead to potential complications due to the involvement of critical areas, such as the respiratory muscles and cardiovascular centers. Additionally, involvement of cardiovascular centers can result in hypotension or other cardiovascular complications. The mechanism behind high spinal anesthesia involves the inadvertent spread of the local anesthetic solution beyond the desired spinal segment. Factors contributing to this phenomenon include an improper dosage, injection site, or patient positioning [33].

Post-Dural Puncture Headache

Post-dural puncture headache (PDPH) is the most common complication of a spinal anesthetic although the incidence has decreased with the development of new, smaller-gauge spinal needles. The incidence is highest among young adults and obstetrical patients with a decreasing risk associated with advancing age. Smaller, non-cutting needles decrease the incidence from as high as 5 % to less than 1 %. The headache occurs as a result of leakage of cerebral spinal fluid through a dural puncture site. This leads to decreased intra-dural pressure, and tension on the meninges and nerves resulting in an intense headache often relieved with recumbency. Cranial nerve palsies may also occur as a result of traction on cranial nerves. Although the headache is not dangerous, the symptoms can be quite debilitating and for a recent parturient may hinder mother–newborn bonding. Conservative management includes bed rest, hydration, and caffeine. When these fail to improve symptoms, an epidural blood patch may be considered [39].

An epidural blood patch is considered the gold standard for managing PDPH, when supportive measures fail. However, the procedure of epidural blood patch itself can lead to another inadvertent dural puncture and other adverse events can occur during a blood patch, such as meningitis or neurological deficits. The minimally invasive, simple procedure of bilateral greater occipital nerve block has been used for treating chronic headaches in patients with PDPH, or in patients who have failed conservative management. Transnasal sphenopalatine ganglion block (SPGB) has also been proposed for the management of postdural puncture headache [40].

Neurologic Complications

Although serious neurologic injury is a rare complication of a spinal anesthetic, many patients will refuse neuraxial anesthesia due to a fear of neurologic injury. Transient radiculopathies occur with an incidence of 6 per 10,000 spinals and generally resolve within 3 months. Cauda equina syndrome, characterized by a sensory deficit in the perianal region, bowel and bladder incontinence, and various motor deficits, may present following regression of the block. It often resolves over weeks to months but may produce lasting neurologic deficits. Incidence of this complication has been reported as 1.2 per 10,000 blocks [41].

Adhesive arachnoiditis is the most devastating neurologic injury. This insidious process occurs several weeks to months following a spinal block with the gradual progression of sensory and motor deficits of the lower

extremities. It is pathologically characterized by proliferation and scarring of the meninges and vasoconstriction of the spinal cord vasculature [42, 43].

Another complication is Transient neurological symptoms which is defined as pain and/or dysasthesia in the back, buttocks, and legs or pain radiating to the lower extremities after initial recovery from spinal anesthesia and resolved within 72 h [44]. Neither sensory nor motor deficits should be present to make this diagnosis. The administration of lidocaine appears to be a significant risk factor for the development of this syndrome with an incidence of 12 % compared to 1.4 % for bupivacaine or tetracaine administration. Lithotomy position and outpatient surgery appear to increase the risk for developing symptoms when lidocaine is administered but are not risk factors with bupivacaine administration. Although neurologic deficits are not present, this syndrome should not be disregarded as an annoyance, as one-third of patients report pain symptoms as severe and may be quite debilitating. Most symptoms resolve within 72 h though some may last for months. In a minority of cases symptoms may persist for greater than 1 month, but in 118 confirmed cases of TNS prospectively evaluated all patients were symptom free by 6 months [45].

Infection

Bacterial or aseptic meningitis may develop following a spinal block with patients presenting with fever, nuchal rigidity, and photophobia. A low index of suspicion should exist for this as bacterial meningitis requires prompt evaluation and treatment while aseptic meningitis resolves spontaneously. Microscopic examination of the cerebral spinal fluid reveals leukocytosis. In aseptic meningitis, gram stain and culture are negative. When clinical suspicion is present, antibiotics should be started while studies are pending [46].

Failed Blocks

A failed, patchy, or incomplete block that yields inadequate anesthesia for a surgical procedure can have significant implications on a patient's perioperative management. Failure can be characterized by an inadequacy in the extent, density, and duration of the block. It may be evident at the time of the procedure or may progress during the surgical case. Supplementation with infiltration of local anesthetic into the surgical field, administration of intravenous sedation or analgesia, or conversion to general anesthesia may be required [47].

Failure rate for spinal block is widely distributed with a range from 1 to 17%. Causes of failed spinal blocks include the obvious inability to successfully access the intrathecal space, poor agent selection, and inappropriate patient positioning following the block. Orifices of non-cutting needles may not completely enter the subarachnoid space allowing loss of anesthetic agent into the epidural space despite adequate flow of CSF. The dura and arachnoid may also act as a flap valve over the opening of the pencil-point needle [48].

Spinal Anesthesia in Cesarean Section

Spinal anaesthesia is the commonest type of anaesthesia used for lower segment caesarean section (LSCS). Compared with epidural technique, spinal anesthesia is quicker and easier to perform, with a definite end point, and a high success rate. It produces rapid, dense and predictable block especially with hyperbaric solutions. There is minimal risk of regurgitation and aspiration of gastric contents. There is minimal transfer of drug across placenta to the foetus and even when transferred, there is minimal risk of foetal toxicity. The mother is awake and is able to enjoy the encounter with her baby [49].

Complications of Spinal Anesthesia

The mother, who could be in labor and not able to clearly understand the implications of anesthesia, should still have an explanation of the procedure and consent should be obtained. The potential complications are shown in Table 1 and these risks along with the possibility of failure of spinal anaesthesia and the need to convert to general anaesthesia should be clearly explained to the mother [50].

Also, Potential complications of spinal anesthesia, as highlighted by [49], encompass a range of issues. Sympathetic blockade during spinal anesthesia can lead to hypotension, attributed to vasodilation and a decrease in systemic vascular resistance. Urinary retention may occur due to the inhibition of reflexes controlling bladder function. Nausea and vomiting can result from the sympathetic blockade and the subsequent gastrointestinal effects. Shivering may arise as a response to the redistribution of blood flow and temperature changes. The use of intrathecal opioids in spinal anesthesia may contribute to respiratory depression or sedation. Lastly, systemic local anesthetic toxicity can occur, posing a risk when excessive amounts of the anesthetic agent are absorbed into the bloodstream, potentially affecting the central nervous system, cardiovascular system, and other organs.

Table (1): Potential complications of spinal anaesthesia [49]

Hypotension (sympathetic blockade)
Urinary retention
Nausea and vomiting
Shivering
Respiratory depression or sedation (if intrathecal opioids are used)
High block or total spinal
Systemic local anaesthetic toxicity
Post dural puncture headache (PDPH)
Neuropathy – may be temporary or permanent
Epidural or spinal abscess or haematoma
Meningitis or arachnoiditis

Monitoring During Intrathecal Spinal Anesthesia

Mandatory monitoring should consist of pulse oximetry, non-invasive blood pressure monitoring and electrocardiogram. The blood pressure should be checked every 2-3 minutes initially as rapid falls are anticipated, necessitating immediate intervention. The hypotension due to sympathetic block may be accentuated by aortocaval compression caused by enlarged uterus in the supine position. Vasopressors such as ephedrine, phenylephrine, mephentermine or metaraminol should be drawn up in a syringe and kept ready before administering spinal anesthesia [51]. The infusions of phenylephrine (100mcg/min) are more effective in preventing hypotension. All patients should be monitored for incidences of tachycardia or bradycardia. Tachycardia associated with labor pain may continue for some time or it may occur due to hypotension. Intra-operatively bradycardia may occur because of higher levels of spinal blockade, or due to vagal stimulation caused by traction on peritoneum. Monitoring is especially important during the time when the uterine sinuses are open, until the suturing is complete, as there is risk of amniotic fluid embolism or venous air embolism. The risk of air embolism may be greater with exteriorization of uterus undertaken by some obstetric practitioners [52].

Bupivacaine and Prilocaine as Local Anesthetics during intrathecal Spinal Anesthesia

Bupivacaine

Bupivacaine is a potent local anesthetic from the amide group, first discovered in 1957 [53]. It is used in regional anesthesia, epidural anesthesia, spinal anesthesia, and local infiltration [53]. Local anesthetics generally block the generation of an action potential in nerve cells by increasing the threshold for electrical excitation [54]. The progression of anesthesia depends on factors such as nerve fiber diameter, myelination, and conduction velocity [54].

Bupivacaine is available in three concentrations: 0.25%, 0.5%, and 0.75% [55]. It is administered via local infiltration, peripheral nerve blocks, spinal anesthesia, epidural anesthesia, and caudal blocks [55].

In recent years, ultrasound-guided nerve blocks have been shown to reduce the risk of local anesthetic toxicity [56]. Visualization of the nerve and surrounding structures decreases the likelihood of injection into a vascular structure, thereby lessening the possibility of reaching toxic levels of bupivacaine in the bloodstream [56].

The dose of bupivacaine depends on the procedure, tissue vascularity, area, number of segments blocked, depth or duration of anesthesia needed, and patient physical condition [57]. Bupivacaine may interact with ergot medications, blood thinners, antidepressants, or monoamine oxidase inhibitors [57]. Allergic reactions to preservative-free amide-type local anesthetics are rare, but true anaphylactic responses are more common with ester local anesthetics or preservatives [57].

At therapeutic levels, bupivacaine blocks voltage-gated Na-channels, preventing Na+ influx, depolarization, and action potential generation [58]. At toxic levels, bupivacaine affects cardiac Na+-channels and neurons in the brain, blocking K+, Ca2+, and NMDA receptors [58]. It also interferes with cellular processes, including oxidative phosphorylation, free fatty acid utilization, and cAMP production [58].

Prilocaine

Prilocaine is a widely used local anesthetic in the amide class [59]. It shares structural similarities with lidocaine [59] and is used for localized pain relief during surgical and medical procedures [59].

Prilocaine exerts its anesthetic effect by binding to sodium channels on the neuronal cell membrane, blocking the influx of sodium ions and preventing action potential propagation [59]. This block is reversible, allowing for the eventual return of nerve function.

Prilocaine has a clinical profile similar to lidocaine and is used for infiltration, peripheral nerve blocks, and spinal and epidural anesthesia [60]. Because it causes significantly less vasodilation than lidocaine, epinephrine is not typically needed to prolong its duration of action [60]. This is advantageous when epinephrine is contraindicated. Prilocaine shows the least systemic toxicity of all amide local anesthetics and is therefore useful for intravenous regional anesthesia [60].

In a study of women undergoing elective cesarean section, hyperbaric prilocaine produced a shorter and more reliable motor block compared to bupivacaine [61].

A literature review found that a dosage range of 40–60 mg of 2% hyperbaric prilocaine is appropriate for surgical procedures involving the lower limb and lower abdomen, lasting up to 90 minutes [62]. This dosage demonstrated comparable onset time to hyperbaric bupivacaine but with a significantly reduced functional recovery time [62]. Patients experienced swift discharge within 4 hours and a diminished incidence of postoperative urinary retention [62].

Another study investigating the use of hyperbaric prilocaine 2% in day surgery found that a dosage of 40 mg was effective, with a low incidence of complications and minimal need for hospitalization [63].

Dexmedetomidine as Adjuvant to either hyperbaric prilocaine or Bupivacaine in intrathecal Anesthesia

Dexmedetomidine, a potent α2 adrenoceptor agonist, has been described as a unique sedative with analgesic, sympatholytic, and respiratory-preserving properties [64]. It is FDA-approved for short-term sedation in the

ICU and for sedation of non-intubated patients during procedures. However, its clinical applications have been greatly expanded in recent decades due to its favorable physiological effects [64].

Dexmedetomidine has been shown to prolong the duration of spinal anesthesia when administered intrathecally or intravenously [65]. The antinociceptive effect is attributed to its direct action on the locus coeruleus and its effects on the spinal cord [65].

Several systematic reviews have investigated the use of dexmedetomidine as an adjuvant to spinal anesthesia. A review of nine randomized controlled trials (RCTs) found that dexmedetomidine prolonged the duration of spinal anesthesia, improved postoperative analgesia, and reduced pruritus, without increasing hypotension or bradycardia [66]. However, these studies were heterogeneous in their methods and outcomes [66].

Another systematic review and meta-analysis of nine RCTs compared dexmedetomidine to local anesthetic alone in neuraxial and peripheral nerve blocks [67]. Intrathecal dexmedetomidine prolonged sensory and motor block duration and time to first analgesic request [67]. However, the trials were small and heterogeneous, and safety data were limited [67].

A meta-analysis of seven trials evaluating the effect of IV dexmedetomidine on spinal anesthesia showed similar results, with prolongation of sensory and motor block, but also an increase in transient bradycardia [68].

Intrathecal dexmedetomidine has also been investigated for its potential role in reducing shivering during cesarean section [69]. It is thought to inhibit the body's thermoregulatory center by blocking the transmission of body temperature information at the spinal cord level [69]. A meta-analysis confirmed that intrathecal dexmedetomidine significantly reduces the incidence of shivering [69].

Several studies have evaluated the effects of dexmedetomidine on nausea and vomiting during cesarean section. While some studies indicate that dexmedetomidine can reduce nausea and vomiting, particularly when used in conjunction with reduced opioid doses [70, 71], others found no significant reduction in the incidence of nausea and vomiting when opioids were not used [70].

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