Review

Spinal anesthesia: an evergreen technique

Simone Di Cianni[1], Maria Rossi[1], Andrea Casati[1†], Caterina Cocco[2], Guido Fanelli[1]

[1] Department of Anesthesia and Pain Therapy, University Hospital, Parma; [2] Department of Anesthesiology and Intensive Care, University of Sassari, Sassari, Italy

Abstract. Spinal anesthesia is a simple technique that provides a deep and fast surgical block through the injection of small doses of local anesthetic solution into the subarachnoid space. The purpose of this review is to provide an overview on recent developments on local anesthetic drugs, side effects, and special techniques of intrathecal anesthesia. Spinal anesthesia can be considered adequately safe, and severe complications are reasonably rare. The cardiovascular effects associated with sympathetic block are more frequent, but successfully treated with volume expansion and administration of vasoactive drugs. It is clear that the total dose of local anesthetic injected into the subarachnoid space is the most important determinant of both therapeutic and unwanted effects of spinal anesthesia. Several studies have also demonstrated the efficacy and safety of using small doses of long acting agents, such as bupivacaine or ropivacaine, to produce an adequately short spinal block in outpatients. Levopivacaine, the pure S(-)-enantiomer of racemic bupivacaine showed a lower risk of cardiovascular and central nervous system (CNS) toxicity than bupivacaine. In the last years we have assisted important changes in the health care organization, with most of the surgical procedures performed on outpatients or on elderly patients with concomitant diseases. This forced us to change the indications and clinical use of intrathecal anesthesia techniques, which have been modified according to the changing needs of surgery. The development of new drugs and special techniques for spinal anesthesia will further improve the clinical use of this old but evergreen technique. (www.actabiomedica.it)

Key words: Spinal anesthesia, local anesthetic, technique, complications

Introduction

Intrathecal anesthesia allows for the production of a deep nerve block in large part of the body through the relatively simple injection of a very small amount of local anesthetic. The first report on clinical use of spinal anesthesia was performed in 1899 by Dr August Bier, who described the intrathecal administration of cocaine (1). Since then, a lot of experience and data had been achieved on physiology, pharmacology, and clinical application of spinal anesthesia. Moreover, technological and pharmaceutic studies have enhanced our clinical practice, while new approaches as well as special techniques have been developed to produce central neuraxial blocks. The greatest challenge of the technique is to control the spread of the local anesthetic through the cerebrospinal fluid (CSF), in order to produce a block that is adequate for the proposed surgery without producing a needless extensive spread.

Spinal anesthesia is a relatively simple technique, which produces adequate surgical conditions by injecting a small amount of drug with easy landmarks, giving a wide popularity to this practice. The aim of this article is to focus on the most recent achievements in terms of knowledge of pharmacology, toxicology and clinical applications of this evergreen technique.

Anatomy and physiology

Several descriptions of the spinal canal anatomy have been reported since the 19th century (2), and the

use of modern radiological imaging technology has provided important insights in understanding anatomical and pathophysiological aspects implicated in spinal anesthesia. The vertebral level at which the spinal cord finishes varies widely from T12 to the L3/L4 intervertebral disc (3); the spinal cord extends to the L1/L2 disc in 51% of people and to the L2/L3 disc or below in 12% (4). A recent magnetic resonance imaging study of 136 adults (5) showed that the median level of termination of the spinal cord for both males and females was the middle of L1 vertebra, a level higher than usually reported (6). The dura mater is a cylinder extending from the foramen magnum to the second segment of the sacrum. It is a dense, connective tissue layer made up of collagen and elastic fibres, and contains the spinal cord and nerve roots that penetrate it. The classical description of the spinal dura mater is of collagen fibers running in a longitudinal direction (7). This had been supported by histological studies (8).

The arachnoid mater represents the most important and active meningeal barrier, delimitating the space of interest in spinal anesthesia: the subarachnoid space. It is formed by two portions: a dense laminar portion covering the dural sac internal surface, and a trabecular portion extending like a spider web around the pia mater (9). The arachnoid mater must not be considered only as a passive container of the cerebrospinal fluid (CSF), but it also actively participates in the transport of anesthetic agents and neurotransmitters involved in spinal block (10).

After atypical course of epidural or spinal blocks some authors also hypothesized the presence of a potential cavity between the dura and arachnoid mater, the subdural compartment. In an ultrastructure evaluation of the dura-arachnoid interface, Reina et al (10) described a dura-subarachnoid border filled with neurothelial cells, but failed to observe any subdural space when surgical manipulation of the meninges was avoided. However, a subdural space appeared if neurothelial cells broke up because of pressure exerted by mechanical forces, as well as air or fluid injection creating fissures within the interface. This concept may explain the variability of the onset and extension of spinal anesthesia by an unintentional subdural injection or catheter migration.

The subdural space contains the spinal nerves, spinal cord and cerebrospinal fluid (CSF). The choroid plexus produces CSF, but there is some evidence of extrachoroidal production. About 500 ml of CSF is produced daily (0.35 ml min^{-1}). The CSF volume in the adult is approximately 150 ml; about half of it is contained in the cranial cavity (11). A very large interindividual variability in the total volume of CSF has been demonstrated with magnetic resonance imaging (12), with volumes of lumbosacral CSF ranging from 28 to 81 ml. Interestingly, the volume of lumbosacral CSF has been demonstrated to be the most important factor affecting the peak sensory block and duration of spinal anesthesia (13, 14). The CSF is a crucial factor determining the effects of intrathecally administered agents, since all drugs we inject into the subarachnoid space dilute into the CSF before reaching their effector site in the spinal cord. Another characteristic that should be considered is the density of human CSF, which is not uniform varying according to sex, age, pregnancy, and illness. The upper boundary of hypobaricity, as defined using oscillometry, varies from 1.00016 to 1.00037 mg/ml or from 1.00003 to 1.00023 mg/ml at 37°C according to patient population (14).

Many factors affect the spinal spread of injected local anesthetics. Nevertheless, the influence of most of them is small, unpredictable and beyond the clinician's control. The major factors are represented by the baricity of the injected drug and the posture of the patient (14). Manipulation of the factors affecting the spread of local anesthetics may be used to produce different types of block, as long as the clinician has a clear understanding of what is involved (15).

The clinical evidence of spinal anesthesia is mainly determined by the total amount of local anesthetic solution injected into the subarachnoid space. The volume and concentration of the injected drug do not exert clinically relevant effects on spinal block characteristics (16,1 7), even if the minimum effective concentration of the local anesthetic solution injected into the spinal canal also depends on its total amount (18, 19).

The mechanism of action of local anesthetic solutions is based on their aptitude of producing conformational changes of voltage-activated Na^+ channels

(20). This results in a reduction and/or block of the current passing through the Na^+ channels, blocking the conduction of the electrical impulse along the axon (20). The usual explanation of the mechanism of nerve block induced by intrathecal injection of local anesthetics was a complete block of the conduction of impulses coming from the periphery and going to the supraspinal nuclei. However, it has been clearly demonstrated that intrathecal injection of local anesthetics also interferes with the function of other neurotransmitters, like the substance P or γ-aminobutirric acid (20). Accordingly, the mechanism by which intrathecal injection of local anesthetics produces surgical anesthesia probably involves more complex interactions, with a disruption of the normal coding of electrical information coming from the periphery to the central nervous system to be analyzed and interpreted at different levels in the spinal cord and supraspinal nuclei (21).

Local anesthetics

The selection of the local anesthetic to be used for spinal anesthesia is usually based on the expected duration of surgery and needs for early patient discharge. Because of the important changes in the health care system organization we have assisted to a significant increase in the number of surgical procedures performed on an outpatient basis, and spinal anesthesia has also become very popular for day-hospital surgery.

Lidocaine in doses ranging from 50 mg to 100 mg is widely used for surgical procedures lasting up to 1 h (22). For shorter surgery the dose can be reduced to 40 mg providing an adequate surgical block with times for complete regression of spinal block of about 2 h and readiness for hospital discharge 3 h after spinal injection (23, 24). The use of doses of spinal lidocaine as low as 20 mg has been described for outpatient procedures with high patient satisfaction and very rapid recovery and discharge, but only with the addition of small doses fentanyl (20 μg) (25).

However, in spite of its wide use and long history, the overwhelming evidence of transient neurologic symptoms associated with spinal lidocaine (20, 26) has raised strong concerns with its use, especially for day case surgery (26). Mepivacaine is another amide local anesthetic with a clinical profile similar to lidocaine. Nevertheless, it is associated with a similarly high incidence of transient neurologic symptoms (27, 28).

Theoretically, procaine and prilocaine could be good alternatives to lidocaine for short spinal anesthesia (20), but they are not extensively accessible for intrathecal administration around the world. A dose of 100 mg of procaine 10% provides similar onset time, shorter resolution of nerve block, and lower incidence of transient neurologic symptoms than the same dose of 5% lidocaine (29). Nonetheless, spinal procaine has also been reported to be associated with a higher failure rate (29, 30) and incidence of nausea and vomiting than lidocaine, with delayed home discharge times (30). Prilocaine used in the same doses of lidocaine provides a similar clinical profile (20), with the advantage of a lower incidence of transient neurologic symptoms (31,32).

Recent studies have shown that a procaine derivative, 2-Chloroprocaine(2-CP), shows ideal characteristics to be used in short outpatients procedures. Thirty mg of 2-CP provides similar results to 80 mg of procaine on anesthesia and patient tolerance (33). Doses ranging between 40 and 50 mg of 1% plain 2-chlorprocaine have been reported to provide adequate surgical block in outpatients undergoing lower limb surgery of 45-60 min duration, while reducing the dose of 2-chloroprocaine to 30 mg may be adequate only for very short procedures (34). Comparing 50 mg of 1% lidocaine and 1% 2-chloroprocaine for outpatient knee arthroscopy, we recently reported that 2-chloroprocaine provided a faster onset of spinal anesthesia, with a more rapid recovery of sensory/motor function, and unassisted ambulation, and a lower incidence of transient neurologic symptoms compared to spinal anesthesia with lidocaine (35).

Long acting agents, such as bupivacaine (with doses ranging between 10 and 20 mg of either plain or hyperbaric solutions) and tetracaine (with doses ranging between 8 and 16 mg of either plain or hyperbaric solutions), are widely used to give spinal anesthesia for surgical procedures lasting up to 2-2.5 hours (20). The use of long acting agents is associated with a lower risk for transient neurologic dysfunction (20, 27, 28,

31). With the increasing concerns on the incidence of neurologic dysfuntions after spinal lidocaine, the use of small doses of long acting agents has also been investigated to provide unfailing spinal anesthesia for short procedures (36). Five to 8 mg bupivacaine (used with plain, hypo- or hyperbaric solutions) have been demonstrated to provide reliable spinal anesthesia for outpatients, with recovery times comparable to those of 40-60 mg lidocaine (37-39).

The efficacy and safety of intrathecal administration of both plain and hyperbaric solutions of ropivacaine have been evaluated in different clinical settings, including orthopedic (40) and urologic surgery (41), as well as in cesarean section and labour pain (42, 43). As for other agents, the use of hyperbaric solutions results in faster onset and higher maximum sensory level, with shorter duration of nerve block (44). Hyperbaric ropivacaine provides a more consistent block, with a faster onset time and quicker mobilization than plain solutions (45). Because of its lower lipophilicity, ropivacaine is also 40-60% less potent than bupivacaine (46). In a volunteer study McDonald et al (47) demonstrated that, when used in similar doses, ropivacaine is associated with a shorter recovery than bupivacaine; thus the use of small doses of ropivacaine could potentially provide some advantages over bupivacaine for outpatient procedures. Gautier et al (48) compared the use of 8 mg ropivacaine with bupivacaine for outpatient knee arthroscopy, and demonstrated that ropivacaine provides earlier recovery of motor function and discharge than the same dose of bupivacaine. Similar findings have been also reported when comparing ropivacaine with levobupivacaine for different outpatient procedures (49, 50).

Additives

Several additives have been associated with intrathecal injection of local anesthetic solutions, mainly aimed at improving the quality and duration of spinal block and postoperative analgesia, or to minimize the dose of local anesthetic injected to reduce the extent and effects of sympathetic blockade.

Epinephrine: epinephrine (in a dose range of 0.1-0.2 mg) is usually used in addition to local anesthetic to both minimize the systemic absorption of local anesthetic agents, and prolong the duration of spinal block (23,51). However, it must also be considered that, even if it does not affect the blood supply of the spinal cord (52), the addition of a potent vasoconstrictor may contribute to the development of transient neurologic symptoms (53), or potentiate the neurotoxic effects of spinal lidocaine (54).

Opioids: Administration of opioids into the subarachnoid space may produce a marked and selective inhibition of the small fibers Aδ and C involved in the conduction of pain sensation. However, they also produce several side effects, including pruritus, nausea, vomiting and respiratory depression in a dose-dependent fashion. A dose of 0.1-0.2 mg morphine added to intrathecally administered local anesthetics has been demonstrated as the best balance between the improvement of the quality of pain control and minimization of side effects (55). Morphine, because of its hydrophilicity, also has an enlarged potential for rostral migration in the CSF, possibly leading to a late respiratory depression. Lipophilic opioids, like fentanyl and sufentanil, have a faster onset of action and lower risk for delayed respiratory depression (56). For this reason they are much more frequently used to potentiate nerve block of local anesthetics without affecting the spread and duration of spinal block (10 to 20 μg fentanyl or 1 to 10 μg sufentanil) (57).

Clonidine: There is overwhelming evidence in literature of the synergistic effects of clonidine and local anesthetics, resulting in marked potentiation of the block induced by the local anesthetic agents on Aδ and C fibers (58); it determines a dose-depended sensory block prolongation and a longer pain-free post operative period. As compared with the addition of opioid drugs, spinal clonidine does not result in pruritus or respiratory depression; however, it can provide a dose dependent decrease of arterial blood pressure and heart rate, and sedation (58). The addition of 15 to 75 μg clonidine improves the quality of spinal block without delaying nerve block resolution and reduces the incidence of urinary retention as compared to opioid agents (59).

Neostigmine: Neostigmine, is a cholinesterase inhibitor with antinociceptive effects when administered intrathecally, probably due to the activation of

both M1 and M2 muscarinic receptors in the spinal cord (60). The main side effect of intrathecal neostigmine is the occurrence of severe nausea and vomiting; however, reducing the doses of neostigmine to 1-5 μg produces significant potentiation of the analgesic effects of local anesthetic and opioid without increasing the incidence of adverse effects (61).

Complications of spinal anesthesia

The literature supports the evidence that severe complications associated with spinal anesthesia are rare enough to permit us to consider spinal block as a safe approach to allow surgery on our patients. Other side effects can be more frequently seen; however, the information of the pathophysiologic changes involved and risk factors associated with the development of complications can help us keep the risks for our patients as low as possible.

Cardiovascular side effects: The frequency of hypotension following spinal anesthesia is 10-40%. The hypotension is related to the extent of sympathetic blockade, which might reduce systemic arteriolar and venous tone. Cardiac output may fall as a result of a decreased venous return. Important hypotension should be treated with appropriate administration of intravenous fluids and well judged use of vasoactive drugs such as ephedrine or phenylepjrine. Cardiac arrest has been reported in healthy patients during the administration of a spinal anesthetic; it occurs suddenly, often preceded by severe bradycardia in an otherwise stable patient.

Postdural Puncture Headache (PDPH): Postdural puncture headache is the most common complication of spinal anesthesia. It happens most frequently in young adults including obstetrics patients, with an incidence of 14%, compared to 7% in individuals older than 70 years. The use of smaller needles with pencil-point tips has markedly reduced the incidence of postdural puncture headaches. These intense headaches occur when cerebrospinal fluid (CSF) escapes through the dural puncture site, resulting in intracranial tension on menigeal vessels and nerves. Treatment consists bed rest, intravenous hydration, and the use of nonsteroidal anti-inflammatory agents. If conventional therapy fails, an epidural blood patch with 10-15 ml of autologous blood injected at the site of the puncture may be necessary to minimize further escape of CSF.

Neurological complications: The frequency of severe neurological deficits following spinal anesthesia is low. In a prospective study of about 40000 cases the incidence of serious neurological deficits was about 0.05% (confidence intervals 0.2-1.1 per 10000) (62). When they occur, they are of great concern to both the patient and clinician. In spite of the low incidence, many patients decline spinal anesthesia because of fear of this complication. The most benign neurologic complication is aseptic meningitis. This syndrome usually presents within 24 hours after spinal anesthesia and is characterized by fever, nucal rigidity and photofobia. Microscopic examination of CSF is characterized by polimorphonuclear leukocytosis; bacterial CSF cultures are negative. Aseptic meningitis requires only symptomatic treatment and usually resolves within a few days.

Cauda equina syndrome presents after regression of the neuroaxial blockade. This syndrome may be permanent, or it may regress slowly over weeks or months. It is characterized by a sensory deficit in the perianal area, urinary and fecal incontinence, and varying deficits in the lower extremities.

The most serious neurologic complication is adhesive arachnoiditis. This reaction usually occurs several weeks or even months after spinal anesthesia. The syndrome is characterized by a gradual progression of sensory deficits and motor limitation in the lower limbs. There is a proliferate reaction of the meninges and vasoconstriction of the spinal cord vasculature.

Spinal cord ischemia and infarction may occur after a prolonged period of arterial hypotension (63). The use of ephinefrine in anesthetic solutions may reduce blood flow to the spinal cord. Traumatic injury to the spinal cord and nerve roots is a rare case of neurologic deficits. A chemical contamination during a wrong sterilization of syringes might be implicated in neurologic complications following spinal anesthesia.

Transient neurological symptoms consisting of severe radicular back pain after neuraxial blockade regression were reported in 1960 following spinal anesthesia with 5% lidocaine. There were no sensory or motor deficits, and the symptoms resolved sponta-

neously within a few days. The incidence was greater with the use of lidocaine compared with bupivacaine and was more common in patients having surgery with the hips or knees in the flexed position (26).

Special technique

The development of special equipment and needles has increased the flexibility of spinal anesthesia, allowing to optimize the advantages and minimize the disadvantages of this technique. The injection of small doses of local anesthetic solutions either more or less dense than the cerebrospinal fluid can allow to restrict the block mostly at one side, and this can help both in minimizing the effects of sympathetic blockade and in optimizing the recovery profile of spinal block. Other techniques have been developed to prolong the block after the first injection either by placing a catheter into the subarachnoid space (continuous spinal anesthesia) or by combining a continuous epidural block with the first spinal injection (combined spinal-epidural anesthesia).

Unilateral spinal anesthesia: There is a small distance between the left and right spinal nerve roots, theoretically preventing the production of an unilateral spinal block; however, a preferential distribution of spinal anesthesia may be obtained by slowly injecting small doses of both hypo- or hyperbaric anesthetic solutions with directional needles, in patients lying in the lateral decubitus position for 10-30 min (64). The use of very small doses of local anesthetic is the most important factor to allow a preferential distribution of spinal block (64, 65): doses ranging between 4 and 8 mg of both hyper- or hypobaric bupivacaine have been reported to provide effectively successful spinal block for one leg surgery with a rate of unilateral sensory and motor block of 40-60% and 60-90%, respectively (64). In order to restrict the block at the operative side we have to consider the use of pencil-point directional needles (like Whitacre or Sprotte type needles) (66), and the use of slow rates of injection (around 0.5-1 ml/min) (64).

Unilateral spinal anesthesia allows to minimize the extent of sympathetic blockade, resulting in less effects on the cardiovascular homeostasis and reduces the incidence of clinically relevant hypotension to 5-7% (67, 68). This also results in a significant acceleration of patient discharge, making unilateral spinal anesthesia an interesting option for outpatient surgery (64).

Combined Spinal/epidural anesthesia (CSE): The aim of this approach is to combine the advantages of the reliable and fast nerve block produced by spinal anesthesia, with the possibility of prolonging anesthesia and analgesia with an epidural catheter. Originally, spinal block was performed at one interspace and the epidural catheter was placed in a different interspace. Afterwards a needle-through-needle technique, in a single interspace, was developed threading a long spinal needle directly through a Tuohy needle or through new "back-eye" or double-lumen modified Tuohy needles (67).

The single interspace needle-through-needle technique provides a better patient acceptance and shorter time to end the practice, with no differences in success rate of spinal anesthesia as compared to the double-segment technique (68). The development of new sets with spinal needles of adequate length and systems allowing to lock the spinal needle, at the Thuoy's hub during spinal injection, enhanced the success rate of this technique. However, the failure rate of spinal anesthesia in a CSE technique still remains slightly higher if compared to the use of a conventional spinal anesthesia technique. Combined spinal-epidural anesthesia also allows to minimize the intrathecal dose of local anesthetic, reducing the effects on cardiovascular function.

Continuous spinal anesthesia: This technique was initially developed by placing an epidural catheter into the subarachoid space. Afterwards, very small polyurethane and nylon catheters (28-32 Gauge) have been developed for continuous spinal anesthesia, which allows to combine the deep and reliable nerve block of spinal anesthesia with the possibility of achieving it gradually and titrating the dose of local anesthetic solution (69). This allows to optimize cardiovascular stability, and is ideally suited for elderly patients with severe co-morbidities (70, 71). More recently new catheters for continuous spinal anesthesia have been developed involving a catheter-over-the-needle system, that can prevent CSF leakage even

without using microcatheters. However, the catheter-over-the needle technique was less successful when compared to both microcatheters and macrocatheters placed through 19-Gauge Tuohy needles, and requires more time to be performed (72, 73).

Conclusions

More than one century has passed since the first description of intrathecal anesthesia was reported in the literature. Only in the last years the improvement in technology and central nervous system imaging allowed to improve our knowledge of some anatomical and pathophysiological aspects of spinal nerve block. In the same time we also assisted to important changes in the health care organization: on one side, the age of patients that we take care of is continuosly increasing, and aging is associated to several concomitant diseases; on the other side, an increasing number of surgical procedures is nowadays performed on outpatients. These important modifications forced us to change the indications and clinical use of intrathecal anesthesia techniques; while the development of new drugs and special techniques for spinal anesthesia requires further studies to improve the efficacy and safety of this old but evergreen technique.

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Correspondence: Prof. Guido Fanelli
Department of Anesthesiology
University Hospital of Parma
Via Gramsci 14 – 43100 Parma, Italy
Tel. +39 0521 702 161
Fax +39 0521 984 735
E-mail: guido.fanelli@unipr.it; www.actabiomedica.it