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REVIEW ARTICLE

Intrathecal drug spread

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Spinal anaesthesia has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anaesthetic. However, the greatest challenge of the technique is to control the spread of that local anaesthetic through the cerebrospinal fluid (CSF), to provide block that is adequate (in both extent and degree) for the proposed surgery but without producing unnecessarily extensive spread and so increasing the risk of complications. The great interpatient variability in spread was observed and described as 'lauenhaft' (waywardness) by August Bier,[10] the first person to use the technique clinically, and has challenged many subsequent workers. In fact, the definitive studies were performed nearly 100 years ago by Arthur Barker, a London surgeon who was the first to use solutions made hyperbaric by the addition of glucose,[7] but his principles have had to be re-learned virtually each time a new drug has been introduced for the technique. This review focuses in particular on work published in the last decade (during which time ropivacaine and levobupivacine were introduced) in trying to provide guidance on making spinal anaesthesia as predictable as possible.

General considerations

Assessment of intrathecal drug spread

Studies of drug distribution usually involve measurements of concentration in a relevant body fluid compartment over time. However, multiple sampling of CSF at one level, let alone at the several needed to build an image of drug distribution through the theca, is not practical and would significantly influence the observations anyway. Thus, indirect indicators of spread are used, the vast majority based on tests of neurological response. Bier's 1899 description of spinal anaesthesia documented the many tests that he used, including "*. . . sensual perception of needle pricks to the thigh, tickling of the soles of the feet, a small incision in the thigh, pushing a large helved needle down to the femur, strong pinching with dental forceps, application of a burning cigar, pulling out pubic hairs, a strong blow with an iron hammer against the tibia, vigorous blows with the knuckles against the tibia, and strong pressure on a testicle*".[10] Most of these tests cause overt tissue damage and are unacceptable clinically, but some indicator of the degree and extent of nerve block is needed before surgery can start, as well as in comparative studies.

An apparently 'adequate' (in extent) spinal may fail because the block has been tested using a stimulus of significantly different modality or intensity than the planned surgery. A simple single stimulus (e.g. pinprick, cold) may be blocked, but spinal cord mechanisms may result in repeated stimuli (temporal summation) or stimuli from adjacent regions (spatial summation), evoking pain and revealing a 'failed block'. Intrathecal block is better than epidural at inhibiting spatial summation,[31] and this partly explains the more profound block produced. In addition, demonstration of the segmental extent of block of one modality does not enable accurate prediction of any other.[149] In general, however, loss of cold sensation is observed at a higher dermatomal level than pinprick,[83 114] which in turn is higher than the level at which touch is lost,[17] although there is variation even in this observation.[18] Many methods can be used to test a block, but they fall broadly into one of two groups: assessment of either afferent (sensory) or efferent (motor or autonomic) function.

Afferent function

Pinprick and cold are probably used most often, but mechanical stimuli such as touch, skin pinch,[152] pressure,[41] Von Frey hairs[76] and gas jets[59] can be used. Generally, loss of sensation to cold occurs before pinprick, and both of these before touch, each stage correlating with inhibition of C, Aδ and Aβ fibres, respectively.[75] Thus, temperature perception is lost before pinprick, is generally at a higher level and is usually assessed

by the application of 'cold' using alcohol,[114] ethyl chloride, a cold gel bag,[30] ice[75] or cooling thermodes,[12] although warming thermodes and warm air[123] can be used. Loss of vibration and proprioceptive sensation have also been used.[101]

More definitive assessment of pain sensation has been attempted with tetanic stimulation using peripheral nerve stimulators,[44 87] and transcutaneous electrical nerve stimulation,[36] both of which correlate well with surgical incision,[116] and assessment of somatosensory evoked potentials.[82] Chemical stimulation with capsaicin, mustard oil, hypertonic saline, bradykinin, serotonin or substance P induce experimental pain but are ineffective on intact skin. Ischaemic limb pain[103] is too diffuse to be of any use in defining extent of block.

Efferent function

As a block extends cephalad, there is progressive impairment of motor as well as sensory function. The commonest method of assessment is the modified Bromage scale[15] (Table 1). This gives no more than a crude mix of information on both the spread and degree of motor block in the lumbosacral distribution. Force transducer systems can be used to measure the degree of motor block at specific joints,[46 154] but the complexities of muscle actions and levels of innervation mean that any estimation of the precise level of block will be poor. Thoracic nerve block paralyses the abdominal wall and intercostal muscles, and can be quantified using electromyography[153] and pulmonary function tests,[43] respectively. Although the effects are proportional to the height of the block, they are too non-specific to be used to identify the level accurately.

Sympathetic block leads to cardiovascular changes. Hypotension and bradycardia are related to block height, but again are too non-specific. Vasomotor responses[47] can be used to detect neuronal integrity, and can be detected by colour and temperature changes in the affected area using thermography,[26] but are less reliable signs[39] and occur at a higher level of block than sensory changes.[26] The vasoconstrictive response in the skin of the upper limb to both pinprick and cold stimulation has been claimed to be a good indicator of block height,[60] although whether it offers anything over subjective response to sensory stimulation is unclear.

Routine methods

Some of the more complex methods described above are impractical in the routine clinical situation and require significant support for research purposes. They also assess very specific aspects of nerve function. At the other extreme, the experienced clinician may use very little formal testing, relying on little more than noting early onset of lower limb weakness and the expected cardiovascular changes, perhaps supplemented by a surreptitious pinch of the surgical wound site. Such confidence is, of course, underpinned by thorough knowledge of how drugs spread through the CSF and the result expected from a particular injection. However, some clinical situations require documentation of block extent (especially Caesarean section), and studies comparing different techniques demand a reliable method of assessment. Cold, most commonly applied as an ethyl chloride spray, is popular, but usually defines a level of block somewhat above that providing 'surgical' anaesthesia. In addition, ethyl chloride is an atmospheric pollutant. Gentle pinprick has the advantages of being simple, repeatable and reproducible and can be applied without patient awareness. It also allows discrimination between 'sharp' and 'dull', and if these two levels of block are close together then the level of 'surgical' anaesthesia is usually not far away either. This is the method of assessment used in the majority of studies considered below.

Table 1 Modified Bromage score used to assess motor power[15]

Grade	Definition
0	No motor block
1	Inability to raise extended leg; able to move knees and feet
2	Inability to raise extended leg and move knee; able to move feet
3	Complete block of motor limb

Mechanisms of drug spread

The CSF of the vertebral canal occupies the narrow (2–3 mm deep) space surrounding the spinal cord and cauda equina, and enclosed by the arachnoid mater. As the local anaesthetic solution is injected, it will spread initially by displacement of CSF and as a result of any currents created within the CSF. The next stage, which may well be the most crucial, is spread due to the interplay between the densities of both CSF and local anaesthetic solution under the influence of gravity. Gravity will be 'applied' through patient position (supine, sitting, etc.) and, in any horizontal position, by the influence of the curves of the vertebral canal. Many factors are said to affect these mechanisms (Table 2),[48] with some having greater impact than others. The key ones are the physical characteristics of CSF and the solution injected, the clinical technique used and the patient's general features. These interrelate in complex ways and it is important that comparative studies are designed in such a way that two groups of patients receive a technique that differs in one factor only. Often that is not the case.

Once bulk spread of the injectate under the influence of the physical forces outlined above is complete, the final stage is diffusion of the drug through the CSF and into the nervous tissue.

CSF characteristics

CSF is an isotonic, aqueous medium with a constitution similar to interstitial fluid. The terms density, specific gravity and baricity define its physical characteristics, but are often used loosely and interchangeably, causing confusion. Precise definitions are as follows.

Table 2 Factors affecting intrathecal spread of local anaesthetics, modified from Greene[48]

Characteristics of the injected solution
Baricity
Volume/dose/concentration
Temperature of injectate
Viscosity
Additives
Clinical technique
Patient position
Level of injection
Needle type/alignment
Intrathecal catheters
Fluid currents
Epidural injection
Patient characteristics
Age
Height
Weight
Sex
Intra-abdominal pressure
Spinal anatomy
Lumbosacral cerebrospinal fluid volume
Pregnancy

Density is the ratio of the mass of a substance to its volume. It varies with temperature, which must be specified.

Specific gravity is the ratio of the density of a substance to a standard. It is usual to relate local anaesthetic solutions at 20°C to water at 4°C.

Baricity is analogous to specific gravity, but the ratio is the densities of local anaesthetic and CSF, both at 37°C.

The units of density are weight per unit volume; the other two characteristics, being ratios, have no units.

The mean density of CSF at 37°C is 1.0003 g litre^{-1}, with a range of 1.0000–1.0006 (± 2SD) g litre^{-1}. It is worth noting that all the physiological variation is within the fourth place of decimals. Unfortunately, however, many investigators fail to measure density to the fourth decimal place, which makes interpretation of their studies difficult. Given the normal variation, it is necessary that solutions that are to be predictably hypobaric or hyperbaric in all patients have baricities below 0.9990 or above 1.0010, respectively.[13] Most glucose-free solutions used intrathecally are just hypobaric[95 100] but behave in a hyperbaric manner if cooled to 5°C before injection.[88 128] Commercially available plain bupivacaine has a baricity of 0.9990,[48] which means that it is only just on the edge of being hypobaric, and is best referred to as 'plain'.

CSF density is lower in women than in men,[121] in pregnant than in non-pregnant women,[113] and in premenopausal women compared with postmenopausal women and men.[81] Theoretically, these differences could lead to differences in the movement of a particular solution in the various patient groups (e.g. a solution that is isobaric in men may be hyperbaric in pregnant women), but the differences between groups are small and probably unimportant clinically.

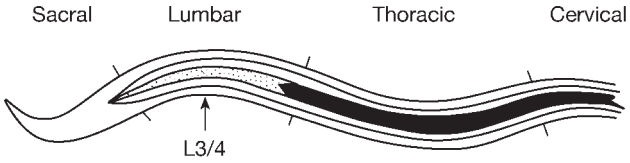

Fig 1 Curves of the vertebral canal influencing movement of drugs according to gravity. Spread is influenced initially by bulk displacement, injection currents and gravity/baricity, then by diffusion through the cerebrospinal fluid and into the central nervous system.

Factors affecting intrathecal spread

Characteristics of the injected solution

Baricity

Almost 100 years ago, Barker was the first to study systematically the factors affecting intrathecal spread. Using glass models of the spinal canal and coloured solutions, he deduced that gravity and the curves of the vertebral column (Fig. 1) could be used to influence the spread of solutions made hyperbaric by the addition of glucose.[7] Babcock employed the opposite approach, using solutions made hypobaric by the addition of alcohol,[5] while Pitkin used alcohol and strychnine in 'Spinocain'.[107] Given the neurotoxic effects of such substances, it is not surprising that the addition of glucose is the only method of altering baricity to remain in routine use. The usual choice for the clinician is between a hyperbaric solution and one with a baricity at, or just below, that of the CSF. Hyperbaric solutions are more predictable, with greater spread in the direction of gravity[138] and less interpatient variability.[16] In contrast, most plain solutions exhibit greater variability in effect and are less predictable,[16 131 148] so that the block may either be too low, and therefore inadequate for surgery, or excessively high, causing side-effects.[135] The greater mean spread of hyperbaric solutions may be associated with an increased incidence of cardiorespiratory side-effects,[91] although this is not always the case,[29 148] and may depend on the concentration of the glucose. Commercially available solutions contain up to glucose 8%, but most of the evidence shows that any concentration in excess of 0.8% will produce a solution that behaves in a hyperbaric manner (Fig. 2), but with somewhat less extensive spread if the glucose concentration is at the lower end of the range.[6 28 29 71 91 133 150] The interplay between baricity and posture is considered later.

Volume/dose/concentration injected

Clearly, it is impossible to change one of these factors without changing another, but this is not always appreciated. For example, many studies purporting to show an effect of volume fail to change the concentration of local anaesthetic, with a consequent increase in the dose administered. When the effect of volume (up to 14 ml) is isolated from other factors, most studies suggest there is no significant influence on mean spread.[8 9 73 79 83 144] However, one study has reported that volume is an important determinant of the

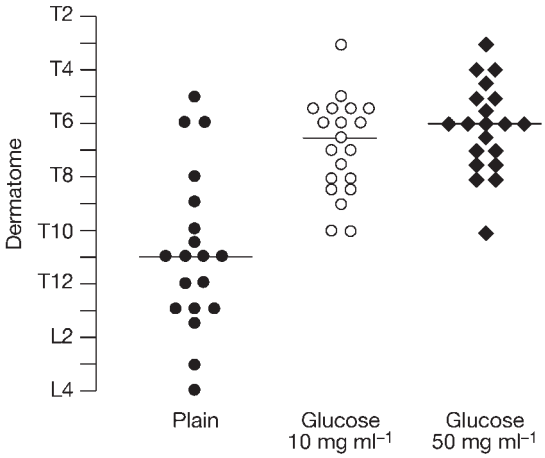

Fig 2 Range of maximum spinal block heights seen with three different solutions of ropivacaine 0.5%, containing glucose 0, 10 and 50 mg ml^{-1}, and with densities of 0.99940, 1.00273 and 1.01531 g ml^{-1} respectively, injected at L2/3 or L3/4. Figure reproduced, with permission, from Whiteside and colleagues.[150]

spread of a truly isobaric solution.[68] Low volume injections (1.5–2 ml) may reduce mean spread.[4 122]

Similar basic concerns apply to studies of the effects of different doses: a change in dose will be accompanied by a change in either volume or concentration. Some studies designed to control for changes in the other factors have shown that increased dose is associated with increased spread,[8 34 66 77 109] and others that there is no difference.[115 122] What really needs to be appreciated is the scale of the effect. If no drug is injected there will be no effect, and a massive overdose (e.g. accidental intrathecal injection during epidural block) will produce a total spinal, but there is not a straight-line relationship in-between. Within the range of doses normally used, a 50% increase in the dose injected will result in an increase of mean spread of only a dermatome or so.[16] Such differences may, on occasion, be statistically significant, but are rarely clinically so, although the increase in duration associated with a larger dose is.

Temperature of the solution

Both CSF and local anaesthetics exhibit a curvilinear decrease in density with increasing temperature. CSF is at core body temperature whereas local anaesthetic solutions are administered at room temperature. There will be some local decrease in CSF temperature (2–3°C with a 2.7 ml bolus; 6–8°C with a 12 ml bolus) immediately after injection,[33 38] but the core temperature is restored within 2 min, so solution density should be reported at body temperature. The consequences of temperature effects are most relevant with plain solutions, bupivacaine 0.5%, for example, being slightly hyperbaric at 24°C (density 1.0032 kg m^{-3}), but slightly hypobaric at 37°C (density 0.9984 kg m^{-3}).[95] Even such minor differences in baricity can cause completely opposite distribution patterns,[21] and may also account for the large variability in the spread of plain bupivacaine when injected at 'room' (which may vary considerably) temperature.[132]

Viscosity

This factor has received little attention, but addition of glucose to an aqueous solution changes viscosity as well as density. Using tetracaine, Okutomi and colleagues[99] compared solutions with a similar specific gravity but different viscosities (containing glucose 10% or NaCl 5%), and others also with a similar specific gravity but only slightly different viscosities (containing glucose 5% or NaCl 2.5%). The most viscous solution (glucose 10%) produced significantly greater mean spread than the others, suggesting that this factor is relevant to spread. Plain solutions are considerably less viscous than those containing glucose, which may be less miscible with CSF. The injected bolus of drug may thus spread further before mixing fully with CSF, but producing a more 'even' distribution as it does so. Very little is new in spinal anaesthesia since Pitkin[107] also considered viscosity important and included starch paste in his 'Spinocain' solution.

Local anaesthetic drugs and additives

Studies of a wide range of local anaesthetic drugs indicate that intrathecal spread is the same, no matter which one is used, as long as the other factors are controlled.[1 45] Solutions containing vasoconstrictors spread in exactly the same way as those without, although block duration may be prolonged.[70 93 133] The addition of other drugs, such as opioids or clonidine, has a dual effect. First, such additions are achieved by mixing the adjuvant and local anaesthetic solutions, usually reducing the density of the latter. In theory this might make the mixture behave in a more hypobaric manner,[100] but no effect has been shown in clinical practice,[11 95 102 124] suggesting that the changes in density are small. The second effect is seen with opioids, which increase mean spread and delay regression,[51] but do so no matter what the route of administration (intrathecal[126] or i.v.[120]). Presumably, this is pharmacological enhancement of subclinical block at the limits of the local anaesthetic's spread through the CSF. Alkalinization of the solution does not increase spread, but does prolong duration.[111]

Clinical technique

Patient position

As has been noted already, the difference between densities of CSF and the solution injected has a major effect on intrathecal drug spread. This is the result of the action of gravity, hyperbaric solutions 'sinking' and hypobaric ones 'floating', so that the degree of caudad or cephalad spread will depend on the interplay between density and patient position. This interplay is the major determinant of the final extent of block with most techniques, although posture has no influence on the spread of a truly isobaric solution.[151]

It is widely believed that injection of a hyperbaric solution in a seated patient will result in a more restricted block. However, a number of studies have shown that the block, while initially more restricted, eventually extends to a level equivalent to that which would have been obtained had the patient been placed supine immediately after injection.[89 108 147] Production of a classical 'saddle block' requires use of relatively small amounts of local anaesthetic in a patient kept in the sitting position for at least 10 min.[151] This will restrict the local anaesthetic to the sacral side of the lumbar lordosis when the supine position is resumed. If larger volumes are used, they will still 'spill over' into the higher lumbar and thoracic segments.

Given that most plain solutions are marginally hypobaric, some cephalad extension of block might be expected if patients are kept seated after injection. Richardson and colleagues[112] found that parturients who received an intrathecal injection of plain bupivacaine in the sitting position as part of a combined spinal epidural technique developed more extensive block than those kept in the lateral horizontal position. These blocks were for labour analgesia, not surgery, but it is noteworthy that many of the blocks in the lateral horizontal group would not have been extensive enough for Caesarean section. Indeed, a failure rate of 25% has been reported when such a technique is used for abdominal delivery, comparing very unfavourably with the zero failure rate of a hyperbaric solution.[67] Keeping the patient seated after injection of the plain solution will result in an adequate block, but has two disadvantages. The first is delay while the block spreads; after injection of a hyperbaric solution the patient is placed supine and other preparations for surgery can be made while the block spreads. The second is the risk of serious hypotension due to venous pooling in the legs as the local anaesthetic reaches and blocks the sympathetic outflow.

Less extreme degrees of tilt are sometimes used to influence spread, usually in an attempt to limit the cephalad spread of a hyperbaric solution and reduce the risk of hypotension. The maintenance of 10° or so of head-up tilt reduces spread,[80] but also has two potentially adverse effects. First, the block may not spread far enough for the projected surgery.[80] Second, there is again the risk of peripheral pooling of venous blood causing serious hypotension. In fact, every authority on spinal anaesthesia from the time of Labat has recommended the reverse: a small degree of head *down* tilt to ensure venous return, thereby maintaining cardiac output and blood pressure. Clinicians are often concerned that this manoeuvre will increase the cephalad spread of a hyperbaric solution and make hypotension more likely, but even a 30° tilt has minimal effect on mean spread, although it does increase variability.[125]

An alternative technique for minimizing sympathetic block is to keep the patient in the lateral position after injection so that only one side of the sympathetic chain is affected. As with 'saddle block', a small volume of local anaesthetic needs to be used and the position maintained for at least 15–20 min for any significant effect,[40] and then the block will tend to spread to the other side once the patient is placed supine for surgery. Because of the need to maintain a left 'tilt' position before delivery by Caesarean section, it has been argued that the spinal anaesthetic should be performed with the patient in the right lateral position to ensure bilateral spread, but this does not seem to influence final block height or its adequacy for surgery.[65] Placing the patient in the lithotomy position immediately after the injection of a hyperbaric solution might be expected to limit cephalad spread by abolishing the lumbosacral curve—the 'slope' down which the local anaesthetic moves under the influence of gravity. However, this was not shown to have an effect on spread, perhaps because even the most extreme positioning does not abolish the curve altogether.[90] The cardiovascular effects were less, probably an indication of the beneficial effects of leg elevation on venous return.

A less commonly used posture during spinal anaesthesia is the prone knee-chest position for lumbar discectomy. The spread of plain bupivacaine 0.5%, 3 ml injected in either the prone or lateral positions is similar.[72] Hypotension was greater in the prone group, although it occurred later.

In most circumstances, intrathecal local anaesthetic appears to stop spreading 20–25 min after injection. However, marked changes in patient posture up to 2 h after injection can lead to significant changes in extent of the block. The effect is independent of solution baricity,[96 108] and probably represents bulk movement of CSF still containing significant concentrations of local anaesthetic. All patient movements should be very gentle and progressive until the block has regressed completely.

Level of injection

Most studies, certainly with plain solutions of bupivacaine, have shown that a higher level of injection results in significantly greater cephalad spread, even when the difference in injection level is only one interspace.[27 79 119 134 140] The results are less consistent with hyperbaric solutions,[117] the effect of gravity perhaps being the more dominant factor with these solutions. However, all of these studies must be reviewed in the light of the more recent demonstration of the difficulty in accurately identifying the level of injection.[14]

Needle type and alignment

The different types of needle bevel impart varying degrees of 'directionality' to the flow of drug solution into the CSF. For instance, fluid leaves the Whitacre needle at an angle of 55° to its plane,[57] and this has been used to facilitate, by directing the orifice appropriately, the production of a unilateral block.[24] However, there is conflicting evidence regarding the effect of cephalad orientation of the orifice. With plain solutions, cephalad orientation of the Sprotte needle produced a block of faster onset but to the same mean level,[61] whereas similar alignment of the Whitacre produced greater spread with less variability.[141] The orientation of the orifice does not seem to influence the spread of hyperbaric solutions.[85 86] Again this may reflect the overriding effect of density/gravity with these preparations.

The alignment of the long axis of the needle is also relevant. Stienstra[130] used a paramedian approach to the subarachnoid space, with significant cephalad angulation of the needle, and demonstrated more extensive spread. It is presumed that this is the result of drug being delivered at a higher level than with the mid-line approach, and with the flow of local anaesthetic solution being more cephalad.

Intrathecal catheters

An intrathecal catheter may be placed for repeated injection or continuous infusion to allow significant prolongation of the block. Such techniques are the preserve of the expert because of the difficulties of catheter insertion and the abnormalities of drug spread that may be produced.[94] The position of the catheter tip, and the direction in which it faces, may combine to produce very abnormal drug distribution.

Fluid currents

Currents generated within the CSF by fluid injection are an obvious cause of spread. Many factors can affect the formation of these currents, notably the size, shape and orientation of the bevel and the speed of injection. It is widely thought that barbotage—the intentional creation of such currents by the repeated aspiration and re-injection of CSF and local anaesthetic—increases spread, but evidence does not confirm this.[69 74 97] Simply varying the speed of injection has been investigated extensively, but with conflicting results. Some studies report greater spread with a faster injection,[3 27 49 58 62] others with slower injection,[129 139] and some report no difference.[2 19 25 143] In general, the evidence suggests that faster injections produce greater spread with plain solutions, but that the effect is less marked with hyperbaric solutions, with some suggestion that slower injection actually produces greater spread.

Glass models of the spinal cord are often used to study such factors, but they omit any representation of the cauda equina and spinal cord, which may act as efficient 'baffles' to the generation of fluid currents.[139] Additionally, a fast injection may produce a bulk movement of CSF and pressure changes that tend to keep the solution near the injection site, whereas a slow injection may allow the solution to spread according to baricity and gravity.[129]

Epidural injection

Administration of an epidural injection of local anaesthetic relatively soon after an intrathecal one causes an extension of the block.[84] This could be due to additional neural block, but an injection of saline can have the same effect,[137] implying that the epidural injection compresses the theca and leads to cephalad spread of CSF containing local anaesthetic.

Patient characteristics

Although there is significant variation in maximum spread between patients given a standard technique, spinal anaesthesia is very reproducible in the individual patient.[136] Clearly, the variability must be due to patient factors, but it is far from clear which is the most significant.

Age

At the extremes of age there are small but significant increases in maximum spread, rate of onset of motor block and cardiovascular instability, regardless of the solution used.[22 104 110 145 146] It is probable that these are secondary to age-related changes in spinal anatomy, nerve physiology and cardiovascular reflexes. However, Hirabayashi[54] compared groups of adolescents and young adults matched in all respects except age and found significantly greater block height in the younger group. The exact reasons for this remain unclear.

Height

Logic might suggest that taller patients would display less cephalad spread for a given amount of local anaesthetic. Indeed, minimum effective doses have been calculated for Caesarean section (0.06 mg cm^{-1} height),[32] but no correlation between height and spread has been found in term parturients.[37 98] Furthermore, only one of the many studies that have looked at the effect of height has shown more extensive spread in shorter patients.[106] The main reason for this is that most of the difference in height between adults is due to the length of the lower limb long bones, not the spine. When spinal length (i.e. distance from C7 to the sacral hiatus) was related to block height, a much better correlation was obtained.[50]

Weight

It is often suggested that epidural fat compresses the dural sac, reduces CSF volume and results in the greater spread observed in obese patients.[106 134] However, these studies used plain solutions, which are known to produce wider variability in block height,[79] and studies with hyperbaric solutions have failed to show a significant relationship.[98 106] In addition, it is recognized that the level of injection in obese patients is often higher than intended,[14] and this can result in greater cephalad spread. Finally, when an obese patient is lying in the lateral position, the distribution of adipose tissue may alter the alignment of the vertebral canal. There are no data available which have controlled these variables in an attempt to determine if weight *per se* has any influence on local anaesthetic spread.

Sex

In general, it is believed that males tend to develop less cephalad spread than non-pregnant females, but there are few objective data. The spread of hyperbaric preparations may be influenced by differences in body shape while the patient is in the lateral position. Males tend to have broader shoulders than hips so that the spinal column has a 'head up' tilt in the lateral position, whereas the reverse is true in females. However, patients are usually turned supine immediately after injection so this effect is likely to be small. Differences in CSF density may be more relevant. This is

higher in males,[121] and will reduce the baricity of the local anaesthetic solution, thereby limiting cephalad spread.

Intra-abdominal pressure

It is often said that raised intra-abdominal pressure increases blood flow through the epidural veins, which then distend and compress the theca to decrease CSF volume. However, this theory was not entirely supported by a magnetic resonance imaging study which found that increasing abdominal pressure decreased CSF volume, but did so by displacing tissue into the vertebral canal through the intervertebral foraminae rather than by changing epidural venous volume.[56] A reduction in CSF volume may influence cephalad spread of local anaesthetic (see below), but no study has distinguished this effect from other causes. Although increased cephalad spread has been demonstrated in twin compared with singleton pregnancies,[64] other factors that could explain the difference (see below) besides increased intra-abdominal pressure.

Increasing intra-abdominal pressure by repeated coughing during the onset of spinal anaesthesia has not been found to influence cephalad spread.[35] This is not surprising given that acute transient changes in CSF pressure are instantaneously transmitted throughout any closed space filled with an incompressible liquid, so no hydrostatic gradients or turbulence develop.

Spinal anatomy

Variations in spinal curvature are only of importance when they influence the gravitational spread of local anaesthetic solutions. Consequently, a scoliosis is unlikely to influence spread unless the patient is kept in the lateral position. A kyphosis, or a change in the normal lumbar lordosis (e.g. in pregnancy), is more likely to have an effect because the anteroposterior curves are crucial to the pattern of spread of a hyperbaric solution in the supine subject. Reduction of the lumbar lordosis by flexion of the hip joint flattens the lumbar lordosis[53] and reduced cephalad spread in one study[127] but not another.[78] Abnormal spinal curvature can be a cause of block failure,[52] particularly if it moves the 'highest' point of the lumbar spine in the supine position from its usual level of L4.[55]

Lumbosacral CSF volume

Total CSF volume in an average adult is about 150 ml, approximately half of which is intracranial. The remainder lies within the spinal subarachnoid space and represents the volume through which the injected solution can distribute. Factors such as age, weight and height all influence lumbosacral CSF volume, which linear regression analysis has suggested is a determinant of spread.[23] This result was obtained by analysis of only 10 patients, but a very restricted block was obtained in a patient with a large CSF volume in spite of repeated injection. Thus, prior removal of CSF would be expected to increase spread, but the results of such studies have been inconclusive.[63 105]

While many factors influence CSF volume, and it may have a crucial effect on intrathecal drug spread, detailed study is, unfortunately, inhibited by the difficulties of measuring CSF volume accurately, even with radiological imaging.

Pregnancy

Many of the physiological changes that occur during pregnancy increase the effect of a local anaesthetic injection. Physical spread of the solution can be increased by changes in the lumbar lordosis,[142] and in the volume and density of the CSF (see above). Cephalad spread is not related to the degree of weight gain during pregnancy,[37] but is greater in twin compared with singleton pregnancies,[64] perhaps due to an effect on intra-abdominal pressure, as discussed above, or through a progesterone-mediated[42] increase in neuronal sensitivity.[20 92] The mechanisms that may be involved include direct effects on membrane excitability, indirect actions on neurotransmitters, increased permeability of the neural sheath, potentiation of endogenous opioids,[118] and potentiation of gamma aminobutyric acid-mediated increases in chloride conductance.

These physical and pharmacological factors add up to a considerable increase in the consequences of an intrathecal injection in the full-term pregnant patient.

Summary

Many factors affect the intrathecal spread of injected local anaesthetics. However, the influence of most of them is small, unpredictable and beyond the clinician's control. The major factors are the baricity of the solution injected and the subsequent posture of the patient. The most predictable effects are produced by the slow injection (into a patient placed supine immediately thereafter) of a small volume of solution that contains glucose, a conclusion which is nearly a hundred years old, but is still not applied universally. Use of glucose concentrations somewhat lower (circa 1%) than are traditional (5–8%) will reduce the risk of excessive spread, but still ensure good quality and extent of block for most of the surgical procedures for which spinal anaesthesia is appropriate. Manipulation of the factors that affect spread may be used to produce different types of block, as long as the clinician has a clear understanding of what is involved.

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