INVESTIGATION OF SOME FACTORS AFFECTING THE SENSORY LEVEL OF SPINAL ANESTHESIA: position, baricity, temperature, needle direction and speed of injection.

(Een studie naar enige factoren die de sensibele blokkade bij spinale anesthesie beïnvloeden: positie, bariciteit, temperatuur, naaldrichting en injectiesnelheid)

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I. Stienstra R, Van Poorten JF. Plain or Hyperbaric Bupivacaine for Spinal Anesthesia. Anesth Analg 1987; 66:171-176.

II. Stienstra R, Van Poorten JF. The Temperature of Bupivacaine 0.5 % Affects the Sensory Level of Spinal Anesthesia. Anesth Analg 1988; 67:272-276.

III. Stienstra R, Van Poorten F, Kroon JW. Needle Direction Affects the Sensory Level of Spinal Anesthesia. Anesth Analg 1989; 68:497-500.

IV. Stienstra R, Gielen M, Van Poorten F, Kroon JW. Spinal Anesthesia with Plain Bupivacaine 0.5 %: Regression of Sensory and Motor Blockade with Different Temperatures of the Anesthetic Solution. Anesth Analg 1989; 69:593-597.

V. Stienstra R, Gielen M, Kroon JW, Van Poorten F. The Influence of Temperature and Speed of Injection on the Distribution of a Solution Containing Bupivacaine and Methylene Blue in a Spinal Canal Model. Accepted for publication in Reg Anesth.

C O N T E N T S

CHAPTER 1

HISTORY

When reading about the history of spinal anesthesia, one cannot but agree with Greene that the introduction of inhalation anesthesia in 1846 was not a random event, but rather the logical consequence of the changes in the political, cultural and religious concepts with regard to pain (1) and that the introduction of local anesthetics rather than intravenous agents into medical practice followed the introduction of ether as the equally logical next step (2).

Around 1850 the coca shrub was brought to Europe by expeditions returning from South America, where native Indians had been chewing its leaves for its fatigue-chasing and cerebral stimulating effects. Whether the indians were aware of its numbing properties is not certain, but it has been reported that the saliva formed while chewing coca leaves was applied to wounds (3,4). In 1855 the German chemist Gaedicke extracted erythroxylin from the coca leaves and in 1859 Albert Niemann isolated the alkaloid cocaine (5), the achievement being reported in 1860 (6), probably by Niemann's teacher Wöhler. Although the numbing effect of cocaine was well known (5,6,7), the search for its therapeutic uses focused mainly on its central stimulating properties. Apart from that, cocaine was used as an aphrodisiac and in the treatment of dyspepsia, cachexia and asthma, as well as in patients suffering from morphin and alcohol addiction (7). Von Anrep, who studied the effects of cocaine in animals, indicated that its local anesthetic properties might be of clinical importance (8), but before him Moréno y Maiz, who would later become physician-in-chief of the Peruvian army, already hinted on the use of cocaine as a local anesthetic in his thesis in 1868 (9). The first however to capitalize on the therapeutic potential of cocaine as a local anesthetic rather than an analgesic was Karl Koller; Koller, who was a resident in the Viennese General Hospital, had developed an interest in ophthalmology. Being displeased with the standard of general anesthesia prevailing at the time in his hospital, he was looking for a substance which, when instilled into the conjuntival sac, would cause anesthesia of the eye (10). His friend and fellow resident Sigmund Freud was greatly interested in the use of cocaine and had recently published an extensive essay on the substance (7). As Sir Robert MacIntosh tells us in his captivating chapter on the history of spinal anesthesia (11), Freud had other interests as well, among them

the ambition to follow an academic career in order to be able to marry his fiancee. Before going on a trip to Hamburg to see her, Freud suggested to Koller that he might study the effect of cocaine on muscular power and asked another friend, Leopold Königstein, to try cocaine as an analgetic in painful conditions of the eye (12). While Freud was in Hamburg enjoying the company of his fiancee, Koller initiated his study on cocaine, independent from Königstein, incidentally. When swallowing some of the drug himself he noticed, as many others before him, the numbing effect of the drug on his lips and tongue. Koller realized that cocaine might be the anesthetic for the eye he had been looking for and set off to investigate the anesthetic effects of cocaine on the eye, first in animal experiments followed by experiments on himself as well as fellow residents and finally in patients. In these experiments he demonstrated the capacity of cocaine to establish complete anesthesia of the cornea. The earliest opportunity to publish his discovery was the annual Heidelberg meeting of the German Ophthalmological Society, but unfortunately Koller was unable to attend this meeting due to financial problems. He therefore asked the organizing committee for permission to have his paper read for him by a colleague, Joseph Brettauer from Triest. Permission was granted and Brettauer not only read the paper on September 15, 1884, but he also gave a practical demonstration using some of the cocaine solution that Koller had given to him. Koller's discovery created a sensation and within weeks cocaine was being investigated and employed all over the world. On October 17, 1884 Koller read a fuller paper about his findings before the Vienna Medical Society (5) and he also published his discovery in the Lancet (13). Although Königstein, who had reached similar conclusions, originally tried to claim that the discovery was his, his conclusions were reported several weeks later (14) and he was finally persuaded, among others by his friend Freud, to concede that the honour belonged to Koller.

It has often been suggested that Koller came to his discovery at the incitement of Freud; when reading however the narrative of Koller's daughter (15) including many letters from Freud to Koller, it becomes clear that Freud had no interest in the local anesthetic properties of cocaine, but had high hopes on its potential in the treatment of morphine addiction. Thus, as is well demonstrated by Liljestrand (16), it was Freud's merit to focus attention on the drug, but the discovery and the introduction of cocaine as a local anesthetic is the excellence of Koller alone.

Koller did not succeed in obtaining the well-deserved assistantship in the academic department of Ophthalmology in Vienna that he wanted so much. In early January 1885, he became involved in an argument with one of Theodore Billroth's house

surgeons, a man called Fritz Zinner (15,17). According to the newspaper of January 7, 1885 (18) the two doctors disagreed on the treatment of an injured finger; during the argument, Zinner met with a slap in the face after calling Koller something that sounded like "impudent Jew". Zinner then challenged Koller to a duel which took place on January 6, 1885, in which Koller managed to graze Zinner, who was carried away to hospital. Duels were of course strictly forbidden in Vienna and this, together with the already prevailing anti-Semitism in Austria, smashed Koller's hopes of an academic career. Being unable to obtain the assistantship in the academic department of Ophthalmology, Koller moved to the Netherlands, where he spent some years working under Cornelius Donders and Herman Snellen. From there he moved to London and finally, in May 1888, he settled in New York where he spent the remainder of his life as an eye specialist, gaining honour, reputation and recognition over the years. In 1928 he wrote a historical notice about the origins of local anesthesia, that was published in both the "Wiener medizinische Wochenschrift" and in the Journal of the American Medical Association (19,20). Karl Koller died in 1944.

Corning, a neurologist, was the first to attempt spinal anesthesia (21), although not in any way as we understand it today. He was under the false impression that injecting cocaine between the spinous processes would result in rapid transportation of the drug to the spinal cord, thus producing anesthesia of the cord. Corning's experiments were carried out in a man and a dog. The man, receiving approximately 120 mg of cocaine which is about four times the lethal dose, was certainly lucky to survive the experiment and what was achieved was probably epidural anesthesia (22); the dog, receiving approximately 13 mg, presumably had spinal anesthesia (22).
Before spinal anesthesia could enter clinical practice, the technique of lumbar puncture had to be invented; in 1891, Essex Wynter published a paper in which he described the attempted treatment of four children suffering from tuberculous meningitis by means of the introduction of a Southey's tube into the subarachnoid space or by puncturing the dura with a knife at the first or second lumbar interspace (23). Although this treatment proved unsuccessful, it may have inspired Heinrich Quincke to perform lumbar puncture in patients suffering from hydrocephalus. Quincke (24) was the first to observe that the spinal cord extended to the second lumbar vertebra and that in order to prevent damage to the cord, lumbar puncture had to be performed in the third or fourth lumbar interspace. He also was the first to describe the technique of lumbar puncture with a needle.

The man who was to combine the pharmacological knowledge of Koller and the technique of Quincke and who is considered to be the father of spinal anesthesia as we know it today, is August Bier. On August 16, 1898 he injected cocaine in the subarachnoid space in order to obtain surgical anesthesia of the lower limb and in his paper published in 1899 he describes six patients who underwent surgery after having received intrathecal doses of 5 to 20 mg of cocaine (25). Convalescence was marked by severe headache and vomiting, which is not surprising in view of the fact that Bier would place his bare finger over the hub of the needle in order to minimize cerebrospinal fluid loss and that he used tap water to dissolve the cocaine crystals (26). In order to investigate the cause of the unpleasant after-effects of spinal anesthesia, Bier had lumbar puncture performed on himself by his assistant Hildebrandt who was to inject 5 mg of cocaine; the experiment failed because the syringe would not fit the needle and some cerebrospinal fluid was lost, most of the cocaine dripping to the floor as well. To save the experiment, Hildebrandt volunteered to undergo spinal anesthesia and that 5 mg of cocaine intrathecally was sufficient to provide analgesia, was unscientifically though unequivocally proven by the fact that subsequently poor Hildebrandt tolerated some of his pubic hair being pulled out, his testes being pulled and sqeezed, being hit on the tibia with an iron hammer and a burning cigar pressed against his leg, all this without causing any pain. The two gentlemen celebrated the success of their investigation the same evening with dinner, wine and cigars, only to find themselves in poor shape for some days afterwards. Bier's symptoms of postural headache and dizziness lasted for nine days and, although admitting that they drank and smoked more than was beneficial and that both of them should have laid down, he suggests that the headaches and vomiting were caused by circulatory disturbances of the central nervous system or by loss of cerebrospinal fluid and he concludes his article with the recommendation that loss of cerebrospinal fluid should be minimized if not avoided.

Independent from Bier and originally unaware of Bier's work, the French surgeon Theodore Tuffier observed that the intrathecal injection of 20 mg of cocaine completely abolished the severe pain caused by an inoperable sarcoma of the iliac bone in a young man who no longer responded to morphine. He then tried the same injection to a lady with a sarcoma of the thigh and to his great surprise was able to remove the tumor without her feeling any pain. Tuffier continued and on November 11, 1899 he presented a first communication about six patients (27) to the Biological Society in Paris (28), a few months after the appearance of Bier's article. Unlike Bier, who had a reserved attitude towards spinal anesthesia, Tuffier was an enthusiastic

advocate of the technique and continued to use it in various operations (29). He improved his technique by paying attention to asepsis, varying the puncture site and patient position after intrathecal injection and he was the first to record a follow-up examination in 60 patients operated under spinal anesthesia (30).
The technique of spinal anesthesia initially gained popularity all over the world with the exception of the United Kingdom, probably because there the prevailing standard of general anesthesia was considered superior to the rest of the world. In the United States reports on the use of spinal anesthesia appeared from Matas (31), Tait and Caglieri (32) and from Bainbridge who used the technique on children (33).

The basic principle and effectiveness of spinal anesthesia with cocaine being established, its popularity was rather limited due to the toxicity and addictive potential of cocaine and a new drug was mandatory. Stovaine was introduced by Fourneau in 1904 (34) and the German chemist Einhorn synthesised procaine in 1905 (35), which was first used in spinal anesthesia by Braun (36). This gave fresh impetus to the development of spinal anesthesia and until the 1920's stovaine was the drug employed most frequently. The English surgeon Arthur Barker advocated the addition of 5 % glucose in order to make the solution hyperbaric, based on his observations in a glass model of the vertebral canal as well as in patients (37,38,39). On the other hand Babcock in Philadelphia added alcohol to stovaine in order to make it hypobaric (40,41).
Although synthesised in 1905, procaine did not gain popularity until Gaston Labat published his famous book on regional anesthesia (42). Labat used procaine crystals dissolved in aspirated cerebrospinal fluid and contrary to Barker advocated the use of the Trendelenburg position in order to secure an adequate blood supply to the brain. To establish high levels of sensory blockade, Labat used barbotage, a technique first described by Le Filliatre (43). George Pitkin used both hypobaric and hyperbaric solutions of procaine with the objective to gain control over the sensory level of blockade (44), but his method did not attain popularity.
The next step was the introduction of the longer acting local anesthetic drugs, tetracaine and dibucaine. Tetracaine was synthesised by Eisleb in 1928 (45) and popularized as a hyperbaric solution by Sise (46), dibucaine was introduced by Uhlmann and Jones (47,48).
In the meantime, one of the major drawbacks of spinal anesthesia, uncontrollable hypotension, had been overcome by the introduction of the pressor drug ephedrine

(49,50). Ephedrine had already been isolated from the Chinese herb ma huang as early as 1887 (51), but it was not introduced into Western medicine until 1926 (52). Lidocaine was synthesised by Löfgren and Lundqvist in 1943 (53,54). In 1957 bupivacaine followed (55), introduced in spinal anesthesia by Ekblom and Widman in 1966 (56). The structural formula of bupivacaine is shown in figure 1.1.

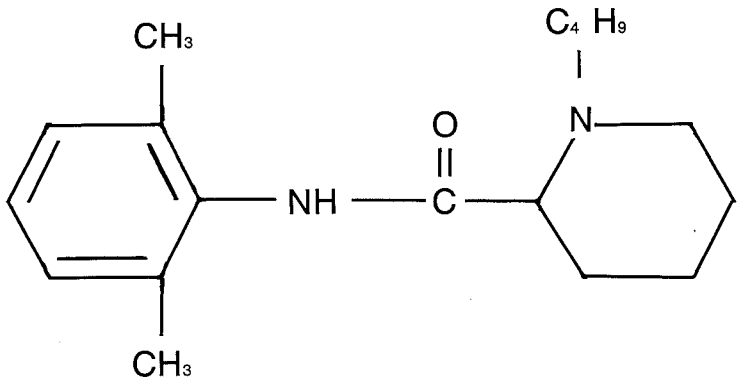

Figure 1.1. Structural formula of bupivacaine.

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CHAPTER 2

INTRODUCTION AND AIMS OF THE STUDY

INTRODUCTION

When injecting local anesthetic solutions into the subarachnoid space, three major factors determine the characteristics of the resulting spinal anesthesia (1,2): Distribution within the cerebrospinal fluid determines the extent of altered neuronal function, uptake determines which functions are affected and elimination determines the duration of altered neuronal function. The determinants of these factors have been well documented (3) and extensively reviewed (1,2). Many factors have been designated to affect the distribution of local anesthetic solutions within the subarachnoid space and consequently the level of sensory blockade; the clinical significance of these factors however varies widely and data are often conflicting.

Increased **patient age** is thought to be associated with higher levels of sensory blockade; this was shown in a statistically significant fashion in some studies (4,5), whereas in other studies there was a statistically not significant tendency to the same effect (6,7).

Cephalad spread is thought to be less in the taller patient, although this has never been studied under controlled conditions. The effect of **patient height** alone would be difficult to study indeed, since other factors e.g. body weight and body mass would almost inevitably be included. Furthermore, rather than having a direct relation with intrathecal distribution, the influence of patient height is more likely to be mediated by other factors such as the volume of cerebrospinal fluid and the number of spinal segments covered by a given volume of cerebrospinal fluid. The acceptance of the effect of patient height on the intrathecal distribution of local anesthetics therefore is based on common sense and clinical impression. Since **sex**-related differences in patient height are not great enough to produce significant differences in sensory levels of blockade (8), the effect is probably small under normal conditions and only clinically relevant in extreme situations.

The **anatomic configuration** of the spinal column will affect the intrathecal distribution of local anesthetic solutions of which the spread is governed by gravity. When the patient is in the supine horizontal position, a hyperbaric solution present in the apex of the lumbar lordotic curve will be promoted to spread downwards in both a thoracic and lumbosacral direction. Reduction of the lumbar lordotic curve by hip flexion has been shown to decrease the cephalad spread of hyperbaric tetracaine in one study (9), and to reduce although not abolish the bimodality observed in the upper level of anesthesia as determined by the inability to appreciate touch in a study using hyperbaric bupivacaine (10). Consequently, the presence of a marked lordotic curve in the upper lumbar region may be expected to decrease the cephalad spread of a hyperbaric solution injected in the lower lumbar region in the supine patient, since it will cause pooling of the local anesthetic solution in the deepest part of the S-shaped lumbar curve (2; Greene NM, personal communication).

The **site of injection** obviously plays a major role. Although spinal anesthesia will rarely if ever be undertaken intentionally above the second lumbar interspace due to the grave risk of damaging the spinal cord which extends to the superior border of the second lumbar vertebra by the spinal needle, injection of a local anesthetic solution into the thoracic subarachnoid space would result in a different distribution pattern. Firstly because of the difference in the site of injection itself, but since the spinal cord occupies a substantial portion of the subarachnoid space above the second lumbar vertebra, the distribution of a local anesthetic solution in a given volume of cerebrospinal fluid would cover more spinal cord segments when injected above the second lumbar vertebra as compared with injection below this level. Furthermore, it has been shown that subarachnoid injection of plain bupivacaine 0.5 % at the second lumbar interspace results in a higher cephalad spread than injection at the fourth lumbar interspace (11).

The **direction of the needle** is supposed to affect intrathecal distribution based on logical assumption. If the needle is directed in a more cephalad direction, the stream of the local anesthetic solution coming from the tip of the needle will expectedly carry the anesthetic solution farther in a cephalad direction than if the same injection were made through a spinal needle inserted at a right angle to the longitudinal axis of the subarachnoid space.

The **volume of cerebrospinal fluid**, or rather the volume of cerebrospinal fluid within the spinal subarachnoid space, will affect the number of spinal segments that are going to be blocked after the intrathecal injection of a given volume of a local anesthetic solution. The total volume of cerebrospinal fluid in normal adults varies from 120 to 150 ml, of which 25 to 35 ml is in the spinal subarachnoid space (12), although this latter volume is also said to be 75 ml (2,13). The effect of the cerebrospinal fluid volume has been well demonstrated in full term parturients, in whom the increased abdominal pressure results in a reduction in cerebrospinal fluid in the lumbar and lower thoracic region of the spinal canal: the dosage required to produce a given level of sensory anesthesia has been shown to be substantially lower in parturients as compared with non-pregnant women (14,15).

Dosage, concentration and volume of anesthetic solution have an inseparable relation with each other since dosage is the product of concentration and volume. Although it has been suggested that volume of local anesthetic solution itself affects distribution (16,17), these studies used varying volumes of an anesthetic solution with the same concentration, thus creating differences in dosage as well. In another study comparing the intrathecal administration of 15 mg of plain bupivacaine in either 2 or 3 ml, it was shown that the higher volume resulted in a higher cephalad spread, whereas injection of 2 ml containing either 10 mg or 15 mg plain bupivacaine resulted in the same level of sensory blockade, indicating that the volume of anesthetic solution rather than dosage affects intrathecal distribution (18). The issue of volume and dosage is further obscured by a study, in which the intrathecal administration of 1 ml containing 7.5 mg of bupivacaine resulted in the same level of sensory blockade as 2 ml containing 15 mg of bupivacaine (19). Contrary to these observations, it was shown that subarachnoid injection of 10 mg of amethocaine in different volumes did not result in significant differences in the maximum level of sensory blockade (20) and that 22.5 mg of bupivacaine in either 3 ml or 4.5 ml of anesthetic solution resulted in the same level of sensory blockade (21). In a well-controlled study designed to elucidate the effects of volume, dosage and concentration on the intrathecal distribution of plain bupivacaine, Sheskey et al. concluded that dosage rather than volume or concentration was the important determinant (22). This view has been confirmed by other studies (23,24). Recently, in a study comparing the intrathecal administration of 12.5 mg of bupivacaine in a volume of either 2.5 ml or 10 ml, the maximum levels of sensory blockade were the same, demonstrating that intrathecal distribution is determined by dosage even when large differences in volume are employed (25). This observation has

been confirmed by other studies comparing the intrathecal injection of 15 mg of bupivacaine in either 3 ml or 6 ml (26,27). Thus, although volume itself may affect intrathecal distribution, the bulk of evidence seems to support the view that dosage is more important.

The **baricity** of the anesthetic solution is determined by the density of the solution relative to the density of cerebrospinal fluid. The density of cerebrospinal fluid at 37 °C is 1.0003 with a standard deviation of 0.0003 (2). Taking into account the small but important variation in the density of cerebrospinal fluid, solutions with a baricity of less than 0.9990 are termed hypobaric and solutions with a baricity of more than 1.0015 are termed hyperbaric (2). Solutions with the same density as cerebrospinal fluid are termed isobaric, although it follows from the already mentioned variability in cerebrospinal fluid density that an isobaric solution can never be isobaric in all patients. Since hypo- and hyperbaric solutions when injected into the cerebrospinal fluid are subject to the effects of gravity, the baricity of the anesthetic solution will affect intrathecal distribution and when using non-isobaric solutions, the position of the patient will likewise be of importance.

AIMS OF THE STUDY

The purpose of the studies to be presented was to investigate different factors influencing spinal anesthesia with bupivacaine 0.5 %.
More specifically, the first study investigated the differences in intrathecal distribution as measured by the maximum sensory level of blockade between the plain and the hyperbaric solutions of bupivacaine 0.5 %, as well as the effect of posture on the intrathecal distribution of the hyperbaric solution.
The second study investigated the temperature-dependent changes in baricity of the plain solution of bupivacaine 0.5 % on intrathecal distribution.
The third study investigated the effect of the direction of the spinal needle on the intrathecal distribution of plain bupivacaine 0.5 %.
The fourth study compared the characteristics of spinal anesthesia as defined by onset, duration and regression of sensory and motor blockade of plain bupivacaine 0.5 % equilibrated to body temperature and to room temperature. The fifth study describes observations made in a spinal canal model regarding the distribution of a solution

containing bupivacaine and methylene blue injected at different temperatures and with different speeds of injection.

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CHAPTER 3

THE EFFECT OF PATIENT POSITION AND BARICITY OF THE BUPIVACAINE SOLUTION ON INTRATHECAL SPREAD [1]

SUMMARY

Three ml of bupivacaine 0.5 %, either plain or in 8 % glucose, was injected intrathecally in three groups of twenty patients. Group 1 received bupivacaine 0.5 % plain; group 2 received bupivacaine 0.5 % in 8 % glucose. Patients in groups 1 and 2 were kept sitting for 3 min after injection. Patients in group 3 received bupivacaine 0.5 % in 8 % glucose and were placed in the supine horizontal position immediately after injection. Observations of patients in group 3 were observer blind and in groups 1 and 2 double blind. The differences between segmental levels of sensory and temperature loss between groups 1 and 2 and between groups 2 and 3 were statistically not significant. Motor blockade of the lower extremities was more intense in the patients who were kept sitting for 3 min (groups 1 and 2). It is concluded that both solutions are equally suitable for spinal anesthesia, provided patients receiving the plain solution are kept sitting for at least 2 min. When using hyperbaric bupivacaine, posture seems to have no influence on cephalad spread.

INTRODUCTION

In recent years, bupivacaine 0.5 % has been used increasingly for spinal anesthesia, both as a plain and as a hyperbaric solution. The hyperbaric solution of bupivacaine has been found to be a safe and reliable anesthetic solution for spinal anesthesia in various studies (1-4). The plain solution of bupivacaine 0.5 % has also been used for spinal anesthesia with good results (5-11). Others, however, found the plain solution of bupivacaine unsatisfactory or only suitable for perineal and lower limb surgery (3,12-16). Since 1982 our department has used the plain solution of bupivacaine 0.5

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% as the sole agent for spinal anesthesia. We have accumulated experience in over 3000 cases in which the plain solution proved an excellent spinal agent for any kind of surgery below the umbilicus. Because of conflicting findings in the literature with regard to the effectiveness of the plain solution, the present study was undertaken to compare the effects of hyperbaric bupivacaine with those of plain bupivacaine under double blind conditions, and the effect of posture when using the hyperbaric solution under observer-blind conditions.

PATIENTS AND METHODS

Sixty patients (ASA I-II) about to undergo urologic surgery under spinal anesthesia were randomly allocated to either a double-blind group (groups 1 and 2) or the open group (group 3). Each group contained twenty patients. Patients in the double-blind groups received 3 ml of a solution containing either bupivacaine 0.5 % plain (group 1) or bupivacaine 0.5 % in glucose 8 % (group 2) and were kept sitting for 3 min after completion of the intrathecal injection of the solution. Patients in group 3 received 3 ml of bupivacaine 0.5 % in glucose 8 % and were turned into the supine horizontal position immediately after injection. The study was approved by the Ethical Committee of the hospital, and oral consent was obtained from all patients.

Premedication consisted of temazepam 10 mg orally the night before the operation. Before the institution of the spinal anesthesia, 500 ml of Ringer's solution was administered by rapid intravenous infusion. Dural puncture was performed with the patient in the sitting position at the L3-L4 interspace by a standard midline or paramedian approach using a 25 gauge spinal needle.

Blood pressure and pulse rate were measured before injection (t = 0) and at 5-min intervals after injection for 20 min (t = 5-20) using an automatic cycling device (Dinamap). ECG was monitored continuously.

Measurement of the height of sensory changes was made 10 and 20 min after injection of the bupivacaine solution. Sensory loss was measured in the anterior axillary line by pin prick using a short bevelled 25-gauge needle. Temperature loss was measured using an ice cube. The segment at which the patient was not capable of recognizing the temperature of the ice cube and the segment of loss of sensation to pin prick were recorded. Motor blockade was assessed 10 and 20 min after injection using a 0-3 scale according to Bromage (17). All punctures and observations were made by the authors themselves; the author making the observations concerning levels of blockade and

degree of motor blockade was "observer blind", i.e., he did not know whether the patient was in the open group or in the double blind group.
Results are expressed as mean ± SEM. Statistical analysis used the Wilcoxon test for matched pairs for intragroup variations and the Mann-Whitney-U test for intergroups comparisons. A P-value less than 0.05 was taken as a significant difference.

RESULTS

No significant statistical differences existed among the three groups with regard to age, height or weight (Table 3.1).

Table 3.1. **Characteristics of the Patients Studied**

	Group 1 (n = 20)	Group 2 (n = 20)	Group 3 (n = 20)	DELTA 1-2	DELTA 2-3
Age (yr)	70 ± 1.72	69 ± 1.61	70 ± 1.59	NS	NS
Height (cm)	175 ± 1.36	173 ± 1.47	173 ± 1.90	NS	NS
Weight (kg)	72 ± 1.61	75 ± 2.52	70 ± 2.54	NS	NS

Group 1: plain bupivacaine, 3 min sitting after injection. Group 2: hyperbaric bupivacaine, 3 min sitting after injection. Group 3: hyperbaric bupivacaine, immediately turned to the supine horizontal position.
NS, no statistically significant difference.
Mean values ± SEM.

The segmental level of temperature loss after 10 min was T-8 in group 1, T-9 in group 2, and T-10 in group 3; after 20 min these levels were T-7, T-7, and T-8, respectively. The segmental level of loss of sensation to pin prick after 10 min was T-9 in group 1, T-10 in group 2, and T-10 in group 3; after 20 min these levels were

T-7, T-8, and T-9, respectively. The differences in sensory levels between groups 1 and 2 and between groups 2 and 3 were statistically not significant, at either 10 or at 20 min (Table 3.2). The ranges of levels are shown in Figure 3.1.

Table 3.2. **Segmental Levels of Loss of Sensation to Temperature (TEMP) and Pin Prick (P.PR) 10 and 20 min after Injection**

	Group 1 (n = 20)	Group 2 (n = 20)	Group 3 (n = 20)	DELTA 1-2	DELTA 2-3
TEMP 10'	T-8 (0.7)	T-9 (0.6)	T-10 (0.6)	NS	NS
TEMP 20'	T-7 (0.7)	T-7 (0.6)	T-8 (0.5)	NS	NS
P.PR 10'	T-9 (0.6)	T-10 (0.5)	T-10 (0.3)	NS	NS
P.PR 20'	T-7 (0.6)	T-8 (0.6)	T-9 (0.4)	NS	NS

Groups as defined in Table 3.1.
NS, not significant.
Mean values ± SEM, SEM in parentheses.

Motor blockade was more intense in the patients who were kept sitting for 3 min (groups 1 and 2), at both 10 and 20 min (Figure 3.2).
Systolic blood pressures decreased in all groups, with decreases significantly below baseline levels after 5, 10, 15 and 20 min in groups 1 and 3; in group 2, decreases were significant after 10, 15 and 20 min. Differences between systolic blood pressures at t = 0 were not significant. Differences between decreases in systolic blood pressures in groups 2 and 3 were not significant at any time; between groups 1 and 2 there was a significant difference between the decreases in systolic blood pressures only after 10 min, at which time the decrease in group 1 was greater.

Table 3.3. Systolic BP (mm Hg) and Heart Rate (beats/min) at Various Times (t) During and After Injection into Subarachnoid Space

	Group 1 (n = 20)	Group 2 (n = 20)	Group 3 (n = 20)	DELTA 1-2	DELTA 2-3
Systolic BP (t = 0)	140 (3.32)	142 (2.97)	145 (4.24)	NS	NS
Systolic BP (t = 5)	130 (3.69) P < 0.01	140 (3.69) NS	136 (4.63) P < 0.05	NS	NS
Systolic BP (t = 10)	122 (4.63) P < .001	135 (4.28) P < 0.05	133 (4.55) P < 0.01	P < 0.02	NS
Systolic BP (t = 15)	122 (3.55) P < 0.01	128 (3.61) P < 0.01	128 (3.09) P < .001	NS	NS
Systolic BP (t = 20)	125 (3.89) P < 0.01	129 (4.52) P < 0.01	130 (3.29) P < .001	NS	NS
Heart rate (t = 0)	75 (3.68)	75 (2.87)	76 (3.14)	NS	NS
Heart rate (t = 5)	76 (3.59) NS	77 (2.94) NS	76 (3.01) NS	NS	NS
Heart rate (t = 10)	75 (3.68) NS	80 (3.55) P < 0.01	75 (2.67) NS	P < 0.05	NS
Heart rate (t = 15)	74 (3.89) NS	78 (3.08) NS	74 (2.71) NS	NS	NS
Heart rate (t = 20)	74 (3.77) NS	77 (2.89) NS	72 (2.90) NS	NS	NS

Groups as defined in Table 3.1.
Mean values ± SEM, SEM in parentheses.

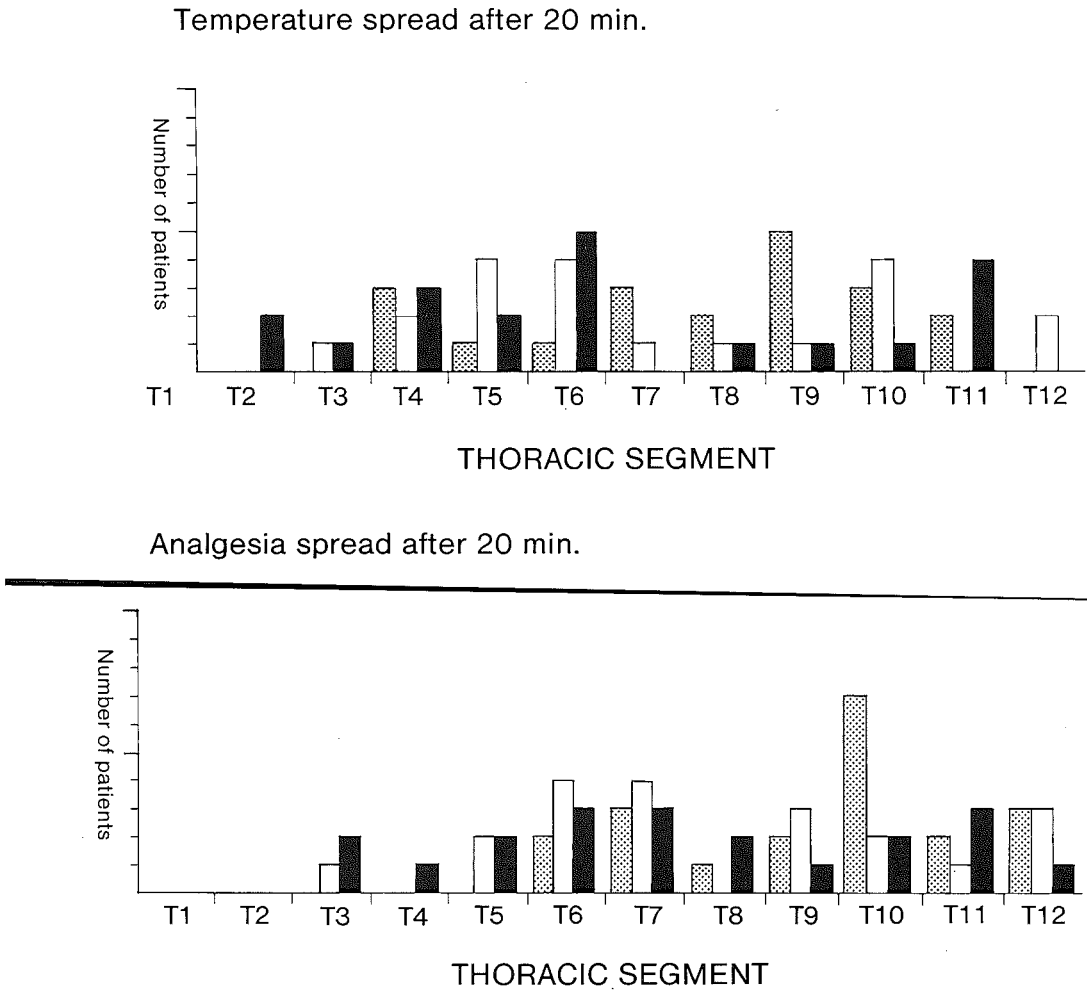

Figure 3.1. Segmental levels of temperature loss (temperature spread) and loss of sensation to pin prick (analgesia spread) 20 min after injection. The horizontal axis shows the thoracic segment at which temperature loss and loss of sensation to pin prick were measured, the vertical axis shows the number of patients.

■ **Group 1: plain bupivacaine, 3 min sitting after injection.**

□ **Group 2: hyperbaric bupivacaine, 3 min sitting after injection.**

▩ **Group 3: hyperbaric bupivacaine, immediately turned to the supine horizontal position.**

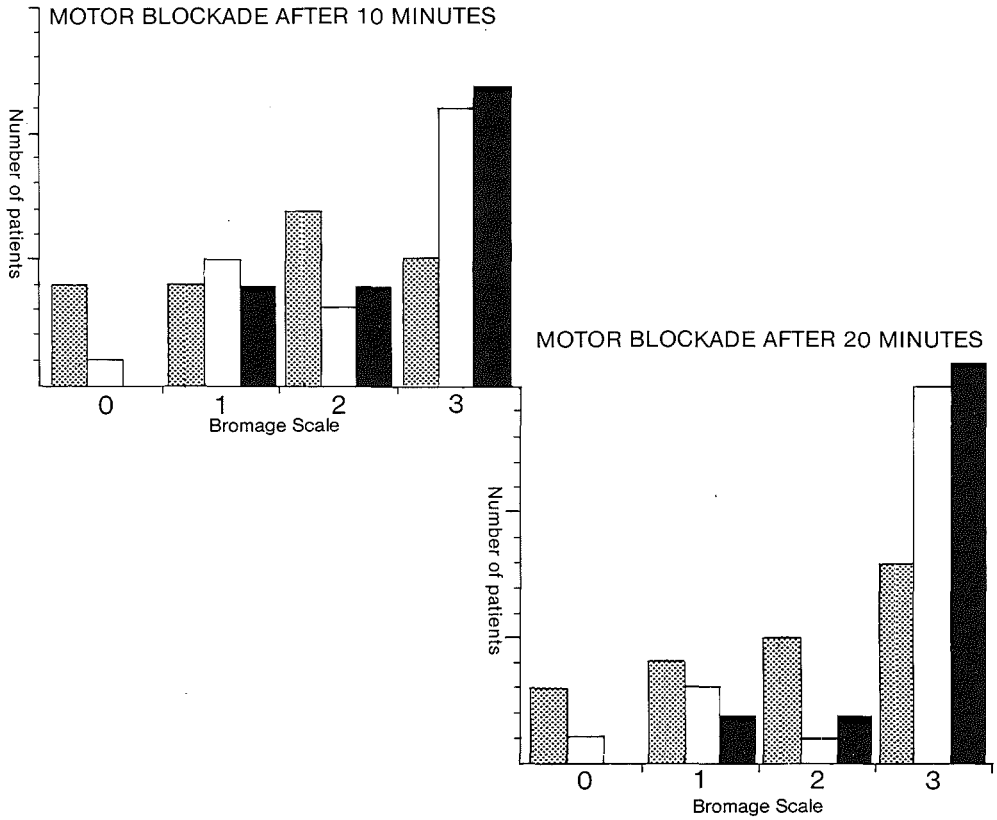

Figure 3.2. **Degree of motor blockade 10 and 20 min after injection. The horizontal axis shows the Bromage scale: 0 = no motor block; 1 = inability to raise the extended leg; 2 = inability to flex the knee; 3 = complete motor block. The vertical axis shows the number of patients.**

■ **Group 1: plain bupivacaine, 3 min sitting after injection.**

□ **Group 2: hyperbaric bupivacaine, 3 min sitting after injection.**

▨ **Group 3: hyperbaric bupivacaine, immediately turned to the supine horizontal position.**

The decrease in blood pressure was so mild in all patients that vasopressors were not required. In groups 1 and 3 there was a small but not significant decrease in heart rate; in group 2 there was a small increase in heart rate that was significant only at 10 min. Intergroup comparison showed that the differences in changes in heart rates between groups 1 and 2 were significant at 10 min. Hemodynamic data are summarized in Table 3.3. None of the patients suffered from postspinal headache.

DISCUSSION

The factors that govern the spread of intrathecally administered solutions have been and still are subject to speculation. Factors playing a major role have been suggested to be the amount of drug given (9,18) or the volume used (5,19). Speed of injection has been suggested as a factor governing spread but has never been tested; barbotage is believed to increase cephalad spread, although it failed to do so in a controlled study (20). Attention has also focused on the influence of posture and the baricity of the solution. Since the work of Barker (21), who studied the behaviour of hyperbaric solutions in a glass tube, local anesthetics for spinal anesthesia have usually been administered as hyperbaric solutions. If the patients are kept in the horizontal position, it has been shown that the use of hyperbaric solutions of tetracaine or bupivacaine result in a higher cephalad spread when compared with the plain solutions (3,13,14,22). However, in a study comparing hyperbaric with isobaric tetracaine in which the patients were kept sitting for approximately 20 sec after injection, there was no difference in cephalad spread (20). Another study reported that the cephalad spread of a plain solution of bupivacaine increases if the patient is kept in the sitting position for 2.5 min (23).

It is interesting to see that all authors who consider the plain solution unsuitable, unpredictable or suitable only for lower limb and perineal surgery perform dural puncture in the horizontal position, turning the patient supine immediately afterwards (3; 12-16). Authors who achieve a good cephalad spread of the plain solution of bupivacaine all perform dural puncture with the patient in the sitting position, keeping the patients sitting for at least 2 min afterwards (9,18,23,24).

In our study, there was no difference in cephalad spread in patients given the hyperbaric and the plain solution in the sitting position. Although this agrees with the results of other studies (18,24), the possibility of a type II error being made must be kept in mind. As can be seen in Figure 3.1, the variation in cephalad spread is

considerable. This could cause masking of an existing significant difference, both between groups 1 and 2 and between groups 2 and 3.
Comparing the sitting patients given hyperbaric bupivacaine with the patients kept horizontal, our study shows that again there was no difference in cephalad spread. This is surprising, because on the basis of baricity one would expect a hyperbaric solution to "sink" in the sitting patient. Indeed, it has been shown that, contrary to common belief, changes in posture cannot be used to control the spread of hyperbaric tetracaine (25) or hyperbaric bupivacaine (26). This suggests that the addition of glucose makes little or no difference with regard to the cephalad spread of an intrathecal solution.

In our study, complete motor blockade was more frequent in the patients kept sitting than it was in patients in the horizontal position; there appeared to be no difference in degree of motor blockade between the patients receiving either the plain or the hyperbaric solution and who were kept sitting for 3 min. In some studies, use of the plain solution has resulted in a higher frequency of complete motor blockade (3,18,24), whereas in other studies this is not so obvious (13,14).

Apart from a significant difference of short duration at 10 min between groups 1 and 2, there were no significant differences with regard to decreases in systolic blood pressure or changes in heart rate, either between groups 1 and 2 or between groups 2 and 3. When performing repeated tests on the same data, there is always a chance of finding a spurious significance; because the aforementioned difference between groups 1 and 2 at 10 min looses significance when Bonferroni's procedure is applied and because a significant difference is not very likely, we feel it is unimportant.

In conclusion, the results of this study indicate that both the plain and the hyperbaric solutions of bupivacaine 0.5 % are equally suitable for spinal anesthesia, provided the patients receiving the plain solution are kept in the sitting position for at least two min. A possible advantage of the plain solution is that duration of action may be longer. Several studies report that anesthesia using a hyperbaric solution has a shorter duration than anesthesia with a plain solution (13,18,22,25,27), although other studies fail to confirm this (20,24). When using a hyperbaric solution, posture has no influence on cephalad spread under the conditions of the present study. Motor blockade was more intense in the patients who were kept sitting, regardless of the solution used.

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CHAPTER 4

THE EFFECT OF TEMPERATURE OF THE BUPIVACAINE SOLUTION ON INTRATHECAL SPREAD [1]

SUMMARY

Three milliliters of plain bupivacaine 0.5 % were injected intrathecally in two groups of 20 patients. Group 1 received a solution that had been equilibrated to 37 °C, group 2 received a solution that had been equilibrated to 4 °C. Patients were kept sitting for 3 min after injection. All observations were observer-blind. The differences between segmental levels of sensory loss between groups 1 and 2 (T-4 and T-9, respectively) and of temperature loss (T-3 and T-8, respectively) 10 and 20 min after injection of bupivacaine were statistically significant. It is concluded that the time needed for thermal equilibration in the cerebrospinal fluid and hence temperature of the injected solution plays an important role in the sensory spread of plain bupivacaine 0.5 %.

INTRODUCTION

It has been shown that anesthetic solutions in vitro equilibrate with body temperature within 1 to 2 min (1,2). Accordingly, it is assumed that the clinically important densities of anesthetic solutions are those measured at 37 °C (3). The baricity of a solution is the density of that solution divided by the density of cerebrospinal fluid. By definition, a solution is isobaric if baricity is 1.0000; if baricity is > 1.0000, the solution is hyperbaric; if less, it is hypobaric.

The plain solution of bupivacaine 0.5 % at a temperature of 4 °C has a density of 1.0040 (courtesy of ASTRA, The Netherlands); because the mean density of cerebrospinal fluid at 37 °C is 1.0003 (1,3), the plain solution of 0.5 % bupivacaine is slightly hyperbaric. At 37 °C, the density of plain bupivacaine 0.5 % is 0.9970

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(courtesy of ASTRA, The Netherlands), i.e., the solution is slightly hypobaric. The present study was undertaken to determine if this difference in baricity has any clinical significance.

PATIENTS AND METHODS

Forty male patients (ASA I-II) scheduled for urologic surgery under spinal anesthesia were randomly allocated to one of two groups. Each group comprised 20 patients. All patients received 3 ml plain bupivacaine 0.5 % while sitting; they were kept in the sitting position for 3 min after completion of the intrathecal injection of the solution and were then turned into the supine horizontal position. Patients in group 1 received a solution that had been previously equilibrated in a stove (MELAG Apparate GmbH W-Germany type 85) to 37 °C for at least 1 day. Patients in group 2 received a solution that had been equilibrated in a refrigerator to 4 °C for at least 1 day. Syringes used to administer the bupivacaine solution were also equilibrated to 37 °C and 4 °C, respectively. The study was approved by the Ethical Committee of our institution and oral consent was obtained from all patients.

Premedication consisted of lorazepam 1 mg orally the night before surgery. Before induction of spinal anesthesia 500 ml Ringer's solution were administered by rapid intravenous infusion, followed, after completion of the intrathecal injection, by 500 ml of a plasma expander (Haemaccel) at a slower rate. Dural puncture was performed with the patient in the sitting position at the L3-L4 interspace using a standard midline or paramedian approach and a 25-gauge spinal needle.

Blood pressure and pulse rate were measured before injection (t = 0) and at 5-min intervals after injection for 20 min (t = 5-20) using an automatic cycling device (Dinamap). ECG was monitored continuously.

Measurements of the levels of sensory changes were made 10 and 20 min after injection of the bupivacaine solution. Sensory loss was measured in the anterior axillary line by pin prick using a short-bevelled 25-gauge needle. Temperature loss was measured using a cold bottle containing a frozen salt solution. The segment at which the patient was not capable of recognizing the temperature of the bottle as well as the segment of loss of sensation to pin prick were recorded. Motor blockade was assessed 10 and 20 min after injection using a 0-3 scale as described by Bromage (4). All punctures and observations were made by the authors under "observer blind" conditions.

Results are expressed as means ± SEM. Statistical analysis used the Wilcoxon test for matched pairs for intragroup variations and the Mann-Whitney-U test for intergroup comparisons. For comparison of differences in motor blockade between the two groups the chi-square test according to Yates was used. $P < 0.05$ was taken as indicative of statistically significant differences.

RESULTS

There were no statistical significant differences between the two groups regarding age, height or weight (Table 4.1).

Table 4.1. Characteristics of the Patients Studied

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
Age (yr)	**63 ± 1.93**	**67 ± 1.95**	**NS**
Height (cm)	**175 ± 1.39**	**175 ± 1.28**	**NS**
Weight (kg)	**78 ± 2.01**	**75 ± 1.46**	**NS**

Group 1: Plain bupivacaine, 37 °C.
Group 2: Plain bupivacaine, 4 °C.
NS, no statistically significant difference.
Data are means ± SEM.

The segmental level of temperature loss after 10 min was T-4 in group 1 and T-10 in group 2; after 20 min, these levels were T-3 and T-8, respectively. The segmental level of loss of sensation to pin prick after 10 min was T-5 in group 1 and T-10 in group 2; after 20 min these levels were T-4 and T-9, respectively. The differences in sensory levels between groups were statistically significant at both 10 and 20 min (Table 4.2).

Table 4.2. **Segmental Levels of Loss of Sensation to Temperature (TEMP) and Pin Prick (P.PR) 10 and 20 min after Injection**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
TEMP 10'	T-4 (0.29)	T-10 (0.51)	P < 0.002
TEMP 20'	T-3 (0.24)	T-8 (0.53)	P < 0.002
P.PR 10'	T-5 (0.30)	T-10 (0.47)	P < 0.002
P.PR 20'	T-4 (0.26)	T-9 (0.48)	P < 0.002

Groups as defined in Table 4.1.
Data are mean values ± SEM, SEM in parentheses.

The ranges of levels are shown in Figure 4.1. The differences in motor blockade between the two groups at 10 and 20 min were not significant. The distribution of motor blockade is shown in Figure 4.2.

Systolic blood pressures decreased in both groups, decreases being significantly below baseline levels after 5, 10, 15 and 20 min, the decrease being more pronounced in group 1. There was no significant difference in systolic blood pressures at t = 0 between groups. Differences between decreases in systolic blood pressures in both groups were significant at t = 10. In three patients in group 1 and one patient in group 2 the decrease in blood pressure necessitated the use of ephedrine. Apart from a significant increase in heart rate at t = 5 in group 1, heart rates did not change significantly; intergroup comparison of the changes in heart rates showed no significant difference. Hemodynamic data are summarized in Table 4.3.

Table 4.3. Systolic BP (mm Hg) and Heart Rate (beats/min) at Various Times (t) during and after Injection into Subarachnoid Space

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
Systolic BP (t = 0)	142 (2.96)	137 (3.80)	NS
Systolic BP (t = 5)	128 (3.45) P < .001	129 (4.22) P < 0.01	NS
Systolic BP (t = 10)	115 (2.62) P < .001	126 (4.14) P < 0.01	P < 0.01
Systolic BP (t = 15)	118 (2.38) P < .001	121 (4.37) P < .001	NS
Systolic BP (t = 20)	116 (2.48) P < .001	123 (4.26) P < .001	NS
Heart Rate (t = 0)	77 (4.02)	74 (3.27)	NS
Heart Rate (t = 5)	81 (3.45) P < 0.05	75 (3.05) NS	NS
Heart Rate (t = 10)	78 (3.35) NS	75 (3.04) NS	NS
Heart Rate (t = 15)	77 (4.82) NS	74 (2.58) NS	NS
Heart Rate (t = 20)	73 (4.10) NS	74 (2.46) NS	NS

Groups as defined in Table 4.1.

Data are mean values ± SEM, SEM in parentheses.

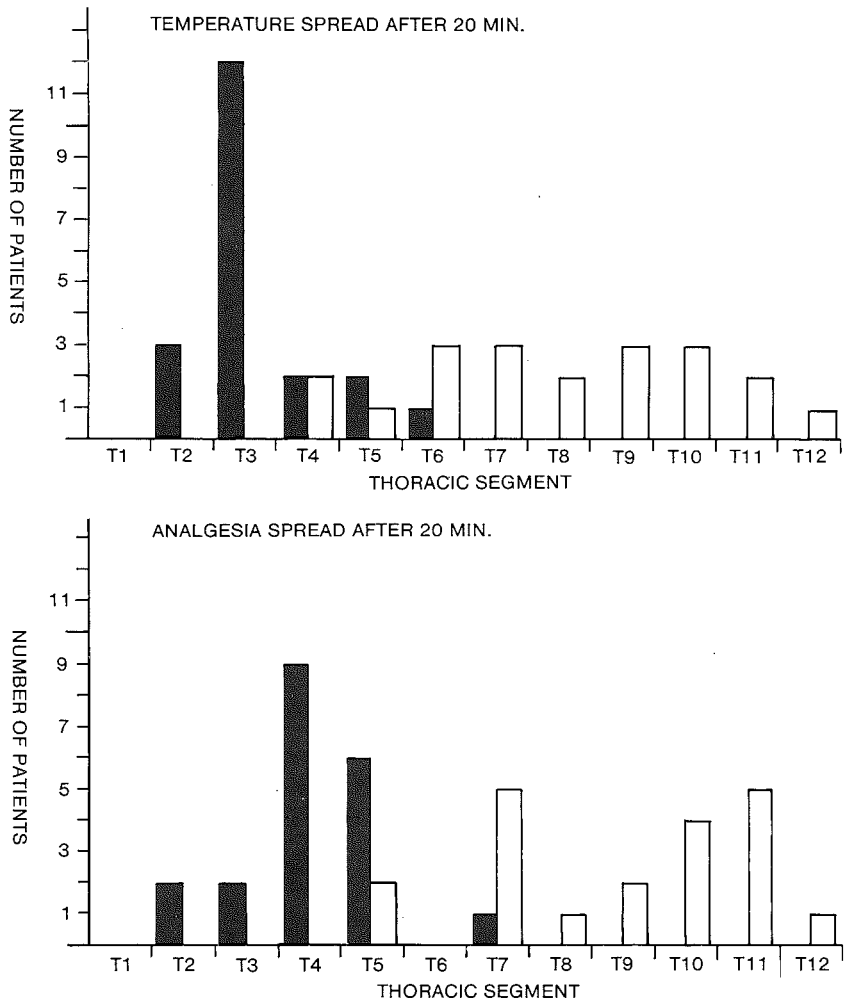

Figure 4.1. Segmental levels of temperature loss (temperature spread) and loss of sensation to pin prick (analgesia spread) 20 min after injection. The horizontal axis shows the thoracic segment at which temperature loss and loss of sensation to pin prick were measured; the vertical axis shows the number of patients. The differences between the two groups regarding temperature and analgesia spread were statistically significant.

■ **Group 1: plain bupivacaine, 37 °C.**

□ **Group 2: plain bupivacaine, 4 °C.**

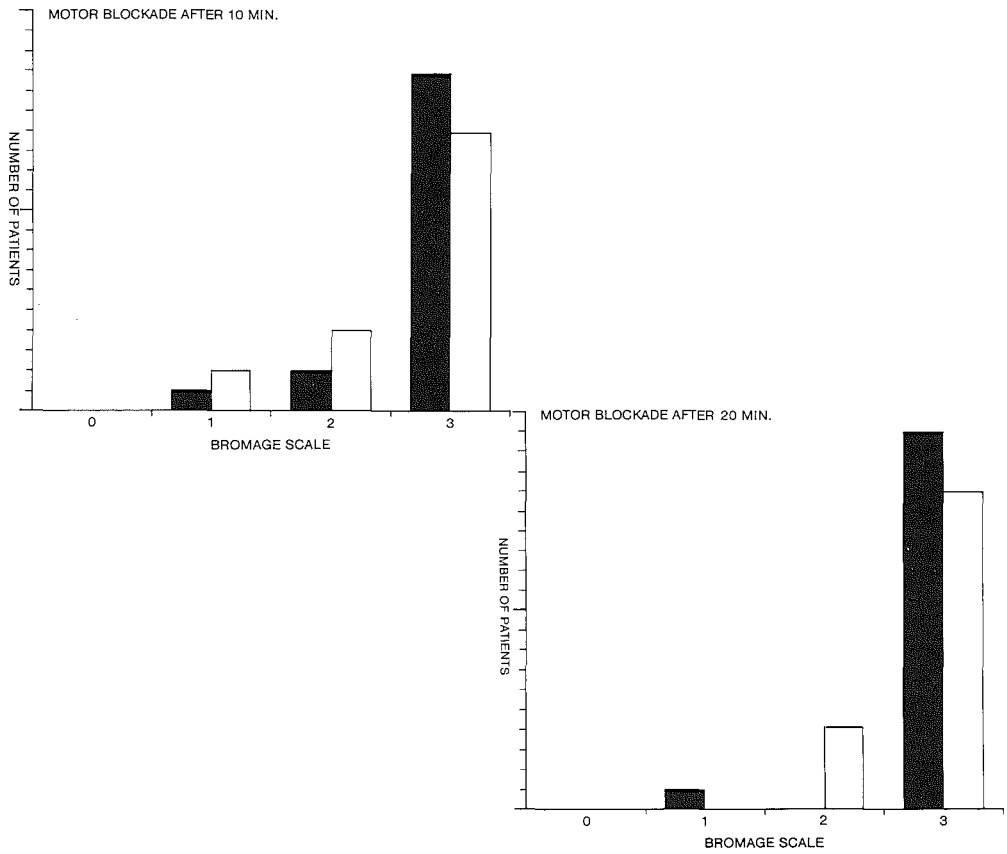

Figure 4.2. **Degree of motor blockade 10 min and 20 min after injection. The horizontal axis shows the Bromage scale: 0 = no motor block; 1 = inability to raise the extended leg; 2 = inability to flex the knee; 3 = complete motor block. The vertical axis shows the number of patients. Differences in motor blockade were statistically not significant.**

■ **Group 1: plain bupivacaine, 37 °C.**

□ **Group 2: plain bupivacaine, 4 °C.**

In one patient in group 2 (analgesia level T-12), analgesia was not sufficient and had to be supplemented with nitrous oxide. One patient in group 2 developed postspinal headache, which was succesfully treated with an epidural blood patch.

DISCUSSION

Although the plain solution of bupivacaine 0.5 % has been recognized as a suitable agent for spinal anesthesia (5-12), one of the major criticisms of its use for this purpose is the fact that predictability with regard to sensory spread is poor (13-22). Among the factors that affect the distribution of local anesthetic solutions in the cerebrospinal fluid, the baricity of the injected solution is well established (3). Although the plain solution of bupivacaine 0.5 % is slightly hypobaric at 37 °C, it is generally regarded and used as an isobaric solution (3).

In an attempt to explain the absence of difference in sensory spread between isobaric and hyperbaric solutions of tetracaine, Levin et al. (23) drew attention to the possibility that the time needed for thermal equilibration of a solution injected at room temperature might be a factor of influence. The assumption that injected solutions reach thermal equilibration in the cerebrospinal fluid within 1 to 2 min is based on the work of Davis and King (1) and Ernst (2); apart from the high room temperatures (27 °C in the former and 23 °C in the latter) both studies were in vitro studies. In none of the studies in which plain bupivacaine 0.5 % was used was temperature of the injected solution controlled. As is shown in this study, injecting bupivacaine 0.5 % at 37 °C not only results in a significantly higher cephalad spread, but also reduces the variability of sensory spread considerably, as is shown by a relatively small SEM of 0.3.

The fact that the cold solution of 4 °C changes from initially slightly hyperbaric to slightly hypobaric during thermal equilibration in the cerebrospinal fluid explains the lower cephalad spread; individual variation in the time needed for thermal equilibration could well explain the greater variability in sensory spread seen with the cold solution. This implies that the time needed for thermal equilibration in the cerebrospinal fluid is an important factor in determining cephalad spread when using plain bupivacaine. It seems reasonable to assume that in most clinics the temperature of the injectate will be the same as room temperature. Because the time needed for thermal equilibration is inversely related to the temperature of the solution, room temperature itself or the temperature of the place of storage of the solution becomes

an important factor. It stands to reason to assume that the ensuing levels of sensory blockade after injecting bupivacaine 0.5 % at room temperature will be somewhere between those seen with solutions of 4 °C and 37 °C. The fact that room temperature will be influenced by geographic location and by the time of year might explain, together with individual variation in the time needed for thermal equilibration, the great variability of sensory spread of plain bupivacaine solutions as seen in the literature.

The decrease in systolic blood pressure was greatest in group 1, as might be expected because of higher cephalad spread, although statistical analysis showed the differences to be significant only at t = 10. When Bonferroni's procedure is applied this difference at t = 10 remains significant. Considering the data, we believe that the lack of significance at t =5, t = 15 and t = 20 should be explained by a type II error being made due to considerable variation in blood pressures.

Apart from a significant increase at t = 5 in group 1, the heart rates showed no significant changes; when Bonferroni's procedure is applied, the increase in heart rate at t = 5 in group 1 loses significance; the conclusion that it involves a spurious statistical significance seems therefore warranted.

As can be seen from Figure 4.2, there were no major differences in motor blockade; in all patients motor blockade was adequate for surgery.

In conclusion, under the conditions of the present study the time needed for thermal equilibration in the cerebrospinal fluid and hence the temperature of the bupivacaine 0.5 % solution is an important factor in determining sensory spread. When using a solution that has been equilibrated previously to 37 °C, predictability of the ensuing level of analgesia is good. In case a high level of sensory blockade using bupivacaine 0.5 % is desired, the solution should be equilibrated to 37 °C.

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CHAPTER 5

THE EFFECT OF THE DIRECTION OF INJECTION ON INTRATHECAL SPREAD [1]

SUMMARY

The effect of the direction of the spinal needle on the sensory level of anesthesia was investigated. Three milliliters of plain bupivacaine 0.5 %, previously equilibrated to 37 °C, were injected intrathecally in two groups of twenty patients, who were kept sitting for 3 minutes after injection. In patients in group 1 a paramedian approach was used with an angle between the spinal needle and the patient's back of 50 ° or less. In patients in group 2 a median or paramedian approach was used, the resultant angle between the spinal needle and the patient's back being between 70 ° and 100 °. The differences between segmental levels of sensory loss between groups 1 and 2 (T 3.4 and T 5.1, respectively) and of temperature loss (T 2.6 and T 4.2, respectively) 30 minutes after injection of bupivacaine were statistically significant. It is concluded that a steep paramedian approach of the subarachnoid space with an angle of less than 50 ° results in a cephalad spread averaging about 1.6 segments greater than when the needle is in the perpendicular position.

INTRODUCTION

One of the factors that can affect the distribution of local anesthetic solutions in the subarachnoid space is the direction of the spinal needle through which injections are made. The possibility that the angle between the spinal needle and the longitudinal axis of the subarachnoid space may affect distribution of anesthetic solution is based on the assumption that if the anesthetic solution is injected through a spinal needle that is pointing in a cephalad direction, the resultant sensory level of blockade will be higher than if the needle is at a right angle with the longitudinal axis of the spinal

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canal (1). The present study was undertaken to determine if in fact the direction of the spinal needle does affect the cephalad spread of plain bupivacaine 0.5 % under controlled conditions.

PATIENTS AND METHODS

Forty male patients (ASA physical status I-II) scheduled for urologic surgery under spinal anesthesia were randomly allocated to one of two groups, each group containing twenty patients. In all patients 3 ml plain bupivacaine 0.5% were injected intrathecally while they were in the sitting position; they were then kept sitting for 3 minutes after injection before being placed in the supine horizontal position. Dural puncture was performed in the L3-L4 interspace using a 25-gauge spinal needle. Patients in both groups received a solution that had been previously equilibrated to 37 °C for at least 24 hours. Syringes used to administer the intrathecal solution were also equilibrated to 37 °C. In patients in group 1 a paramedian approach was used, in which the angle between the spinal needle and the patient's back was at most 50 °. In patients in group 2 a median or paramedian approach was used, in which the angle between the spinal needle and the patient's back was between 70 ° and 100 °. The angle between the needle and the frontal plane was measured with a protractor. In patients in group 1 the point of needle entry was immediately lateral to the lower border of the processus spinosus of L4, in patients in group 2 the point of entry was level with the L3-L4 interspace. Thus in patients in group 1 entry in the subarachnoid space with the tip of the needle pointing cranially was achieved, whereas in patients in group 2 the position of the needle was more or less horizontal.

Premedication consisted of lorazepam 1 mg orally the night before surgery. Before induction of spinal anesthesia 500 ml Ringer's solution were administered by rapid intravenous infusion, followed, after completion of the intrathecal injection, by 500 ml of a plasma expander at a slower rate. Bupivacaine solutions were injected at a rate of 0.2 ml/sec.

Blood pressure and pulse rate were measured before injection (t = 0) and 15 and 30 min after injection (t = 15 and t = 30) using an automatic cycling device (Dinamap). ECG was monitored continuously.

Measurement of the level of sensory changes was made 30 min after injection of the bupivacaine solution. Sensory loss was measured in the anterior axillary line by pinprick using a short bevelled 25-gauge needle. Temperature loss was measured using a cold bottle containing a frozen salt solution. The segment at which the patient was not capable of recognizing the temperature of the bottle as well as the segment at which there was loss of sensation to pinprick were recorded. Motor blockade was assessed 30 min after injection using a 0-3 scale as described by Bromage (2).
All punctures and observations were made by the authors under "observer blind" conditions.

The study was approved by the Ethics Committee of our institution and oral consent was obtained from all patients.

Results are expressed as means ± SEM. Statistical analysis used the Wilcoxon test for matched pairs for intragroup variations and the Mann-Whitney-U test for intergroup comparisons. $P \leq 0.05$ was taken indicative of statistically significant differences.

RESULTS

The average angle between the spinal needle and the patient's back was 40 ° (range 20-45, SEM 1.4) in group 1 and 86 ° (range 70-90, SEM 1.2) in group 2.
The differences between the two groups regarding age, length and weight were not significant (Table 5.1).

The segmental level of temperature loss after 30 min averaged T 2.6 in group 1 and T 4.2 in group 2. The segmental level of loss of sensation to pinprick after 30 min averaged T 3.4 in group 1 and T 5.1 in group 2. Both these differences were statistically significant (Table 5.2). The ranges of levels are shown in Figure 5.1. All patients had complete motor blockade of the lower limbs after 30 min.

Table 5.1. **Characteristics of the Patients Studied**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
			NS
Age (yr)	73 ± 1.86	72 ± 2.39	NS
Height (cm)	173 ± 1.43	177 ± 1.73	NS
Weight (kg)	72 ± 2.12	74 ± 2.34	

Group 1: Angle between spinal needle and longitudinal axis of spinal canal less than 50 °.
Group 2: Angle between spinal needle and spinal canal 70 ° to 100 °.
NS, no statistically significant difference.
Data are means ± SEM.

Table 5.2. **Segmental Levels of Loss of Sensation to Temperature (TEMP) and Pin Prick 30 min after Injection**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
TEMP	T-2.6 (0.24)	T-4.2 (0.39)	P < 0.01
PIN PRICK	T-3.4 (0.27)	T-5.1 (0.37)	P < .002

Groups as defined in Table 5.1.
Data are mean values ± SEM, SEM in parentheses.

Systolic blood pressures decreased in both groups, decreases being significantly below baseline levels after 15 and 30 min. Baseline systolic blood pressures as well as the decreases in systolic blood pressure were similar in the two groups. The decrease in blood pressure necessitated the use of ephedrine (15 mg intravenously plus 35 mg

intramuscularly) in 7 patients in group 1 and in 4 patients in group 2.
The heart rates in either group showed no significant changes, nor were there significant differences in baseline heart rates between groups. Hemodynamic data are summarized in Table 5.3.

Table 5.3. **Systolic BP (mm Hg) and Heart Rate (beats/min) at Various Times (t) during and after Injection into Subarachnoid Space**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
Systolic BP (t = 0)	139 (3.21)	135 (3.21)	NS
Systolic BP (t = 15)	115 (4.02) P < .001	118 (3.50) P < .001	NS
Systolic BP (t = 30)	122 (3.79) P < .001	118 (3.64) P < .001	NS
Heart Rate (t = 0)	78 (3.70)	74 (1.80)	NS
Heart Rate (t = 15)	78 (3.43) NS	74 (2.28) NS	NS
Heart Rate (t = 30)	76 (2.70) NS	75 (2.42) NS	NS

Groups as defined in Table 5.1.
Data are mean values ± SEM, SEM in parentheses.

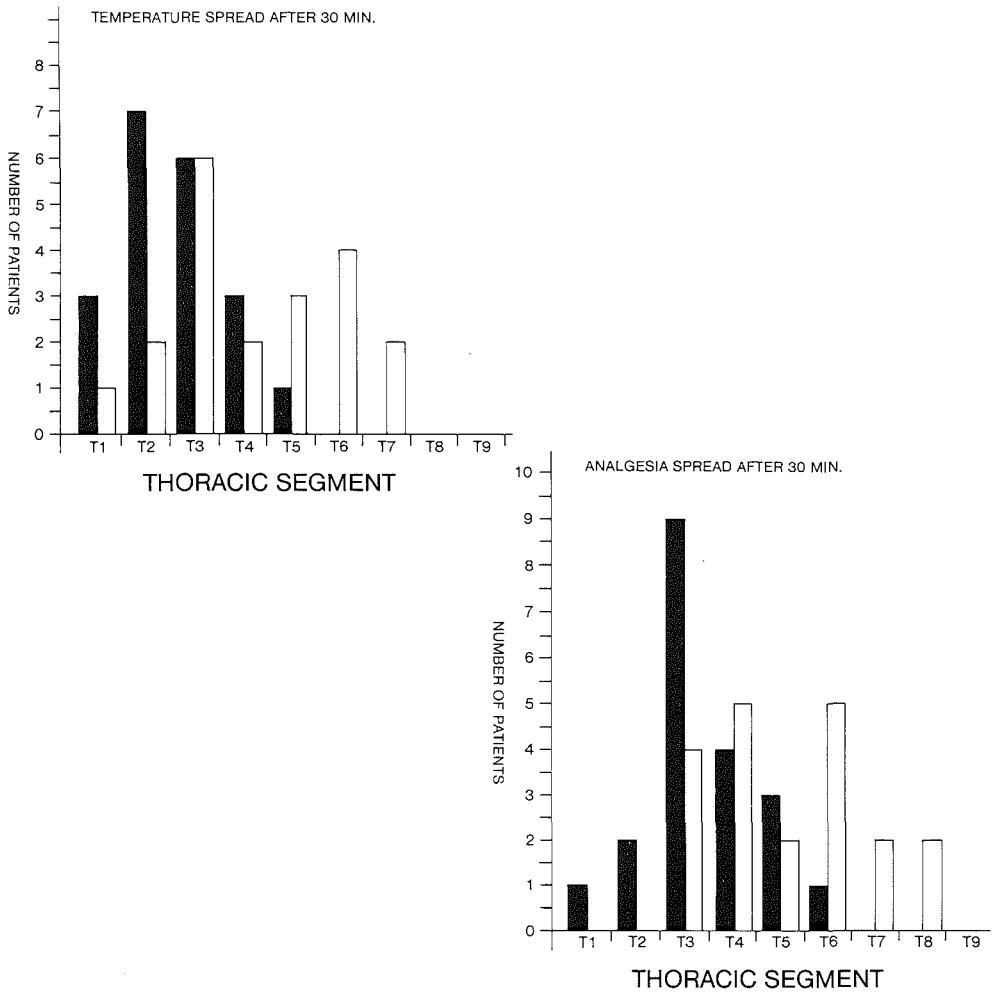

Figure 5.1. Segmental levels of temperature loss (temperature spread) and loss of sensation to pin prick (analgesia spread) 30 min after injection. The horizontal axis shows the thoracic segment at which temperature loss and loss of sensation to pin prick were measured; the vertical axis shows the number of patients. The differences between the two groups in segmental levels of loss of temperature and pin prick discrimination were statistically significant.

■ **Group 1: Angle between spinal needle and longitudinal axis of spinal canal less than 50 °.**

□ **Group 2: Angle between spinal needle and spinal canal varying from 70 ° to 100°.**

Operative conditions were good; none of the patients required analgetic supplementation. None of the patients developed postspinal headache.

DISCUSSION

Many factors affect the intrathecal spread of anesthetic solutions (1). One of the major problems therefore in determining the influence of one factor is to effectively control the others. That this may be difficult if not impossible, is proven by the many controversies that still exist regarding the effect of some of these factors. In the case of bupivacaine 0.5 % the difficulty in achieving effective control of all known and unknown determinants of intrathecal spread is clearly illustrated by the great variability of sensory spread as seen in the literature. Since it has been shown that equilibration of the plain solution of bupivacaine 0.5 % to 37 °C prior to intrathecal administration considerably reduces the variability of the ensuing sensory blockade (3), we administered a bupivacaine solution equilibrated to body temperature in order to minimize variability between the two groups of patients.

This study shows that changing the position of the spinal needle from a conventional more or less perpendicular entry into a reduced angle of entry of less than 50 ° results in a statistically significant increase in cephalad spread of 1.6 to 1.7 segments. It should be emphasized however that the clinical significance of this difference is quite limited compared to other factors affecting the sensory level of spinal anesthesia.

In a study comparing different directions of the bevel of the spinal needle in combination with different speeds of injection, Neigh et al. (4) found that the direction of the bevel of a conventional spinal needle had no effect on sensory spread. However, when using a Whitacre needle (where the fluid is ejected at 90 ° to the longitudinal axis of the needle), they found that injecting in a cephalad direction resulted in a higher cephalad spread as compared with injecting in a caudad direction or injecting through a conventional spinal needle. Although with conventional spinal needles the maximum acuteness of the angle between needle and longitudinal axis of the spinal canal is obviously limited, the result of reducing the angle of the needle with the tip pointing in a more cephalad direction is essentially the same as injecting through a Whitacre needle in a cephalad direction.

It has been shown that use of the plain solution of bupivacaine 0.5 % is associated with a higher frequency of complete motor blockade of the lower limbs than the

hyperbaric solution (5,6,7). Indeed, in our study all patients in both groups had complete motor blockade of the lower limbs after 30 minutes.

The decreases in systolic blood pressure as compared with baseline levels were statistically significant in each group, both after 15 and 30 minutes. The differences in decreases between the two groups were not significant. It should be noted however, that variation in both groups was large and that 11 patients received ephedrine. There were no statistical significant changes in heart rates.

In conclusion, when using the plain solution of bupivacaine 0.5 % equilibrated to 37 °C, using a steep paramedian approach of the subarachnoid space with an angle between spinal needle and longitudinal axis of the spinal canal of less than 50 °, the resulting sensory blockade will average about 1.6 segments higher as compared with the conventional more or less perpendicular approach. The clinical significance of this finding is small.

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CHAPTER 6

DIFFERENCES IN ONSET AND REGRESSION OF SENSORY AND MOTOR BLOCKADE FOLLOWING INTRATHECAL ADMINISTRATION OF PLAIN BUPIVACAINE AT DIFFERENT TEMPERATURES [1]

SUMMARY

Onset, -defined as the time between injection and achievement of the highest level of sensory blockade-, duration and regression of sensory and motor blockade after the intrathecal administration of 3 ml plain bupivacaine 0.5 %, previously equilibrated to either 37 °C or 20 °C, were studied in two groups of twenty patients. In patients receiving the solution equilibrated to 37 °C, the maximum level of sensory blockade was significantly higher (T 4.6 versus T 7.5), variability was smaller (SEM 0.33 versus 0.58) and duration of the sensory level of blockade at or above T 6, T 8 and T 10 significantly longer (56 min versus 20 min, 101 min versus 59 min and 131 min versus 77 min, respectively). There were no significant differences with regard to onset of sensory and motor blockade or either the time needed both for the sensory level of blockade to regress two segments from its highest level and to the first lumbar segment, or the duration of complete motor blockade of the lower limbs. It is concluded that the intrathecal administration of a bupivacaine solution previously equilibrated to 37 °C as compared with a solution injected at room temperature results in a higher, more predictable maximum sensory level of blockade with longer duration at or above T 6, T 8 and T 10.

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INTRODUCTION

The plain solution of bupivacaine 0.5 % has been established as an useful local anesthetic agent for spinal anesthesia(1-5), although the predictability of the maximum level of sensory analgesia is reported to be poor (6-15). Since it has been shown that keeping the patients seated for 2.5 min after intrathecal injection increases cephalad spread (16), satisfactory high levels of sensory blockade have been reported (16-21). Recently we demonstrated that equilibrating the bupivacaine solution to 37 °C prior to injection results in a higher and more predictable level of maximum cephalad spread (22). The present study was undertaken to compare the onset, duration and regression of sensory and motor blockade when using the plain solution of bupivacaine 0.5 % previously equilibrated to either 37 °C or 20 °C.

PATIENTS AND METHODS

Forty male patients (ASA physical status I-II) scheduled for urologic surgery were randomly allocated to one of two groups, each group comprising 20 patients. All patients received 3 ml plain bupivacaine 0.5 % while they were in the sitting position. The sitting position was maintained for 3 minutes after completion of the intrathecal injection, after which the patients were placed in the supine horizontal position. Dural puncture was performed at the L3-L4 interspace using a midline or paramedian approach and a 25-gauge spinal needle. The bupivacaine solution was injected at a rate of 0.2 ml/sec. Patients in group 1 received a solution that had previously been equilibrated to 37 °C for at least 24 hours. Patients in group 2 received a solution that had been equilibrated to 20 °C for at least 24 hours. Syringes used to administer the bupivacaine solution were also equilibrated to 37 °C and 20 °C, respectively. The study was approved by the Ethics Committee of our institution and informed consent was obtained from all patients.

Premedication consisted of lorazepam 1 mg orally the night before surgery. Before the institution of spinal anesthesia, 500 ml of Ringer's solution were administered by rapid intravenous infusion, followed, after completion of the intrathecal injection, by 500 ml of a plasma expander (Haemaccel) at a slower rate. Using an automatic cycling device, blood pressure and pulse rate were measured before injection and at 5-min intervals after injection until the patients were returned to the ward. ECG was monitored continuously.

Measurement of the level of sensory changes was made at 10-min intervals during the first 30 min and at 15-min intervals thereafter until regression to the first lumbar segment. Sensory loss was measured in the anterior axillary line using a short bevelled 25-gauge needle. The segment at which there was loss of sensation to pinprick was recorded. For comparisons, the average levels of sensory blockade after 10, 20, 30, 60 and 120 min were used. Motor blockade of the lower limbs was assessed using a 0-3 scale as described by Bromage (23) at the same intervals as the measurements of the level of sensory changes until regression from 3 to 2 on the Bromage scale.
All inductions of spinal anesthesia were made by the authors (RS and FvP); all observations were made by one author (JWK) under "observer blind" conditions.
Results are expressed as means ± SEM. Statistical analysis used the Mann-Whitney-U test for intergroup comparisons. $P \leq 0.05$ was taken indicative of statistically significant differences.

RESULTS

There were no statistically significant differences between the two groups with respect to age, height and weight (Table 6.1).
The onset of sensory blockade, defined as the time between injection and achievement of the highest level of sensory blockade, averaged 21.0 min in group 1 and 23.5 min in group 2, the difference not being statistically significant. The sensory level of blockade averaged T 4.6 (range: T 2 - T 7) in group 1 and T 7.5 (range: T 3 - T 12) in group 2; this difference was statistically significant. The average levels of sensory blockade remained significantly higher in group 1 at all times (10, 20, 30, 60 and 120 min after injection).
Two-segment regression, defined as the time between achievement of the highest level of sensory blockade and its regression to a level two segments lower, averaged 61 min in group 1 and 79 min in group 2; this difference was not statistically significant. Regression to L1, defined as the time between achievement of the highest level of sensory blockade and its regression to the first lumbar segment, averaged 167 min in group 1 and 156 min in group 2, the difference not being statistically significant.

Table 6.1. **Characteristics of the Patients Studied**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
Age (yr)	66 ± 1.85	71 ± 1.62	NS
Height (cm)	174 ± 1.45	173 ± 1.30	NS
Weight (kg)	78 ± 1.84	74 ± 2.05	NS

Group 1: Plain bupivacaine, 37 °C.
Group 2: Plain bupivacaine, 20 °C.
NS, no statistically significant difference.
Data are means ± SEM.

All patients had complete motor blockade of the lower limbs after 30 min; The onset of complete motor blockade of the lower limbs averaged 13 min in group 1 and 14 min in group 2; the difference was statistically not significant. Regression of motor blockade from 3 to 2 on the scale of Bromage took 151 min in group 1 and 159 min in group 2, a difference that was not statistically significant.
The data on onset, level of sensory blockade and regression are shown in Table 6.2. The regression of the sensory level of blockade as a function of time is shown in Figure 6.1. Figure 6.2 shows the durations of sensory blockade at or above T 10, T 8 and T 6, which were respectively 131 min, 101 min and 56 min in group 1 and 77 min, 59 min and 20 min in group 2; these differences were statistically significant. Figure 6.3 shows the number of patients with a sensory level of blockade at or above T 10 as a function of time.

Table 6.2. **Onset and Regression of Motor Blockade and Maximum Level of Sensory Blockade**

	Group 1 (n = 20)	Group 2 (n = 20)	DELTA 1-2
ANALGESIA ONSET (min)	21.0 ± 1.43	23.5 ± 2.18	NS
MAXIMUM BLOCK	T 4.6 ± 0.33	T 7.5 ± 0.58	P < .001
2 S REGRESSION (min)	61 ± 5.4	79 ± 7.2	NS
L 1 REGRESSION (min)	167 ± 7.2	156 ± 9.8	NS
MOTOR BL. ONSET (min)	13 ± 1.3	14 ± 1.3	NS
MOTOR BL. REGRESSION BROMAGE 3 -- 2 (min)	151 ± 9.6	159 ± 8.1	NS

Groups as defined in Table 6.1. ANALGESIA ONSET = Average time from injection to maximum level of sensory blockade. MAXIMUM BLOCK = Average maximum level of sensory blockade as measured by pin prick. 2 S REGRESSION = Time between achievement of the highest level of sensory blockade and its regression to a level two segments lower. L 1 REGRESSION = Time between achievement of the highest level of sensory blockade and its regression to the first lumbar segment. MOTOR BL. ONSET = Average time from injection to complete motor blockade of the lower limbs (Bromage 3). MOTOR BL. REGRESSION BROMAGE 3 -- 2 = Average time from achievement of complete motor blockade of the lower limbs (Bromage 3) to the ability of moving the feet (Bromage 2).
NS, no statistically significant differences.
Data are means ± SEM.

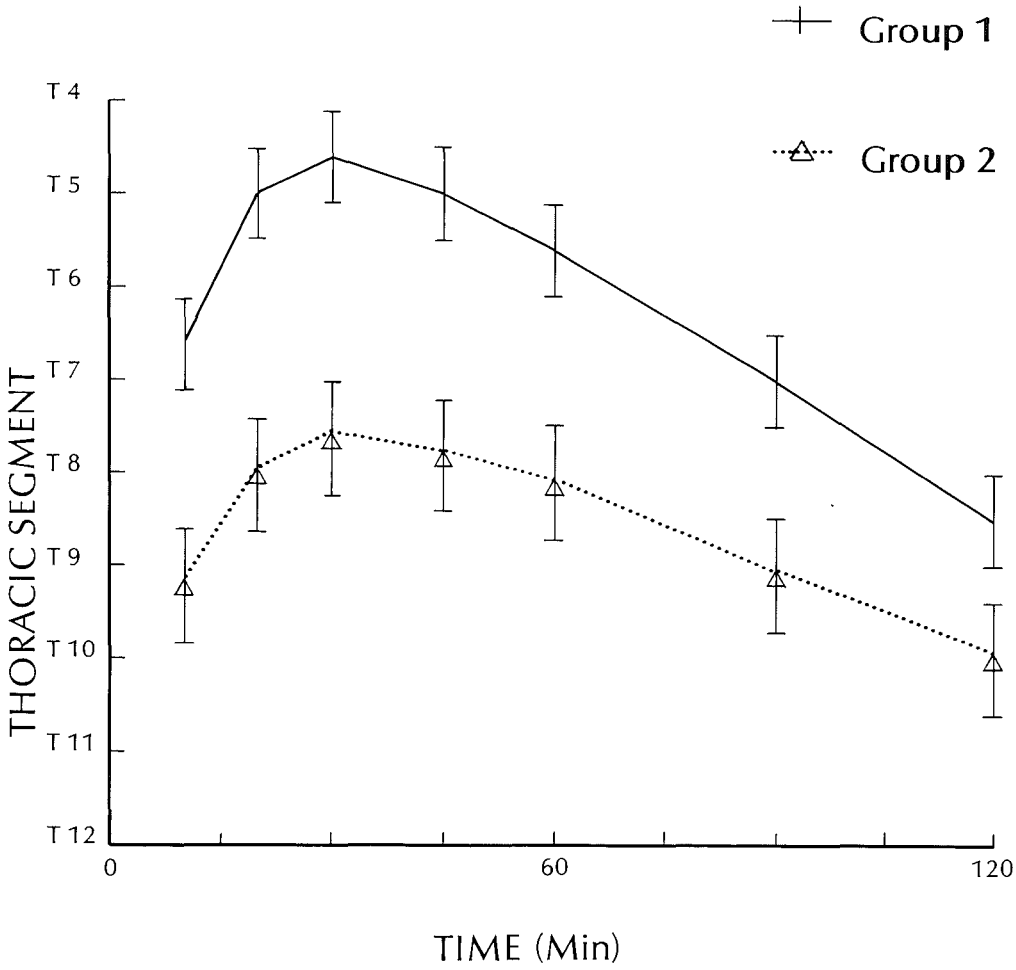

Figure 6.1. Regression of the average sensory levels of blockade as a function of time. The horizontal axis shows the time in min after intrathecal injection of 3 ml plain bupivacaine 0.5 %; the vertical axis shows the average thoracic segment at which loss of sensation to pin prick was measured. Vertical bars represent SEM. The differences between the two groups, which were compared at 10, 20, 30, 60 and 120 min, were significant. Group 1: Plain bupivacaine, 37 °C. Group 2: Plain bupivacaine, 20 °C.

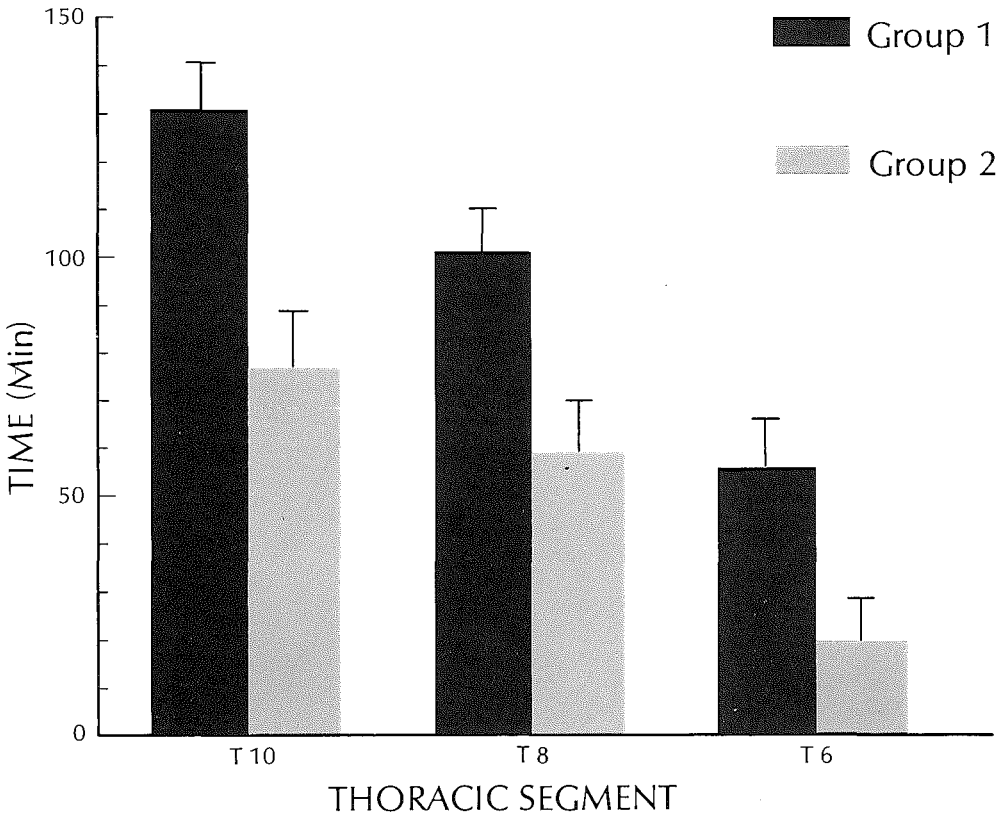

Figure 6.2. Average duration of sensory blockade at or above T-10, T-8 and T-6. The horizontal axis shows the thoracic segment; the vertical axis shows the time interval in min from the first to the last measurement at which the sensory level of blockade as determined by pin prick was at or above the specified thoracic segment. Vertical bars represent SEM. The differences between the two groups in duration of sensory blockade at or above T-10, T-8 and T-6 were significant. Group 1: Plain bupivacaine, 37 °C. Group 2: Plain bupivacaine, 20 °C.

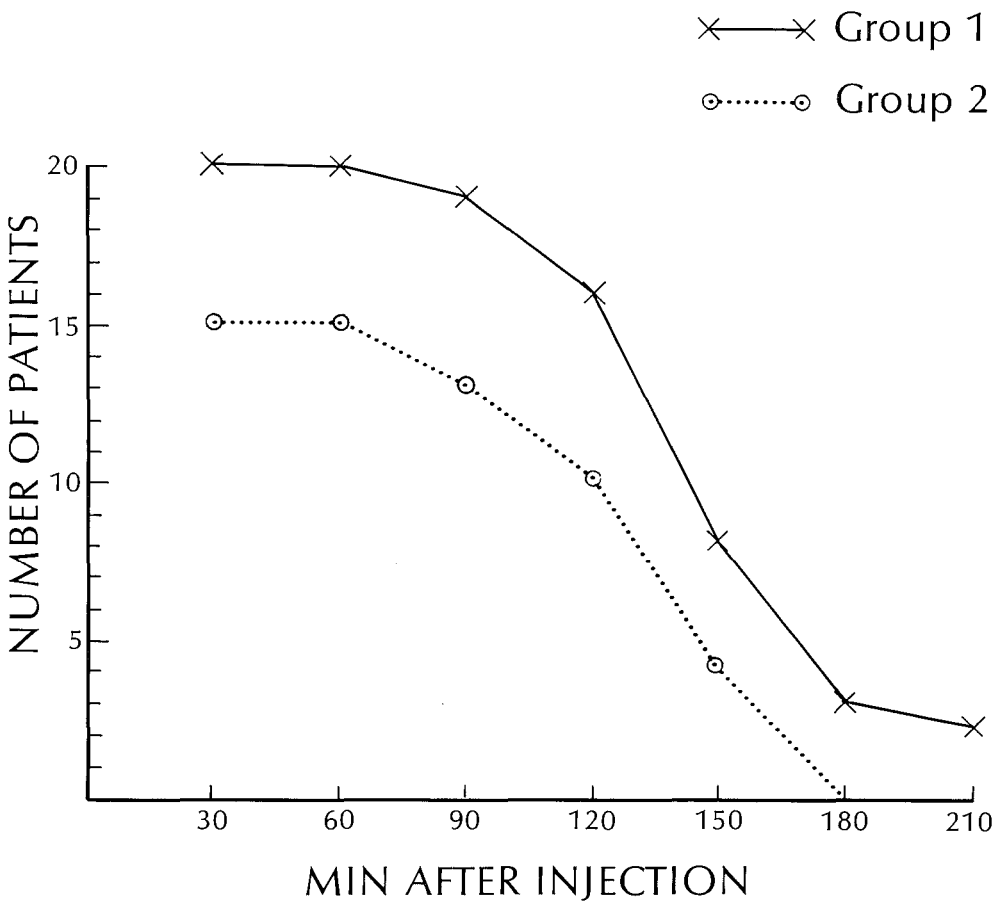

Figure 6.3. The number of patients with a sensory level of blockade as determined by pin prick at or above T-10 as a function of time after injection. The horizontal axis shows the time in min after intrathecal injection of 3 ml plain bupivacaine 0.5 %; the vertical axis shows the number of patients with a level of sensory blockade at or above T-10. Group 1: Plain bupivacaine, 37 °C. Group 2: Plain bupivacaine, 20 °C.

Baseline systolic blood pressures and heart rates were similar in the two groups. Systolic blood pressures decreased in both groups, decreases being more pronounced in group 1. In five patients in group 1 and in one patient in group 2 the decrease in blood pressure necessitated the administration of ephedrine (15 mg intravenously plus 35 mg intramuscularly).

In group 1, three patients were given 0.5 mg alfentanil intravenously during surgery: in one of the 3 the level of sensory blockade at the time (120 min after intrathecal injection) was at T 12; the two other patients experienced pain (one during manipulation of the peritoneum in the inguinal region, the other during traction on the spermatic cord) while the level of sensory blockade was at T 7 (105 and 140 min after intrathecal injection). In group 2, one patient was given 0.5 mg alfentanil intravenously during surgery because of pain at a time when the level of sensory blockade was T 12 (75 min after intrathecal injection). In none of these patients were other or repeated analgetics necessary.

One patient (group 1, 67 years) suffered from post-spinal headache, which was succesfully treated with an epidural blood patch after three days.

DISCUSSION

That many factors affect the intrathecal spread of local anaesthetic solutions (24) is amply demonstrated by the many conflicting data seen in the literature regarding the characteristics of spinal anesthesia when using plain bupivacaine 0.5 %. Despite apparent similarities in methodology, differences in times to onset, maximum levels of sensory blockade achieved and regression of anesthesia exist, indicating that apart from the variability caused by different investigators, there must be unknown factors that exert a considerable influence. In our study, the average time to onset of maximum cephalad spread was more than 20 min in both groups; although this finding contrasts with some studies reporting shorter onset times (16,25,26), it agrees with others (27).

The maximum level of sensory blockade was significantly higher in patients given the bupivacaine solution previously equilibrated to 37 °C; also, variability of this higher maximum level was significantly less than in patients receiving the 20 °C solution as illustrated by the smaller SEM. These results are consistent with those of a previous study (22). Compared with cerebrospinal fluid of 37 °C, the plain solution of bupivacaine 0.5 % is isobaric at 20 °C and slightly hypobaric at 37 °C; this explains the higher maximum level of sensory blockade in patients in group 1.

As might be expected with a higher maximum level of sensory blockade, time to two-segment regression of the sensory level was shorter in group 1 than in group 2, although the difference did not reach statistical significance. The time for regression of the sensory level to the first lumbar segment was also not significantly different; since the maximum level of sensory blockade was higher in group 1, regression to the first lumbar segment obviously involved more segments, indicating that the average time for regression per segment is shorter in group 1. As can be seen from figure 6.1, the average levels of sensory blockade were significantly higher in group 1 at all times. Two more practical ways of assessing the differences in regression are a) the duration, defined as the average time that the sensory level of blockade is at or above a certain thoracic segment, or b) the number of patients with a sensory level at or above T 10 as a function of time. The former is shown in figure 6.2, the latter in figure 6.3. As shown in figure 6.2, the sensory level of blockade remains significantly longer at or above T 6, T 8 and T 10 in patients in group 1 than in patients in group 2. This means that the shorter average time for regression per segment notwithstanding, the previous equilibrating of the bupivacaine solution to 37 °C as compared with the use of a solution at room temperature results not only in a higher, more predictable level of sensory analgesia, but also provides a sensory block with a longer duration.

As can be seen from figure 6.3, in five patients in group 2 the sensory level of analgesia remained below T 10, whereas in group 1 the level of sensory blockade was above T 10 in all patients.

Two of the patients in group 1 needed analgetic supplementation while the level of sensory blockade at the time was T 7; one patient experienced pain during manipulation of the peritoneum in the inguinal region, the other during traction on the spermatic cord. This indicates that in these two patients the intensity of sensory blockade was insufficient for visceral stimulation; this phenomenon has been observed in another study, in which a patient experienced pain on bladder distension while the sensory level of blockade was T 6 (26). It is conceivable that the intensity of sensory blockade varies inversely with the number of dermatomes blocked especially where the higher thoracic dermatomes are concerned and that when using a plain bupivacaine solution previously equilibrated to 37 °C with the intention of achieving a high level of sensory blockade, a higher dose of bupivacaine may be necessary in order to secure adequate analgesia for all patients.

When 15 mg or more of the plain solution of bupivacaine 0.5 % are administered with the patients in a sitting position, motor blockade of the lower limbs is reported to be 80-100 % complete (16-22,25-29). In our study, motor blockade of the lower limbs was complete in all patients and duration of complete motor blockade was similar in both groups.

The decreases in systolic blood pressures in relation to baseline levels were more pronounced in group 1 which is consistent with the higher maximum level of sensory blockade in this group. Ephedrine, which was given when physical signs of low blood pressure were apparent or when systolic blood pressure fell below 90 mm Hg, was administered to five patients in group 1 and to one patient in group 2.

In conclusion, under the conditions of the present study the use of a solution of plain bupivacaine 0.5 % previously equilibrated to 37 °C as compared with a solution of 20 °C results in a significantly higher, more predictable level of sensory blockade. Onset of sensory and motor blockade, the time needed for regression of two segments and for regression to the first lumbar segment as well as for regression of complete motor blockade to class 2 on the scale of Bromage were similar. Average durations of sensory blockade at or above T 6, T 8 and T 10 were significantly longer in patients receiving the solution of 37 °C.

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CHAPTER 7

OBSERVATIONS IN A SPINAL CANAL MODEL [1]

SUMMARY

Three ml of a solution (BMB) containing 4.81 mg bupivacaine base and 0.029 mg methylene blue per ml were injected in the middle of a vertically mounted spinal canal model containing 0.9 % NaCl at 37 °C. The BMB solution injected was either equilibrated to 37 °C (Exp. I) or to 22 °C (Exp. II). Each experiment was conducted 8 times, 4 times with a high speed of injection (± 0.6 ml/sec) and 4 times with a slow speed of injection (0.05 ml/sec). The density of the BMB solution was determined at 37 °C and at 22 °C and found to be, respectively, slightly hypobaric and slightly hyperbaric relative to the 0.9 % NaCl solution of 37 °C. Three min after completion of the injection, nine 1-ml samples were drawn simultaneously from the site of injection and from 8 sampling sites situated equally above and below the site of injection at 5 cm intervals, which were subsequently analyzed for methylene blue concentrations. Injection of the BMB solution equilibrated to 37 °C resulted in a distribution directed mainly upward, whereas injection of the BMB solution equilibrated to 22 °C showed distribution in a mainly downward direction. Variation in methylene blue concentrations was large and no definite differences based on different speeds of injection were observed. It is concluded that small differences in baricity result in largely different distribution patterns that could explain the variability in sensory levels of blockade when using an isobaric solution for spinal anesthesia.

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[1]**Accepted for publication in a modified form as: Stienstra R, Gielen M, Kroon JW, Van Poorten F. The Influence of Temperature and Speed of Injection on the Distribution of a Solution Containing Bupivacaine and Methylene Blue in a Spinal Canal Model. Reg Anesth.**

INTRODUCTION

Among the factors affecting the distribution of local anesthetic solutions within the subarachnoid space, the density of the solution is well recognized (1). The density of a local anesthetic solution relative to the density of cerebrospinal fluid determines whether a solution is considered hypobaric, isobaric or hyperbaric. Because it has been shown, in vitro, that local anesthetic solutions rapidly equilibrate to body temperature within 1-2 min (2,3), the clinically relevant density of a solution is the density measured at 37 °C (1). Density varies inversely with temperature; in the case of local anesthetic solutions which are considered to be isobaric, differences in temperature of the solution may cause a change in baricity. The density of the plain solution of bupivacaine 0.5 % differs only slightly from the density of cerebrospinal fluid and, consequently, is usually termed isobaric (1), although at 37 °C it is in fact slightly hypobaric. That this difference in baricity has clinical implications was shown in a study, in which equilibration of plain bupivacaine 0.5 % to body temperature prior to intrathecal injection resulted in a higher and more predictable level of sensory blockade as compared with a bupivacaine solution previously equilibrated to 4 °C (4). Since it has been demonstrated that, when using the plain solution of bupivacaine 0.5 % for spinal anesthesia, keeping the patients seated for 2.5 min after injection results in a higher cephalad spread (5), many anesthesiologists keep their patients seated for 2 or more min when using plain bupivacaine. The present study was undertaken to determine, in a vertically mounted spinal canal model, whether the small differences in baricity due to differences in temperature result in different distribution patterns during the first 3 min after injection and whether different speeds of injection affect distribution.

METHODS

The model (figures 1 and 2) was made of glass. It consisted of a tube widening slightly at both ends, with a length of 88.2 cm and a cross-sectional area of 1.45 cm^2 resulting in a total volume capacity of 136 ml. The tube contained 9 holes in the longitudinal direction, each 5 cm apart, the fifth hole being exactly in the middle of the tube. The holes were filled with silicone caps, through which 18-gauge sampling needles (with the bevels ground off) were placed in the center of the tube.

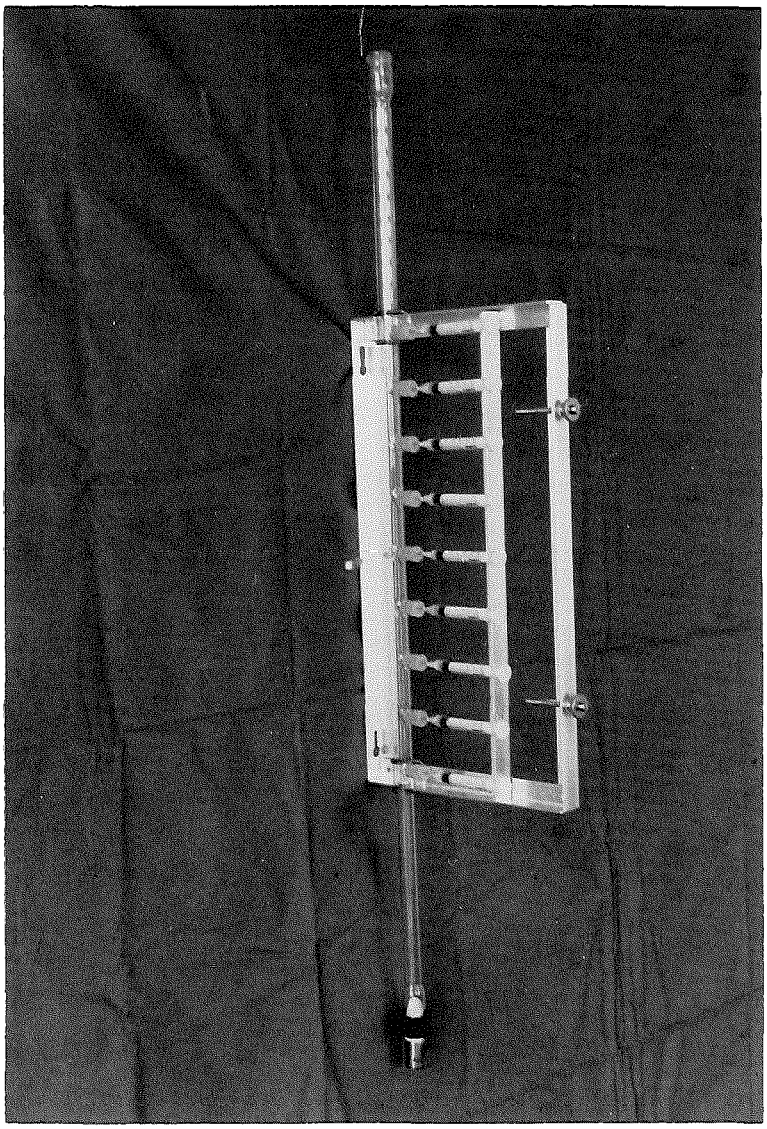

Figure 7.1. The glass model of the spinal canal, used in the experiments.

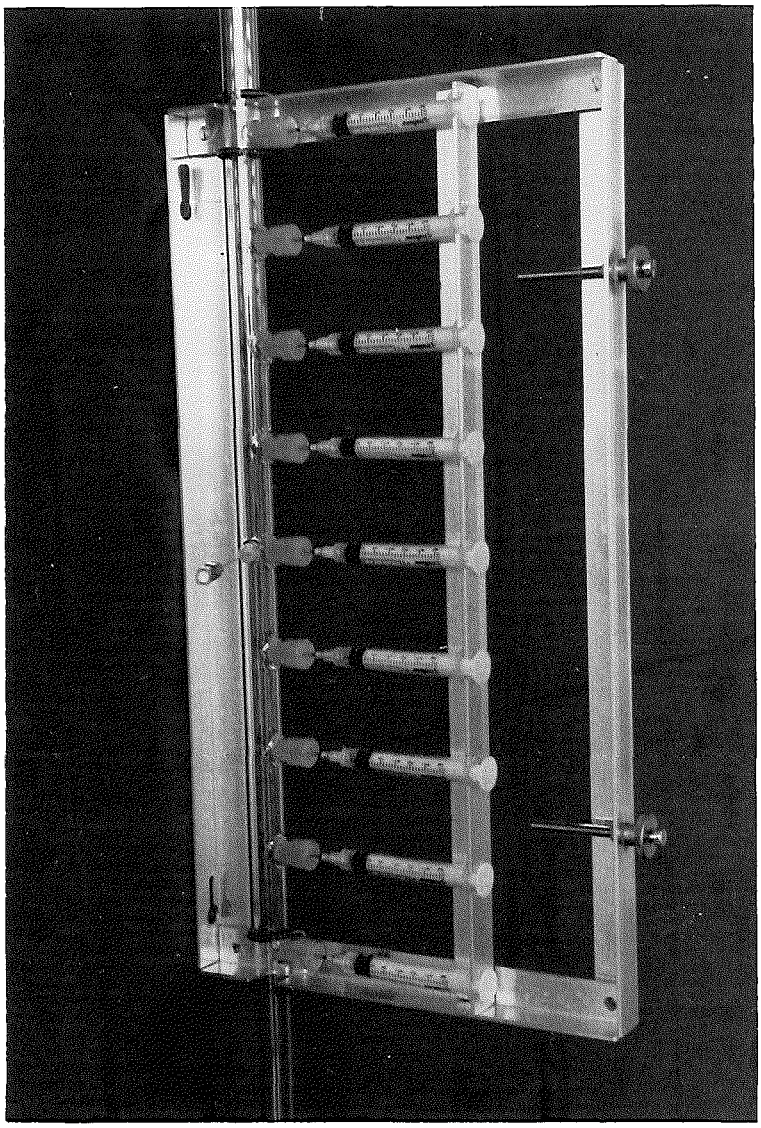

Figure 7.2. Detail of the middle portion of the model, showing more clearly the sampling device, the site of injection and the 9 sampling sites.

The syringes attached to the sampling needles and their pistons were fitted in a metal frame fixed to the glass tube, in such a manner that 9 one-ml samples could be drawn simultaneously in one movement. Opposite the fifth sampling hole was the injection site, a hole fitted with a silicone cap through which a 25 gauge spinal needle was placed. The model was open at the top and closed at the bottom with a screw cap containing a rubber reservoir of 4 ml, in order to allow free flow from both sides during sampling. The model was filled with normal saline (0.9 % NaCl) and mounted vertically in the middle of a cabinet along with a second glass tube containing saline in which an AIS Thermodig N 800 digital thermometer was placed; this was used as a temperature reference. In the middle of the cabinet, a thermostat was mounted, connected with a heater and a blower outside the cabinet. The blower was connected to a rubber hose that blew warm air in the bottom of the cabinet. The cabinet had a glass door, which allowed continuous reading of the temperature and observation of each experiment. When the temperature of the saline solution in the reference tube reached 37.3 °C, the glass door was opened slightly until the temperature started to drop.

Injections were made with a solution (BMB) containing 4.81 mg bupivacaine base and 0.029 mg methylene blue per ml. Before the experiments, the densities of both this solution and of plain bupivacaine 0.5 % at 22 °C and at 37 °C were determined, as well as the density of the saline solution at 37 °C (Research Laboratories, Erasmus University Rotterdam).

In a pilot study, 3 ml of the BMB solution at room temperature was injected into the model; after 3 min, nine 1-ml samples were drawn simultaneously and subsequently analyzed for both bupivacaine base and methylene blue concentrations. Bupivacaine base concentrations were determined according to the HPLC method; methylene blue concentrations were measured with a spectrofotometer at 660 nm. The resulting methylene blue concentration as a function of the bupivacaine base concentration in the nine samples was found to be represented by a linear relationship with a correlation coefficient of $r = 0.9972$. It was concluded from the pilot study that, when injecting a mixture containing bupivacaine and methylene blue, the resulting distribution of bupivacaine is identical and proportional to that of methylene blue so that, in order to visualize the distribution of bupivacaine, the less laborious determination of methylene blue concentrations will suffice.

Two experiments were done. Both were conducted with the model at 37 °C. In experiment I, 3 ml of the BMB solution, previously equilibrated to 37 °C, were injected through the 25 gauge spinal needle. In experiment II, 3 ml of the BMB

solution at room temperature (22.0 °C - 22.3 °C) were injected. Each experiment was conducted 8 times, four times with the speed of injection as fast as possible and four times at a slow speed of injection of 0.05 ml/sec. Injection times were monitored with a stopwatch. Three min after completion of the injection nine 1-ml samples were drawn simultaneously, which were subsequently analysed for methylene blue concentrations. After each sampling the spinal needle as well as the sampling needles were removed and the model was rinsed, after which new needles and syringes were placed and both the model and the temperature reference tube were filled with fresh saline.

RESULTS

Table 7.1 shows the densities of plain bupivacaine 0.5 % and the BMB solution at 22 °C and 37 °C, as well as the density of the 0.9 % NaCl solution at 37 °C. As can be seen from Table 1, both plain bupivacaine 0.5 % and the BMB solution employed by us are slightly hyperbaric at 22 °C and slightly hypobaric at 37 °C when compared to saline of 37 °C.

Table 7.1. Densities of the Solutions at Different Temperatures

Temperature (°C)	22	37
NaCl 0.9 %		**0.9997**
Plain bupivacaine 0.5 %	**1.0037**	**0.9994**
BMB Solution	**1.0035**	**0.9991**

BMB Solution: The solution used in the experiments contained 4.81 mg bupivacaine base and 0.029 mg methylene blue per ml.

The average injection time in the high speed experiments was 5.9 sec (range 5.3-6.4) in experiment I and 5.0 sec (range 4.3-6.1) in experiment II.
The temperature of the saline solution could be kept between 36.7 °C and 37.3 °C during all experiments by opening and closing the glass door of the cabinet.
In experiment I, the methylene blue could be seen to extend mainly in an upward direction from the site of injection, well beyond the highest sampling site (no.1), with occasional currents spiralling downward. In experiment II, the opposite was observed, the bulk of the methylene blue moving downward from the site of injection beyond the lowest sampling site (no. 9) with occasional currents spiralling upward in what seemed to be a quite random fashion. Although in both experiments the injections made at a high speed created clearly more turbulence, no visual differences in distribution could be observed when compared to the experiments in which injections were made at a slow speed of 0.05 ml/sec.
The methylene blue concentrations in the eight series of experiment I, although showing a large variation at identical sampling sites, showed a similar distribution with the highest concentrations upward from the site of injection. When comparing the series using a high speed of injection with the series using a slow speed of injection, the methylene blue concentrations found in the latter were generally higher.
In experiment II, the distribution pattern was also similar with the highest concentrations of methylene blue downward from the site of injection; as well as in experiment I, large variation in methylene blue concentrations at identical sampling sites was seen. When comparing the series using a high speed of injection with the series using a low speed of injection, there were no clear differences between the average methylene blue concentrations at identical sampling sites with the exception of the lowest sampling site (no. 9), where the highest concentrations were found in the series using a slow speed of injection. The average values of methylene blue concentrations are summarized in Table 2. Figure 3 shows a graph of the differences in methylene blue concentrations between experiments I and II.

Table 7.2. **Average Values of Methylene Blue Concentrations in Nanograms per ml (± SEM)**

Sample Site	Exp. I HS (n = 4)	Exp. I SS (n = 4)	Exp. II HS (n = 4)	Exp. II SS (n = 4)
1	1939 (278)	2553 (198)	41 (33)	7 (7)
2	1582 (271)	2401 (309)	148 (51)	138 (106)
3	1686 (93)	2245 (169)	296 (87)	414 (196)
4	1806 (182)	2054 (216)	636 (196)	760 (191)
5	1442 (163)	1683 (226)	1457 (77)	1454 (22)
6	936 (254)	1235 (172)	1901 (223)	1628 (157)
7	804 (305)	989 (67)	1671 (106)	1679 (143)
8	503 (165)	635 (124)	1538 (73)	1663 (120)
9	455 (158)	362 (48)	1194 (193)	1634 (89)

Exp. I: 3 ml of a solution (BMB) containing 4.81 mg bupivacaine base and 0.029 mg methylene blue per ml equilibrated to 37 °C injected at high speed (HS) or slow speed (SS) into model containing normal saline of 37 °C.

Exp. II: 3 ml of BMB solution equilibrated to 22 °C injected at high speed (HS) or slow speed (SS) into model containing normal saline of 37 °C.

Sample sites situated 5 cm apart in the longitudinal direction of the model, numbered 1 to 9 from the top downward. Injection site located opposite sample site no. 5.

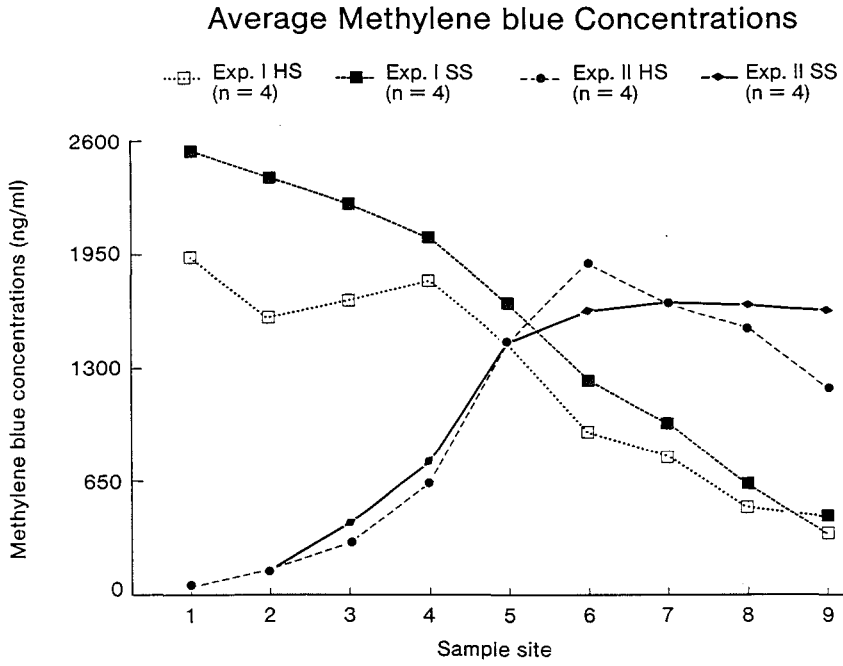

Figure 7.3. **Graph of the average methylene blue concentrations. The horizontal axis shows the sampling sites. The sampling sites were positioned in the longitudinal direction of the model, 5 cm apart and distributed evenly around the midpoint of the model. They are numbered 1 to 9 from the top downward. The vertical axis shows the methylene blue concentrations in ng/ml. Each value represents the average of 4 series. Exp I: 3 ml of a solution (BMB) containing 4.81 mg bupivacaine base and 0.029 mg methylene blue per ml equilibrated to 37 °C injected into model containing normal saline at 37 °C, injected at high speed (HS) or slow speed (SS). Exp. II: 3 ml of BMB solution equilibrated to 22 °C injected into model containing normal saline at 37 °C, injected at high speed (HS) or slow speed (SS). SEM bars have been omitted for the sake of presentation.**

DISCUSSION

It should be emphasized that the volume capacity of our spinal canal model was large compared with the amount of cerebrospinal fluid present in the spinal subarachnoid space; the objective of the experiments, however, was to study differences in fluid dynamics under different conditions, and as such, it was deemed unnecessary to aim for a close resemblance to the in vivo situation, which would demand a technically more complicated and more expensive device.

Cerebrospinal fluid has a density of 1.0003 at 37 °C (6); the density of the plain solution of bupivacaine 0.5 % as determined in this study was 1.0037 at 22 °C and 0.9994 at 37 °C. Thus, the plain solution of bupivacaine 0.5 % is slightly hyperbaric at room temperature and slightly hypobaric at body temperature. In the experiments, the different temperature-dependent densities of the BMB solution cause a comparable change in baricity when compared to the density of normal saline at 37 °C.

Although the difference in density between the BMB solution and normal saline at 37 °C is very small, the resulting distribution pattern as observed visually and as reflected in methylene blue concentrations in all 8 series of experiment I is that of a hypobaric solution.
The difference between the density of the BMB solution at room temperature and normal saline of 37 °C is larger, and consequently, the results from experiment II not only confirm the hyperbaric state of the BMB solution at room temperature when compared to normal saline at 37 °C, but as the average methylene blue concentrations found in experiment II were in general lower than those found in experiment I, they also suggest that spread below the lowest sampling site (no. 9) in this experiment was more extensive than spread above the highest sampling site (no. 1) in experiment I.
In a study comparing the injection of plain bupivacaine 0.5 % at 4 °C and 21 °C in a spinal canal model containing normal saline at 21 °C, Beardsworth et al. (7) found that injecting bupivacaine at 4 °C in the vertically positioned model resulted in a hyperbaric distribution after 20 min, whereas injection of bupivacaine at 21 °C showed a symmetrical distribution around the site of injection; this agrees with the densities given in their study, which show that, compared to normal saline at 21 °C, bupivacaine was hyperbaric at 4 °C and isobaric at 21 °C. Where the results from our study agree with theirs with regard to the hypothermic injection, they differ with respect to the isothermic injection. This difference may be explained on the basis of the small, but

apparently relevant change in baricity from bupivacaine related to normal saline when their densities are compared at 37 °C instead of at 21 °C.

In our study, we took the samples 3 min after completion of the injection; we did that first of all because, in most clinical studies using the plain solution of bupivacaine 0.5 % for spinal anesthesia, the patients are kept seated for 2 to 3 min after intrathecal injection. Secondly, the longer the time interval between injection and sample-taking, the more the in-vitro conditions will deviate from in- vivo conditions due to uptake and elimination of the local anesthetic from the cerebrospinal fluid in the latter.

One of the major drawbacks of the plain solution of bupivacaine 0.5 % in spinal anesthesia is that predictability of the ensuing level of sensory blockade is poor (8-17), unless the bupivacaine solution is equilibrated to body temperature prior to intrathecal administration (4,18). Although many factors govern the spread of an intrathecally administered solution (1) and extrapolation of in-vitro observations to in-vivo situations should be done with caution and reservation, it seems reasonable to conclude from this study that the observed large difference in distribution caused by a small, temperature-dependent change in baricity, has its clinical reflection in an unpredictable intrathecal spread when using a solution that, at room temperature, is slightly hyperbaric relative to cerebrospinal fluid and that, depending on the density of the cerebrospinal fluid, will change from slightly hyperbaric to slightly hypobaric in most patients during thermal equilibration in the cerebrospinal fluid.

In the series using a high speed of injection, the speed of injection was approximately 10 times as fast as in the series using a slow speed of injection. In experiment I, the methylene blue concentrations at identical sampling sites were generally lower in the series using a high speed of injection as compared with the series using a low speed of injection; although it should be stressed that the variation in methylene blue concentrations was large, this observation may reflect a more extensive spread beyond the highest sampling point with the higher speed of injection.
In a study in which several more or less isobaric local anesthetic solutions were injected into a spinal canal model, increasing the speed of injection fourfold and twelvefold resulted in a more extensive spread of the local anesthetic solution (19). Clinically, however, these extreme differences in speed of injection are hardly feasible, and it has been shown that no differences in the maximum sensory level of anesthesia result from increasing the speed of injection twofold (20) or fivefold (21).

In conclusion, the present study shows that the temperature-dependent difference in baricity of the BMB solution from slightly hyperbaric at 22 °C to slightly hypobaric at 37 °C relative to normal saline at 37 °C, results in contrary distribution patterns of the BMB solution in 37 °C normal saline when injected at either 22 °C or 37 °C. The fact that the plain solution of bupivacaine 0.5 % exhibits a comparable temperature-dependent difference in baricity relative to cerebrospinal fluid at 37 °C offers, apart from other factors influencing intrathecal spread, an explanation for the large variability in the maximum level of sensory blockade when using the plain solution of bupivacaine 0.5 % at room temperature or a lower temperature for spinal anesthesia.

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CHAPTER 8

SUMMARIZING CONCLUSIONS

Although the results and conclusions of the different studies described in Chapters 3-7 are addressed in the DISCUSSION section of each chapter, some aspects are elaborated upon in greater detail in the following.

The fact that many factors affect the distribution of intrathecally administered local anesthetic solutions, implies that it is extremely difficult to study one factor while keeping all other factors constant at the same time. Moreover, the level of sensory anesthesia is determined in a subjective manner. This is well illustrated by apparently similar studies yielding conflicting results. One of the major causes is probably the large variation in observations resulting from the inability to effectively control all factors involved in combination with relatively small sample sizes; this increases the risk of a statistical type II error being made, which means erroneous retention of the null hypothesis, resulting in the false conclusion that there is no significant difference while in reality there is. For instance, it has been shown that injecting plain bupivacaine through the second lumbar interspace when compared with injection through the fourth lumbar interspace increases the average maximum level of sensory blockade by four dermatomes (1). Yet in some studies, spinal anesthesia is administered through different interspaces rather than through one, and this will increase the variation in the observed maximum levels of sensory blockade, especially since it was demonstrated by radiography that in as much as 50 % of the cases the spinal needle did not rest in the predicted interspace (2). Similarly, differences in age, height and weight which are relatively large yet evenly distributed among the different groups of patients to be studied, may not give rise to a significant difference between the groups with respect to age, height and weight, but they will surely contribute to an increased variation in the ensuing maximum levels of sensory blockade and the risk of a type II error being made, thus masking an existing significant difference in these maximum levels. Inter-patient variability may well be a factor of influence, although it has never been studied; intra-patient variability probably plays no major role, as was shown in a study in which individual patients acted as their own controls by receiving more than one spinal anesthesia and from which it was concluded that the

predictability of the maximum level of sensory blockade of the second anesthesia from the first anesthesia was highly significant (3). Caution is therefore mandatory when interpreting the absence of statistically significant differences.

In our first study (chapter 3), one of the conclusions was that keeping the patients receiving the hyperbaric solution in the sitting position for 3 min, did not result in a significantly lower maximum level of sensory blockade when compared with the patients immediately turned into the supine horizontal position; a lower level might have been expected on the basis of baricity, although it can also be argued that a time difference of 3 min is too small to make a difference, so that turning the patients into the supine horizontal position after 3 min will still allow the distribution of the hyperbaric solution in the cephalad direction to catch up with the distribution seen in the patients that were turned into the supine horizontal position immediately after injection, resulting in comparable levels. In a study comparing the effects of posture and baricity with 5 ml 0.5 % bupivacaine, a group of 10 patients receiving hyperbaric bupivacaine in the sitting position which was maintained for 2 min had the same average maximum level of sensory blockade as a group of 10 patients receiving the same amount in the lateral horizontal position (4). In a study with 4 ml hyperbaric bupivacaine administered to patients in the sitting position which was maintained for 2 to 25 min after which the patients were turned into the supine horizontal position followed by a 15 ° head-down tilt, it was shown that turning the patients into the Trendelenburg position as late as 42 min after injection increased the maximum level of sensory blockade with 3.1 segments (5). On the other hand, in a study comparing the intrathecal administration of hyperbaric tetracaine to patients that were either in the lateral horizontal position and turned supine immediately after injection or in the sitting position which was maintained for 2 min, it was found that the maximum level of sensory blockade was significantly lower in the patients sitting for 2 min (6); it was concluded from this study that while a hyperbaric solution spread under the effect of gravity, posture could not be used to control its spread. In a study with hyperbaric bupivacaine comparing the effect of a 15 ° head-down tilt during 10 min after injection with the horizontal position, the average maximum levels of sensory blockade were, although higher in the head-down group, statistically not significant (7). In a study comparing the effect of a 10 ° head-down tilt during 60 sec with the supine horizontal position after the injection of hyperbaric bupivacaine and tetracaine, the maximum level of sensory blockade was not increased by the Trendelenburg position (8). It should be emphasized that all these studies (4-8) as well as ours showed large

variations in the maximum levels of sensory blockade, which makes it difficult if not impossible to draw an unanimous conclusion; since it has been amply demonstrated that hyperbaric solutions of bupivacaine and tetracaine compared with the plain solution when administered in the lateral horizontal position result in a higher cephalad spread (4,6,9-13), the conclusion that hyperbaric solutions spread under the effect of gravity seems justified, whereas the effects of changes in posture after completion of the intrathecal administration of a hyperbaric solution on subarachnoid distribution remain controversial.

Plain bupivacaine is generally regarded as an isobaric solution (14). However, at 37 °C, plain bupivacaine has a density of 0.9993 g/ml (14); the density of cerebrospinal fluid at 37 °C is 1.0003 g/ml; the baricity of plain bupivacaine at 37 °C therefore is 0.9990 (0.9993/1.0003) and as such it is slightly hypobaric. When the density of plain bupivacaine at room temperature (22 °C) is compared to the density of cerebrospinal fluid at 37 °C, the baricity is 1.0034 (1.0037/1.0003, chapter 7, page 84, Table 7.1) and as such it is hyperbaric. In our second study (chapter 4) we demonstrated that differencecs in baricity of plain bupivacaine due to different temperatures at the time of intrathecal injection resulted in a significant difference in the average maximum level of sensory blockade. The distribution of plain bupivacaine equilibrated to 37 °C as seen in our study was clearly that of a hypobaric solution, with a smaller variation in the maximum levels of sensory blockade than usually seen with plain bupivacaine injected at room temperature, an observation that has been confirmed in our third and fourth study (chapters 5 and 6). Solutions with densities well beyond the upper and lower limits of the density of cerebrospinal fluid will obviously be hyperbaric or hypobaric respectively at body temperature; a hyperbaric solution will remain hyperbaric when injected at room temperature, and provided the difference in density is large enough, a solution hypobaric at body temperature will remain so at room temperature. With isobaric solutions, the situation is different; if a solution is isobaric at 37 °C, it will be slightly hyperbaric at room temperature. In the case of plain bupivacaine, the density of which is near that of cerebrospinal fluid, the question is whether or not the small differences in densities between plain bupivacaine and the cerebrospinal fluid of an individual patient which will inevitably be present in most patients due to small variations in the density of the latter, are large enough to influence intrathecal distribution. The observation that plain bupivacaine, although regarded as an isobaric solution, behaves like a hypobaric solution when previously equilibrated to 37 °C, indicates that a relatively small change in the density of an

"isobaric" solution due to a change in temperature is large enough to change the profile of this solution into a hypobaric solution. This view is supported by the observations made in the spinal canal model study (chapter 7), where the injection of a solution containing bupivacaine and methylene blue with a baricity at 37 °C -relative to the normal saline solution used in the experiments- of 0.9994 (0.9991/0.9997, chapter 7, page 84, Table 7.1), resulted in a largely hypobaric distribution pattern. When the same solution was injected at room temperature with a baricity of 1.0038 (1.0035/0.9997, chapter 7, page 84, Table 7.1), the distribution showed a largely hyperbaric pattern. Although the use of results obtained in in-vitro experiments to explain in-vivo observations should be done with caution, the in-vitro results at least indicate that small, temperature-dependent changes in density that are in the same order of magnitude as those seen with plain bupivacaine under in-vivo conditions, can lead to a change in baricity large enough to change the distribution pattern. When plain bupivacaine is injected at room temperature, it will initially be slightly hyperbaric in most patients, changing to slightly hypobaric somewhere during thermal equilibration to 37 °C in the cerebrospinal fluid. It stands to reason that variation in the maximum level of sensory blockade is enlarged by differences in the time needed for thermal equilibration and variation in the density of cerebrospinal fluid of individual patients, and this, apart from other factors, may explain the poor predictability of the ensuing maximum level of sensory blockade reported in the literature when using plain bupivacaine at room temperature for spinal anesthesia. In view of the above it is concluded that the plain solution of bupivacaine is not truly isobaric, other than accidentally in an individual patient.

In our third study (chapter 5), we demonstrated that reducing the angle between the spinal needle and the longitudinal axis of the spinal canal to < 50 °, increased the average maximum level of sensory blockade by 1.6 to 1.7 segments; although the clinical importance of this observation is limited, it illustrates that when the variation in the maximum levels of sensory blockade is reduced by previously equilibrating the plain bupivacaine solution to 37 °C, an in itself small difference can be brought to light with statistical significance.

In our fourth study (chapter 6), we studied the differences in sensory and motor block characteristics following the intrathecal administration of plain bupivacaine equilibrated to either 37 °C or 20 °C. When a given dose of bupivacaine results in a high maximum level of sensory blockade, as is the case when the solution is given at body

temperature, it means that the amount of bupivacaine available per spinal segment is less than in a situation in which the same dose results in a lower maximum level of sensory blockade with less spinal segments blocked. The logical consequence of this is, that the time for regression per spinal segment will be shorter when the maximum level of sensory blockade is higher. However, clinically more important than the time needed for regression of a spinal segment, is the duration of sensory blockade at a given level, i.e. the time that the sensory level of blockade is at or above a given dermatome. As was shown in our study, durations at T 6, T 8 and T 10 were significantly longer in the patients receiving bupivacaine at body temperature when compared with bupivacaine given at room temperature. Based on these observations, the conclusions of our second study (chapter 4) can be extended: Equilibration of the plain solution of bupivacaine 0.5 % to 37 °C prior to intrathecal injection as compared with a solution injected at room temperature, results in a higher, more predictable maximum level of sensory blockade with longer duration of sensory blockade at the sixth, eighth and tenth dermatome.

CONCLUSIONS

-The solutions of plain bupivacaine 0.5 % and hyperbaric bupivacaine 0.5 % are equally suitable for spinal anesthesia, provided patients receiving the plain solution are kept sitting for at least 2 min.

-When using hyperbaric bupivacaine 0.5 % for spinal anesthesia, keeping the patients in the sitting position during injection and for 3 min thereafter seems to have no influence on cephalad spread.

-When using plain bupivacaine 0.5 % for spinal anesthesia, the time needed for thermal equilibration in the cerebrospinal fluid and hence the temperature of the injected solution affects the intrathecal distribution of that solution.

-When using plain bupivacaine 0.5 % for spinal anesthesia previously equilibrated to 37 °C, the resulting maximum level of sensory blockade is higher and more predictable as compared with the maximum level of sensory blockade following the intrathecal administration of the same solution equilibrated to 4 °C or 20 °C.

-The intrathecal administration of plain bupivacaine 0.5 % previously equilibrated to 37 °C results in a sensory block of longer duration at the 6th, 8th and 10th dermatome as compared with the same solution injected at room temperature.

-When using plain bupivacaine 0.5 % for spinal anesthesia previously equilibrated to 37 °C, using a steep paramedian approach of the subarachnoid space reducing the angle between the spinal needle through which injections are made and the longitudinal axis of the spinal canal to < 50 ° increases the maximum level of sensory blockade by approximately 1.6 segments as compared with the conventional more or less perpendicular approach.

-When using plain bupivacaine 0.5 % for spinal anesthesia injected at room temperature, the large variation in the resulting maximum levels of sensory blockade can in part be explained by the change in baricity that will occur in most patients during thermal equilibration to body temperature following intrathecal administration.

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CHAPTER 9

SUMMARY

Chapter 1 describes the history of spinal anesthesia, starting with the discovery of the local anesthetic properties of cocaine and the introduction into clinical practice of lumbar puncture, and ending with the introduction of bupivacaine for spinal anesthesia in 1966.

Chapter 2 describes the factors that are supposedly influencing the intrathecal spread of local anesthetic solutions as well as the aims of this thesis.

Chapter 3 describes an investigation studying the intrathecal distribution as measured by the maximum level of sensory blockade of plain bupivacaine and hyperbaric bupivacaine, as well as the effect of different patient positions on the distribution of hyperbaric bupivacaine.

Chapter 4 describes the effect on intrathecal distribution of injecting plain bupivacaine previously equilibrated to either 37 °C or 4 °C. The difference in baricity of bupivacaine at these temperatures and the role of thermal equilibration in the subarachnoid space are discussed.

Chapter 5 describes the effect of different angles between the spinal needle and the longitudinal axis of the subarachnoid space on the intrathecal distribution of plain bupivacaine, equilibrated to body temperature prior to injection in order to minimize variation in the maximum levels of sensory blockade.

Chapter 6 describes a study investigating the differences in sensory and motor block characteristics following the intrathecal injection of plain bupivacaine equilibrated to either 37 °C or 20 °C.

Chapter 7 describes the observations made in a spinal canal model, in which a solution containing bupivacaine and methylene blue was injected at either 37 °C or 22 °C with different speeds of injection, as well as the differences in distribution under these

conditions 3 min after injection as measured by methylene blue concentrations in samples taken at various sites situated equally above and below the site of injection.

Chapter 8 describes some aspects of statistics, patient position and baricity in greater detail and summarizes the conclusions.

CHAPTER 10

SAMENVATTING

In hoofdstuk 1 wordt een beschrijving gegeven van de geschiedenis van de spinale anesthesie, van de ontdekking van de locaal-anesthetische eigenschappen van cocaine en de introductie van de lumbale punctie in de geneeskunde, tot de introductie van bupivacaine voor spinale anesthesie in 1966.

Hoofdstuk 2 beschrijft de factoren waarvan verondersteld wordt dat zij de intrathecale verspreiding van locaal-anesthetica beïnvloeden alsmede de doelstellingen van dit proefschrift.

In hoofdstuk 3 wordt een onderzoek beschreven, waarin de intrathecale verspreiding van glucosevrije en hyperbare bupivacaine wordt bestudeerd aan de hand van het maximale niveau van sensibele blokkade, evenals de invloed van verschillen in positie van de patiënt op de intrathecale verspreiding van hyperbare bupivacaine.

Hoofdstuk 4 beschrijft de invloed op de intrathecale verspreiding van glucose-vrije bupivacaine die voor injectie geëquilibreerd is op 37 °C respectievelijk 4 °C. Het verschil in de bariciteit van bupivacaine bij deze temperaturen alsmede de rol van thermische equilibratie in de subarachnoïdale ruimte worden besproken.

Hoofdstuk 5 beschrijft de invloed van verschillende hoeken tussen de spinale naald en de lengte-as van de subarachnoïdale ruimte op de intrathecale verspreiding van glucose-vrije bupivacaine, die tevoren op lichaamstemperatuur geëquilibreerd was teneinde de variabiliteit van de maximale niveaus van sensibele blokkade te beperken.

In hoofdstuk 6 wordt een onderzoek beschreven, dat de verschillen in de kenmerken van sensibele en motorische blokkade na de intrathecale toediening van glucose-vrije bupivacaine geëquilibreerd op 37 °C respectievelijk 20 °C bestudeert.

Hoofdstuk 7 beschrijft de waarnemingen in een model van de subarachnoïdale ruimte, waarin een oplossing bevattende bupivacaine en methyleenblauw geëquilibreerd op 37

°C respectievelijk 22 °C met verschillende snelheden werd geïnjecteerd, alsmede de verschillen in verspreiding onder deze condities 3 min na injectie door middel van de bepaling van methyleenblauw concentraties in monsters, die op verschillende plaatsen gelocaliseerd op gelijke afstanden boven en onder de plaats van injectie genomen werden.

In hoofdstuk 8 wordt dieper ingegaan op enige aspecten betreffende de statistiek, positie van de patiënt en bariciteit en worden de conclusies samengevat.

CURRICULUM VITAE

Rudolf Stienstra was born in Rotterdam, The Netherlands on July 1, 1950. He obtained his secondary school certificate (H.B.S.-B) at the Peter Stuyvesant College, Willemstad, Curaçao, Dutch Antilles, in 1970. In 1970 he started to study medicine at the Medical Faculty, Erasmus University Rotterdam, from which he graduated in 1977. From 1977 till 1979 he was a resident in Internal Medicine at the Zuiderziekenhuis Rotterdam (Head: Prof. Dr. W.H. Bïrkenhäger). Specialization in Anesthesiology followed at the department of Anesthesiology, Academical Hospital Rotterdam-Dijkzigt (Dr. B. Dworacek, later Prof. Dr. W. Erdmann). During this specialization, he worked two months at the department of Anesthesiology of the Academical Hospital of Trondheim, Norway (Head: Prof. Dr. H. Breivik) and in 1982 he was certified as an anesthesiologist by the Committee for the Registration of Qualified Medical Specialists of the Royal Netherlands Medical Association. Since 1982, he has been working as a staff anesthesiologist at the Reinier de Graaf Gasthuis, Delft, The Netherlands.