Comparison of glucose 7.5% and 0.75% with or without phenylephrine for tetracaine spinal anaesthesia

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Purpose: To investigate whether a marginally hyperbaric tetracaine solution with or without phenylephrine could produce consistent blocks as compared with a conventionally hyperbaric tetracaine solution injected at L₃₋₄ interspace with the patient in the lateral position.

Methods: We studied 120 ASA I or II patients scheduled for elective surgery to the lower limb. Patients were randomly divided into four equal groups to receive spinal anaesthesia using tetracaine 0.5% in glucose 0.75% or 7.5%, with or without phenylephrine 0.125%. Neural block was assessed in a double-blind manner by cold, pinprick, and touch sensation, and a modified Bromage scale after the injection of the study drug.

Results: The median (10th, 90th percentiles) peak dermatomal level to pinprick obtained by the solutions in glucose 0.75% was T₁₀ (L₁, T₅), which was lower than that obtained by the solution in glucose 7.5% extending to T₅ (T₁₀, T₃) and T₅ (T₁₀, T₂) with or without phenylephrine, respectively ($P < 0.0001$). The addition of phenylephrine prolonged the time to two-segment regression but did not change the maximum extent of blocks.

Conclusions: A marginally hyperbaric tetracaine with or without phenylephrine produced consistent blocks with spread restricted to the lower thoracic segments when administered

intrathecally at the L₃₋₄ interspace with the patient in the lateral position.

Objectif: Rechercher si une solution quasi hyperbare de tétracaïne avec ou sans phényléphrine peut produire des blocs constants comparativement à une solution de tétracaïne hyperbare conventionnelle injectée dans l'espace L₃₋₄ chez un patient en position latérale.

Méthodes: L'étude porte sur cent vingt patients ASA I et II programmés pour une chirurgie non urgente au membre inférieur. Les patients étaient répartis aléatoirement en quatre groupes égaux pour recevoir une rachianesthésie à la tétracaïne 0,55% dans le glucose 0,75% ou 7,5% avec ou sans phényléphrine 0,125%. Après une injection effectuée en double aveugle, le bloc nerveux était évalué par le froid, la piqure d'aiguille et la sensation tactile ainsi que sur une échelle de Bromage modifiée.

Résultats: Le niveau maximal métamérique médian (10^e, 90^e percentiles) mesuré à la piqure d'aiguille à T₁₀ (L₁, T₅) avec les solutions glucosées 0,75% était inférieur à celui produit par la solution glucosée 7,5% qui s'étendait à T₅ (T₁₀, T₃) et T₅ (T₁₀, T₂) avec et sans phényléphrine ($P < 0,0001$). L'ajout de phényléphrine a prolongé l'intervalle de la régression de deux segments mais n'a pas modifié l'extension supérieure du bloc.

Conclusion: Une solution quasi hyperbare de tétracaïne avec ou sans phényléphrine a produit des blocs constants avec une extension limitée aux segments thoraciques inférieurs lorsque administrée par la voie sous-arachnoïdienne chez le patient en décubitus latéral.

Key words

ANAESTHETIC TECHNIQUES: spinal;
LOCAL ANAESTHETICS: tetracaine;
CATECHOLAMINES: phenylephrine;
PHYSICS: baricity.

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One of the most important factors influencing the extent of spread of spinal anaesthesia is the baricity of the local anaesthetic solution injected. It is easily manipulated by changing the concentration of glucose solution. There have been many studies comparing the effects of different baricities to search for an ideal anaesthetic solution that could produce predictable blocks with little risk of unnecessarily extensive spread.¹⁻⁹ Recently, a marginally hyperbaric bupivacaine solution containing a low

concentration of glucose was shown to produce consistent blocks when injected at the L₃₋₄ interspace.¹ However, in the study, lumbar puncture was performed with the patient in the sitting position. Blocks administered at the L₂₋₃ interspace with patients in the lateral position led to extensive blocks.

The present study was conducted to determine whether a marginally hyperbaric local anaesthetic solution administered at the L₃₋₄ interspace with the patient in the lateral position produced consistent spinal block using the long acting agent, tetracaine. The anaesthetic behaviour and haemodynamic consequences produced by the dilute solution were compared with those produced by a conventionally hyperbaric solution. In addition, we examined prolongation of the blocks with phenylephrine.

Methods

After institutional review board approval, 120 ASA I or II patients scheduled for elective surgery to the lower limb were enrolled in the study. Informed written consent was obtained from all participants. Patients with a contraindication to spinal anaesthesia, major back problems, or neurological disease were excluded.

Premedication consisted of 0.05–0.1 mg·kg⁻¹ atropine and 0.5–1 mg·kg⁻¹ hydroxyzine *im* approximately one hour before anaesthesia. After an intravenous infusion of acetated Ringer's solution was initiated in a hand or forearm at a rate of 10 ml·kg⁻¹·hr⁻¹, the patients were placed in the lateral decubitus position. Lumbar puncture was performed at the L₃₋₄ interspace with a 25-ga Quincke needle using the midline approach. After obtaining free reflux of cerebrospinal fluid (CSF), 0.1 ml of CSF was taken for the measurement of specific gravity, and the test solution (2–3 ml based on patient height: <150 cm, 2.0 ml; 150–159 cm, 2.2 ml; 160–169 cm, 2.4 ml; 170–179 cm, 2.6 ml; 180–189 cm, 2.8 ml; >190 cm, 3.0 ml) was administered at a rate of 0.1 ml·sec⁻¹ with the bevel of the needle oriented toward the dependent side. After injection of study solution, 0.1 ml CSF was again aspirated and reinjected in order to confirm correct placement of the needle tip.

Patients were randomly assigned to one of four groups (*n* = 30 in each group) according to the solution injected. Group I received tetracaine 0.5% in glucose 7.5%; Group II received tetracaine 0.5% in glucose 0.75%; Group III received tetracaine 0.5% in glucose 7.5% and phenylephrine 0.125%; and Group IV received tetracaine 0.5% in glucose 0.75% and phenylephrine 0.125%. The solutions were prepared immediately before injection by dissolving 20 mg crystalline tetracaine hydrochloride in a combined solution of 3 ml glucose 10% or 1% with 1 ml of distilled water or

TABLE I Physical characteristics of solutions studied

Group	I	II	III	IV
Specific gravity	1.037	1.009	1.038	1.011
pH	7.776	7.796	7.615	7.516
Osmolality (mOsm·L·kg ⁻¹)	497	86	556	162

The solution for Group I was tetracaine 0.5% in glucose 7.5%; Group II tetracaine 0.5% in glucose 0.75%; Group III tetracaine 0.5% in glucose 7.5% and phenylephrine 0.125%; Group IV tetracaine 0.5% in glucose 0.75% and phenylephrine 0.125%. All local anaesthetic solutions were measured at 37°C.

phenylephrine 0.5%. The physical characteristics of the solutions are shown in Table I. The specific gravity of each solution and CSF was measured at 37°C by a refractometer.

Patients were immediately placed supine and remained level during the rest of the study period. All variables were assessed in a double-blinded manner by an investigator who was unaware which solution had been injected. The dermatomal levels of blockade of light touch, temperature, and pinprick discrimination, as well as the degree of motor block, blood pressure and heart rate were measured 2, 5, 10, 15, 20, 25, and 30 min and thereafter every 30 min after intrathecal injection of the local anaesthetic unless sedation or surgery prevented assessment. The loss of each sensory modality was determined by the patient's verbal response to the stimulus applied bilaterally in the mid-clavicular line starting caudad and moving cephalad. The dull, hinged end of a sterile safety pin was used to examine light touch; an alcohol soaked swab for temperature; the sharp tip of a safety pin for pinprick. The degree of motor block was assessed by a modified Bromage scale from 0 to 4 (0 = able to move hip, knee, ankle, toes; 1 = unable to move hip, able to move knee, ankle, and toes; 2 = unable to move hip and knee, able to move ankle and toes; 3 = unable to move hip, knee and ankle, able to move toes; 4 = unable to move hip, knee, ankle, toes). Blood pressure was measured using an automated sphygmomanometer, and heart rate was determined by electrocardiogram. Hypotension was treated with 5 mg ephedrine *iv* if systolic arterial pressure decreased by >25% of the preanaesthetic value or if symptoms, such as nausea or dizziness, became apparent.

Results are expressed as mean ± SE or median and 10th and 90th percentiles. Continuous variables were compared using one-way analysis of variance (ANOVA) and the Student-Newman-Keuls (SNK) test. Haemodynamic values were analyzed using data that showed a maximum decrease after spinal injection. Differences in the time course of dermatomal level of analgesia to pinprick among the four solutions were

TABLE II Patient characteristics

Group	I	II	III	IV
Sex (M/F)	13/17	19/11	14/16	17/13
Age (yr)	49-3	45-4	50-3	49-4
Height (cm)	159-2	162-2	160-3	161-2
Weight (kg)	61-2	62-2	61-2	64-3
Dose (mg)	11.5-0.3	12.0-0.3	11.6-0.3	11.8-0.3

Data are mean $\pm$ SE. No differences among groups.

Patients in Group I received tetracaine 0.5% in glucose 7.5%; those in Group II tetracaine 0.5% in glucose 0.75%; those in Group III tetracaine 0.5% in glucose 7.5% and phenylephrine 0.125%; those in Group IV tetracaine 0.5% in glucose 0.75% and phenylephrine 0.125%.

FIGURE Time course of dermatomal level of loss of pinprick sensation after spinal anaesthesia. Mean $\pm$ SE. Patients in Group I received tetracaine 0.5% in glucose 7.5%; Group II tetracaine 0.5% in glucose 0.75%; Group III tetracaine 0.5% in glucose 7.5% and phenylephrine 0.125%; Group IV tetracaine 0.5% in glucose 0.75% and phenylephrine 0.125%. Groups I and III are different from Groups II and IV as analyzed by repeated measures ANOVA and Scheffe's F tests.

assessed with repeated measures ANOVA and Scheffe's F tests. The peak level of sensory block and the degree of motor block were compared using the Kruskal-Wallis test and the SNK test. Chi-square analysis with the Bonferroni correction was used to compare the number of patients given ephedrine. $P < 0.05$ was considered significant.

Results

Patient characteristics and the dose of tetracaine administered did not differ among the four study groups (Table II). No patient was given hypobaric solutions in comparison with CSF, which ranged from 1.005 to 1.008 in specific gravity at 37°C.

All the spinal anaesthetic solutions produced satisfactory anaesthesia, including motor block, for surgery proposed. The time course of the upper segmental level of analgesia to pinprick for 210 min after spinal anaesthesia is displayed in the Figure, where differences were detected in the anaesthetic behaviour between the glucose 7.5% solutions (Groups I and III) and 0.75% solutions (Groups II and IV). There were no differences in the peak dermatomal levels to any of the three types of stimuli between groups I and III or between groups II and IV (Table III). However, the glucose 7.5% solutions of Groups I and III produced more extensive blocks than did the glucose 0.75% solutions of Groups II and IV ($P < 0.0001$). Whereas all patients in Groups I and III obtained loss of pinprick sensation to the level higher than T₁₂, three and six patients in Groups II and IV, respectively, did not. The mean time taken to achieve the peak dermatomal level of loss of sensation to pinprick did not differ among the four groups. One patient each in Groups I and III developed loss of pinprick sensation to the level higher than T₁, felt uneasy, and could not breathe deeply. There was no difference in the maximum degree of motor block among the four groups. The mean time for the sensory blocks to pinprick to regress to two segments below the maximum were prolonged with the use of glucose 0.75% solutions as well as with the addition of phenylephrine.

All the spinal anaesthetic solutions produced similar decreases in arterial blood pressure and heart rate. However, a difference existed in the number of patients receiving ephedrine between the groups given glucose 7.5% solutions and the groups given glucose 0.75% solutions. Patients in Group I received more doses of ephedrine than those in Groups II and IV ($P < 0.05$).

Discussion

The present study was undertaken to examine whether a marginally hyperbaric tetracaine solution with or without phenylephrine produced consistent blocks compared with a conventionally hyperbaric tetracaine solution injected at L₃₋₄ interspace with the patient in the lateral position. All the test solutions produced similar motor and sufficient sensory blocks for surgery to the lower limb. However, the peak dermatomal levels of sensory blockade were less cephalad with marginally hyperbaric tetracaine 0.5% (glucose 0.75%) solutions than with glucose 7.5% solutions, which sometimes caused an unnecessary high blockade.

Although most recent studies have been performed using lidocaine or bupivacaine,¹⁻⁷ tetracaine was chosen for this investigation for the following reasons: First, there was a need for a long acting local anaesthetic for the type of surgery planned for this study population.

TABLE III Perioperative characteristics

Group	I (n = 30)	II (n = 30)	III (n = 30)	IV (n = 30)
Peak dermatomal level to cold	T ₄ (T ₈ , T ₁)	T ₉ ‡ (T ₁₂ , T ₄)	T ₄ (T ₈ , T ₁)	T ₁₀ ‡ (L ₁ , T ₄)
Peak dermatomal level to pinprick	T ₅ (T ₁₀ , T ₂)	T ₁₀ ‡ (L ₁ , T ₅)	T ₅ (T ₁₀ , T ₃)	T ₁₀ ‡ (L ₁ , T ₅)
Peak dermatomal level to touch	T ₇ (T ₁₁ , T ₃)	T ₁₁ ‡ (L ₄ , T ₈)	T ₇ (T ₁₁ , T ₃)	T ₁₁ ‡ (L ₃ , T ₇)
Time to peak dermatomal level to pinprick (min)	23.2 ± 1.0	26.2 ± 1.5	23.5 ± 1.0	25.2 ± 1.2
Maximum motor block	4 (3, 4)	4 (3, 4)	4 (4, 4)	4 (4, 4)
Time to 2-segment regression (min)	94 ± 5	122 ± 7*	123 ± 9*	201 ± 11§
Maximum decrease in heart rate (%)	9.3 ± 1.9	6.5 ± 2.5	9.2 ± 2.0	8.8 ± 2.7
Maximum decrease in SAP (%)	14.8 ± 3.6	12.9 ± 2.3	16.5 ± 2.2	10.7 ± 2.8
No. patients given ephedrine	13	5‡	12	5‡
Mean doses of ephedrine (mg)	4.8 ± 1.3	1.3 ± 0.6†	2.7 ± 0.7	1.2 ± 0.5†

Values are median (10th, 90th percentiles) or mean ± SE.

SAP = systolic arterial pressure.

Patients in Group I received tetracaine 0.5% in glucose 7.5%; Group II tetracaine 0.5% in glucose 0.75%; Group III tetracaine 0.5% in glucose 7.5% and phenylephrine 0.125%; Group IV tetracaine 0.5% in glucose 0.75% and phenylephrine 0.125%.

‡P < 0.05 vs Groups I and III. *P < 0.05 vs Groups I and IV. §P < 0.05 vs Groups I, II and III. †P < 0.05 vs Group I.

Second, it is well established that the addition of phenylephrine prolongs the duration of tetracaine spinal anaesthesia,¹⁰ whereas the effects of phenylephrine on spinal anaesthesia with bupivacaine is questionable.¹¹ Third, tetracaine is most readily available as crystals in Japan so that solutions containing various concentrations of glucose can be prepared easily.

Extensive spread after the intrathecal administration of hyperbaric local anaesthetic solution has been demonstrated previously. For example, Brown *et al.*⁹ showed that the hyperbaric tetracaine solution produced higher sensory levels (T_{5,5}) than did the isobaric (T_{9,5}) or the hypobaric (T_{10,8}) solutions. Similar findings were reported in studies performed by Bannister *et al.*⁵ and Van Gessel *et al.*⁴ using bupivacaine either 8% or 5%, respectively. Therefore, it is believed that the increased cephalad spread results from gravitational distribution of a hyperbaric solution to the lowest point of the thoracic curvature in the supine subject. In addition, it seems that this phenomenon holds true for almost any hyperbaric solution and that the concentration of glucose has little effect on distribution once enough glucose has been added to increase baricity of the solution to a certain level. Lee *et al.*⁸ showed that tetracaine solutions containing >1% glucose behaved similarly.

However, our results clearly show that a marginally hyperbaric tetracaine solution may behave differently from a conventionally hyperbaric solution and support previous findings in different study designs. Sanderson *et al.*¹ showed that bupivacaine 0.5% in glucose 0.8% produced consistent blocks when injected intrathecally with a patient seated. Therefore, it has been proposed

that a solution, of specific gravity only slightly in excess of that of CSF, can only move slowly down the slope created by the lumbar lordosis in the supine. Thus, in horizontal patients less extensive and variable blocks are produced.

The effects of a plain tetracaine solution were not compared in the present study because of its poor performance. We found, in a preliminary study, that tetracaine 0.5% in distilled water with phenylephrine 0.125%, which is slightly hypobaric at 37°C, produced variable and unreliable blocks. While some patients developed sensory block to T₃, four of 12 patients given this solution required another spinal or additional epidural anaesthesia. Similar findings have been reported in the literature. Brown *et al.*⁹ found that the spread of analgesia produced by hypobaric tetracaine solutions was similar to that produced by isobaric solutions but that only 55% of patients had a successful motor block and adequate anaesthesia for surgery. Plain bupivacaine, which is hypobaric at 37°C, also has a reputation for unpredictable spinal distribution.¹²

Haemodynamic stability appears to be another advantage of a marginally hyperbaric solution. Although we failed to show any differences in the maximum decrease in systolic blood pressure or heart rate after spinal anaesthesia among the solutions, the number of patients treated for hypotension or symptoms such as nausea or dizziness was smaller in the glucose 0.75% groups than in the glucose 7.5% groups.

Concern regarding the safety of local anaesthetic may also lead us to recommend the use of a lower concentration of glucose. Most of the recently reported cases of neuro-

logical sequelae following spinal anaesthesia were associated with hyperbaric local anaesthetic solutions.¹³⁻¹⁶ Although the results from prospective clinical¹⁷ and animal studies¹⁸ suggest that glucose has little effects on the neurotoxicity, the final concentration of local anaesthetic in the sacral portion of CSF is probably higher with hyperbaric solutions than with other solutions.¹⁹

There was no difference in the effects of phenylephrine between the conventionally hyperbaric solutions and the marginally hyperbaric solutions in the present study. The addition of phenylephrine prolonged the duration of tetracaine spinal anaesthesia, but did not change the extent or quality of the blocks for about 60 min. The addition of phenylephrine makes the solution a little heavier. However, it seems that the change in the baricity, by adding phenylephrine, is not large enough to change the movement of the solution in CSF.

It is of interest that, despite more widespread distribution, blockade produced with glucose 7.5% solutions regressed more quickly than that with glucose 0.75% solutions. It has been suggested that the greater spread of the solutions can permit more rapid uptake into the blood from the anaesthetized nervous tissue.²⁰ The delayed regression seems to benefit a marginally hyperbaric solution, especially when the maximum cephalad spread of spinal anaesthesia is barely sufficient for the surgical procedure.

In conclusion, tetracaine 0.5% in glucose 0.75% with or without phenylephrine 0.125%, which is marginally hyperbaric, can produce consistent blocks with spread restricted to the lower thoracic segments causing less haemodynamic variability when administered intrathecally at the L₃₋₄ interspace with a patient in the lateral position. The ideal distribution of local anaesthetic administered intrathecally is high enough for the proposed surgery without serious respiratory or circulatory depression. The marginally hyperbaric solutions employed in the present study seem suitable for surgery of the perineum and lower extremities. However, although none of the patients studied received additional anaesthesia for surgery, some patients given glucose 0.75% solutions did not obtain sensory block to the inguinal region. It may be necessary to investigate whether the administration of the marginally hyperbaric tetracaine solution injected at the L₂₋₃ interspace or at a higher rate can extend the cephalad spread safely.

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