Causes and Prediction of Maldistribution during Continuous Spinal Anesthesia with Isobaric or Hyperbaric Bupivacaine

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Background: Many cases of cauda equina syndrome after maldistribution of local anesthetics during continuous spinal anesthesia have been reported. In experiments, a caudad route of catheter travel and the use of hyperbaric agents have been shown to induce these limited blocks. The aim of this clinical study was to verify this hypothesis and seek a predictive factor for the maldistribution of bupivacaine.

Method: Continuous spinal anesthesia *via* a 19-gauge end port spinal catheter was performed in 80 elderly patients randomly assigned to receive either isobaric or hyperbaric solutions. Successive injections of 2.5 mg bupivacaine were performed at 5-min intervals until a sensory level at or cranial to T8 was obtained. Maldistribution was defined by a sensory level caudal to T12 despite a total dose of 17.5 mg of either isobaric or hyperbaric bupivacaine. After surgery, all catheters were injected with contrast media and examined radiographically.

Results: The frequency of maldistribution was not significantly different in the isobaric and hyperbaric groups. A caudally oriented catheter tip was found to be a major cause of maldistribution ($P < 10^{-5}$). A thoracic sensory level could be reached in all patients presenting a limited block by simply changing the baricity of the bupivacaine, the position of the patient, or both. The sensory level obtained 10 min after the first injection of 2.5 mg isobaric or hyperbaric bupivacaine was found to be a predictive factor of maldistribution.

Conclusions: Hyperbaric solutions do not appear to be a clinical factor in the development of limited block. The principle factor causing the maldistribution of bupivacaine is the caudal orientation of the tip of the end-hole catheter rather than its level or the route of catheter travel. (Key words: Anesthetic techniques; bupivacaine; cauda equina syndrome; continuous anesthetics; local anesthetics; neurologic complications; spinal anesthesia.)

CONTINUOUS spinal anesthesia (CSA) allows the titration of small amounts of local anesthetics to achieve the appropriate level of anesthesia with only minimal hemodynamic changes.[1–3] However, the safety of this technique has been questioned because of reports of associated neurologic sequelae.[4–7] The mechanisms underlying these neurologic lesions include the maldistribution of local anesthetics that remain confined to the lumbar and sacral regions.[8–10] When a thoracic sensory level is not achieved, successive injections of local anesthetic are administered, thereby increasing the risk of neurotoxic concentrations and the resulting cauda equina syndrome.[8–10] Experimental studies using a model of the subarachnoid space have highlighted two major causes of limited block: sacral positioning of the catheter and the injection of hyperbaric solutions.[8–10] However, few clinical studies have examined the causes of restricted distribution during CSA, and although it appears likely that the malpositioning of the catheter and subsequent poor distribution of the drug play an important role, this remains to be fully documented in humans.[11,12] In some cases of maldistribution with isobaric[2,13] or hyperbaric[11,13] solutions, a sacrally positioned tip of the spinal catheter, a sacral pooling of a radiographic dye, or both have been identified. The principal aim of this study was to determine if the level or orientation of the tip of the catheter and the baricity of the anesthetic solution were explicative factors for the maldistribution of 0.5% bupivacaine during CSA. In addition, we tried to identify a clinical means to predict limited block.

Materials and Methods

After we obtained approval from our institution's ethics committee and informed patient consent, 80 pa-

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tients aged 70 yr or older who were scheduled for elective lower limb surgery were included in this prospective, blinded, randomized study. Contraindications to spinal anesthesia, the inability to identify pinprick stimulation, or both were used as exclusion criteria. All patients were premedicated with an intramuscular injection of 1 mg/kg hydroxyzine and 1 mg/kg meperidine. Continuous spinal anesthesia was performed at the L2–L3 or L3–L4 interspace using a 16-gauge Tuohy needle (Perican by B Braun, Melsungen, Germany) with the patient lying in the lateral position. Once the subarachnoid space had been identified by the return of clear cerebrospinal fluid, the needle was rotated so that the bevel was directed cranially and a 19-gauge end port epidural catheter (Vygon, Ecouen, France) was introduced to a distance of 4 cm. The needle was withdrawn and the catheter secured in place with a sterile dressing. The patient was turned to lie in a horizontal supine position and the easy aspiration of cerebrospinal fluid *via* the catheter was verified to ensure its subarachnoid location.

Patients were randomly allocated to two groups in which they received either isobaric or hyperbaric bupivacaine. The injected isobaric solution was 0.5% plain bupivacaine (Marcaine; Astra Pharmaceutical Products, Nanterre, France), whereas the hyperbaric solution was 0.5% bupivacaine with 8% dextrose (Marcaine). The anesthesiologist was blinded to the administered solution. The induction dose was 2.5 mg bupivacaine injected over 3 s (0.5 ml plus 0.2 ml to fill the catheter). Ten minutes after induction, if the upper sensory block was caudal to T8, additional doses of 2.5 mg bupivacaine were injected at 5-min intervals to obtain a sensory level equal or cranial to T8. The total dose of bupivacaine administered was limited to 17.5 mg, corresponding to seven injections of 2.5 mg bupivacaine. The upper sensory level was assessed using the pinprick method using an 18-gauge needle, every 5 min, until a T8 level was obtained. The upper level was assessed again 20 min later. Maldistribution of bupivacaine was defined by a limited lumbosacral block (sensory level caudal to T12) 5 min after the seventh injection of 2.5 mg bupivacaine. If maldistribution of bupivacaine occurred, the anesthetist had the choice of changing either the baricity of the anesthetic solution, the position of the patient, or both to obtain a sensory level compatible with the planned surgical technique.

When the patient had been transferred to the recovery room and lay in a horizontal supine position, 4 ml radiographic dye was injected into the spinal catheter

and a conventional anteroposterior roentgenogram of the lumbosacral spine was obtained. The contrast media used was a hyperbaric iodine solution (Iopamidol 200; 4 ml = 800 mg iodine, specific gravity = 1.22; Schering Pharmaceutical, Lys-Lez-Lannoy, France). This procedure allowed the assessment of the spinal puncture level, length of catheter insertion, route of catheter travel, level and orientation of the tip of the catheter and diffusion of the contrast media. The intrathecal route of the catheter was considered to be coiled at the puncture level if its radiographic image was limited topographically to the spinal puncture level, cephalad if it took a cranial route, and caudad if it took a sacral direction. The orientation of the tip of the catheter was defined as cephalad when pointed cranialy and caudad when pointed sacrally. The radiographic analysis was performed by two neuroradiologists, both blinded to the obtained upper level of blockade and the patient's group. All patients were examined daily during the first 5 postoperative days to assess any neurologic deficits.

Statistical Analysis

Continuous data were expressed as means ± SD, and discrete data were expressed as medians with ranges. Continuous data were compared using the two-tailed Student's *t* test. Discrete data were compared using nonparametric Mann-Whitney and Kruskal-Wallis tests. Categorical data were compared using chi-square or Fisher's exact tests for 2 × 2 tables and chi-square or G tests for larger tables. A Spearman rank test was used to test the correlation between discrete data. A probability value <0.05 was considered to indicate significance. When multiple tests were performed, Bonferroni's correction was applied. To study the discriminant capacity of the upper sensory level obtained 10 min after the first 2.5 mg bupivacaine injection to predict a maldistribution, we constructed receiver-operator characteristic curves for both groups, plotting for each upper sensory level. In the abscissa, 1 minus specificity, and the ordinate indicated the sensitivity. Areas under the receiver-operator characteristic curves were obtained by the trapezoidal rule and their standard deviations from the variance. The area under the receiver-operator characteristic curve represents the discriminant capacity of the test. An area of 0.5 corresponds to a nondiscriminant test, and an area of 1 corresponds to an ideally discriminant test.[14]

Results

Forty patients were enrolled in each group. Except for age and weight, both groups were comparable (table 1).

Table 1. Patient Characteristics

	Isobaric Group (n = 40)	Hyperbaric Group (n = 40)	P
Age (yr)	85 ± 6	82 ± 6	0.019
Weight (kg)	58 ± 11	63 ± 12	0.032
Height (cm)	162 ± 7	163 ± 8	NS
Sex ratio (female/male)	32/8	31/9	NS
ASA physical status (II/III/IV)	16/17/7	22/16/2	NS

All values, except for sex and ASA status, are expressed as mean ± SD.
NS = not significant.

Spread of Anesthesia

Sixty-four of 80 patients, 29 in the isobaric and 35 in the hyperbaric group, reached a sensory level equal or cranial to T8 5 min after their total dose of bupivacaine, which ranged from 2.5 to 15 mg (fig. 1). The number of patients reaching a T8 sensory level after each bupivacaine injection was not significantly different between the two groups (fig. 1). The dose of bupivacaine required to reach T8 was 7.5 mg (range, 2.5-15 mg) in the isobaric and 5 mg (range, 2.5-15 mg) in the hyperbaric group (NS). The time necessary to achieve this level was 20 min (range, 10-35 min) in the isobaric group and 15 min (range, 10-35 min) in the hyperbaric group (NS). Five minutes after the last injection, the mean level of anesthesia was higher in the hyperbaric group (T7 [range, T8-T5]) than in the isobaric group (T8 [range, T8-T6]) ($P = 0.0006$). Twenty minutes after the last injection of bupivacaine, the anesthetic spread was comparable in both groups (T7 [range, T9-T4]).

In six patients, four in the isobaric group and two in the hyperbaric group, the sensory level ranged from T12 to T9, 5 min after the maximal dose of 17.5 mg bupivacaine. The level of anesthesia was still adequate to allow surgery to be performed.

Maldistribution of bupivacaine occurred in the remaining 10 patients, 7 in the isobaric and 3 in the hyperbaric group (NS), as the spread of anesthesia 5 min after a total dose of 17.5 mg bupivacaine was below T12 and limited to the lumbar and/or sacral segments. To obtain an appropriate thoracic sensory level, at least T12 for knee surgery and T10 for hip surgery, the baricity of the bupivacaine and/or the position of patient were modified. In the isobaric group, four patients then received 5 to 7.5 mg doses of hyperbaric bupivacaine in the Trendelenburg position, whereas the remaining three patients received 5 mg of isobaric bupivacaine in the lateral decubitus position. In the hyperbaric group,

the required thoracic levels were reached in two patients using only the Trendelenburg position without reinjection and in the remaining patient using both the Trendelenburg position and an additional 5 mg dose of hyperbaric bupivacaine.

Neither general anesthesia nor intravenous supplementation were required for surgery in any of the 80 patients.

Radiologic Study

No statistical differences were noted between the two groups concerning the spinal puncture level, intrathecal length, route of the catheter, or the catheter tip's level and orientation (table 2). A more cranial catheter tip level was directly related to a more cranial spinal puncture level ($P < 0.001$) and a cephalad route of catheter travel ($P < 0.001$). Similarly, a caudal level of the catheter tip was related to a caudal spinal puncture level and a caudad route of catheter travel. A cranial catheter tip orientation was found to be correlated with a cranial catheter tip level ($P < 0.001$) and a cephalad route of catheter travel ($P < 0.001$). A similar relation was found among a caudal tip orientation, a caudal tip level, and a caudad route of catheter travel. No correlation was found between the spinal level of puncture and either the route of catheter travel or the catheter tip's orientation. No significant intergroup differences
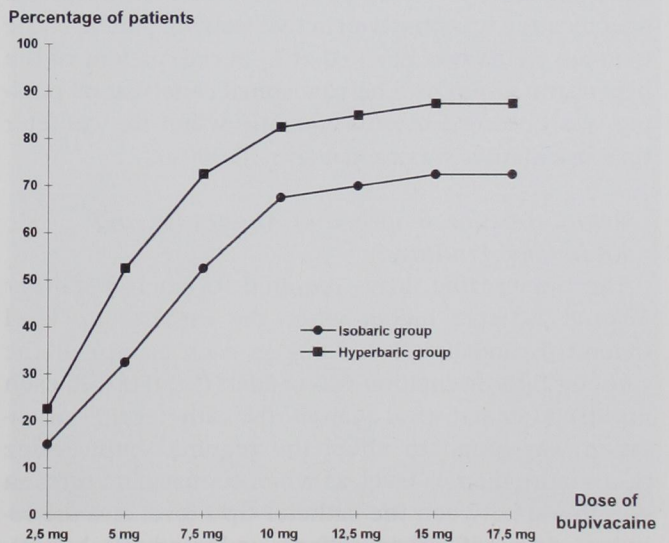

Fig. 1. Cumulative proportion of patients reaching a sensory level equal to or cranial to T8 after each injection of either 2.5 mg isobaric or hyperbaric bupivacaine. There is no statistical difference between the two groups.

Table 2. Radiologic Data Concerning the Spinal Catheters

	Isobaric Group (n = 40)	Hyperbaric Group (n = 40)	Percentage of Total Population
Level of puncture			
T12–L1	1	1	2.5
L1–L2	3	5	10
L2–L3	20	19	48.75
L3–L4	11	13	30
L4–L5	5	2	8.75
Route of catheter travel			
Cephalad	27	30	71.25
Coiled at the puncture level	9	7	20
Caudad	4	3	8.75
Tip orientation			
Cephalad	34	35	86.25
Caudad	6	5	13.75
Tip level*	L_2 [L_5–T_{11}]	L_2 [L_5–T_{11}]	
Intrathecal length† (cm)	3.9 ± 1.7	4.0 ± 1.5	

There were no statistical differences between the two groups.

* Tip level expressed as median [range].

† Intrathecal length expressed as mean ± SD.

were noted concerning the four parameters for catheter position.

Homogeneous lumbothoracic diffusion of the contrast media in the subarachnoid space was noted in 32 of the isobaric and 37 of the hyperbaric patients (NS). Sacral pooling was seen in six isobaric and two hyperbaric patients (NS). A mixed subdural and subarachnoid opacification was observed in two isobaric patients. The contrast media was blocked at L_2 in one patient of the hyperbaric group by a narrow spinal canal. Sacral pooling was observed more frequently when the catheter tip's orientation was caudal ($P < 0.0001$).

Relation between Spread of Anesthesia and Radiologic Findings

The bupivacaine doses required to reach a sensory level at T_8 were higher when the catheter tip level extended caudally ($P < 0.001$ in each group) or the catheter tip's orientation was caudal ($P < 0.001$ in each group). After statistical analysis, the catheter tip's orientation was found to effect the required bupivacaine doses more than its level, as when cephalad no relation was found between the catheter tip's level and the required doses of either isobaric or hyperbaric bupivacaine. Similarly, with a caudal tip orientation, the catheter tip's level and the required bupivacaine doses were not related.

The occurrence of maldistribution of bupivacaine was greater with caudally extended catheter tip levels ($P < 0.001$ in each group) and caudal catheter tip orientations ($P < 0.0002$ in the isobaric and $P < 0.003$ in the hyperbaric groups). After statistical analysis, the catheter tip's orientation was found to effect the maldistribution of isobaric or hyperbaric bupivacaine more than its level, as when the orientation was cranial no relation was found between the catheter tip's level and the occurrence of maldistribution of bupivacaine. Similarly, with a caudal catheter tip orientation, the catheter tip's level and the occurrence of maldistribution of bupivacaine were not related. The spinal puncture site and maldistribution of bupivacaine were unrelated in both patient groups. The diffusion of the contrast media in the 10 cases involving maldistribution of bupivacaine provided the images of eight sacral poolings (fig. 2), one mixed subdural and subarachnoid opacification, and one narrow spinal canal. In the remaining 70 patients, when maldistribution of bupivacaine did not occur, the contrast media diffusion was lombothoracic in 69 cases (fig. 3) and mixed, subdural, and subarachnoid in one. A highly significant direct relation was shown to exist between maldistribution of bupivacaine and the sacral pooling of contrast media (kappa statistic = 0.875).[15]

The maximal sensory level was higher when the catheter tip's level extended cranially ($P < 0.0001$) or the orientation ($P < 0.0001$) was cephalad. Once again, the tip's orientation had a greater effect than its level.

Clinical Factor Predictive of Maldistribution of Bupivacaine

The discriminant capacity of the upper sensory level obtained 10 min after the first 2.5 mg bupivacaine injection to predict distribution was high in both the isobaric (area under receiver-operator characteristic curve, 0.98 ± 0.04) and hyperbaric group (area under receiver-operator characteristic curve, 0.97 ± 0.06). No maldistribution occurred if the upper sensory level was cranial or equal to L3 in the isobaric group (fig. 4) and L5 in the hyperbaric group (fig. 5).

Side Effects

One patient in the isobaric group suffered from a severe postdural puncture headache with bilateral deafness and the loss of taste and smell 24 h after operation. These symptoms resolved without sequelae after only conservative treatment. No cases of cauda equina syn-
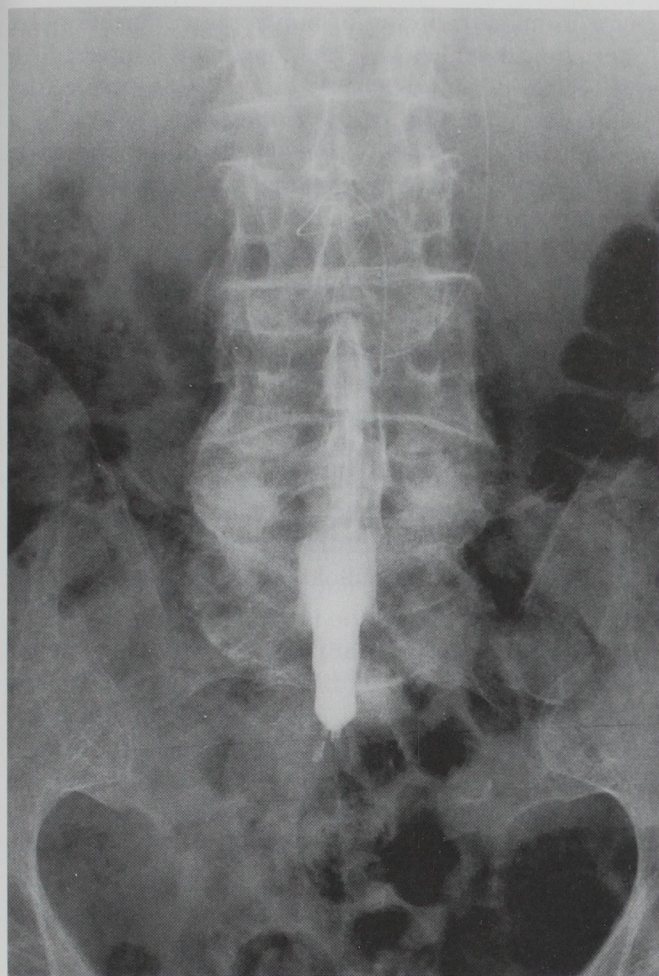
Fig. 2. Anteroposterior view of the lumbar spine after injection of 4 ml Iopamidol 200. This radiograph obtained in a patient with maldistribution of bupivacaine shows the tip of the catheter has a caudad orientation, and the contrast media has pooled in the dural cul-de-sac. This is the most frequently seen image of maldistribution.

drome or persistent paresthesia were observed in the 80 patients.

Discussion

Our results show that during CSA performed with a 19-gauge end-holed catheter, maldistribution of bupivacaine results essentially from a caudal orientation of the tip of the catheter and not from the level of the tip or from the baricity of the injected solution. If after 10 min of the induction dose of 2.5 mg bupivacaine the sensory level reached L3 with an isobaric solution or

L5 with a hyperbaric solution, no maldistribution was noted.

A precise definition of maldistribution of anesthetic solution during CSA has never been given, nor is there a consensus on the sensory level or dose at which it occurs. Many studies have demonstrated inadequate anesthesia despite successful catheter insertion.[2,16-20] In some well-documented clinical studies, the obtained sensory levels were clearly limited at the sacral[11] or lumbar[13,21-23] dermatomes. These levels corresponded to the restricted diffusion of dye solutions in experimental studies using a model of the subarachnoid space, where the dyes accumulated in the sacral cavity.[8-10] As such, we considered that maldistribution had occurred
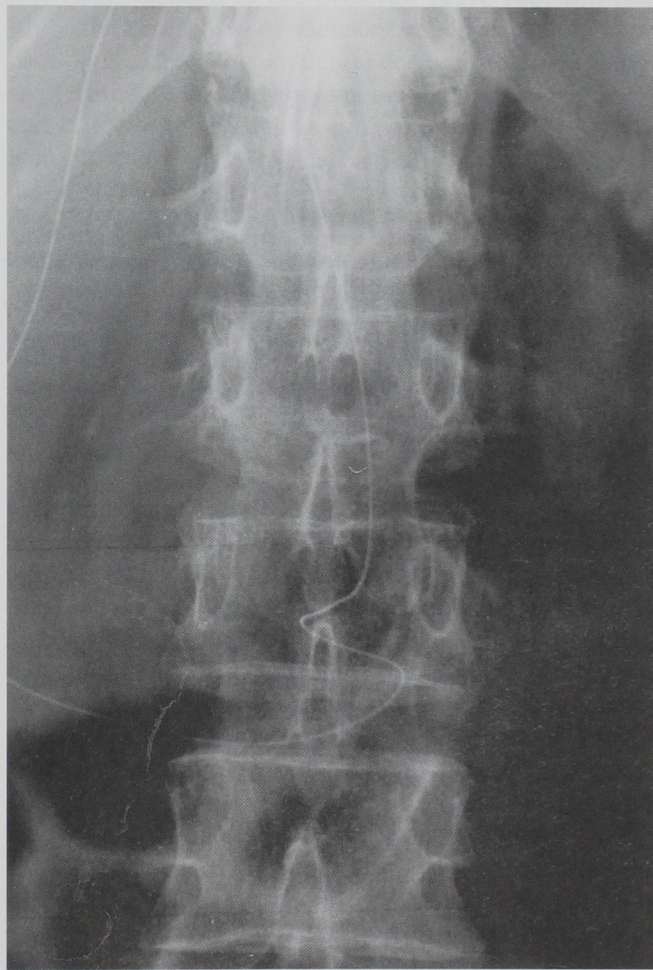

Fig. 3. Anteroposterior view of the lumbar spine after injection of 4 ml Iopamidol 200. This radiograph obtained in a patient without maldistribution of bupivacaine shows the tip of the catheter has a cephalad orientation and the contrast media diffused homogenously in the lumbar and thoracic regions.
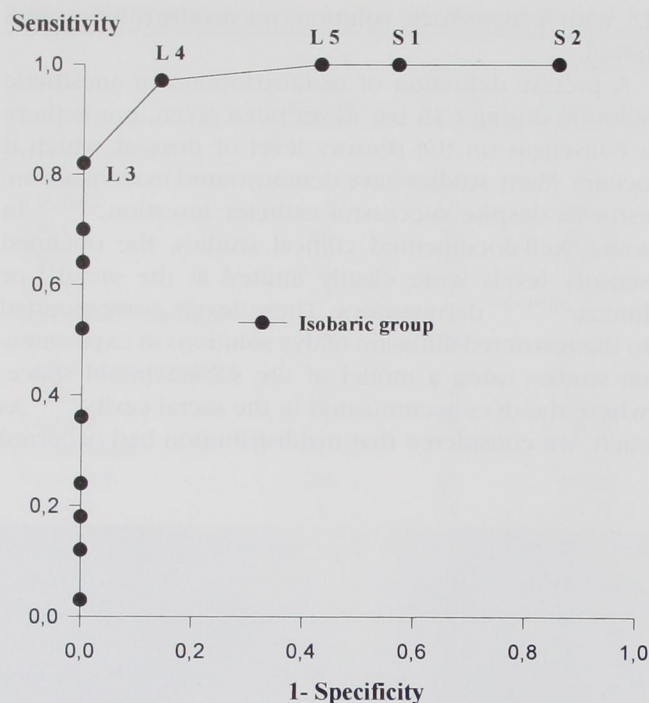
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Fig. 4. Receiver–operator characteristic curve for upper sensory level obtained 10 min after the first 2.5 mg isobaric bupivacaine injection to predict maldistribution. The area under the receiver–operator characteristic curve is 0.98 ± 0.04. For a given upper sensory level, the abscissa value is the ratio of the number of maldistributions occurring in patients with an upper sensory level greater or equal to this threshold to the number of maldistributions occurring in all patients. No maldistribution occurred if the upper sensory level was greater or equal to L3 in the isobaric group.

in our study when anesthesia was limited to the sacral or lumbosacral segments. The dose of local anesthetic above which maldistribution is likely to occur is classically considered to be greater than the dose that would have been given if the single-injection technique was used.[4] In the elderly, doses as low as 5 mg bupivacaine (either isobaric or hyperbaric) have resulted in very extensive sensory blockades.[13] Therefore the maximal dose of 17.5 mg used in this study would appear to be sufficiently high to clearly identify the occurrence of bupivacaine maldistribution.

In this study, 10 bupivacaine maldistributions occurred, 7 in the isobaric group and 3 in the hyperbaric group (NS). To demonstrate a difference between the two groups, we would have had to include 190 patients in each group (α risk = 0.05; β risk = 0.20). In contrast to the findings of previous experimental studies,[8–10] hyperbaric solutions do not appear to be a clinical risk

factor in maldistribution of bupivacaine. Furthermore, other clinical studies have demonstrated limited block with isobaric bupivacaine.[2,13,19,20,22,23] Conversely, the orientation of the tip of the catheter appears to be a major factor in the distribution of isobaric or hyperbaric bupivacaine in CSA. Experimental studies investigating the maldistribution of local anesthetics have not studied the tip orientation but rather the route of catheter travel. They demonstrated a relation between a caudal direction taken by the catheter and the restricted diffusion of the dye solution.[8–10] In our study, the route of the catheter, tip level, and tip orientation are three interdependant parameters. The occurrence of maldistributions of bupivacaine was most frequently observed with a caudal tip orientation, often associated with catheters having a sacral route and caudal tip level. Two clinical studies examined the extent of sensory blockade in relation to the radiologically localized position
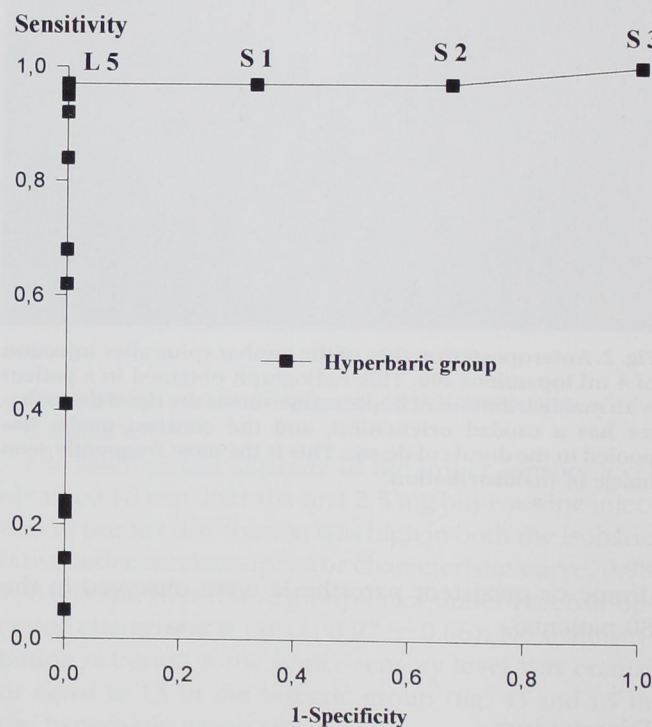

Fig. 5. Receiver–operator characteristic curve for upper sensory level obtained 10 min after the first 2.5 mg hyperbaric bupivacaine injection to predict maldistribution. The area under the receiver–operator characteristic curve is 0.97 ± 0.06. For a given upper sensory level, the abscissa value is the ratio of the number of maldistributions occurring in patients with an upper sensory level greater or equal to this threshold to the number of maldistributions occurring in all patients. No maldistribution occurred if the upper sensory level was greater or equal to L5 in the hyperbaric group.

of the spinal catheter.[19,24] Van Gessel *et al.*[24] injected hypobaric bupivacaine through 20-gauge catheters with three side ports in patients in the lateral decubitus position. Although 7% of the catheters were positioned caudally, no maldistribution occurred and no correlation was found between the level of the tip of the catheter and the achieved sensory level. In the lateral decubitus position, the anteroposterior curves of the spinal column do not influence the distribution of local anesthetic, even when the catheter is caudad. In contrast, when anesthetics are injected in patients lying in a supine horizontal position, even hypobaric solutions can accumulate in the sacral cavity.[21] In the study by Standl and Beck,[19] isobaric bupivacaine was administered through 28-gauge end-port catheters in patients lying in the supine position. They showed that caudally directed catheters increased the onset time of analgesia and the dose of isobaric bupivacaine required to achieve a T10 level. However, neither the level nor orientation of the catheter tip were studied, and the correlation between the route of catheter travel and maldistribution of bupivacaine was not considered.

Our results concerning the catheter's route correspond with those of Van Gessel *et al.*,[24] who reported that 21% of 20-gauge spinal catheters had been unintentionally coiled at the puncture level and 7% positioned caudally, and often associated with a higher puncture level than that assumed clinically. Using 28-gauge microcatheters, other authors reported that when inserted 4 cm or more, 31% were directed caudally.[25] Many cases of inadequate anesthesia have been reported when using microcatheters.[2,11,17,19,22,23] These findings may be due to the high frequency of sacral positioning and the low rate of injection imposed by the catheter's low diameter.[8-10] However, limited block has also been reported when using 20-gauge catheters,[13,16,18,20,21] with a frequency as high as 18%,[20] without the influence of injection speed on the distribution of isobaric bupivacaine.[26] Why should we then discourage the use of microcatheters,[27] especially as cauda equina syndromes have also been described[4,7] using 20-gauge catheters? Further, it has been suggested that CSA should be abandoned in cases of limited block to avoid possible neurologic complications.[6,10,20] In our study, changing the baricity of the anesthetic solution, the patient's position, or both allowed adequate sensory levels to be achieved. When surgery was performed in the supine position, placing the patient in the Trendelenburg position and injecting hyperbaric bupivacaine provided adequate sensory levels. When surgery was performed in the lateral decubitus position, the injection of isobaric bupivacaine alone allowed anesthesia of the thoracic segments to be obtained. Other measures have been proposed: withdrawal of the catheter,[4,8,9] use of multiple side-port catheters,[8] or insertion of the catheter <2 cm.[25] Considering experimental results[8-10] and the data from this study, it appears that the measures proposed to avoid pooling of the anesthetic solutions caudal to the peak of the lumbar curve may prevent or treat maldistributions. However, the efficiency of such measures should be validated in other large series using both large-bore and microcatheters.

The danger appears to lie in missing the diagnosis rather than in the occurrence of maldistribution. When missed, potentially neurotoxic doses of local anesthetic, particularly 5% lidocaine,[28,29] can accumulate in the sacral curve and cause damage to the posterior nerve roots. In our study, the description of a sensory level predictive of maldistribution after a low induction dose allows early diagnosis of the condition and implementation of avoidance measures. Recently, the cauda equina syndrome was documented after the clinical use of bupivacaine,[30] and high doses of this drug have been shown to cause prolonged sensory blocks in animals.[28] The role of glucose in the neurologic complications[29,31] of CSA have not been proved in experiments.

Although the 4 ml injection of hyperbaric contrast media cannot reproduce the distribution of successive 0.5 ml injections of hyperbaric and less yet isobaric bupivacaine, all eight images showing sacral pooling of the contrast media were associated with eight cases of maldistribution of either isobaric or hyperbaric bupivacaine. Furthermore, analyzing the contrast media's diffusion clarified the two cases of maldistribution of bupivacaine involving cephalad catheter tips: one narrow spinal canal and one mixed subdural and subarachnoid opacification.[32-34]

In conclusion, this is the first clinical study that demonstrates the correlation between the position of the spinal catheter and the maldistribution of local anesthetics. A caudal orientation of the tip of an end-holed spinal catheter is a major factor of restricted block. Maldistribution can be predicted 10 min after the injection of 2.5 mg of either isobaric or hypobaric bupivacaine using the obtained sensory level, thus avoiding the subarachnoid injection of high anesthetic doses and allowing avoidance measures to be implemented quickly. These findings should limit the occurrence of cauda equina syndrome after CSA. Further work oriented toward technical advances, such as adapting the needle's bevel and the multiple side-port catheter's design, could be of interest in preventing the maldistribution of local anesthetics.

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