Incidence of Transient Neurologic Symptoms after Hyperbaric Subarachnoid Anesthesia with 5% Lidocaine and 5% Prilocaine

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Background: Hyperbaric 5% lidocaine has been associated with transient neurologic symptoms (TNSs) after spinal anesthesia. A prospective, masked, randomized study was conducted to compare the incidence of TNSs after spinal anesthesia with hyperbaric 5% lidocaine or 5% prilocaine to assess the utility of prilocaine as an alternative to lidocaine in patients having short surgical procedures.

Methods: The number of patients to be enrolled (100 per group) was determined by power analysis (80%, P = 0.05) considering an incidence of TNSs after spinal anesthesia with lidocaine of at least 11% according to data reported in other studies. Two hundred patients scheduled for elective surgery expected to last <60 min were allocated at random to receive spinal anesthesia with hyperbaric 5% lidocaine or hyperbaric 5% prilocaine. Three to 5 days after spinal anesthesia, all patients were interviewed by an anesthesiologist who was blinded to the group assignment and details of the anesthetic and surgical technique using a standardized symptom checklist. Patients with symptoms underwent neurologic examination.

Results: Both groups were comparable with regard to demographic data and details of the surgical and anesthetic procedures. The incidence of TNSs in both groups was low and differences were not found (4% in the lidocaine group and 1% in the prilocaine group). The mean age of patients with TNSs (58 yr) was higher than that of patients without TNSs (48 yr; P = 0.05). No relation with any of the other variables was found.

Conclusions: The low incidence of TNSs among lidocaine-anesthetized patients (4%) may account for the lack of significant differences between hyperbaric 5% lidocaine and 5% prilocaine and to the insufficient power of the study to exclude the possibility of a type II error. (Key words: Local anesthetics; spinal anesthesia; spinal.)

LIDOCAINE has been used extensively for spinal anesthesia, especially for short surgical procedures, with a remarkable safety record. Despite its wide use, few peripheral nerve problems were reported until 1990. In 1991, Rigler et al. described four cases of cauda equina syndrome after continuous spinal anesthesia, in three of which 5% hyperbaric lidocaine was administered. Subsequently, recent reports have suggested an association between transient neurologic symptoms (TNSs) and the use of hyperbaric lidocaine in spinal anesthesia, although there is a high variability with regard to the incidence of transient radicular symptoms found in these studies.

Prilocaine is a local anesthetic of the amide type. Its pharmacologic properties resemble those of lidocaine. It has been used for all types of infiltration and regional nerve block anesthesia as well as for spinal anesthesia. To our knowledge, no case reports of TNSs after spinal anesthesia with prilocaine have been published.

This prospective, masked, randomized study was designed to determine the incidence of TNSs in patients having surgery who were to receive hyperbaric subarachnoid anesthesia with 5% lidocaine or 5% prilocaine to assess the utility of prilocaine as an alternative to lidocaine in patients scheduled for short surgical procedures.

Materials and Methods

The study was approved by our hospital ethical committee and all patients gave written informed consent. We studied patients classified as American Society of Anesthesiologists physical status I, II, and III who were aged 18–80 yr and scheduled for elective orthopedic,
urologic, gynecologic, vascular, and general surgery procedures expected to last <1 h under spinal anesthesia. Exclusion criteria consisted of history of neurologic disorders that may affect the lower extremities, diabetes mellitus, high alcohol intake (>60 g/day), chronic back pain, and protrusion of intervertebral disk.

The patients were assigned to receive 5% hyperbaric lidocaine (B/Braun Medical, S.A., Rubí, Barcelona, Spain) or 5% hyperbaric prilocaine (B/Braun Medical) according to a computer-generated list by simple random sampling. Patients were numbered consecutively by a blinded observer and allocated to one of the anesthetic solutions. The number of patients to be enrolled in this study (n = 200, 100 per group) was determined by power analysis (80%, P = 0.05) considering an incidence of TNs after spinal anesthesia with lidocaine of at least 11% according to data of recently published studies\(^5\) and a low occurrence of TNs after spinal anesthesia with prilocaine (<1%) in our experience. To maintain the methodologic strictness of the working team, a maximum study period of 9 months was established.

After cannulation of a peripheral vein and starting routine monitoring, 10 ml/kg lactated Ringer’s solution was infused. After skin preparation with a 10% solution of povidone-iodine (Betadine, Asta-Médica, Madrid, Spain) with the patient in the sitting or in the left or right decubitus position, 2 ml 1% mepivacaine was injected for local anesthesia of the skin and subcutaneous tissue using a 20-gauge needle (at the discretion of the attending anesthesiologist). Dural puncture was performed using a 25-gauge pencil-point spinal needle (Pencan; B/Braun Medical; or Pajunk, Geisingen, Germany). A 22- and a 24-gauge Pajunk needle was used in two patients because of lumbar puncture was difficult. Once correct needle position was identified by free flow of cerebrospinal fluid, approximately 0.20 ml cerebrospinal fluid was aspirated, and the local anesthetic was injected. The dose of local anesthetic was calculated in relation to the type of operation and the patient’s height. Onset of block was defined as sensory block at the level at which the operative procedure should be carried out. The segmental level of sensory block to pinprick was assessed at 10-min intervals for 30 min after block placement. Maximum height of block was recorded. The Bromage scale was used to test motor blockade (3 = unable to move feet or knees; 2 = unable to flex knees, barely able to move feet; 1 = barely able to flex knees, no impairment of foot movement; 0 = no impairment of movement of legs and feet). The anesthesiologist who administered the spinal anesthesia (and collected the data on sensory and motor block) was not blinded to the study groups. Complications of the anesthetic technique (number of punctures, paresthesias during dural or hemorrhagic puncture) were recorded.

All patients were contacted by telephone 3–5 days after spinal anesthesia by an anesthesiologist who was unaware of the drug given or details of the anesthetic technique. To ensure standardized data collection, a symptom checklist similar to that reported by Hampel et al.\(^5\) was used. Transient neurologic symptoms were defined as pain or dysesthesia or both in the buttocks, thighs, or lower limbs occurring after recovery from the anesthetic.\(^5\) All patients who reported TNs were referred to this blinded anesthesiologist, who again evaluated the patient and performed a neurologic examination.

Categorical variables were analyzed using the chi-square (χ²) test and Fisher’s exact test and continuous variables with the Student’s t test when differences between both treatment arms and patients with and without TNs were analyzed. Significance was defined as P < 0.05. The SAS (Cary, NC) computer software package for Windows (version 6.11; Microsoft, Redmond, WA)\(^15\) was used to perform statistical analyses.

**Results**

During the 9-month study period, 200 patients were enrolled in the study; 98 of them were assigned to the group to receive hyperbaric 5% lidocaine (mean osmolality, 780 ± 60 mOsm/l) and 102 to receive hyperbaric 5% prilocaine (760 ± 50 mOsm/l). Two blocks in the prilocaine group provided inadequate surgical anesthesia, and general anesthesia was required. None of the two patients with inadequate spinal anesthesia reported TNs, but these patients were excluded from the final analysis because of the possibility that local anesthetic was not placed intrathecally.

Of the 98 patients treated with 5% hyperbaric lidocaine, there were 57 men and 41 women whose mean age was 49 ± 17 yr, mean weight was 72.3 ± 12.2 kg, and mean height was 166.2 ± 10.9 cm. The group of 100 patients treated with 5% hyperbaric prilocaine included 66 men and 34 women with a mean age of 47 ± 14 years, mean weight of 73.7 ± 11.2 kg, and mean height of 166.4 ± 9.7 cm. Relevant aspects of the surgical and anesthetic procedures did not differ significantly between treatment groups, except for a more rapid
onset of anesthesia in the group receiving lidocaine compared with those receiving prilocaine (3.6 vs. 4.2 min; table 1). There were no significant differences between the 5% lidocaine and 5% prilocaine groups in the number of patients undergoing orthopedic (33 vs. 22), urologic (15 vs. 14), gynecologic (6 vs. 6), vascular (28 vs. 34), or general surgical procedures (16 vs. 24). The duration of surgery was also similar (46 ± 19.6 min in the lidocaine group vs. 48.6 ± 24.6 min in the prilocaine group).

Symptoms suggestive of TNSs developed in four patients (4.1%) in the lidocaine group and in one patient (1%) in the prilocaine group (P = 0.2). There were no differences between patients with and without TNSs in terms of mean weight, mean height, mean dose of anesthetic injected, use of local anesthesia, midline approach, site of dural puncture, motor blockade, height of block, attempts at dural puncture, position during operation, and duration of surgery. The mean age of patients with TNSs was significantly greater than the mean age of patients without TNSs (58 vs. 48 yr; P < 0.05). The five patients with TNSs were placed in the sitting position at dural injection and achieved complete motor blockade. Perioperative anesthetic complications were not recorded except for paresthesia in one patient in the lidocaine group.

In the group of four patients receiving lidocaine, neurologic symptoms occurred 12–24 h after surgery. Three patients were positioned supine during operation and one was prone. In all patients, the intensity of pain was mild and corresponded to L5–S1 dermatomes. All patients were treated with nonsteroidal anti-inflammatory drugs, as routinely prescribed by the attending surgeon immediately after surgery. Radicular symptoms disappeared in 48 h, except in one patient in whom symptoms lasted 10 days. The single patient with TNSs given prilocaine was in the supine position for knee arthroscopy. Symptoms developed 24 h after surgery and were located at the level of L5–S1 dermatomes. Pain intensity was mild and disappeared in 72 h. In all patients with TNSs, results of neurologic examinations done 1 week after the interview were within normal limits.

Nine patients without TNSs had backache, six of
whom experienced pain at the site of injection, and three had low back pain. Two of these patients were placed in a lithotomy position. Multiple attempts at dural puncture were carried out in four of the six patients with pain at the site of injection. Three patients reported mild headache that resolved spontaneously.

Discussion

The incidence of TNs after spinal anesthesia with 5% hyperbaric lidocaine varies in reported studies. In 1969, Phillips et al.\textsuperscript{1} reported the results of a prospective review of 10,440 patients who received lidocaine for spinal anesthesia. There were 30 (0.3%) patients with transient peripheral nerve symptoms. This study was not randomized, lidocaine spinal anesthesia was used mainly for obstetric procedures, and neither pain duration and severity nor localization of neurologic symptoms were defined. A standardized questionaire for measuring TNs also was not used.

Recently, Schneider et al.\textsuperscript{3} reported four cases of TNs (4.5%) among 88 patients anesthetized with 5% hyperbaric lidocaine. In the study by Tarkkila et al.,\textsuperscript{4} 27 (10.2%) of 265 patients anesthetized with 5% hyperbaric lidocaine reported TNs. These studies were nonrandomized. In a prospective nonrandomized study of Hampl et al.,\textsuperscript{5} TNs occurred in 44 of 120 (37%) patients receiving 5% lidocaine. Limitations of this study, however, have been recognized by the authors themselves and by others.\textsuperscript{16} The study was not randomized; the anesthetic technique, surgical procedure, and intraoperative management varied; and the anesthesiologist in charge of the anesthetic procedure was not blinded. In a recent randomized study done by the same authors,\textsuperscript{17} they reported an incidence of 37%, although the sample size was small (n = 25). Accordingly, the incidence of TNs after spinal anesthesia with 5% hyperbaric lidocaine may vary from 15% to 53% (95% confidence interval). In this randomized study and in a previous one,\textsuperscript{18} details of a priori power calculations were not provided. In the randomized, double-blinded, prospective study of Pollock et al.,\textsuperscript{7} there was no difference in the incidence of TNs (16%) between the patients receiving 5% hyperbaric lidocaine (n = 55) and those receiving 2% isobaric lidocaine (n = 52), although the incidence of TNs was significantly greater in patients undergoing arthroscopy compared with those having hernia repair (13% vs. 5%).

Ours is a randomized, prospective, masked study in which demographic variables and relevant aspects of the surgical and anesthetic procedures in both study groups, lidocaine and prilocaine, were comparable. All patients were assessed in the postoperative period by a single anesthesiologist using a standardized questionnaire to prevent subjective interpretations regarding evidence of TNs. We found a much lower incidence of TNs in both groups than had previously been reported. However, the follow-up method used to assess the presence of neurologic problems is a crucial aspect of elucidating the true incidence of TNs. Bias may arise whether follow-up is carried out on the next day after surgery or by telephone after discharge from the hospital some days later. Patients interviewed on the ward are more likely than patients interviewed by telephone to report minor symptoms, so that the incidence of TNs may be overestimated. In contrast, recall bias may occur when patients are interviewed 3 or more days after surgery. In both cases, it would be necessary to assess the validity, reliability, and inter- and intraobserver reproducibility of the predetermined set of questions.

Patients with TNs were significantly older than patients without TNs (mean age, 58 vs. 48 yr; P < 0.05). Phillips et al.\textsuperscript{1} compared the incidence of neurologic symptoms of their study (0.3%) with that reported by Dripps and Vandam\textsuperscript{19} (0.7%) and suggested that the difference might be explained on the basis of the patients' older age (25.2 yr vs. 40.6 yr, respectively).

The cause of TNs is still unknown. In vitro and in vivo experimental studies suggesting the neurotoxic potential of 5% lidocaine have been reported,\textsuperscript{20,21} but there are no data regarding the neurotoxicity of prilocaine. Recently, 2% hyperbaric lidocaine has been implicated as a cause of toxicity in spinal anesthesia.\textsuperscript{7,17,22}

The lithotomy position may increase the vulnerability of nerve fibers exposed to 5% lidocaine by stretching lumbosacral nerve roots.\textsuperscript{3} Freedman et al.\textsuperscript{23} found a higher incidence of TNs after spinal anesthesia with lidocaine when patients were in the lithotomy position compared with the supine position (21.8 vs. 2.9%, respectively). Pollock et al.\textsuperscript{7} also indicated that patient position may be an important contributing factor to TNs based on the higher incidence of TNs in patients undergoing arthroscopy compared with those having inguinal hernia. Most of our patients (74%) were operated on in the supine position, which may help explain the lower incidence of TNs in this study.

Although TNs occurred in 4% of patients anesthetized with lidocaine and in 1% of those given prilocaine,
no differences between both anesthetic agents were found. This is related to an insufficient statistical power of the study despite the fact that sample size was calculated considering an incidence of TNSs after spinal anesthesia with lidocaine of at least 11% according to data published in the literature.5,6 The low incidence of TNSs in the lidocaine group found in our study compared with figures reported in previous studies may account for the lack of statistically significant differences between both groups. On the other hand, the occurrence of a case of TNSs among patients in the prilocaine group was a relatively unexpected finding. Therefore, the question of whether lidocaine causes a higher incidence of TNSs than prilocaine was not definitively answered in our study, although it seems evident that the incidence of TNSs is much lower than that previously reported.

Given the low incidence of TNSs after spinal anesthesia with 5% hyperbaric lidocaine, more than 500 patients would have to be recruited in future trials to detect differences as found in the present study. In any case, only randomized studies with a standardized measurement of TNSs, previous training of the observer(s), and a larger sample size may provide conclusive data on the incidence of TNSs with the use of 5% hyperbaric lidocaine and 5% hyperbaric prilocaine for spinal anesthesia.

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