SUPPLEMENT

*Muhammet Gozdemir
Bunyamin Muslu
Huseyin Sert
Burhanettin Usta
Ruveyda Irem Demircioglu
Hulya Kasikara*

Department of Anesthesiology, Turgut
Ozal University School of Medicine,
Ankara, Turkey

Transient neurological symptoms after spinal anesthesia

Abstract

Purpose: The aim of this study was to investigate the incidence of transient neurological symptoms (TNS) after spinal anesthesia with levobupivacaine, bupivacaine, articaine or lidocaine.

Methods: The patients (n=400) were randomly assigned to receive spinal anesthesia with levobupivacaine, bupivacaine, articaine or isobaric lidocaine. Onsets of sensory and motor block were recorded. On postoperative days 1, 2 and 3, patients were interviewed by an investigator blinded to the spinal anaesthetic agent used. The patients were classified as having TNS if there was pain in the hips, thighs and/or lower limbs following recovery from anesthesia.

Results: Time to maximum sensory block was significantly longer in the articaine group than the lidocaine group. The incidence of TNS was much less after spinal anesthesia with levobupivacaine, bupivacaine and articaine than after lidocaine.

Clin Invest Med 2016; 39 (6): S106-S110.

Correspondence to:

Muhammet Gözdemir, MD,
Department of Anesthesiology, Turgut Özal University School of Medicine
Address: Alparslan Türkeş Caddesi No. 57 06510 Ankara, Turkey
E-mail: doktormuhammet@yahoo.com

Transient neurological symptoms (TNS) after spinal anesthesia are characterized by postoperative pain or dysaesthesia in hips or lower extremities. These symptoms were first described by Schneider *et al.* in 1993 in four patients who had undergone spinal anesthesia with hyperbaric 5% lidocaine [1], and were investigated further in subsequent larger studies [2].

Compared to lidocaine, bupivacaine and articaïne are less commonly associated with TNS after spinal anesthesia [3-9]. We have previously reported that the incidence of TNS in patients who underwent isobaric subarachnoid anesthesia was lower with levobupivacaine (5 mg/ml) compared to lidocaine (20 mg/ml); but our study group were small. A literature search revealed only a few studies that mentioned the incidence of TNS after spinal anesthesia with articaïne and levobupivacaine [9-11]. The aim of this study is to determine the incidence of TNS in patients who underwent isobaric subarachnoid anesthesia with levobupivacaine (5 mg/ml), articaïne (20 mg/ml), bupivacaine (5 mg/ml) or lidocaine (20 mg/ml).

Materials and Methods

After receiving approval by the local ethics committee, we enrolled 400 patients. All patients had an ASA score of I or II, and received spinal anesthesia in order to undergo minor orthopedic, caesarean section, varicose vein, inguinal hernia and appendectomy operations. Patients with the history of diabetes mellitus, morbid obesity, allergy to the anesthetics used in the study, acute or chronic back pain, spinal canal stenosis, vertebral abnormality, or previous back surgery, were excluded from the study.

Patients were assigned randomly by the authours via a sealed envelope method to receive either levobupivacaine (Chirocaine® 5 mg/ml, Abbott, Nycomed, Pharma, Elverum, Norway), bupivacaine (Bustesin® 5 mg/ml, Idol, Vem, Topkapı, Istanbul, Turkey), articaïne (Ultracain D-S fort® 20 mg/ml, Sanofi Aventis, Luleburgaz, Kırklareli, Turkey) or lidocaine (Jetmonal® 20 mg/ml, Adeka, Samsun, Turkey). All drugs were prepared as 3 ml doses and were drawn into syringes by an independent anesthesia resident so that the anesthetist performing the injection was unaware of which drug has being given. Patients were routinely monitored. At the L 2-3 or L 3-4 interspace, a 27-gauge pencil point type needle (Pencan®, B. Braun, Melsungen AG, Melsungen, Germany) was inserted in the sitting position. Free flow of cerebrospinal fluid was verified and the anesthetic was injected. Height of sensory block and motor block was controlled at 3, 5, 10, 15 and 30 min, and thereafter at 30-minute intervals.

All patients hospitalized at the hospital one day after the operation, and were examined again before discharge from the hospital. Patients were also interviewed on the next two days by telephone. TNS was defined as pain and/or dysaesthesia in the area of the hips, thighs, and/or lower limbs occurring after recovery from anesthesia, and which was not directly attributable to surgery. The time from block cessation to the onset of TNS was recorded. Postoperative pain, including TNS, was treated with dexketoprofen trometamol (25 mg tablets two times a day).

One week after spinal anesthesia, patients who had experienced TNS were interviewed by telephone. Questions regarding the symptoms and their duration included headache, backache, pain in the operation area and pain in the thighs, buttocks, calves or elsewhere.

Statistical Analysis

The number of patients enrolled in this study was determined based on our preliminary study and a power of 80% and significant difference for rate of TNS amount four groups with a significance level of 5%. Required sample size was calculated as 78 patients for each group.

All statistical calculations were performed using SPSS for Windows software, version 15.0 (SPSS Inc, Chicago, IL). Normal distribution of the collected data was tested by the Shapiro-Wilk test. ANOVA was used for analyses of the normally distributed parameters and Kruskal Wallis test was used to evaluate of the non-normally distributed parameters. Mann-Whitney-U test was used for comparison of non-normally distributed parameters for between the two groups. $p < 0.008$ was considered statistically significant with Bonferroni correction. The overall incidence of TNS was compared between groups via the chi square test. Values were presented as mean $\pm$ SD or median (range) in manuscript, figures and tables and $p < 0.05$ was accepted statistically significant.

Results

The levobupivacaine and bupivacaine groups did not differ significantly in terms of time to achievement of maximum motor block when compared with others; however, in the lidocaine group, this time was significantly longer compared to the articaïne group ($p = 0.001$, Table I). Time to maximum sensory block was significantly longer in the articaïne group than in the lidocaine group ($p = 0.001$, Table I) but there were no significant differences found in other intergroup comparisons.

Table 1. Characteristics of patients and variables of spinal anesthesia

	Characteristics of patients and variables of spinal anesthesia				
	Levobupivacaine Group (n=100)	Bupivacaine Group (n=100)	Articaine Group (n=100)	Lidocaine Group (n=100)	<i>p</i>
Gender (male/female)	35/65	43/57	40/60	38/62	0.699
Age (years; median, range)	32.17 (17-74)	31.53 (18-66)	37.77 (18-82)	31.10 (18-68)	0.216
Height (cm; mean±SD)	167±8	168±6	167±9	167±9	0.329
Weight (kg; mean±SD)	78±10	78±12	78±8	78±10	0.984
Duration of surgery (minutes; median, range)	45 (20-154)	40 (20-154)	40 (20-148)	45 (20-105)	0.565
Types of operation					
Cesarean section	50	46	47	52	
Inguinal hernia	12	6	9	8	
Minor orthopedic	14	15	7	10	
Appendectomy	3	7	9	6	
Varicose vein	11	16	13	11	
Plenoidal sinus	10	10	15	13	
Maximum motor block grade	3	3	3	3	
Time to maximum motor block (minutes; median, range)	10.59 (3-60)	9.70 (3-60)	10.72 (3-30)	7.51 (3-30) *	0.002
Time to maximum sensory block (minutes; median, range)	6.50 (3-15)	7.56 (3-30)	5.81 (3-30)&	8 (3-30)§	0.007

* $p < 0.001$ (Lidocaine Group versus Articaine group), & $p < 0.001$ (Levobupivacaine Group versus lidocaine group), § $p < 0.005$ (Lidocaine Group versus Articaine group).

The incidence of TNS did not differ among patients receiving levobupivacaine, bupivacaine and articaine ($p=0.838$, Table III). Levobupivacaine, bupivacaine and articaine were associated with less frequency of TNS than lidocaine. TNS developed in five patients (5/100, 5%) in the levobupivacaine group, in seven patients (7/100, 7%) in the bupivacaine group, in six patients (6/100, 6%) in the articaine group and in twenty seven patients (27/100, 27%) in the lidocaine group ($p=0.001$, Table II). Of these 45 patients who reported TNS, all complained of bilateral symptoms. At the one-week follow-up interview, no patient exhibited continued TNS. The distribution of the patients' TNS-related pain is summarized in Table II. In more than half of these patients, the pain extended across multiple regions, including the buttocks, thighs and lower legs (Table II). Among the 45 patients in the

four groups who experienced TNS, the severity of pain ranged from 1/10 to 6/10 (median 3/10).

TNS degree of pain as 1-6/10, and described it as radiating to the buttocks and lower extremities. The pain developed on the day following surgery and resolved within 72 hours. Cold and pinprick tests showed no hyperalgesia or sensory loss, and deep tendon reflexes were normal. Lumbar radiographs showed no abnormalities. These findings were compatible with TNS. The patients with TNS in the all groups all responded well to treatment with a nonsteroidal anti-inflammatory drug.

Discussion

The occurrence of TNS after spinal anesthesia appears to be related to the type of local anesthetic used [3]. Lidocaine has been found to be associated with TNS more than several other

local anesthetics [3] and as a result, the avoidance of TNS via the use of alternatives to lidocaine has become a topic of discussion. Bupivacaine, for example, has been found to have a low incidence of TNS [3-6]. Levobupivacaine is similar to bupivacaine in anesthetic properties [8] and likewise it would be expected to have a low incidence of TNS. Articaïne application for local, regional and spinal anesthesia has been reviewed previously [12]. In recent years, spinal articaïne appears to have a shorter duration of impact and rare cases of TNS have been reported [7, 12]. The present study was, therefore, designed specifically to investigate TNS incidence with these four local anesthetic agents.

We found that after spinal anesthesia with levobupivacaine and bupivacaine the incidence of TNS were much lower compared to lidocaine (5%, 7% *vs.* 27% of patients). This finding is consistent with previous studies of bupivacaine [2, 4-6], and is also consistent with the single study in the literature that has investigated TNS after the use of levobupivacaine [11]. In that study, none of the 30 patients who underwent spinal anesthesia with levobupivacaine developed TNS.

Spinal articaïne has a low incidence of TNS, and a similar duration of impact with lidocaine [7, 8]. After spinal anesthesia with articaïne, recovery of motor function was faster and time to spontaneous voiding significantly shorter [7, 8]. Our findings are similar to this study of spinal anesthesia with articaïne (6%).

After lidocaine spinal anesthesia, the reported incidence of TNS has varied from 0% to 40% [6, 13-16]. The incidence in our study fell within this range, at 27%. We used a 2%, lidocaine solution. Previous studies have investigated the incidence of TNS with the following concentrations of lidocaine: 2% or 5% [11, 12]; 1% or 5% [11]; and, 2 %, 1% or 0.5% [4].

In conclusion; we found that the incidence of TNS after spinal anesthesia was much less after levobupivacaine, bupivacaine and articaïne than after lidocaine; however, it appears that TNS may occur in association with levobupivacaine and articaïne.

References

1. Schneider M, Ettlin T, Kaufmann M, Schumacher P, Urwyler A, Hampl K, Von hochstetter A. Transient neurologic symptoms after hyperbaric subarachnoid anesthesia with 5% lidocaine. *Anesthesia and Analgesia* 1993; 76: 1154-1157.
2. Camponovo C, Wulf H, Ghisi D, Fanelli A, Riva T, Cristina D, Vassiliou T, Leschka K, Fanelli G. Intrathecal 1% 2-chloroprocaine *vs.* 0.5% bupivacaine in ambulatory surgery: a prospective, observer-blinded, randomised, controlled trial. *Acta Anaesthesiologica Scandinavica* 2014; 58: 560-566.
3. Zaric D, Pace NL. Transient neurologic symptoms (TNS) following spinal anaesthesia with lidocaine versus other local anaesthetics. *Cochrane Database of Systematic Reviews* 2009; 15: CD003006.
4. Pollock JE, Neal JM, Stephenson CA, Wiley CE. Prospective study of the incidence of transient radicular irritation in patients undergoing spinal anesthesia. *Anesthesiology* 1996; 84: 1361-1367.
5. Freedman JM, Li DK, Drasner K, Jaskela MC, Larsen B, Wi S. Transient neurologic symptoms after spinal anesthesia: an epidemiologic study of 1,863 patients. *Anesthesiology* 1998; 89: 633-641.
6. Keld DB, Hein L, Dalgaard M, Krogh L, Rodt SA. The incidence of transient neurologic symptoms after spinal anesthesia in patients undergoing surgery in the supine position. Hyperbaric lidocaine versus hyperbaric bupivacaine. *Acta Anaesthesiologica Scandinavica* 2000; 44: 285-290.
7. Dijkstra t, Reesink JA, Verdouw BC, Van Der Pol WS, Feberwee T, Vulto AG. Spinal anesthesia with articaïne 5% *vs* bupivacaine 0.5% for day-case lower limb surgery: a double-blind randomized clinical trial. *British Journal of Anaesthesia* 2008; 100: 104-108.
8. Hendriks MP, De Weert CJ, Snoeck mm, Hu HP, Pluim ma, Gielen MJ. Plain articaïne or prilocaine for spinal anesthesia in day-case knee arthroscopy: a double-blind randomized trial. *British Journal of Anaesthesia* 2009; 102: 259-263.
9. Förster JG, Kallio H, Rosenberg PH, Harilainen A, Sandelin J, Pitkänen MT. Chloroprocaine *vs.* articaïne as spinal anaesthetics for day-case knee arthroscopy. *Acta Anaesthesiologica Scandinavica* 2011; 55: 273-281.
10. Mcleod GA, Burke D. Levobupivacaine. *Anesthesia* 2001; 56: 331-341.
11. Breebaart MB, Vercauteren MP, Hoffmann VL, Adriaansen HA. Urinary bladder scanning after day-case arthroscopy under spinal anesthesia: comparison between lidocaine, ropivacaine, and levobupivacaine. *British Journal of Anaesthesia* 2003; 90: 309-313.
12. Kallio H, Snäll EV, Luode T, Rosenberg PH. Hyperbaric articaïne for day-case spinal anesthesia. *British Journal of Anaesthesia* 2006; 97: 704-709.
13. Ostgaard G, Hallaråker O, Ulveseth OK, Flaatten H. A randomized study of lidocaine and prilocaine for spinal anesthesia. *Acta Anaesthesiologica Scandinavica* 2000; 44: 436-440.
14. Salazar F, Bogdanovich A, Adalia r, Chabás e, Gomar C. Transient neurologic symptoms after spinal anesthesia using isobaric mepivacaine and isobaric lidocaine. *Acta Anaesthesiologica Scandinavica* 2001; 45: 240-245.

15. Pollock JE. Transient neurologic symptoms: etiology, risk factors, and management. *Regional Anesthesia* 2002; 27; 581-586.
16. Fanelli G, Danelli G, Zasa M, Baciarello M, Di Cianni S, Leone S. Intrathecal ropivacaine 5 mg/ml for outpatient knee arthroscopy: a comparison with lidocaine 10 mg/ml. *Acta Anaesthesiologica Scandinavica* 2009; 53: 109-115.