Original Research Article

The incidence of transient neurologic syndrome in obstetric and non-obstetric patients with spinal 0.5% hyperbaric bupivacaine and 5 % hyperbaric lignocaine - A randomized double blind control study

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Abstract

Background: Lignocaine has been used for spinal anesthesia since 1948 for many decades without any serious complications. In subjects who were recovering from lignocaine spinal anaesthesia, Transient Neurologic Symptoms (TNS) have been reported. In pregnant women, small doses of spinal anaesthesia are known to produce higher levels of spinal anaesthesia compared to non-pregnant women. The aetiology of TNS is still poorly understood and the incidence of TNS has been reported to be low in pregnancy.

Materials and methods: We conducted a randomised controlled clinical trial on 200 subjects who were admitted to Dhanalakshmi Srinivasan Medical College and Hospital. 100 obstetric subjects were randomised to receive either 1.1 ml of 5% lignocaine (Group 1 – OL, n=50) or 2 ml of 0.5% bupivacaine (Group 2 – OB, n=50). 100 non obstetric subjects were randomised to receive either 2 ml of 5% lignocaine (Group 3 – NL, n=50) or 3 ml of 0.5% bupivacaine (Group 4 – NB, n=50). Incidence of Transient Neurological Symptoms was our primary outcome variable.

Results: Out of 50 people with OL none had TNS. The proportion of subjects developing TNS was 2%, 4% and 4% respectively in OB, NL and NB groups. None of the factors such as degree of motor

blockade, age, weight, occurrence of hypotension, lowest SBP, lowest DBP, lowest heart rate had a significant association with occurrence of TNS.

Conclusions: The incidence of TNS in OL group was 0. The occurrence of transient neurologic symptoms with intrathecal lidocaine among obstetric patients in the supine surgical position appears to be infrequent and also without any serious complications.

Key words

Transient Neurologic Symptoms (TNS), Lignocaine, Pregnant women, Spinal anesthesia, Bupivacaine, Lidocaine.

Introduction

Spinal anesthesia is a form of neuraxial blockade achieved centrally by injecting local anesthetic agents into the subarachnoid space. August bier [1] performed the first spinal anesthesia in 1898 using cocaine, which was the first known local anesthetic. Other local anesthetics were then introduced gradually. Lignocaine has been used for spinal anesthesia since 1948 for many decades without any serious complications [2], but there are reports of several neurological complications in the last few decades [3, 4]. The major cause for using lignocaine for spinal anesthesia [5, 6] is its appropriateness for ambulatory surgery, quick onset of action and recovery, shorter duration of action with intense motor and sensory blockade. All local anaesthetics have a potential to cause neurotoxic effects depending on the dosage, duration of exposure [4]. There is a risk of permanent nerve damage, with all local anaesthetics when they were administered in higher concentration or for longer periods of time [7].

In subjects who were recovering from lignocaine spinal anaesthesia after a single injection, a new adverse effect [4] "Transient Neurologic Toxicity" was reported in 1993. New terms arose in the following years such as "Transient Radicular Irritation" [8-10] and "Transient Neurologic Symptoms (TNS)". There is appearance of Transient Neurologic Symptoms, which includes mild to severe pain arising from the gluteal region with radiation to both the lower extremities [11], inside a few hours to twenty four hours after recovering fully from an uneventful spinal anaesthesia. Even though MRI, Electrophysiological testing and several neurological tests could not detect any abnormalities with TNS [12] resulting from use of lignocaine, it has been understood as a sign of probable neurotoxicity [13] of lignocaine. In Pregnant women, small doses of spinal anaesthesia are known to produce higher levels of spinal anaesthesia compared to non-pregnant women because of decreased vertebral canal space and also the CSF volume and also increased sensitivity of spinal nerves to local anaesthetic agents [14-16], caused by higher progesterone levels in the last trimester. The incidence of TNS has also been reported to be lower in pregnancy [15, 16]. Studies with different concentrations and doses of lignocaine have shown that the incidence of TNS was not dose or concentration dependent and the aetiology is still poorly understood [5, 6, 17].

Objectives

The objective of our study was to compare the incidence of TNS in obstetric and non-obstetric patients with spinal 0.5% hyperbaric bupivacaine and 5 % hyperbaric lignocaine.

Materials and methods

We conducted a randomised controlled clinical trial on 200 subjects who were admitted to Dhanalakshmi Srinivasan Medical College and Hospital from August 2013 to August 2014 after obtaining clearance from the hospital ethical committee. Our study population included 100 obstetric women posted for elective caesarean section and 100 non obstetric women posted for

surgeries like hernia repair, eversion of sac and appendectomy. We excluded all subjects with neurologic disorders, hypertension, diabetes mellitus, and backache.

We divided the study population into 4 groups. 100 obstetric subjects were randomised to receive either 1.1 ml of 5% lignocaine (Group 1 – OL) or 2 ml of 0.5% bupivacaine (Group 2 – OB). 100 non obstetric subjects were randomised to receive either 2 ml of 5% lignocaine (Group 3 – NL) or 3 ml of 0.5% bupivacaine (Group 4 – NB). All subjects were pre medicated with 1 mg midazolam i.m. 45 minutes before surgery. The obstetric patients were given 30 ml of 0.3 mol solution of sodium citrate 30 minutes before surgery and 150 mg of oral ranitidine the night before surgery and again 2 hours before surgery. The subarachnoid space was accessed at the L3-L4 interspace in the midline using a 25 gauge Quincke's needle. The allocated local anaesthetic was injected into the subarachnoid space after free flow of CSF. The subjects were maintained on a continuous flow of intravenous fluids, titrated according to the blood pressure. Lowest systolic and diastolic blood pressure, heart rate were noted. After surgery, all the subjects were taken to ICU, where they remained until complete recovery from their spinal anesthesia. All subjects received inj. diclofenac i.m. on the night of surgery, tab. diclofenac 50 mg twice daily from the first post-operative day for 4 days, for pain relief. After shifting from ICU, the subjects were then interviewed on the first, second, fourth and seventh day of their hospital stay. During post-operative assessment, a symptom check list was used for standardised data collection. If the subject reported TNS and related symptoms, they were asked to identify the location of their symptoms and a complete neurological examination was performed in subjects with significant symptoms. The collected data was entered in microsoft excel and analysed with SPSS Trial version 12.0. Incidence of Transient Neurological Symptoms was our primary outcome variable. The main explanatory variables were type of local anaesthetic used, obstetric status of the patient, hypotension, degree of motor and sensory blockade.

Other relevant variables analysed were demographic and anthropometric variables like age, weight. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables with confidence intervals. The association between proportion of subjects with transient neurologic symptoms and relevant variables was assessed by cross tabulation and comparison of percentages. Chi square test was used to test statistical significance. P value < 0.05 was considered statistically significant.

Results

A total of 200 subjects were included in the final analysis. Out of the 200 subjects, 100 were obstetric and remaining 100 were non-obstetric cases. Out of these 50 in each group received lidocaine and the other 50 received bupivacaine.

In our study, the mean age of obstetric subjects in lidocaine group (n=50) was 25.86 (±2.49) years while in bupivacaine group (n=50), it was 26.28 (± 3) years. The mean age of non-obstetric subjects in lidocaine group (n=50) was 30.34 (±8.62) years, while in bupivacaine group (n=50) it was 32.42 (±11.19) years. In our study, the mean weight of obstetric subjects in lidocaine group (n=50) was 63.18 (±3.78) kg while in bupivacaine group (n=50), it was 65.54 (±4.27) kg. The mean weight of non-obstetric subjects in lidocaine group (n=50) was 64.88 (±6.18) kg, while in bupivacaine group (n=50) it was 59.94 (±11.35) kg. The differences across the four groups in terms of age and weight were statistically significant as shown in **Table - 1** (P value < 0.005).

Out of 50 people with OL, 11 (22.0%) had achieved maximum sensory level of T4, 19(38.0%) achieved up to T5 level, 19(38.0%) achieved up to T6 level was and 1(2.0%) subject achieved up to T7. Out of 50 people with OB,

17(34.0%) had achieved maximum sensory level of T4, 16(32.0%) achieved up toT5 level, 17(34.0%) achieved up to T6 level. out of 50 people with NL, 4(8.0%) had achieved maximum sensory level of T4, 12(24.0%) achieved up toT5 level, 34(68.0%) achieved up to T6 level. out of 50 people with NB, 9(18.0%) had achieved maximum sensory level of T4, 19(38.0%) achieved up toT5 level, 22(44.0%) achieved up to T6 level. The difference in the proportion of maximum sensory level across groups could not be statistically tested (**Table - 2**).

Table - 1: Comparison of baseline parameters between 4 study groups.

Parameter	OL (N=50)	OB (N=50)	NL (N=50)	NB (N=50)	F-Statistic	P value
Age	25.86±2.49	26.28±3.00	30.34±8.62	32.42±11.19	9.453	<0.001
Weight	63.18±3.78	65.54±4.26	64.88±6.18	59.94±11.35	6.280	0.004

Table - 2: Comparison of maximum sensory level with group of study population (N=200).

Group	Maximum sensory level			
	T4	T5	T6	T7
OL (N=50)	11(22.0%)	19(38.0%)	19(38.0%)	1(2.0%)
OB(N=50)	17(34.0%)	16(32.0%)	17(34.0%)	0(0%)
NL (N=50)	4(8.0%)	12(24.0%)	34(68.0%)	0(0%)
NB (N=50)	9(18.0%)	19(38.0%)	22(44.0%)	0(0%)

*****No statistical test was applied –due to 0 subjects in one of the cells

Table - 3: Comparison of mean of degree of motor block across study groups (N=200).

Group	Mean	Std. Deviation	F-Statistic	P value
OL(N=50)	3.92	0.2740	0.7472	0.525
OB(N=50)	3.86	0.3505		
NL(N=50)	3.94	0.2399		
NB(N=50)	3.92	0.2740		

Table - 4: Comparison of group with TNS and hypotension of study population (N=200).

Parameter	OL (N=50)	OB (N=50)	NL (N=50)	NB (N=50)	P value
TNS, (N(%))	0 (0%)	1 (2.0%)	(4.0%)	2(4.0%)	*
Hypotension (N(%))	4 (8.0%)	4 (8.0%)	7(14.0%)	4(8.0%)	0.66

No statistical test was applied –due to 0 subjects in one of the cells

The mean degree of motor block in obstetric subjects in lidocaine group was 3.92±0.2740, it was 3.86±0.3505 in bupivacaine group, the mean degree of motor block of non-obstetric subjects in lidocaine group was 3.94± 0.2399, it was 3.92±0.2740 in bupivacaine group, the differences across the four groups in terms of degree of motor block was statistically not significant (p value0.525) (F statistics 0.7472) (**Table - 3**).

Out of 50 people with OL none had TNS. The proportion of subjects developing TNS was 2%, 4% and 4% respectively in OB, NL and NB groups. Out of 50 people with OL 8%had hypotension's. The proportion of subjects developing hypotension was 8%, 14%and 8% respectively in OB, NL and NB group. The difference in the proportion of group across hypotension could not be statistically tested (**Table - 4**).

Discussion

Lidocaine has been used for spinal anesthesia since 1948, seemingly without causing concern.

However, during the last 10 years, a number of reports have appeared implicating lidocaine as a possible cause [18-20] of neurologic complications after spinal anesthesia. In our study, the incidence of TNS after spinal anaesthesia with lignocaine in obstetric subjects, who underwent caesarean section was nil. The main research question we addressed was whether the incidence of TNS with lidocaine in obstetric patients was less than that in non-obstetric patients and whether the incidence of TNS in lidocaine group was more than that in bupivacaine group. The incidence of TNS with bupivacaine in obstetric subjects was higher than lidocaine group at 2%. The incidence of TNS in non-obstetric subjects in lignocaine group (4%) versus the bupivacaine group (4%) was the same and hence was not statistically significant. On the whole, the incidence of TNS in obstetric group was 1% and in the non-obstetric group, it was 4%, the difference in which was not statistically significant. This then raised questions as to reason for small incidence. One may wonder whether pregnancy in and of itself played a role in minimising the occurrence of this syndrome. We however, believe that the supine surgical position is a more possible explanation for small incidence of TNS in our study. Similar to our study, Aouad MT, et al. (2001) in their study observed that the incidence of TNS was zero with 95% confidence interval of 0% to 3% in both the groups in their study on 200 women, who were scheduled for cesarean delivery. They concluded that the frequency of postoperative TNS [15] does not exceed 3% in patients undergoing cesarean delivery at term using hyperbaric lidocaine 5% or hyperbaric bupivacaine 0.75%. In the obstetric population Lidocaine spinal anesthesia is commonly used for various obstetric procedures. Philip J, et al. (2001) [16] in their study observed the incidence of transient neurologic symptoms with lidocaine was 3% with 95% confidence interval = 0.1%–17.8% and that with bupivacaine was 7% with 95% confidence interval of 0.9%–23.5%, which was statistically not significant. The large incidence in their study could be explained by the fact that their patients did not receive any post-operative analgesics. But our patients, received standardized analgesics post operatively which could have reduced the incidence of TNS to a minimum. In contrast to our study Keld DB, et al. (2000) [21] observed a higher incidence of 26% of TNS (nine patients) in the lidocaine group compared to 3% (one patient) in the bupivacaine group (3%) ($P<0.01$). Contrary to our study, Zaric D, et al. (2005) [20] in their systematic review on 1347 patients observed that 117 developed TNS and the relative risk for developing TNS after spinal anesthesia with lidocaine was higher than with other local anesthetics (bupivacaine, prilocaine, procaine, and mepivacaine), was 4.35 with 95% confidence interval of 1.98 to 9.54. Zaric D, et al. (2009) [19] in their systematic review on sixteen trials reporting on 1467 patients observed that 125 developed TNS and the use of lidocaine for spinal anesthesia increased the risk of developing TNS. The incidence of hypotension, degree of motor blockade were not statistically significant between the four groups in our study , but the statistical significance of difference in level of maximum sensory blockade attained and TNS incidence between the four groups could not be tested as shown in Table - 2, 3 and 4. There was a clinical difference in the maximum sensory level among the four groups, because the non-obstetric patients received a larger volume and amount of drug, as demanded by the procedure. This cannot influence the TNS, as its occurrence is not dose dependent.

The choice of local anaesthetic is determined by the type and duration of surgery and by the intensity of motor blockade that is required. The increase in day care surgery has generated a need for a local anaesthetic with a quick onset and short duration of action that allows for a speedy recovery and early discharge. So far, this profile is fulfilled only by lignocaine. We conducted our study in a group of subjects in which possible confounding variables were controlled. All subjects satisfied strict inclusion criteria. All subjects were in supine position for their surgery.

All received spinal anaesthesia in a standardised manner using local anaesthetic preparations that contained no additives. Aguilar JL, et al. (2004) in their review [22] had opined that intrathecal administration of local anesthetics is known to increase glutamate concentration in cerebrospinal fluid leading to transient neurologic syndrome. Studies with different concentrations and doses of lidocaine have shown that the risk of TNS was not dose- or concentration dependent as shown by Hampl, et al. (1996) [8] and Pollock, et al. (1999) [12]. All forms of lidocaine have been associated with TNS: Hyperbaric – Tong, et al. (2003) [23], Isobaric – Hampl, et al. (1996) [8]; and when diluted with cerebrospinal fluid – Pollock, et al. (1999) [12].

Lignocaine had historically been considered as a preferable spinal anesthetic agent, for short procedures, because of its short duration of action. Although bupivacaine is an excellent choice, its long duration of action makes it less useful for short procedures. In our study, the incidence of TNS after spinal anesthesia with lignocaine in patients in supine position was small and without any serious sequelae. In Pregnant women, small doses of spinal anaesthesia are known to produce higher levels of spinal anaesthesia compared to non-pregnant women because of compression of inferior vena cava causing shunting of blood to the venous plexus in the vertebral canal. This decreases the vertebral canal space and also the CSF volume. Hence, the anaesthetic agent will dilute in smaller CSF volume than in non-obstetric women [15]. Studies with different concentrations and doses of lignocaine have shown that the incidence of TNS was not dose or concentration dependent and the aetiology is still poorly understood.

Conclusion

The occurrence of transient neurologic symptoms with intrathecal lidocaine among obstetric patients in the supine surgical position appears to be infrequent and also without any serious complications. In our study, the incidence of TNS after spinal anaesthesia with lignocaine in obstetric subjects, who underwent caesarean section, was nil while it was 2% in bupivacaine obstetric group. However, there is a need for larger randomized studies to be conducted under similar controlled conditions to conclusively ascertain the incidence of transient neurologic symptoms with lidocaine in a similar population.

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