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ORIGINAL RESEARCH

Assessment of myotoxic effect of bupivacaine after continuous peripheral nerve blocks: A biochemical study

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ABSTRACT:
Background: The growing popularity of regional anaesthesia techniques has prompted interest into the investigation of localanaesthetic (LA)-induced tissue damage. Myotoxicity caused by LA agents was first described by Brun in striated muscles.Hence; the present study was conducted for assessing myotoxic effect of bupivacaine after continuous peripheral nerve blocks. **Materials & methods:** A total of 20 patients were enrolled in the present study. Complete demographic and clinical details of all the patients were obtained. Insertion of femoral nerve catheter was done in all the patients. This was followed by administration of 20 ml of bupivacaine. Muscle samples were obtained 14 days after the administration of bupivacaine followed by assessment of histologic section. Muscle damage was graded as follows: Grade 0: No damage, Grade 1: Mild damage, Grade 2: Moderate damage and grade 3: Marked lesion. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. **Results:** Myotoxic effect was found to be present in 45 percent of the patients while in the remaining 55 percent of the patients, Myotoxic effect was absent. While comparing the age-wise and gender-wise distribution of patients non-significant results were obtained. **Conclusion:**Mild to moderate muscle and Myotoxic changes do occur after the administration of bupivacaine suggesting of irreversible skeletal muscle damage.

Key words: Bupivacaine, Myotoxic

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INTRODUCTION

The growing popularity of regional anaesthesia techniques has prompted interest into the investigation of localanaesthetic (LA)-induced tissue damage. Myotoxicity caused by LA agents was first described by Brun in striated muscles in 1959, and has continued to garner interest as a serious complication of peripheral nerve blocks. Although thought to be a rare and subclinical adverse effect of LAs in humans, several cases of clinically important myotoxicity have been reported in the literature, mostly after retrobulbar blocks.[1- 3]

Subcellular pathomechanisms of local anesthetic myotoxicity are still not completely revealed. However, excessively increased intracellular [Ca^2] levels have been shown to have the key role in myocyte injury. In this respect, bupivacaine and, to a smaller extent, ropivacaine both induce Ca^2 release from the SR, and simultaneously inhibit Ca^2 reuptake into the SR, resulting in persistently increased [Ca^2] levels. In contrast, less myotoxic drugs such as tetracaine may inhibit Ca^2 release, without affecting Ca^2 reuptake.[4- 6] Hence; the present study was conducted for assessing myotoxic effect of bupivacaine after continuous peripheral nerve blocks.

MATERIALS & METHODS

The present study was conducted in the department of biochemistry and anesthesia and it included assessment of myotoxic effect of bupivacaine after continuous peripheral nerve blocks. A total of 20 patients were enrolled in the present study. Complete demographic and clinical details of all the patients were obtained. Insertion of femoral nerve catheter was done in all the patients. This was followed by administration of 20 ml of bupivacaine. This was followed by subsequent continuous infusion of bupivacaine. Muscle samples were obtained 14 days after the administration of bupivacaine followed by assessment of histologic section. Muscle damage was graded as follows: Grade 0: No damage, Grade 1: Mild damage, Grade 2: Moderate damage and grade 3: Marked lesion. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Chi-square test was used for assessment of level of significance.

RESULTS

In the present study, a total of 20 patients were analyzed. Mean age of the patients of the present study was 43.5 years. 40 percent of the patients belonged to the age group of more than 40 years.25 percent of the patients belonged to the age group of less than 25 years. Out 20 patients included in the present study, 12 were males while the remaining were females.

In the present study, Myotoxic effect was found to be present in 45 percent of the patients while in the remaining 55 percent of the patients, Myotoxic effect was absent. In the present study, while comparing the age-wise and gender-wise distribution of patients non-significant results were obtained.

Table 1: Demographic details

Parameter		Number of patients	Percentage of patients
Age group (years)	Less than 25	5	25
	25 to 40	7	35
	More than 40	8	40
Gender	Males	12	60
	Females	8	40

Table 2: Myotoxic effect

Myotoxic effect	Number of patients	Percentage of patients
Grade 0	11	55
Grade 1	6	30
Grade 2	3	15
Grade 3	0	0

Table 3: Correlation of Myotoxic effect with age

Age group (years)	Number of patients with Myotoxic effect	Number of patients without Myotoxic effect	p- value
Less than 25	2	3	0.124
25 to 40	3	4	
More than 40	4	4	

Table 4: Correlation of Myotoxic effect with gender

Gender	Number of patients with Myotoxic effect	Number of patients without Myotoxic effect	p- value
Males	5	7	0.858
Females	4	4	

DISCUSSION

Regional blocks improve postoperative analgesia and postoperative rehabilitation in children and in adult patients. Continuous peripheral nerve blocks have been proposed as safe and effective techniques for postoperative pain relief and chronic pain therapy, particularly in small children. The local anesthetic solution during continuous blocks comes into contact with muscles.[7- 9]Hence; the present study was conducted for assessing myotoxic effect of bupivacaine after continuous peripheral nerve blocks.

In the present study, a total of 20 patients were analyzed. Mean age of the patients of the present study was 43.5 years. 40 percent of the patients belonged to the age group of more than 40 years. 25 percent of the patients belonged to the age group of less than 25 years. Out 20 patients included in the present study, 12 were males while the remaining were females. Zink W et al compared the long term myotoxic effects of both drugs in a clinically relevant setting. Femoral nerve catheters were inserted in anesthetized pigs, and either 20 mL of bupivacaine (5 mg/mL) or ropivacaine (7.5 mg/mL) was injected. Subsequently, bupivacaine (2.5 mg/mL) and ropivacaine (3.75 mg/mL) were continuously infused (8 mL/h) over 6 h. Control animals were treated with corresponding volumes of normal saline. After 7 and 28 days, respectively, muscle samples were dissected at the former injection sites, and histological patterns of muscle damage were blindly scored (0 = no damage to 3 = marked lesions/myonecrosis) and compared. No morphological tissue changes were detected in control animals. In the observed period, both local anesthetics induced morphologically identical patterns of calcific myonecrosis, formation of scar tissue, and a marked rate of fiber regeneration. However, bupivacaine's effects were constantly more pronounced than those of ropivacaine. In a period of 4 wk after peripheral nerve block, both long-acting local anesthetics, bupivacaine and ropivacaine, produced calcific myonecrosis suggestive of irreversible skeletal muscle damage. In comparison with ropivacaine, however, the extent of bupivacaine-induced muscle lesions was significantly larger.[8]

In the present study, Myotoxic effect was found to be present in 45 percent of the patients while in the remaining 55 percent of the patients, Myotoxic effect was absent. Zink W et al compared the effects of bupivacaine and ropivacaine on skeletal muscle tissue in equipotent concentrations. Femoral nerve catheters were inserted into anesthetized minipigs, and 20 mL of either bupivacaine (5 mg/mL) or ropivacaine (7.5 mg/mL) was injected. Subsequently, bupivacaine (2.5 mg/mL) and ropivacaine (3.75 mg/mL) were continuously infused over 6 h. Control animals were treated with corresponding volumes of normal saline. Finally, muscle samples were dissected at injection sites. After processing and staining, histological patterns of muscle damage were blindly examined, scored (0 = no damage to 3 = myonecrosis), and statistically analyzed. After normal saline, only interstitial edema was found. Bupivacaine treatment caused severe tissue damage (score, 2.3 +/- 0.7), whereas ropivacaine induced fiber injury of a significantly smaller extent (score, 1.3 +/- 0.8). Furthermore, bupivacaine, but not ropivacaine, induced apoptosis in muscle fibers. In summary, both drugs induce muscle damage with similar histological patterns. Compared with bupivacaine, which induces both necrosis and apoptosis, the tissue damage caused by ropivacaine is significantly less severe. They concluded that ropivacaine's myotoxic potential is more moderate in comparison with that of bupivacaine.[9]

In the present study, while comparing the age-wise and gender-wise distribution of patients non-significant results were obtained. Hussain N et al summarized the existing myotoxicity evidence and empirically examined its implications. Databases were searched for all in vitro animal and human studies evaluating LA-induced myotoxicity.

Studies were stratified by design. Data sought included the model examined, LA used, injury mechanisms, nature of damage, and extent of recovery. For human studies, they also aimed to estimate prevalence and recovery rates. One hundred and fifteen studies, mainly animal and ophthalmic, were included. Myotoxicity risk factors included higher concentrations and prolonged exposure to LA, and use of bupivacaine. Injury mechanisms involved early and late aberrations to cytoplasmic calcium (Ca2þ) homeostasis by the sarcoplasmic reticulum Ca2þ ATPase. Incidence in ophthalmic studies was 0.77% (392 of 50 618). Inflammatory changes within a few days after exposure marked the onset of myotoxicity, and myo-degeneration followed within the first week post-exposure. Time to recovery in human muscles ranged between 4 days to 1 yr. None/partial and complete recovery were observed in 61% and 38% of patients, respectively. Across all experimental models, skeletal muscles exposed to LA consistently display myotoxic effects. Evidence is robust in animal and ophthalmic studies, and displays a concerning signal with continuous adductor canal block use in human case reports.[10]

CONCLUSION

From the above results, the authors concluded that mild to moderate muscle and Myotoxic changes do occur after the administration of bupivacaine suggesting of irreversible skeletal muscle damage.

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