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Original Research Article

A prospective study on the association between spinal anesthesia and obesity

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Abstract

Purpose: To compare the outcomes of spinal anesthesia in obese and non-obese patients. **Methods:** In this study, 199 patients who underwent total knee replacement arthroplasty (TKRA) were categorized into obesity group (n = 61) and non-obesity group (n = 138). Anesthesia was considered successful if a bilateral T12 sensory blockage occurred within the first 15 min of injection of intrathecal drug. Parameters that influence spinal anesthesia were analyzed using logistic regression by means of multiple variables that independently influence the outcome of spinal anesthesia.

Results: It was observed that the independent predictors for successful anesthesia in the patients were dose of bupivacaine (odds ratio at 95 % confidence interval = 2.08; range: 1.61 - 2.67) and obesity status (odds ratio at 95 % confidence interval = 2.83; range: 1.21 - 6.49). The outcome of the multivariate analysis also indicated that the dose of bupivacaine, body mass index (BMI) and obesity were predictors of spinal anesthesia. It was also found that the period of the sensory blockage due to bupivacaine was longer in the obesity group than in the non-obesity group.

Conclusion: Sensory blockage in bupivacaine anesthesia during TKRA is influenced by dose of bupivacaine, obesity and BMI.

Keywords: Spinal anesthesia, Total knee replacement arthroplasty, Bupivacaine, Obesity, Body mass index, Logistic regression

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INTRODUCTION

Spinal anesthesia involves the injection of a local anesthesia into the subarachnoid space, using a fine needle [1]. In recent years, factors that influence the extent of sensory loss in connection with spinal anesthesia have been extensively studied [2,3]. Moreover, the position of the patient during injection, speed of injection, spinal space, specific gravity of the solution, dosage, BMI, age, gender, and height have all been investigated [4]. These parameters influence the degree of blockage of sensory nerve in study subjects who undergo anesthesia during surgery [5]. Several reports indicate that the effect of BMI on spinal anesthesia is debatable in view of mixed outcomes.

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As a consequence of modern food habits, more and more obese patients are seen in operation theatres (OTs) these days, a situation which necessitates studying the effect of obesity on spinal anesthesia [6]. Studies on the impact of obesity on anesthesia have produced contrasting outcomes [7]. However, some previous studies have reported positive associations between obesity and level of sensory blockage [8]. This positive relationship between obesity and spinal anesthesia was attributed to reduced CSF volume due to the large amounts of epidural fat [8]. However, the extent of blockade is also influenced baricity of local anesthetics and there also studies which demonstrate the are confirmation of local anesthetics in uneven blockade heights [2].

However, it has also been reported that there was no difference between the median effective dose (ED_{50}) of anesthesia for successful surgery between obese and non-obese patients [9]. Thus, the impact of obesity on spinal anesthesia is not yet properly understood. Moreover, prolonged spinal anesthesia beyond the specific surgery time causes uneasiness to the patients and long admission in the hospital. It is therefore essential to study the characteristics of spinal anesthesia among obese subjects because these patients usually go throughout patient surgery [3,7].

The present investigation focused on prospective and observational studies on changes in duration of spinal anesthesia among obese and nonobese patients. The study included the comparison of the neuraxial blockade levels between the obesity and non-obesity patient groups at the time of induction of anesthesia, and at the end of surgery. The study also involved determination of independent parameters that may influence the outcome of spinal anesthesia, using multivariate analysis. Parameters such as age, gender, and anesthesia dose were subjected to logistic regression analysis to identify the parameters or the factors that establish the level of the final anesthesia on completion.

EXPERIMENTAL

Subjects and study design

The prospective investigation was started in June 2015 and ended in July 2016. The study complied with National Institutes of Health guidelines [10] and was approved by the Hospital Review Board and Ethical Committee (No. HSP-2015-03-023/E).All patients who participated in this study gave prior consent. Patients preparing

for TKRA were enrolled in the study. The patients were categorized according to the physical status of the ASA which ranged from I to III as shown in Table 1. Patients were excluded if they had one or more of the following conditions: (i) high central fever, (ii) diabetes mellitus, (iii) previous episodes of spinal surgery, (iv) infectious fever with core temperature, (v) infection at injection site, (vi) circulatory shock, (vii) coagulopathy, and (viii) creased intracranial.

 Table 1: Physical status classification by American

 Society of Anesthesiologists (ASA)

ASA	Description		
classification			
ASA I	Healthy normal patient		
ASA II	Patient having mild systemic disease		
ASA III	Patient having severe systemic		
	disease		
ASA IV	Patient having severe and life		
	threatening systemic disease		
ASA V	Patient who is not expected to		
	survive without surgery		
ASA VI	Patient declared brain-dead		
Class E	Emergency cases		

The obesity criteria recommended by the World Health Organization (WHO) was used for classification of the study subjects into two groups, i.e., obesity group and non-obesity group (Table 2). Subjects with BMI greater than 30.0 kg/m² were classified as non-obese (NO, total population = 138), while subjects with $BMI \ge 30.0$ kg/m² were classified as obese (O, total population = 61). The Body Mass Index (BMI) which is a simple index for weight-to-height determination was used to classify underweight and obese subjects. The BMI was calculated by dividing the body weight by the square of height in meters (kg/m^2) . The characteristics of patients. including their age, sex and medical information are shown in Table 3.

 Table 2: Body Mass Index (BMI) classification as per Asian criteria

Classification	Principal cut-off points BMI (kg/m ²)
Healthy weight	18.50-22.98
Overweight	23.00-24.89
Pre-obesity	24.98-29.98
Type1 obesity	30.00-40.00
Type 2 - severe obesity	40.10-50.00
Type 3 - morbid obesity	> 50

Table 3: Hollmen scale for sensory blockage

Grade	Definition
0	Full sensation
1	Weak sensation
2	Recognized as light touch
3	Loss of sensation

Study protocol

The patient's measurements were conducted by a ward nurse on duty and the BMI of each was determined using MS Excel. The weight and height of the patients were measured in kilograms and meters, respectively, in standing position, one day before the surgery.

Study subjects were given 10 ml per kg of Ringer's lactate (RL) solution 15 - 20 min prior to spinal anesthesia inside a standard surgery chamber. They were maintained on 5 ml/kg/h dose of RL solution thereafter, and hydroxyl ethyl starch was given at 7 ml/kg/h during the surgery period. Oxygen gas was supplied using a face mask at 6 L/min during the surgery process. The administration of the spinal anesthesia began from the spinal puncture in its lateral point at the L4-5 interspaced with the help of a 25 gauge spinal needle [8]. About 5 - 8 mg/ml of bupivacaine solution was injected into the patients by the anesthesiologists using a 2-ml syringe for 20-30 s, depending on the BMI of the patients. The needle with the orifice pointing cephalad was positioned supinely and horizontally along with the patient.

Successful induction of the anesthesia was indicated by the blockage of bilateral T12 sensor that could be pinpricked for 15 min with intrathecal having a sensory or motor block scale \geq 2, while successful induction of total knee replacement arthroplasty anesthesia was considered as anesthetic induction with a sensory block \geq T12 level beyond the surgical end and sensory or motor block scale \geq 2 [6].On the other hand, anesthetic failure was taken as failed induction or sensory nerve blockade lower than T12 [11]. For multivariate logistic regression analysis, successful anesthesia was considered to be the endpoint and assessment for the tourniquet pain was carried out.

Measurements

Measurement of the length of the vertebral column from its spinous process was done on the 7th cervical vertebra to the patient's sacral hiatus in its lateral position. During the surgery, the sensory level and motor block were estimated for 20 min, and at 5 min intervals after administration of the intrathecal drug. The levels of sensory and motor blockages were also estimated at the end of the surgery. Assessments based on pinpricking of the sensory levels were evaluated based on the Hollmen scale [12] as described in Table 3.

The sensations of the patients were assessed by pinpricking with a 25 G needle bilaterally along the mid-clavicular line. Where there was a difference in the level of sensory blockage, the lower level of blockage was chosen. Thus, motor blockage was classified based on the Bromage scale [13] which is on the lower limbs (Table 4).

Table 4: Description of Bromage score

Grade	Degree of block
0	Nil (0%)
4	Partial (33%)
2	Almost complete (66%)
3	Complete (100%)

Hypotension was defined as reduction in systolic arterial pressure ≥ 20 %, or mean value more than 55 mmHg. In cases of occurrence of hypotension, 5 mg dose intravenous ephedrine bolus was administered. If there was a drop in pulse rate (less than 50 beats per minute), 0.5 mg dose of atropine was administered. The time taken for the appearance of the first postoperative pain was recorded, as well as the first time of self-void after the completion of the surgery.

Statistical analysis

Statistical analysis was carried out using SPSS software (SPSS Inc, version 21, Chicago, IL, USA). Mann-Whitney U-test was used to compare continuous data, while categorical variables were compared using Chi-square test. The categorical variables are presented in terms of absolute numbers (n) and relative frequencies (%), and the variables are presented as means and medians.

Univariate and multivariate statistical analyses were used to study the logistic regression models for predicting successful spinal anesthesia in the studied population. Initially, the possibility of successful anesthesia was first predicted using the multivariate model that contained only variables which were found significant from the univariate analysis (p < 0.05). The predictor variables were chosen based on a backward Wald from the list of patients with a significance value of p < 0.05 and the BMI values were included in the categorical and continuous variables.

RESULTS

The prospective study comprised 226 patients of which 27 were excluded because of other health issues such as high fever, diabetes mellitus, and previous episodes of spinal surgery. The remaining and eligible 199 patients who completed the study protocol were included in the analysis.

Comparative statistics on spinal anesthesia characteristics and its perverse events between the NO and O groups are presented in Table 5. The demographic and clinical parameters were found to be correlated among the two groups as evident from Table 5. In addition, the dose of bupivacaine administration was not similar in the groups. As per definition, incidence of failure of anesthesia was considerably lower in the O group (9 failures, 13.43 %), when compared with the NO group (39 failures, 29.32 %). These results are shown in Table 6.

 Table 5: Characteristics of patients and their clinical information

Variable	Non choolter	Ohaoitu	P-
Variable	Non-obesity	Obesity	•
	group	group	value
Age of the	71 (64 - 74)	71 (67 -	0.42
patient (years)		76)	
Height (cm)	151 (148 -	151 (147 -	0.23
0 ()	155)	155)	
Weight (kg)	57 (54 - 63)	77 (73 -	0.001
		83)	
BMI (kg/m ²)	26.1 (24 -	34.1 (32.5	0.001
	28.1)	- 35.9)	
Gender	23/127	12 / 6Ź	0.95
(male/female;			
n)			
Vertebral	59 (51 - 65)	57 (50 -	0.066
column length		63)	
(cm)		00)	
ASA (I/II/III)	27 / 86 / 25	11/42/8	0.63
Bupivacaine	8 (5 - 8)	8 (5 - 8)	0.83
dose (mg)	0 (0 0)	0 (0 0)	0.00
Duration of	112 (101 -	107 (94 -	0.12
	``	114)	0.12
surgery (min)	117)		0.44
Tourniquet	97 (86 - 108)	90 (82 -	0.11
time		102)	
(in min)			

There was no significant difference regarding the failure of anesthesia induction between the obesity and the non-obesity groups. However, the level of sensory blockage in the induction of anesthesia at the end of the surgery was significantly higher in the obesity group, when compared with the non-obesity group (induction in the NO vs O group = T8; T10 - T6 vs. T9; T11 - T7, p = 0.03).

There were no reports of surgical pain during surgery in both groups, and there was no significant difference in the incidents of tourniquet pain, nausea, and bradycardia between the two groups. Moreover, there was no significant difference in the time taken to feel the first postoperative pain between the two groups (Table 6). **Table 6:** Spinal anesthesia characteristics andassociated adverse events

Variable	Non-obesity	Obesity	P-value
Vallable	group	group	<i>r-</i> value
Anesthetic	94 / 39	58/9	0.014
success vs.	(29.32 %)	(13.43 %)	
failure of			
anesthesia (n/n)	124/6/420	61 / 4	0.14
Success of anesthesia vs.	134 / 6 (4.29 %)	61 / 4 (6.15 %)	0.14
failure of	70)	(0.15 /8)	
induction of			
anesthesia (n/n)			
Sensory blockage	T8 (T10 - T6)		0.03
peak level at		(T11 - T7)	
anesthesia			
	10 (0 10)	10	0 4 4 0
Sensory nerve	12 (9 - 16)	13 (11 - 17)	0.140
blockage peak (min)		(11 - 17)	
Tourniquet pain	16 (10.67 %)	4	0.43
(n, %)		(6.15 %)	0110
Sensory nerve	11 th Thoracic	`12 th ´	0.39
blockade level	vertebra	Thoracic	
upon completion		vertebra	
Hypotension (n,	6 (4.48 %)	0 (6.56 %)	0.51
%) Ephedrine dose	6 (6 - 6.5)	6 (6 - 8.0)	0.32
(mg)	0 (0 - 0.5)	0 (0 - 0.0)	0.52
Mean blood	61 (57 - 66)	60 (55 - 6)	0.43
pressure baseline	- (()	
(mmHg)			
Lowest mean	58 (55 - 61)	57 (55 - 60)	0.34
blood pressure			
(mmHg) Des dus andia (n		0 (40 70 0/)	0.44
Bradycardia (n, %)	7 (7.45 %)	8 (13.79 %)	0.11
Vomiting (n, %)	4 (4.26 %)	2 (3.45 %)	0.64
Nausea (n, %)	8 (8.51 %)	6 (10.34 %)	0.87
Shiver (n, %)	7 (7.45 %)	1 (1.72 %)	0.16
First report of	180	180	0.01
postoperative	(150 - 200)	(160 - 200)	0.01
pain (min)	(100 200)	(100 200)	
Duration of stay in	6 (5 - 8)	7 (5 - 9)	0.22
hospital (days)			

Univariate analyses on predictors of successful anesthesia showed that BMI \ge 30 kg/m², weight and dose of bupivacaine (in milligram) were important predictors for successful anesthesia (Table 7). Multivariate analysis on predictors of successful anesthesia revealed that BMI \ge 30 kg/m² (odds ratio at 95 % CI: 2.83; range: 1.21 -6.49), and dose of bupivacaine (odds ratio at 95 % CI: 2.08; range: 1.61 - 2.67) were independently associated with the success of spinal anesthesia (Table 8).

However, when BMI was incorporated as a continuous variable in the analysis, the parameters were also independently associated with the success of spinal anesthesia (odds ratio at 95% CI: 1.08; range: 1.07 - 1.26).

Variable	Success	Failure of	Odds	P-
	of anesthesia (n = 152)	anesthesia (n = 48)	ratio (95% Cl)	value
Age (in years)	72 (66 - 77)	72 (68 - 79)	0.98 (0.94 -	0.12
Weight (kg)	66 (57 - 77)	58 (54 - 69)	1.02) 1.06 (1.03	0.003
Height (cm)	151 (148 - 155)	150 (147 - 155)	1.09) 1.04 (0.98	0.31
BMI ≥30 kg/m²	58 (38.16 %)	9 (18.75)	1.11) 3.30 (1.18	0.02
BMI (kg/m²)	28.75 (24.8 - 32.7)	26.95 (24.5 - 29.4)	5.43) 1.10 (1.04	0.01
Length of Spinal column	57 (52 - 63)	55 (49 - 63)	1.17) 1.01 (0.97	0.05
(cm) dose of bupivacaine (mg)	8 (7 - 9)	7 (7 - 8)	1.06) 2.1 (1.57	0.01
			2.63)	

 Table 7:
 Univariate analysis of obesity and nonobesity groups for predictors of successful anesthesia

 Table 8: Multivariate analysis of obesity and nonobesity groups for predictors of successful anesthesia

Covariate	Coefficient	Odds ratio (95% Cl)	<i>P-</i> value
Categorical			value
data variable			
$BMI \ge 30$	1.03	2.83 (1.21 -	0.01
kg/m^2		6.49)	0.0.
Dosage of	0.73	2.08 (1.61 -	< 0.01
bupivacaine		2.67)	
(mg)		,	
Constant	- 5.09	0.004	-
value			
Continuous			
data variable			
BMI (kg/m ²)	0.11	1.08 (1.07 -	< 0.01
		1.26)	
Dosage of	0.72	2.12 (1.62 -	< 0.01
bupivacaine		2.71)	
(mg)	7.04	0.000	
Constant	- 7.94	0.002	-
value			

DISCUSSION

This prospective study presents an inclusive comparison of various parameters related to spinal anesthesia between obesity and nonobesity groups. These parameters aid in determining the outcome of the spinal anesthesia based on BMI. In fact, the study was strictly based on the BMI charts which were categorized into two different groups of patients who underwent TKRA.

In this study, no significant difference was observed between the anesthetic and surgical characteristics of the patients in both groups. However, the success rate of anesthesia was considerably higher in the obese patients. Moreover, the post-surgery pain report and the time of first self-void were of lengthier duration in obese patients. A higher BMI of \geq 30 kg/m² was related to the success of anesthesia in addition to the dose of intrathecal bupivacaine. Several conflicting reports on the direct association of obesity with spinal anesthetics are available in the literature [14,15]. Thus, the mechanism spinal blockage is not underlying fullv understood.

However, it has been observed that the volume of CSF plays a vital role in determining the duration and extent of spinal blockage [7]. Another study showed that the volume of CSF is correlated with the peak level of sensory blockage [7,8]. In the present prospective study, characteristic of patients such as age, height, weight, and BMI were regarded as potent factors that influence inter-individual variations. A study has reported a direct relationship between obesity and distribution of sensory blockage [16]. It has been MRN scan that the volume of CSF in obese patients is greatly reduced [9]. However, the mechanism involved in the reduction of volume of CSF in obese patients is not properly understood. The only possible explanation is that the reduction in CSF volume may be because of increased intraabdominal pressure [17].

There were also observations of increased blood flow via the lumbar vertebral plexus [18]. This is due to the blockage of the inferior vena cava caused by increased pressure in the abdomen pressure in obese patients. This may be due to the weight of the abdominal contents and swelling in the extradural vein. Moreover, the extradural vein compresses the cerebrospinal fluid space, resulting in a reduction in its volume in obese patients [19]. This may explain the improvement in effect of anesthesia in obese patients.

Study limitations

Some limitations are associated with this study. In the first place, the doses of bupivacaine

applied to both the groups were not fixed. Secondly, the study was entirely observational and prospective in nature. It is therefore recommended that a single and pre-set dose of bupivacaine be used in subsequent investigations. Thirdly, the injection level should have been made higher in obesity patients. Lastly, the patients used in the study were mostly comprised of aged women between the ages of 60 and 70 years.

CONCLUSION

These results suggest that the period of bupivacaine spinal block is prolonged in obese patients, relative to non-obese patients. Multivariate analysis also show that bupivacaine dose, BMI and obesity are important predictors of spinal anesthesia. It is recommended that a fixed dose of bupivacaine should be used in future studies to confirm the effect of obesity on spinal anesthesia.

DECLARATIONS

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Conflict of interest

No conflict of interest is associated with this study

Authors' contributions

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by them. LS and PL contributed equally to this manuscript. LS and PS did the overall study. LS, PS, FF, LC, SW, RW, WL, BZ and LG analyzed the results and developed the concept. LS, PS, SW, RW, BZ and LG wrote the manuscript.

REFERENCES

- Serpell MG, Fettes PDW, Wildsmith JAW. Pencil point spinal needles and neurological damage. Br J Anaesth2002; 89 (5): 800–801
- 2. Logan MR, McClure JH, Wildsmith JA. Plain bupivacaine: an unpredictable spinal anaesthetic agent. Br J Anaesth 1986; 58: 292–296.

- Corning JL. Classical File', Survey of Anesthesiology. NY Med J 1885; 42: 483-486
- Schnider TW, Minto CF, Bruckert H, Mandema JW. Population pharmacodynamic modeling and covariate detection for central neural blockade. Anesthesiology 1996; 85: 502–512.
- Hocking G, Wildsmith JA. Intrathecal drug spread. Br J Anaesth 2004; 93: 568–578.
- Patel AV, Hildebrand JS, Gapstur SM. Body mass index and all-cause mortality in a large prospective cohort of white and black U.S. Adults. PLoS One 2014; 9: e109153
- Hogan QH, Prost R, Kulier A, Taylor ML, Liu S, Mark L. Magnetic resonance imaging of cerebro spinal fluid volume and the influence of body habitus and abdominal pressure. Anesthesiology 1996; 84:1341–1349.
- Barclay DL, Renegar OJ, Nelson EW Jr. The influence of inferior vena cava compression on the level of spinal anesthesia. Am J Obstet Gynecol 1968; 101: 792–80
- Kim WH, Lee JH, Ko JS, Ahn HJ, Park SK, Gwak MS, et al. The effect of body mass index on spinal anaesthesia for total knee replacement arthroplasty: A doseresponse study. Anaesth Intensive Care 2012; 40: 410– 416.
- 10. www.osp.od.nih.gov/sites/default/files/NIH_Guidelines.ht ml
- Ginosar Y, Mirikatani E, Drover DR, Cohen SE, Riley ET. ED50 and ED95 of intrathecal hyperbaric bupivacaine co-administered with opioids for cesarean delivery. Anesthesiology 2004; 100: 676–682.
- Capogna G, Celleno D, Laudano D, Giunta F. Alkalinization of local anesthetics. Which block, which local anesthetic? RegAnesth1995; 20: 369–377
- Bromage PR, Burfoot MF, Crowell DE, Pettigrew RT. Quality of epidural blockade. I. influence of physical factors. Br J Anaesth 1964; 36: 342–352.
- Taivainen T, Tuominen M, Rosenberg PH. Influence of obesity on the spread of spinal analgesia after injection of plain 0.5% bupivacaine at the L3-4 or L4-5 interspace. Br J Anaesth1990; 64: 542–546.
- 15. Leino KA, Kuusniemi KS, Palve HK, Tiusanen HT, Tuppurainen TT. The effect of body mass index on the spread of spinal block in patients with rheumatoid arthritis. J Anesth 2011; 25: 213–218.
- McCulloch WJ, Littlewood DG. Influence of obesity on spinal analgesia with isobaric 0.5% bupivacaine. Br J Anaesth 1986; 58: 610–614.
- 17. Robinson LS. The collateral circulation following ligation of the inferior vena cava; injection studies in still born infants. Surgery 1949; 25: 329–347
- Blomberg R. The dorso median connective tissue band in the lumbar epidural space of humans: an anatomical study using epiduroscopy in autopsy cases. Anesth Analg 1986; 65: 747–752.
- Carvalho B, Collins J, Drover DR, Atkinson Ralls L, Riley ET. ED (50) and ED (95) of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. Anesthesiology 2011; 114: 529–535.