

## A Prospective Study Determining the Impact of Spinal Anaesthesia on Perioperative Hyperglycemia in Diabetic Patients Undergoing Lower Limb Orthopaedic Surgeries

Sujeet Kumar<sup>1</sup>, Rajesh Kumar Choudhary<sup>2</sup>, Vijayendra Prasad<sup>3</sup>

<sup>1</sup>Senior Resident, Department of Anaesthesia, BMIMS Pawapuri, Nalanda, Bihar, India

<sup>2</sup>Senior Resident, Department of Anaesthesia, BMIMS Pawapuri, Nalanda, Bihar, India

<sup>3</sup>Associate Professor and HOD, BMIMS Pawapuri, Nalanda, Bihar, India

Received: 10-07-2023 Revised: 15-08-2023 / Accepted: 22-09-2023

Corresponding Author: Dr. Rajesh Kumar Choudhary

Conflict of interest: Nil

### Abstract

**Aim:** The aim of the present study was to assess the effect of spinal anaesthesia on perioperative hyperglycemia in diabetic patients undergoing lower limb orthopaedic surgeries and also to state the trend of perioperative hyperglycemia.

**Material & Methods:** A prospective study conducted in the Department of Anaesthesia for the duration of 12 months including 100 patients having either Type I or Type II Diabetes Mellitus controlled on either oral hypoglycaemic drugs or injectable insulin aged 30 to 65 years, belonging to either sex and American Society of Anesthesiologists (ASA) physical status II and III undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia.

**Results:** The mean age, weight, height and duration of anaesthesia was 50.52±12.68 years, 62.8±5.6 kg, 160.8±4.6 cm and 104.6±10.5 respectively. Mean BG value preoperatively or 10min before induction was 111.58±11.084. Then at SI, there was statistically significant decrease in BG value to mean value 106.84±13.57. 30min after SI, mean BG value was 108.72±18.92. This value was lower as compared to the pre-operative BG value, but not statistically significant. 1hr after SI, BG value was 110.60±12.228. This value was also lower as compared to the pre-operative BG value, but not statistically significant. 2hrs after SI, BG value increased to mean value 121.86±18.442. Even, 3 hrs after SI, BG value continued increasing and the mean value became 124.12±16.004. 4 hrs after SI, BG value was maximum with the value being 126.24±15.385. There was statistically significant difference (p=.000). Blood glucose (BG) value decreases till 1hr after surgical incision (SI), and then increases till 4th hr after SI. This change in blood glucose values is statistically significant at SI, 2nd hr after SI, 3rd hr after SI and 4th hr after SI.

**Conclusion:** Spinal anaesthesia blunts surgical stress response and hence, at SI, BG values decrease. But BG values increase at other times in perioperative period owing to the regression of sensory analgesia.

**Keywords:** Spinal Anaesthesia, Perioperative, Hyperglycemia, Diabetic.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

Surgery is considered to be the combination of numerous factors including anaesthesia, medication, tissue trauma, blood loss, and temperature changes. All these factors cause metabolic changes. Together, they produce perioperative adaptive stress response. [1,2,3] Surgery and anaesthesia elicit a stress response that produces marked neurophysiological changes with release of adrenaline, noradrenaline, cortisol, glucagon, and growth hormone. This increase in counter-regulatory hormones and cytokines raises glucose levels and increases insulin resistance. In susceptible patients, this may result in significant hyperglycemia. [4] Surgery is also associated with increased stress response which

results in sympathetic activations and the release of pituitary hormones that accelerate glycogenolysis and gluconeogenesis and result in stress hyperglycaemia. [5]

Stress hyperglycaemia is defined as any blood glucose concentration >7.8 mmol/l (140 mg/dl) without evidence of previous diabetes by the American Diabetes Association and American Association of Clinical Endocrinologists consensus. [6] Stress-induced hyperglycaemia is common and more than 50% occurs in previously non-diabetic patients. [7,8] Perioperative stress-induced hyperglycaemia is reported in 20–40% of patients

undergoing general surgical procedures. [9-11] The magnitude of stress hyperglycaemia relates to the extent of surgical procedures, the technique of anaesthesia, the anatomic location of the surgery, and the types of intraoperative fluids. [12,13] The associated factors for the incidence of stress hyperglycaemia include age, body mass index, duration of surgery, baseline blood glucose level, and intraoperative blood transfusion. [7,14,15] However, a prolonged, high magnitude stress response has harmful effects on metabolism and immune function.

Surgical stress also causes hypothalamic activation of the sympathetic nervous system. This in turn results in increased secretion of catecholamines from the adrenal medulla and release of norepinephrine from presynaptic nerve terminals. High catecholamine levels have catabolic effect. They inhibit insulin release and also enhance glycogenolysis, hepatic glucose production and peripheral insulin resistance, producing hyperglycemia. [16] that also attenuate protein anabolism, wound healing and the activity of the immune defense system after surgery by causing hyperglycemia, thereby increasing perioperative morbidity and mortality. [17-20] There are three main methods for attenuating surgical stress response including neural blockade by epidural or spinal anesthesia, which prevent nociceptive signals from the surgical area from reaching the central nervous system. This inhibitor effect involves both afferent and efferent pathways. Cortisol response is suppressed by neural blockade from T4 to S5. Other methods are intravenous administration of high-dose of strong opioid analgesics which block hypothalamic pituitary gland function and infusion of anabolic hormones such as insulin that causes change in the hormonal status of the patient. [21]

Hence the aim of study was to assess the effect of spinal anaesthesia on perioperative hyperglycemia in diabetic patients undergoing lower limb orthopaedic surgeries and also to state the trend of perioperative hyperglycemia

### Material & Methods

A prospective study conducted in the Department of Anaesthesia, BMIMS Pawapuri, Nalanda, Bihar,

India for the duration of 12 months including 100 patients having either Type I or Type II Diabetes Mellitus controlled on either oral hypoglycaemic drugs or injectable insulin aged 30 to 65 years, belonging to either sex and American Society of Anesthesiologists (ASA) physical status II and III undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia.

### Inclusion Criteria

Only patients having preoperative blood glucose level between 80-120mg/dl were included in the study.

### Methodology

After obtaining approval from the Hospital Ethics Committee and written informed consent from the patients. Patients on recent intravenous or oral steroid therapy within 30 days, although inhaled steroids were permitted, known case of chronic obstructive respiratory disease and asthma on intravenous steroid therapy; having coagulation abnormalities, hypovolemia or hypotension, pre-existing severe bradycardia, or ejection fraction 20% from basal HR) and hypotension (mean atrial pressure 20% from basal BP) were recorded and managed as per the standard protocols. When blood glucose concentrations exceeded 180mg/dL, it was treated as hyperglycaemia as per continuous insulin infusion (CII) protocol. When blood glucose concentrations lowered below 60mg/dl, it was treated as hypoglycaemia as per the standard protocol.

### Statistical Analysis

Statistical testing was conducted with the statistical package for the social science system version (SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Ages, weight, height, duration of anaesthesia and blood glucose (BG) values were reported as mean  $\pm$  standard deviation. Comparison of BG before, during and after surgery was done using Student's t-test. For statistical test,  $P < 0.05$  was taken to indicate a significant difference.

### Results

**Table 1: Demographic characteristics (age, weight, and height) and duration of anaesthesia**

Variables	Mean $\pm$ SD
Age in years	50.52 $\pm$ 12.68
Weight (kg)	62.8 $\pm$ 5.6
Height (cm)	160.8 $\pm$ 4.6
Duration of anaesthesia (min)	104.6 $\pm$ 10.5

The mean age, weight, height and duration of anaesthesia was 50.52 $\pm$ 12.68 years, 62.8 $\pm$ 5.6 kg, 160.8 $\pm$ 4.6 cm and 104.6 $\pm$ 10.5 respectively.

**Table 2: Blood glucose (BG) values (mg/dl)**

Time	Mean±SD
10 min before induction	111.58±11.084
SI	106.84±13.57
30 min after SI	108.72±18.92
1hr after SI	110.60±12.228
2hr after SI	121.86±18.442
3hr after SI	124.12±16.004
4hr after SI	126.24±15.385

Mean BG value preoperatively or 10min before induction was 111.58±11.084. Then at SI, there was statistically significant decrease in BG value to mean value 106.84±13.57. 30min after SI, mean BG value was 108.72±18.92. This value was lower as compared to the pre-operative BG value, but not statistically significant. 1hr after SI, BG value was 110.60±12.228. This value was also lower as

compared to the pre-operative BG value, but not statistically significant. 2hrs after SI, BG value increased to mean value 121.86±18.442. Even, 3 hrs after SI, BG value continued increasing and the mean value became 124.12±16.004. 4 hrs after SI, BG value was maximum with the value being 126.24±15.385. There was statistically significant difference (p=.000).

**Table 3: Trend of blood glucose (BG) values taking BG value at 10min before induction as reference value (mg/dl)**

Time	Mean±SD	P Value
SI	4.736±7.833	.005
30min after SI	.902±12.478	.720
1hr after SI	.928±14.276	.732
2hr after SI	-10.230±22.098	.012
3hr after SI	-12.500±15.076	.000
4hr after SI	-16.634±15.635	.000

Blood glucose (BG) value decreases till 1hr after surgical incision (SI), and then increases till 4th hr after SI. This change in blood glucose values is statistically significant at SI, 2nd hr after SI, 3rd hr after SI and 4th hr after SI.

### Discussion

Spinal anesthesia (SA) is a commonly performed regional anesthesia technique in current practice. Drops of cerebrospinal fluid during SA provide an objective criterion for application field compared to other neuraxial anesthesia procedures. Even so, failure of SA is observed depending different causes (failed lumbar puncture, dose selection, drug solution error, anatomical abnormalities, solution=density, inactive local anesthetic solution and local anesthetic resistance). [22]

The stress of surgery results in increased levels of gluco-regulatory hormones (catecholamines, cortisol, glucagon, and growth hormone) and excessive release of interleukin-6 and interleukin-1. The counter-regulatory response produces alterations in carbohydrate metabolism, including insulin resistance, increased hepatic glucose production, impaired peripheral glucose utilization, and relative insulin deficiency. [17,18] The mean age, weight, height and duration of anaesthesia was 50.52±12.68 years, 62.8±5.6 kg, 160.8±4.6 cm and 104.6±10.5 respectively. Mean BG value preoperatively or 10min before induction was

111.58±11.084. Then at SI, there was statistically significant decrease in BG value to mean value 106.84±13.57. 30 min after SI, mean BG value was 108.72±18.92. This value was lower as compared to the pre-operative BG value, but not statistically significant. 1hr after SI, BG value was 110.60±12.228. This value was also lower as compared to the pre-operative BG value, but not statistically significant. 2hrs after SI, BG value increased to mean value 121.86±18.442. Even, 3 hrs after SI, BG value continued increasing and the mean value became 124.12±16.004. 4 hrs after SI, BG value was maximum with the value being 126.24±15.385. There was statistically significant difference (p=.000). During anesthesia induction and surgery, insulin concentration may decrease due to  $\alpha$  adrenergic inhibition of  $\beta$ -cell secretion. Plasma glucose concentrations increase in perioperative period. In fact, anaesthesia itself results in hyperglycemia, which is then further aggravated by the surgical procedure. The initial increase in plasma glucose after injury is due to activation of glycogenolysis. But later hepatic gluconeogenesis becomes the major factor in liver glucose release because liver glycogen stores are limited. The usual mechanisms that maintain glucose homeostasis are ineffective in the perioperative period and catabolic hormones promote the production of glucose, thereby resulting in hyperglycemia. [5,19,20]

Blood glucose (BG) value decreases till 1hr after surgical incision (SI), and then increases till 4th hr after SI. This change in blood glucose values is statistically significant at SI, 2nd hr after SI, 3rd hr after SI and 4th hr after SI. Poon et al [23] achieved better stress response control by combining epidural anesthesia with general anesthesia. Opioids also suppress the stress response by inhibiting hypothalamic pituitary gland function. In a study of lower abdominal surgery, 50 µg/kg fentanyl suppressed the stress response by reducing growth hormone, cortisol, and glucose concentrations. But, systemic opioids may be insufficient to suppress this response in upper abdominal surgeries. In other study of cholecystectomies using 100 µg/kg fentanyl, the stress response was suppressed; however, patients also required postoperative ventilator support. Most studies of neural blocks have assessed the effect of epidural anesthesia, but, few have addressed spinal anesthesia and stress. Moller et al [24] (1984) compared stress responses following spinal and general anesthesia in abdominal hysterectomies, and reported that spinal anesthesia had a temporary inhibitory effect, which was correlated with the sensorial block level. According to Basem et al [25] (2013) for all patients combined, mean glucose increased slightly from preoperative to incision, substantially from incision to surgery midpoint, and then remained high and fairly stable through emergence, with nondiabetic patients showing a greater increase. For nondiabetics, the mean increase in glucose concentration was more in patients given dexamethasone than placebo. However, there was no dexamethasone effect in diabetics. They assessed this response in patients undergoing non-cardiac surgery under general anaesthesia.

### Conclusion

Spinal anaesthesia blunts surgical stress response and hence, at SI, BG values decrease. But, BG values increase at other times in perioperative period owing to the regression of sensory analgesia.

### References

- Barton RN. The neuroendocrinology of physical injury. *Baillieres Clin Endocrinol Metab* 1987; 1(2): 355-74.
- Chrousos GP. Stressors, stress, and neuroendocrine integration of the adaptive response. The 1997 Hans Selye Memorial Lecture. *Ann NY AcadSci* 1998;851:311-35
- Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2000; 85:109–12.
- Dortch JD, Eck DL, Ladlie B, TerKonda SP. Perioperative glycemic control in plastic surgery: review and discussion of an institutional protocol. *Aesthetic Surgery Journal*. 2016 Jul 1;36(7):821-30.
- Burton D, Nicholson G, Hall G. Endocrine and metabolic response to surgery. *Continu Educ Anaesthesia Crit Care Pain* 2004;4:144–7.
- Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, Inzucchi SE, Ismail-Beigi F, Kirkman MS, Umpierrez GE. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes care*. 2009 Jun;32(6):1119.
- Knaak C, Wollersheim T, Mörgeli R, Spies C, Vorderwülbecke G, Windmann V, Kuenz S, Kurpanik M, Lachmann G. Risk factors of intraoperative dysglycemia in elderly surgical patients. *International Journal of Medical Sciences*. 2019;16(5):665.
- Dave JA, Engel ME, Freercks R, Peter J, May W, Badri M, Van Niekerk L, Levitt NS. Abnormal glucose metabolism in non-diabetic patients presenting with an acute stroke: prospective study and systematic review. *QJM: An International Journal of Medicine*. 2010 Jul 1;103(7):495-503.
- Kwon S, Thompson R, Dellinger P, Yanez D, Farrohi E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. *Annals of surgery*. 2013 Jan;257(1):8.
- Maitra S, Kirtania J, Pal S, Bhattacharjee S, Layek A, Ray S. Intraoperative blood glucose levels in nondiabetic patients undergoing elective major surgery under general anaesthesia receiving different crystalloid solutions for maintenance fluid. *Anesthesia, essays and researches*. 2013 May;7(2):183.
- Shi Z, Tang S, Chen Y, Yang J, Jiang B, Liu X, Zhou X, Pan X, Yang J, Wu J, Hu H. Prevalence of stress hyperglycemia among hepatopancreatobiliary postoperative patients. *International Journal of Clinical and Experimental Medicine*. 2013;6(9):799.
- Desborough JP, Hall GM. Modification of the hormonal and metabolic response to surgery by narcotics and general anaesthesia. *Baillière's clinical anaesthesiology*. 1989 Sep 1;3(2):317-34.
- Saringcarinkul A, Kotrawera K. Plasma glucose level in elective surgical patients administered with 5% dextrose in 0.45% NaCl in comparison with those receiving lactated Ringer's solution. *Medical journal of the Medical Association of Thailand*. 2009 Sep 1;92(9):1178.
- Moorthy V, Sim MA, Liu W, Chew ST, Ti LK. Risk factors and impact of postoperative hyperglycemia in nondiabetic patients after cardiac surgery: A prospective study. *Medicine*. 2019 Jun;98(23).

15. Jämsen E, Nevalainen PI, Eskelinen A, Kalliovalkama J, Moilanen T. Risk factors for perioperative hyperglycemia in primary hip and knee replacements: a prospective observational study of 191 patients with osteoarthritis. *Acta Orthopaedica*. 2015 Mar 4; 86(2):175-82.
16. Molina PE. Neurobiology of the stress response: contribution of the sympathetic nervous system to the neuroimmune axis in traumatic injury. *Shock* 2005;24(1):3-10.
17. Alberti KG. Role of counterregulatory hormones in the catabolic response to stress. *J Clin Invest* 1984; 74(6):2238-48.
18. Weismann C. The metabolic response to stress: an overview and update. *Anesthesiology* 1990; 73:308-27.
19. Singh M. Stress response and anaesthesia. *Indian Journal of Anaesthesia* 2003; 47:427-434.
20. Fereshteh Amiri, Ali Ghomeishi, Seyed Mohammad, Mehdi Aslani, Sholeh Nesioonpour, Sara Adarvishi. Comparison of Surgical Stress Responses During Spinal and General Anesthesia in Curettage Surgery. *Anesth Pain Med* 2014 August; 4(3): e20554.
21. Moller IW, Hjortso E, Krantz T, Wandall E, Kehlet H. The modifying effect of spinal anaesthesia on intra- and postoperative adrenocortical and hyperglycaemic response to surgery. *Acta Anaesthesiol Scand*. 1984;28(3):266-9.
22. Fettes PD, Jansson JR, Wildsmith JA. Failed spinal anaesthesia: mechanisms, management, and prevention. *British journal of anaesthesia*. 2009 Jun 1;102(6):739-48.
23. Poon KS, Chang WK, Chen YC, Chan KH, Lee TY. Evaluation of stress response to surgery under general anesthesia combined with spinal analgesia. *Acta Anaesthesiologica Sinica*. 1995 Jun 1;33(2):85-90.
24. Møller IW, Hjortso E, Krantz T, Wandall E, Kehlet H. The modifying effect of spinal anaesthesia on intra- and postoperative adrenocortical and hyperglycaemic response to surgery. *Acta anaesthesiologica scandinavica*. 1984 Jun;28(3):266-9.
25. Abdelmalak BB, Bonilla AM, Yang D, Chowdary HT, Gottlieb A, Lyden SP, Sessler DI. The hyperglycemic response to major noncardiac surgery and the added effect of steroid administration in patients with and without diabetes. *Anesthesia & Analgesia*. 2013 May 1;116(5):1116-22.