

Intraoperative blood glucose level changes between obese and non-obese non-diabetic patients undergoing general anaesthesia for craniotomy surgeries

Abstract

Background: Surgery causes a considerable metabolic stress in the non-diabetic and more so in a diabetic subject. In non-diabetic subjects the stress response is more in obese population than in non-obese due to the presence of insulin resistance. The severity of surgery as well as the type of anesthesia influences the magnitude of the counter regulatory response. The study was undertaken to observe the effect of stress of surgery in obese and non-obese non-diabetic patients undergoing craniotomy under general anesthesia.

Methods: A Prospective randomized parallel group study was done on a total of 100 patients. They were divided into two groups non-obese patients and obese patients comprising of 50 patients in each group depending on their BMI. If at any time intraoperative CBG was found to be more than or equal to 150mg/dL, calculated dose of human soluble insulin was given as intravenous bolus equal to the amount of CBG/100 units.

Results: 36% patients in obese population developed at least one episode of hyperglycemia (CBG \geq 150 mg/dL) but only 20% in non-obese population did so. Insulin consumption was significantly higher in obese population than in non-obese population to maintain normoglycemia. The relative risk of becoming hyperglycemic in obese compared to non-obese is 1.80 (95% CI 0.92 to 3.51)

Conclusion: We conclude that stress induced hyperglycemic response in patients undergoing craniotomy surgery under general anaesthesia is common in non-diabetic obese non-obese population.

Keywords: blood glucose level, obese, non-obese, non-diabetic, general anaesthesia, craniotomy surgeries

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Introduction

Surgeries are considered to be the combination of multiple factors including tissue damage, fasting, blood-loss, effects of medication and temperature changes from a metabolic point of view.¹ Combinations of all these factors give rise to stress response. The stress response to surgery is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system.² The ultimate effect of these various endocrine changes is increased catabolic activity by increased secretion of catabolic hormones like cortisol and glucagon. The effect of these endocrine and metabolic changes ultimately leads to increased neoglucogenesis and hyperglycemia. So this stress response may be quantified by the incidence of hyperglycemia. The metabolic changes appear to be proportional to the severity of the surgical trauma with plasma cortisol and blood glucose concentration rising slightly during minor surgical procedures but significantly during major operations.³

Advances over the last decade have expanded our understanding of the role of adipocytes in biology, and this has begun to provide mechanistic insights into the causal relationship between obesity and diabetes. It is now clear that adipocytes function as endocrine glands with wide-reaching effects on other organs including the brain. Most likely, the complex orchestration of the relationship

between adipose tissue, Insulin action, and glucose homeostasis evolved out of survival needs to maintain fuel supplies when food was scarce. Now in Western society, obesity with its accompanying morbidities has reached epidemic proportions and the need for scientific advances to identify new therapeutic approaches are very much required.^{4,5}

Hence the present study was undertaken to know the incidence of intraoperative hyperglycemia in terms of capillary blood glucose \geq 150 mg/dl in non-obese and obese non-diabetic patients and requirement of rescue insulin therapy in each group.

Materials and methods

Total of 100 patients were enrolled for this prospective randomized parallel group study after obtaining institutional ethics committee clearance. Fifty patients were considered in each group to obtain normal distributed data. Informed consent was obtained from the subjects or their relatives before enrolment. Patients underwent preoperative evaluation and were checked against the exclusion criteria such as patient refusal, pregnancy, extremes of ages, severe cardiovascular and respiratory diseases in this study. Before taking the patient to operation theatre blood sample was drawn for capillary blood glucose.

In the operating room, venous cannulation was done in a large peripheral vein of hand using a 18G polyurethane intravenous (I.V) cannula and a three way stop cock was attached. Patients received sodium chloride 0.9% solution as maintenance fluid and as per calculated hourly infusion rate according to their body weight. Fluid deficit arising from overnight fasting was corrected by the maintenance fluid. Fifty percent of total deficit was corrected in the first hour and the remaining fifty percent was corrected in next two hours. Blood loss and other plasma losses were approximately calculated from mops and suction drain bottle. These losses up to the transfusion threshold (blood loss >15% of body weight) was replaced volume per volume with succinylated polygelatin (Gelofusine®). All patients were premedicated with 0.2mg glycopyrrolate I.V, 1mg midazolam I.V, ranitidine 50mg I.V, fentanyl 2mcg/kg I.V and ondansetron 4mg I.V five minutes prior to induction of anaesthesia. Following preoxygenation, induction of anaesthesia was done with 2mg/kg propofol intravenously and tracheal intubation facilitated by inj. rocuronium 0.6mg/kg. Anaesthesia was maintained with 66% Nitrous Oxide and 1% Isoflurane in 33% Oxygen, on controlled ventilation. Intravenous fentanyl 0.5mcg/kg at hourly intervals was administered for intraoperative analgesia. Muscle relaxation was maintained with intravenous atracurium 0.5mg/kg followed by 0.1mg/kg at 30 minutes intervals or as clinically judged.

All patients had baseline blood glucose measurement performed immediately prior to the start of intravenous infusion of any fluid. There after CBG levels were measured half hourly till the end of surgery and half an hour after end of surgery. Glucose concentration was determined in fresh capillary blood by reflectance photometry using an Accu-Check® Active blood glucose monitor (Roche Diagnostics, Mannheim, Germany; Unit of measure: mg/dL, measuring range: 10–600mg/dL or 0.56–33.6mmol/L). If at any time during the study, CBG was found to be >150mg/dL, calculated dose of human soluble insulin (= CBG/100units) was given as I.V. bolus.

Results

Data were summarized by descriptive statistics namely mean and standard deviation (SD) for numerical variables and counts and percentages for categorial variables. Numerical variables were compared between groups by student’s independent samples t-test if normally distributed or by Mann-Whitney U test if otherwise. Chi-

Table 2 Capillary blood glucose level in intraoperative and postoperative period with respect to base line value

Group statistics for capillary blood glucose (CBG)					
CBG	Non-obese		Obese		p value
	Mean±SD	Median	Mean ±SD	Median	
CBG pre-operative	91.12±14.873	90.5	91.96±13.723	91	0.77
CBG 0mins	92.72±17.978	89	91.54±13.194	91	0.709
CBG 30mins	94.92±19.391	91	93.10±14.379	92.5	0.583
CBG 60mins	98.12±19.188	94	99.98±17.665	97.5	0.615
CBG 90mins	104.73±23.887	98	110.06±21.197	108	0.246
CBG 120mins	110.41±24.536	108	121.97±22.059	124	0.026
CBG 150mins	117.86±25.575	114.5	132.71±21.474	136	0.009
CBG 180mins	123.26±23.491	121	143.92±19.962	146	0.001
CBG post-operative	132.44±28.854	128	143.92±33.682	140.5	0.070

CBG; Capillary blood glucose

square test or Fischer’s exact test were employed for intergroup comparison of categorical variables. All analysis were two tailed and p<0.05 was considered statistically significant.

It was seen that there was no statistically significant difference between the groups in terms of the demographic characteristics of the patients namely age, sex and ASA physical status distribution and duration of surgery. There was statistically no significant difference in FBS, PPBS and baseline CBG values between two groups. However there is statistically significant difference between weight and BMI as there are patients from two groups- obese and non-obese (Table 1).

CBG values at 0 and 30minutes were comparable in both groups. However mean CBG at 60minutes interval and thereafter at every 30minutes was higher in obese population than in non-obese population. The difference in CBG readings from 120minutes onwards were statistically significant (p<0.05) (Table 2). At 90minutes the non-obese population shows a 7.20% increase in mean CBG while obese population shows 8.72% increase in CBG. The difference between two groups was only 1.52%. But the difference between two groups gradually increases with duration of surgery. At 120minutes CBG increase in non-obese population was 21.17% from baseline while in obese population was 32.63% from baseline and the results were statistically significant. Further, as the duration of surgery increases the difference gradually increases.

Table 1 Difference between weight and BMI as there are patients from two groups-obese and non-obese

Demographic and baseline clinical profile			
Variables	Non-obese (mean±SD)	Obese (mean±SD)	P value
Age(in yrs)	38.52±12.299	42.32±13.227	0.140
Height (in cm)	158.58±10.933	161.49±8.107	0.125
Duration of anaesthesia (min)	201.80±60.210	178.90±62.933	0.066
FBS (mg/dl)	89.42±11.234	90.90±11.151	0.510
PPBS (mg/dl)	111.90±12.534	108.38±13.651	0.182
Weight (in kg)	51.96±11.030	81.10±8.375	0.000
BMI	20.44±3.420	31.04±1.037	0.000

FBS; Fasting blood glucose, PPBS; Post prandial blood glucose

10 out of 50 patients in non-obese population and 18 out of 50 patients in obese population developed at one episode of hyperglycemia (CBG \geq 150mg/dl) during surgery (Figure 1).

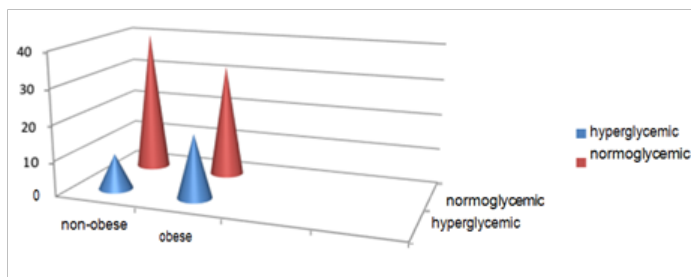


Figure 1 Incidence of hyperglycemia in non-obese and obese population.

This was done by Fisher's exact test 2-tailed p value 0.118 with RR (95% CI) of hyperglycemia(full intraoperative duration) in obese compared to non-obese is 1.80 (0.92 to 3.51).

The average insulin requirement per 30minutes intraoperatively went on increasing in both non-obese and obese population, with increase in obese population more than non-obese population but the results were comparable (Figure 2). The total insulin requirement in non-obese population had a mean of 0.64units and that of obese population had a mean of 1.47units and the difference was statistically significant (p=0.02) (Figure 3). The post operative insulin requirement in non-obese had a mean of 0.38units and that in obese population had a mean of 0.77units and the difference was statistically significant (p= 0.01).

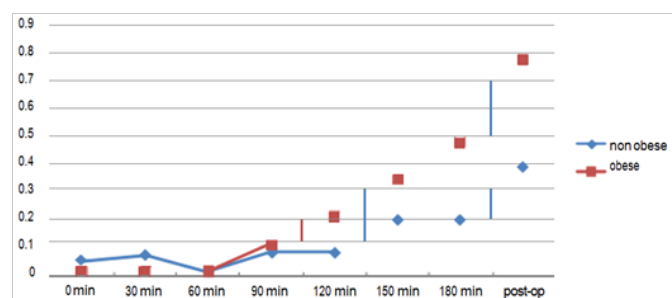


Figure 2 Insulin requirement in units per hour intraoperatively and postoperatively.

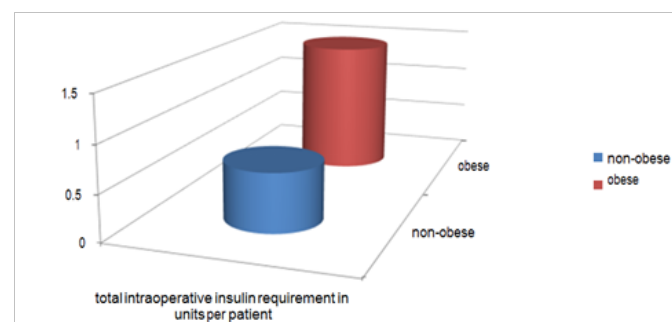


Figure 3 The total insulin requirement in non-obese population.

Discussion

Surgery is a stress response induced by neurohormonal changes that affects glucose metabolism even in non-diabetic subjects. Due to presence of insulin resistance in obese patients the response is more than in non-obese population.

Seshiah V showed that surgery causes a considerable metabolic stress in the non-diabetic and more so in a diabetic subject.⁶ The stress response to surgery is mediated by neuroendocrine system essentially by stimulating the adrenomedullary axis. The neuroendocrine system comes into play to maintain fuel requirements by glycogenolysis and gluconeogenesis through stress hormones like catecholamines, glucagon, cortisol and growth hormone. In a non-diabetic there is enough insulin secretion to utilize the fuel produced by the stress hormones and thus glucose homeostasis is maintained. This compensatory role of insulin is less possible in type 2 diabetic subjects. Rothenberg and Loh-Trivedi documented that surgery elicits a stress response that is directly proportional to the degree of tissue trauma.⁷

A recent study by Adams HA et al suggested that the principal mechanism lies with the elevation of sympathetic tone with a consequent release of cortisol and catecholamines during surgery.⁸ These hormones, in turn, lead to relative insulin hyposecretion, insulin resistance, and increased protein catabolism. Anaesthesia also principally affects glucose metabolism through the modulation of sympathetic tone; however, in vitro evidence exists that insulin secretion is suppressed by inhalational agents with consequent increase in serum glucose level. The sympathoadrenal stimulation as a consequence of surgery and anaesthesia is associated with severe metabolic changes simultaneous with these changes there is marked inhibition of insulin secretion. In this study the capillary blood glucose levels between two groups became significant after 120minutes of anaesthesia.

Baruah MP & Ranabir S,⁹ Mohan V & Deepa R¹⁰ Wasir JS and coworkers¹¹ revealed that Indian and people from other Asian origin are more prone to develop cardiovascular mortality and morbidity with a lower BMI possibly because of the presence of visceral adiposity. According to them increased overall and gender-specific prevalence of the metabolic syndrome (49.2% overall; 41.4% in males; 55.3% in females) was observed by using the definition which included modified cut-off points of non-obligatory, BMI and impaired fasting glucose (>100mg/dl) in addition to other defining parameters.

Results of the study of Smiley DD and associates,¹² Rehman HU and Mohammed K,¹³ Umpierrez GE,¹⁴ Scherpereel PA and Tavernier B¹⁰ showed that the severity of surgery as well as the type of anesthesia influence the magnitude of the counter regulatory response. Circulating catecholamines, cortisol, and glucagon concentration and blood glucose concentration are higher in patients undergoing general anesthesia than regional and epidural anesthesia. Similarly study of Tilak V, and coworkers¹⁵ also revealed the same results. In this study, surgery were done under general anesthesia and showed raised capillary blood glucose level in intraoperative and postoperative period with respect to base line value as shown in Table 2 and changes were statistically significant (p<0.05) after 120minutes of anaesthesia intraoperatively.

This study followed the WHO surgical safety guideline checklist which emphasized a perioperative target blood glucose of 108–180mg/dl.¹⁶ Sebranek JJ and co workers¹⁷ suggested perioperative target blood glucose of 140–180mg/dl and IV Insulin has the advantage of being quickly titratable with a rapid onset of action. The result of this present study was also consistent with that of Desborough JP,¹⁸ Umpierrez GE and co workers¹⁴ and Mizock BA¹⁹ regarding stress response to trauma and surgery which comprises a

number of hormonal changes initiated by neuronal activation of hypothalamic–pituitary–adrenal axis. The overall metabolic effect is catabolism of stored body fuels. In general, the magnitude and duration of the response are proportional to the surgical injury and the development of complications.

Kahn BB and coworkers,⁴ Reaven GM⁵ showed that “Insulin resistance” usually denotes resistance to the effects of Insulin on glucose uptake, metabolism, or storage. Insulin resistance in obesity and type 2 diabetes mellitus (NIDDM) is associated with decreased Insulin-stimulated glucose transport and metabolism in skeletal muscle and adipocytes by altering suppression of hepatic glucose output. Insulin is a critical regulator of almost all aspects of adipocyte biology.

A study by Furnary AP and associates,²⁰ Singh M²¹ showed that general anesthesia may limit the perception of sensations due to injury, but does not abolish the response completely as hypothalamus reacts to the noxious stimuli even in the deeper planes of anesthesia. All the intravenous agents and volatile anesthetics in normal doses have minor influence on the endocrine and metabolic function. Severity of surgery and the type of anesthesia influence the magnitude of the counter regulatory response which is evidenced by increase in circulating catecholamines, cortisol and glucagon concentration and blood glucose as well.

Coursin DB and co workers,¹¹ Desborough JP,¹⁸ Mizock BA¹⁹ said that an increase in blood glucose levels during surgery is expected as part of the surgical stress response. Surgical injury can cause metabolic and hormonal changes resulting in hyperglycemia. The contributing factors for perioperative hyperglycemia are decrease in Insulin secretion and an increase in Insulin resistance; an increase in counter regulatory hormones; an increase in gluconeogenesis and a decrease in glucose utilization. In this study, the mean capillary blood glucose level also significantly increased till the end of the surgery.

But, Hermanides J and coworkers²² stated that high mean glucose is less harmful when glucose variability is low, and patients with identical mean glucose can have different mortality rates with high glucose variability. This study was also showed increasing trend of capillary blood glucose level in intraoperative and postoperative period with respect to base line value as shown in and the changes were significant statistically ($p < 0.05$) intraoperatively after 120minutes of anaesthesia.

Furnary AP & associates²⁰ showed that use of an intravenous Insulin infusion protocol is effective during the intraoperative and immediate postoperative period. In this study the total intraoperative insulin requirement and postoperative insulin requirement was more in obese population than in non-obese population and the difference was statistically significant ($p < 0.050$).

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Conflict of interest

Author declares there is no conflict of interest towards this article.