Journal of Anesthesia & Clinical Research
ISSN: 2155-6148

Sardar et al., J Anesthe Clinic Res 2013, 4:6
DOI: 10.4172/2155-6148.1000329

Research Article Open Access

Stress Response to Total Abdominal Hysterectomy under General Anesthesia in Type 2 Diabetic Subjects

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Abstract

Aims: This study was designed to investigate the hemodynamic alteration and changes of glycemic, cortisol and electrolytes status in total abdominal hysterectomy of type 2 diabetic subjects under general anesthesia.

Subjects and method: Fourty subjects under general anesthesia for total abdominal hysterectomy were recruited and thrice blood samples were collected from each subject, before anesthesia (PT_0), 10 minutes after incision (PT_1) and 10 minutes after extubation (PT_2). Plasma glucose was measured by glucose-oxidase method, serum C-peptide and serum cortisol by chemiluminescence's based ELISA technique (Immulite, USA). Serum electrolytes were measured by Dry Chemistry method (DT-60, USA)

Results: All the subjects were hemodynamically stable during surgery. Plasma glucose increased significantly in PT2. Serum cortisol was significantly higher in PT_1 and PT_2 than PT_0.

Conclusions: Total abdominal hysterectomy under general anesthesia in well controlled type 2 diabetic subjects is accompanied by a hyperglycemic response which results from rise of insulin antagonists like cortisol.

Keywords: Stress response; Anesthesia; Type2 diabetes; Total abdominal hysterectomy

Introduction

Inevitably, diabetic patients presenting for incidental surgery, or surgery related to their disease, will place an increasing burden on anesthetic services. Perioperative morbidity and mortality are greater in diabetic than in nondiabetic patients [1]. This is due to the pathophysiology that is more complicated in diabetic than in nondiabetic subjects. Stress response to surgery and anesthesia, counter regulatory hormones, preoperative fasting states, dehydration and insulin deficiency complicate the situation. These lead to abnormal metabolism of carbohydrate, protein and fat as well as electrolyte imbalance. In response to stress during surgery and anesthesia- the biochemical parameters like stress hormone (cortisol, epinephrine, glucagon and growth hormone), plasma glucose, ketone bodies, blood urea nitrogen, lactate, free alanine, pyruvate, C-peptide and electrolytes being altered [2-4].

Surgery and anesthesia invoke a neuroendocrine stress response with release of counter-regulatory hormones, which results in peripheral insulin resistance, increased hepatic glucose production, impaired insulin secretion, and fat and protein breakdown, with potential hyperglycemia and even ketosis in some cases. The degree of this response depends on the complexity of the surgery and on post-surgical complications. In addition to counter-regulatory hormone excess and relative insulin deficiency, fasting and volume depletion contribute to metabolic decompensation [5].

The stress response leads to secretion of many anabolic and catabolic hormones and if the stress response is prolonged, the continuous hyper metabolic state may result in exhaustion of essential components of the body e.g. glucose, fat, protein, minerals, causing loss of weight, fatigue, decreased resistance, delayed ambulation and increased morbidity and mortality [6].

Studies documented that a number of factors can influence plasma electrolytes during surgery. Among the electrolytes potassium is most important for diabetic subjects due to glucose-potassium co-transport. Insulin and epinephrine stimulate potassium uptake into cells while hyper osmolarity causes translocation of potassium out of cells and into the extracellular potassium for extra cellular space [5].

The present study was designed to explore the metabolic and stress response to lower abdominal surgery under general anesthesia in type 2 diabetic subjects, particular focus on serum glucose, C-peptide, cortisol and electrolytes which may help for better anesthetic management of type 2 diabetic subjects.

Subjects and Methods

Fourty subjects who were admitted in BIRDEM hospital in fit physical condition (ASA Class I & II) and received total abdominal hysterectomy under general anesthesia were studied. Patients taking steroid or analgesics drugs, and obese or malnourish subjects were excluded from the study.

Design of general anesthesia

Thiopental, halothane, fentanyl, vecuronium, nitrous oxide with oxygen.

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Received May 29, 2013; **Accepted** June 24, 2013; **Published** June 26, 2013

Citation: Sardar K, Hafizur Rahman M, Abdur Rashid M, Omar Faruque M, Liaquat Ali, et al. (2013) Stress Response to Total Abdominal Hysterectomy under General Anesthesia in Type 2 Diabetic Subjects. J Anesthe Clinic Res 4: 329. doi:10.4172/2155-6148.1000329

Preparation of the subjects

Patients were recruited 1 week before surgery while undergoing preoperative evaluation and testing in the hospital. The purpose of the study was explained in details to each subject. The evaluation consisted of nursing and anesthesia functional health evaluation, provision of information regarding the surgery and obtaining appropriate laboratory testing. After recruitment into the study, informed written consent and demographic data were obtained. Weight and height of individual were recorded accordingly. All the patients took 7.5 mg medazolam at bed time the night before surgery. Patients were fasted for 6-8 hours prior to surgery and morning dose of antidiabetic therapy was omitted.

Conduction of anesthesia

On arrival at preoperative room an 18 G vasofix intravenous cannula was inserted into right anticubital vein for obtaining blood sample and another one was inserted into the left cephalic vein near to wrist for administration of fluid and other medications. The patients were next brought to the operating room where they underwent anesthesia and surgery. The anesthetic protocol was strictly maintained in all patients and consisted of an intravenous induction using thiopental sodium 5 mg/kg body weight, vecuronium 0.1 mg/kg body weight and fentanyl 1.5 µg/kg body weight. Once intubated with an endotracheal tube, anesthesia was maintained with inhaled O_2/N_2O (1:2) and appropriate dialing of halothane. Anesthesia is maintained with halothane as required to ensure adequate depth of anesthesia assessed by pulse, BP, tearing and sweating. Vecuronium 0.02 mg/kg body weight every 20 minutes and fentanyl 0.5 µg/kg body weight every 30 minutes is continued until 20 minutes before the anticipated end of surgery. Series of pulse rate, systolic and diastolic blood pressure were recorded pre, per and post operatively. Preoperative, preoperative and postoperative values were recorded as P_0, P_1 and P_2. SpO_2, ECG, temperature, sweating and tearing is monitored continuously. Temperature was maintained within normal limit. The patients were received normal saline with appropriate volume as per 4-2-1 rule. After operation the patients were extubated with intravenous Neostigmine 0.05 mg/kg body weight and Atropine 0.02 mg/kg body weight. The time of introduction of anesthesia, incision, end of surgery and extubation was recorded properly.

Sample collection

Three samples (8-10 ml) were collected through right handed cannula with all precautions. The first blood sample was drawn just before anesthesia (PT_0), 2nd sample 10 minutes after incision (PT_1) and 3rd sample 10 minutes after extubation (PT_2). Two ml of blood from each sample was kept in a test tube containing sodium fluoride and potassium oxalate in 1:3 ratios to prevent glycolysis and coagulation and remaining blood was taken in a plain test tube. Both tubes were immediately placed into ice cold water. The samples were centrifuged at 3000 rpm for 15 minutes and serum was stored at -40°C until further analysis.

Plasma glucose was measured by glucose-oxidase method (Randox, UK). Total Cholesterol and TG was measured by enzymatic-colorimetric method. Serum electrolytes were measured by Dry Chemistry method (DT-60, USA). Serum C-peptide and cortisol was measured by chemiluminescence based EIA method (Immulite, USA).

Statistical analysis was performed using SPSS (Statistical Package for Social Science) software for Windows version 10 (SPSS Inc., Chicago, Illinois, USA).

Results

Clinical and Biochemical characteristics of the study subjects

Mean ± SD age and BMI of the studied subjects were 43 ± 7 years and 24.6 ± 3.1 kg/m^2 respectively, systolic and diastolic blood pressure were 140 ± 15 mmHg and 85 ± 10 mmHg respectively; pulse was 84 ± 14 per minute and duration of surgery was 81 ± 15 minutes (Table 1).

The systolic, diastolic blood pressure and pulse rate of pre operative (P_0), per operative (P_1) and post operative period (P_2) values were expressed as mean ± standard deviation were not significantly different (Table 2).

Plasma glucose was significantly higher in PT_2 in comparison to PT_0 (p=0.0001) and PT_1 (p=0.0001). On the other hand the mean ± SD values of serum C-peptide were not significantly different in those time points (Table 3). Serum cortisole (ng/ml) level was significantly (p=0.003) higher in PT_1 (14 ± 6) than PT0 (12 ± 5). The value in PT_2 (33 ± 8) was increased about three times higher than PT_0 (PT_0 vs PT_2, p=0.0001; PT_1 vs PT_2, p=0.0001) (Table 3). The mean ± SD of serum sodium and serum potassium values were almost similar and within normal limit during the surgery (Table 3).

Discussion

Various aspects of anesthesia and surgery cause stress induced hemodynamic, endocrine and metabolic changes in type 2 diabetic

Age (yrs)	43 ± 7
BMI (kg/m^2)	24.6 ± 3.1
Systolic BP (mmHg)	140 ± 15
Diastolic BP (mmHg)	85 ± 10
Pulse (per minute)	84 ± 14
Duration of surgery (minutes)	81 ± 15
TG (mg/dl)	135 (55-310)
Cholesterol (mg/dl)	197 (125-298)
Creatinine (mg/dl)	1.0 ± 0.12
SGPT (U/l)	26 ± 7
Urea (mg/dl)	25 ± 6
Uric acid (mg/dl)	3.6 ± 1.2

Table 1: Clinical and biochemical characteristics of the study subjects (n=40).

Group	Systolic BP (mmHg)	Diastolic BP (mmHg)	Pulse/minute
P_0	140 ± 15	85 ± 10	84 ± 14
P_1	140 ± 27	88 ± 23	82 ± 11
P_2	137 ± 22	85 ± 13	83 ± 13

Results are expressed as M ± SD. P_0=Preoperative, P_1=Peroperative, P_2=Postoperative

Table 2: Perioperative haemodynamic status of the study subjects (n=40).

	PT_0	PT_1	PT_2
Plasma Glucose (mmol/l)	5.9 ± 1.9[a]	6.0 ± 1.8[a]	9.6 ± 2.7[b]
C-peptide (ng/ml)	2.16 ± 0.90	2.0 ± 0.95	2.0 ± 1.24
Cortisol, (ng/ml)	12 ± 5	14 ± 6[b]	33 ± 8[c]
Serum sodium (mmol/l)	137 ± 6	137 ± 6	136 ± 7
Serum potassium (mmol/l)	4.14 ± 0.62	4.10 ± 0.64	4.11 ± 0.66

Results are expressed as M ± SD. PT_0=Preoperative (before anesthesia), PT_1=Peroperative (10 minutes after incision), PT_2=Postoperative (10 minutes after extubation). Values in column with different superscripts are significantly different each other when using student paired 't' test.

Table 3: Perioperative glycemic, insulinemic, serum cortisol and serum electrolytes status of the study subjects (n=40).

subjects due to stimulation of the sympatho-adrenergic system. Appropriate dosing of intravenous and inhalational anesthetic agents can minimize the hemodynamic alteration during surgery. Knutgen reported that in diabetic subjects with severe autonomic neuropathy, hypotensive reactions are seen very often during the operation and also demonstrated that the hemodynamic stability in the perioperative period depends on the severity of autonomic dysfunction [7]. Diabetes with severe autonomic neuropathy has a high risk of blood pressure instability. The subjects in the present study were hemodynamically stable all over the period under common general anesthetic procedure. The subjects had good glycemic control before anesthesia, thus the chance of autonomic neuropathy was less frequent among the subjects as well as adequate depth of anesthesia was maintained. Probably due to this reason they were hemodynamically stable all over the perioperative period.

In the present study plasma glucose level is higher in P_1 but it is significantly higher ($p<0.01$) in the P_2 (Table 3) state. Seshiah showed that surgery causes a considerable metabolic stress in the non-diabetic and more so in a diabetic subject [8]. The stress response to surgery is mediated by neuroendocrine system essentially by stimulating the adreno-medullary 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 [9]. Another study suggests that the principal mechanism lies with the elevation of sympathetic tone with a consequent release of cortisol and catecholamines during surgery [10]. These hormones, in turn, lead to relative insulin hyposecretion, insulin resistance, and increased protein catabolism. Anesthesia also principally effects 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 present study shows that serum C-peptide concentration is not decreased significantly along with the course of anesthesia but there is a tendency to decrease. This suggests that the depth of anesthesia was maintained adequately and thus C-peptide response was not significant. Other factors may be involved in this mechanism and this needs further exploration.

Carli reported that total abdominal hysterectomy with halothane or isoflurane anesthesia leads to two fold reduction in serum cortisol level. But with the onset of surgery, serum cortisol concentration increased rapidly [11]. Mizutani et al. showed that cortisol concentration during medazolam/fentanyl/oxygen/air anesthesia combined with epidural anesthesia in patients undergoing total abdominal hysterectomy and also compared with another group of patients sevoflurane/nitrous oxide/oxygen anesthesia combined with epidural anesthesia [12]. Castillo et al. reported that serum cortisol and other hormonal levels are significantly higher during intravenous anesthesia than during balanced anesthesia [13]. During total abdominal hysterectomy of type 2 diabetic subjects under common general anesthetic procedure in the present study, it has found that serum cortisol concentration increased to some extent 10 minutes after incision and three times increased 10 minutes after extubation (Table 3) which is supported by the published data. The data suggests that the used anesthetic technique did not prevent surgical stress response of type 2 diabetic subjects fully although they were hemodynamically stable.

In conclusion, lower abdominal surgery under general anesthesia in well controlled type 2 diabetic subjects is accompanied by a hyperglycemic response which results from rise of insulin antagonists like cortisol rather than fall of insulin secretion.

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