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Evaluation of the Effect of Perioperative Blood Sugar Level on Surgical Site Infections in Patients Undergoing Total Mastectomy

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Abstract

Background: Stress hyperglycemia during surgeries has been reported to increase the possibility of surgical site infections (SSIs) and worsen the patient's prognosis.
Objectives: The aim of the present study was to evaluate the correlation between perioperative blood sugar level and SSIs in patients undergoing mastectomy.
Methods: In this prospective case-control study, 158 female patients undergoing mastectomy were included with diabetes as an exclusion criterion. Blood glucose levels were measured in 5 phases for each patient.
Results: Among 158 studied patients, 8 (5.5%) developed SSIs. Four patients (2.74%) in the control group and 4 patients (50%) in the case group had hyperglycemia in at least one of the stages. Logistic regression analysis demonstrated associations between SSI development and any blood glucose value of more than 150 mg/dL. It seems that age, medical history, current smoking, tumor characteristics, previous chemoradiotherapy, surgical duration, administration of prophylactic antibiotics, and other surgical factors have not been significantly correlated with SSI.
Conclusions: As hyperglycemia is an easily controllable factor, the control of blood sugar levels during the perioperative period is recommended in patients undergoing breast surgeries to decrease SSI rates.

Keywords: Blood Sugar Level, Mastectomy, Surgical Site Infection

1. Background

Surgical site infections (SSIs) are among the common causes of postoperative morbidity, which also increase mortality, hospital re-admission, and hospitalization duration in patients undergoing surgery (1, 2). Hyperglycemia during hospitalization, especially in traumas and surgeries, occurs approximately in one-third of patients. Acute transient (stress) hyperglycemia during surgeries has been reported to increase the possibility of SSIs and worsen the patient prognosis as well (1, 3-5). Previous studies have reported that regardless of the history of diabetes, higher blood glucose values are associated with higher risks of SSIs and glycemic control has been shown to reduce the risk of SSIs in various types of surgeries (6, 7). However, glycemic control is not well established in postoperative care strategies (8). Although mastectomies, which are the most common oncologic surgeries, are considered clean surgeries and low rates of SSIs are expected in these procedures, SSI rates for mastectomies are quite significant. The growing incidence of resistant bacterial strains in hospital-acquired infections is also a matter of concern in this regard (9-11).

2. Objectives

The aim of the present study was to evaluate the association between perioperative blood glucose levels and SSIs in patients undergoing mastectomy.

3. Methods

3.1. Study Population

In this prospective case-control study, 158 female patients with the diagnosis of breast cancer, who were candidates for a total mastectomy, were included. This investigation was conducted at the general surgery department of Imam Reza Hospital of Mashhad, Khorasan province, Iran, between March 2013 and March 2016. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (code number: 900850). All participants gave full informed written consent prior to inclusion in the study. Patients with a previously-diagnosed diabetes mellitus, a history of antibiotic use within the previous 30 days, under treatment with corticosteroids, and those who were reluctant to participate in the study, were excluded. The demographic data, including age and a full history of medical conditions consisting of hypertension, hyperlipidemia, ischemic heart disease (IHD), previous chemotherapy or radiotherapy, previous breast surgery, other pharmacologic cancer therapies (steroids, etc.), current smoking, alcohol use, and American Society of Anesthesiologists (ASA) score, were provided for each patient. Patients with SSIs were considered as cases and patients, who were infection-free by the 30th postoperative day, were considered as controls.

3.2. Patient Management

Blood glucose levels were measured in 5 phases for each patient. First, before entering the operating room; second, at the time of anesthesia induction; third, during the surgery; fourth, in the recovery room; fifth, 24 hours postoperatively by capillary glucometer. The patients would be categorized in the hyperglycemic group if they had any glucose value of more than 150 mg/dL. Otherwise, the patients were included in the normo-glycemic group. The patients were randomly selected by each surgical team to be operated on. All patients were managed by the standard protocol and the routine surgical procedure. Antibiotic prophylaxis was used. At the end of the surgery, the wound was closed and a drain was placed at the anterior chest wall and axilla as needed. Wound care strategies were done after surgery. After discharge, patients were educated to wash the wound every 24 hours with soap and water and covered it by sterile gauze pads. They were also trained to measure the amount of the drain. Intraoperative variables, including duration of surgery, type of mastectomy (radical vs. modified radical mastectomy), prophylactic and postoperative antibiotics, estimated blood loss, drains used, and lymph node dissection were recorded as well.

Postoperatively, the patients were visited daily in the hospital ward and, then, followed up by phone calls or direct observation in the outpatient clinic for at least 30 days. They were followed with the cancer staging reports, postoperative antibiotics, and other wound complications, such as flap necrosis, dehiscence, hematoma, and seroma formation. An SSI would be diagnosed clinically if any sign of SSI occurred, including pain or tenderness, localized swelling, redness or heat, purulent drainage from the superficial or deep incision, and fever more than 38°C.

3.3. Statistical Analysis

All statistical analyses were performed, using SPSS 19 statistical software. Continuous variables were reported as mean ± SD. Categorical variables were reported as absolute numbers and percentages. Analysis of the data distribution was assessed by the Kolmogorov-Smirnov test. Normally-distributed continuous variables were compared, using the unpaired *t*-test. The Mann-Whitney U test was used for those variables that were not normally distributed. Categorical variables were analyzed, using either the chi-square test or Fisher's exact test. Logistic regression analysis was conducted to obtain adjusted estimates of the odds ratio and to identify the association between blood glucose level and SSIs, using SPSS. Two-sided P values of less than 0.05 were considered to indicate statistical significance for all statistical tests.

4. Results

Among 158 studied patients, 8 (5.5%) developed SSIs. The mean ± SD age of the patients was 48.2 ± 11.9 years, 53.75 ± 11.61 years for cases, and 48.12 ± 11.75 for the control group; 5 patients were current smokers and 8 were addicted to some kinds of opiate. Ninety patients (56.96%) denied the history of medical conditions, 36 had a history of hypertension, 17 had dyslipidemia, and 13 had a positive history of IHD. The detailed characteristics of patients are presented in Table 1.

Among the patients, 5.1% (8 patients) had a history of breast cancer in the contralateral breast, 152 (96.2%) were presented as primary tumors, and 6 (3.8%) had the recurrence of a primary tumor. A total of 39 of 158 patients (25.3%) had preoperative chemoradiotherapy. According to the ASA physical status classification system, 142 of the patients (89.9%) were categorized as ASA I and 16 (10.1%) as ASA II (Table 2).

Prophylactic antibiotics were prescribed for 12 patients (7.6%). All patients took cefazolin and cephalexin postoperatively; 55 of the patients (34.8%) underwent total mastectomy and 103 (65.2%) had modified radical mastectomy. The mean ± SD duration of surgery was 2.92 ± 0.65 hours overall, 3.25 ± 0.65 hours in the case group, and 2.89 ± 0.64 in the control group. In 55 of the patients (34.8%), axillary lymph node dissection (ALND) accompanied mastectomy. No patient underwent sentinel lymph node dissection. Pectoral surgical drains were inserted in 27 patients (17.1%) and combined pectoral and axillary drains were placed in 131 patients (82.9%) (Table 3).

A total of 36 of the patients (22.8%) had at least one blood glucose value over 150 mg/dL and were considered as hyperglycemic; the other 122 patients (77.2%) were included in the normo-glycemic group. Four patients (2.74%) in the

Table 1. Detailed Characteristics of Patients in the Case and Control Groups

	Total No. (%)	Control Group	Case Group	P Value (Fisher's Exact Test)
Smoking	5 (3.16)	5	0	1.000
Addiction	8 (5.06)	6	2	0.057
No previous medical disease	93 (58.9)	87	3	0.278
Hypertension	36 (22.78)	34	2	1.000
Hyperlipidemia	17 (10.76)	14	3	0.054
Ischemic heart disease	13 (8.23)	11	2	0.138

Table 2. Presentation and ASA Classification in the Control and Case Groups

	Total No. (%)	Control Group	Case Group	P Value (Fisher's Exact Test)
Presentation				0.138
Primary tumor	152 (96.2)	145	7	
Recurrence	6 (3.8)	5	1	
Previous chemoradiotherapy	39 (25.3)	35	4	0.191
ASA classification				0.568
ASA I	142 (89.9)	135	7	
ASA II	16 (10.1)	15	1	

Table 3. Type of Surgery and Surgical Drains in the Control and Case Groups

	Total No. (%)	Control Group	Case Group	P Value (Fisher's Exact Test)
Type of surgery				0.051
Total mastectomy	55 (34.8)	55	0	
MRM	103 (65.2)	95	8	
ALND	55 (34.8)	55	0	0.051
Surgical drains				0.352
Pectoral	27 (17.1)	27	0	
Pectoral + axillary	131 (82.9)	119	8	

control group and 4 (50%) in the case group had hyperglycemia during at least one stage. The mean glucose levels in every 5 phases of measurement in the case and control groups are summarized in Table 4.

Table 4. Blood Glucose in the Control and Case Groups[a]

	Total	Control Group	Case Group
BG1	107.91 ± 35.33	106.12 ± 32.72	150.5 ± 58.45
BG2	117.86 ± 43.68	115.5 ± 36.54	179.12 ± 99.00
BG3	120.75 ± 45.54	117.93 ± 38.08	184.88 ± 105.77
BG4	120.97 ± 34.75	119.27 ± 32.45	163.00 ± 53.67
BG5	114.49 ± 39.09	111.94 ± 34.76	145.88 ± 60.35

[a]Values are expressed as mean ± SD.

A comparison of the mean age of cases and controls showed no statistically significant difference between these groups (independent sample *t*-test: P = 0.220). There was no significant difference between the case and control groups considering the history of smoking, addiction, history of hypertension, IHD, and dyslipidemia.

Variables associated with tumor characteristics, including primary tumor versus the recurrence of a primary tumor, ASA score, and previous chemoradiotherapy were similar in the case and groups. There was no significant difference between groups regarding the history of cancer in the contralateral breast. Factors regarding surgical procedure, which included the mean duration of surgery (Mann-Whitney U test; P = 0.183), prescription of prophylactic antibiotics (Fisher's exact test: P = 0.647), type of surgery, ALND, and type of the used surgical drains, did not have significant association with the development of SSI.

Logistic regression analysis demonstrated associations between SSI development and any blood glucose value of more than 150 mg/dL (Table 5).

5. Discussion

Several studies have demonstrated a significant association between perioperative blood glucose level and SSI development in different eras, including cardiovascular and

Table 5. Associations Between SSI Development and any Blood Glucose Value of More Than 150 mg/dL

	Odd Ratio	95% Confidence Interval	P Value
BG1	6.32	1.35 - 29.5	0.019
BG2	5.81	1.35 - 25	0.018
BG3	3.68	0.82 - 16.6	0.089
BG4	5.81	1.35 - 25	0.018
BG5	2.60	0.49 - 13.9	0.26

general surgery, ICU, and trauma patients, regardless of the history of diabetes (8, 12-16). These studies are limited among patients undergoing mastectomy. Vilar-Compte et al. (1) in 2008 indicated that in patients undergoing mastectomy, elevated blood glucose values during surgery and/or the immediate postoperative period correlate with the increased risk of SSI. They showed that any blood glucose of more than 150 mg/dL increases the risk of developing postoperative SSIs (1). In the present study, logistic regression analysis demonstrated an association between SSI development and any blood glucose value of more than 150 mg/dL as well. In Ruiz-Tovar et al.'s study, a cut-off point of 128 mg/dL was established with patients, whose glucose exceeded this having a 4.7-fold higher risk of SSI (6). The analysis of the quantitative correlation between the blood glucose levels and infection rate has also been established in some studies (1, 8, 14). This issue was not concerned in our study. In the current study, age, medical history, current smoking, tumor characteristics, previous chemoradiotherapy, duration of surgery, and other surgical factors, as well as prophylactic antibiotic did not seem to have a significant association with the SSI post-surgically. Vilar-Compte et al. reported different results; age more than 50 and preoperative chemoradiotherapy were risk factors for infection occurrence (1, 11). They explained the role of advanced age with the progressive incidence of medical conditions, especially diabetes and hypertension, in older patients. Advanced age, chemoradiotherapy, and duration of surgery have been mentioned as risk factors for infection in other studies (15, 17). The effect of solo radiotherapy and chemotherapy was not explored in our analysis. Davis reported ASA score of 3 or higher, surgical time of 2 hours or longer, and current smoking status as significant risk factors (18). In our study, we found no association between ASA score and SSI development, although no patient had ASA score of 3 or higher. As shown in previous articles (18), ALND was not a risk factor for SSI occurrence.

The rate of SSIs in this study was 5.8%, which is rational considering the clean base of this kind of surgery (1). Some studies have reported a higher incidence of postoperative wound infections (1, 11), which could not be compared due to the lack of firm criteria for diagnosis or could show a high prevalence of hospital-acquired infections in their settings.

In the present study, hyperglycemia was associated with an increased rate of SSIs in each of the 5 levels of measurement. The results of the timing of hyperglycemia in the literature are inconstant (8, 14, 19). It seems that hyperglycemia during the perioperative period is a consequence of the stress-induced increase in counter-regulatory hormones, which diminishes immune response as in patients with diabetes (1). Regarding the role of diabetes as a risk factor of postoperative infection, 4 types of comparison have been made in the literature:

1) In some studies, the association between hyperglycemia and SSI has been investigated in patients with diabetes (14, 15). Actually, in these studies, the effect of glycemic control in patients with diabetes was concerned; the results showed an increased risk of infection in patients with diabetes, experiencing hyperglycemia in the perioperative period (20).

2) In some other studies, the comparison has been made between patients with newly-diagnosed hyperglycemia and hyperglycemia in patients with a known history of diabetes, which have shown a more adverse outcome in the newly-diagnosed patients (8, 21).

3) Diabetes had also been investigated as an independent risk factor post-surgically in patients with and without SSIs (1).

4) In our study, diabetes was an exclusion criterion in order to investigate the net effect of stress-induced hyperglycemia. No advantage of perioperative antibiotic prophylaxis has (PAP) been reported in mastectomies (22).

Vilar-Compte et al. (1) found no difference in SSI rates or other important outcomes associated with PAP in patients undergoing mastectomy and concluded that not prescribing PAP is permitted in this group of patients. Similarly, in our study, the prescription of prophylactic antibiotics (Fisher's exact test: P = 0.647) did not have a significant association with the development of SSIs. Other wound complications, including necrosis, hematoma, and seroma formation in association with perioperative hyperglycemia have been concerned in other studies (11), but we did not discuss this matter. This study was limited by the low number of participants, which necessitates larger studies in this matter in the future. Obesity was investigated by most of the similar articles, which were not probed in our analysis because of too missing data. Another missing aspect of our study is the microbiology of SSIs, which is recommended to be approached in the future.

5.1. Conclusions

Conclusively, our analysis demonstrated a significant association between perioperative blood glucose level and

SSI development in all 5 steps of measurement. As hyperglycemia is an easily modifiable factor, glycemic control during the perioperative period is recommended in patients undergoing breast surgeries to lower SSI rates.

Footnotes

Authors' Contribution: Project implementation: Dawood Mafinezhad, Reza Taheri, and Seyed Esmaeil Nezhad Hoseini. Idea and project manager: Mohammadreza Motie.

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