

## Original Article

# Prevalence of stress hyperglycemia among hepatopancreatobiliary postoperative patients

Zeya Shi<sup>1,2</sup>, Siyuan Tang<sup>1</sup>, Yuxiang Chen<sup>3</sup>, Jinxu Yang<sup>4</sup>, Bo Jiang<sup>2</sup>, Xiaoming Liu<sup>2</sup>, Xu Zhou<sup>2</sup>, Xiaoji Pan<sup>2</sup>, Juan Yang<sup>2</sup>, Jinshu Wu<sup>2</sup>, Hongjuan Hu<sup>1</sup>, Binbin Ji<sup>1</sup>, Xiaolin Lin<sup>1</sup>, Sanmei Chen<sup>1</sup>, Juan Zhang<sup>2</sup>

<sup>1</sup>School of Nursing Central South University, Changsha 410013, China; <sup>2</sup>People's Hospital of Hunan Province, Changsha 410005, China; <sup>3</sup>Biomedical Engineering Institute Central South University, Changsha 410008, China; <sup>4</sup>Luohe Medical College, Luohe, Henan 462002, China

Received August 10, 2013; Accepted September 13, 2013; Epub September 25, 2013; Published September 30, 2013

**Abstract:** Objective: The aim of this study was to determine the prevalence of stress hyperglycemia and its association with mortality among hepatopancreatobiliary postoperative patients admitted. Methods: Retrospectively analysis was made on 706 cases of the hepatopancreatobiliary postoperative patients from three Grade A hospitals in Hunan province from November 2011 to June 2012, including the incidence and risk factors of patients with stress hyperglycemia. Results: The incidence of stress hyperglycemia of pancreatic postoperative patients was 34.28%. The incidence of pancreatic surgery, simple cholecystectomy and biliary tract and liver surgery in patients with stress hyperglycemia was 63.08%, 20.83% and 32.21%, respectively. Stress hyperglycemia was associated with the first postoperative glucose values, duration of surgery, whether the anemia and the presence or absence of hypoproteinemia ( $P < 0.05$ ), but was no related with sex, weight and previous history ( $P > 0.05$ ). Conclusion: Stress hyperglycemia is common among emergency admissions and these patients have significantly higher mortality rate compared to other patients ( $P = 0.001$ ). Postoperative first blood glucose levels, duration of surgery, whether the anemia and the presence or absence of hypoproteinemia were stress hyperglycemia risk factors for patients.

**Keywords:** Hepatopancreatobiliary postoperative patients, postoperative, stress hyperglycemia, prevalence

## Introduction

Stress-induced hyperglycemia (SHG) is a common problem in patients admitted to the Intensive Care Unit (ICU), even when glucose homeostasis has previously been normal. SHG is that there is no history of diabetes in the stress case, two times fasting blood glucose 7.0 mmol/L or random glucose 11.1 mmol/L [1]. Hyperglycemia is a near-universal finding in diabetic persons suffering catabolic illnesses and may worsen prognosis, although this possibility is controversial. The presence of hyperglycemia is associated with an increased risk of infectious complications in surgical patients, and indirect evidence indicates that maintenance of euglycemia can reduce the risk of infection.

Regarding stress hyperglycemia among patients with myocardial infarction there are a lot reports [2-5].

Lerario et al [6] made a retrospective analysis of 2262 patients with myocardial infarction (IAM) admitted in a cardiologic emergency unit evaluating the prevalence of DM (diabetes) and stress hyperglycemia (SHG). They found that besides 12.1% of subjects were previously referred to be diabetic (men: 10.7% and women: 15.8%), diabetes was effectively diagnosed in 24.8% (M: 22.9%, W: 29.7%) and stress hyperglycemia in 13.6% (M: 14.3%, W: 11.7%) indicating that glycemic alterations were effectively observed in 37.2% of the patients with IAM (M: 37.2%, W: 41.4%). In DM subjects IAM events occurred earlier, total intra-hospital mortality was higher (DM: 20.7%, ND: 13.8%, SHG: 13.4%) and less surgical procedures were performed (ND: 33.8%, DM: 21.7%, SHG: 18.0%) [4].

However, up to now, there is no report about the prevalence of stress hyperglycemia among

## Stress hyperglycemia and hepatopancreatobiliary surgery

**Table 1.** Stress hyperglycemia incidence for the three different groups of surgical patients

Surgery classification	cases	SHG cases	SHG incidence
Pancreatic surgery	65	41	63.08
Simple cholecystectomy	48	10	20.83*
Other biliary tract and liver surgery	593	191	32.21* <sup>▲</sup>
Total	706	242	34.28* <sup>▲</sup>

Note: \*compared with pancreatic surgery,  $P < 0.05$ ; <sup>▲</sup>compared with simple cholecystectomy,  $p > 0.05$ ; <sup>▲</sup>compared with simple cholecystectomy,  $P < 0.05$ .

**Table 2.** Single factor analysis of pancreatic postoperative patients with stress hyperglycemia

		occurred SHG	No occurred SHG	$\chi^2$	P
Gender (cases)	male	109	205	0.062	0.803
	female	133	259		
Previous surgery (cases)	yes	88	206	0.193	0.679
	no	154	303		
Intraoperative blood transfusion (cases)	yes	36	20	24.943	0.000*
	no	205	443		
Anemia (cases)	yes	135	71	126.344	0.000*
	no	107	392		
hypoproteinemia (cases)	yes	146	48	199.572	0.000*
	no	96	415		
Age (years)		56.082±12.167	53.648±13.327	-2.442	0.015*
postoperative first time blood glucose (mmol/L)		10.097±3.193	7.583±1.878	-11.277	0.000*
Weight (KG)		56.173±11.392	56.656±10.491	0.491	0.623
Operation duration time (h)		4.312±2.184	3.386±2.032	-5.595	0.000*
Blood loss amount (ml)		203.206±291.949	124.968±158.086	-3.883	0.000*

Note: \* $P < 0.05$ .

hepatopancreatobiliary postoperative patients. The aim of this study was to determine the prevalence of stress hyperglycemia and its association with mortality among hepatopancreatobiliary postoperative patients admitted to emergency department and identify the risk factors for better control blood sugar and improving patient outcomes. In this study, we conducted a retrospective analysis of 706 cases of hepatopancreatobiliary postoperative patients and explore stress hyperglycemia and its risk factors after hepatopancreatobiliary surgery. The results go as follows.

### Subjects and methods

#### Subjects

In this study, 706 cases of hepatopancreatobiliary postoperative patients were recruited from the three Grade A hospitals in Hunan province in November 2011 to June 2012. Of which 314 cases were male, aged 14 to 86 years, average (54.86±12.98) years old; female 392 cases,

aged 9 to 83 years old, on average (54.18±13.00) years; cholelithiasis, 48 cases, 21 cases of duodenal diverticulum, 44 cases of duodenal papilla cancer, 593 cases of severe cholangitis.

#### Investigation method

The data from 706 cases of hepatopancreatobiliary postoperative patients was gathered, which included age, gender, whether anemia, whether the dysproteinemias, previous surgery history, duration of surgery, the first postoperative glucose and postoperation stress hyperglycemia. Then various data was analyzed by SPSS13.0 software, measurement data was expressed as  $\bar{x} \pm s$ , the numeration data was employed as rate (%),  $\chi^2$  test was used in the comparison between two samples. The logistic multiple factors method was used to analyze effects of various factors on stress hyperglycemia.  $P < 0.05$  was considered statistically significant difference.

## Stress hyperglycemia and hepatopancreatobiliary surgery

**Table 3.** Logistic regression analysis of stress hyperglycemia in hepatopancreatobiliary postoperative patients

Variables	Regression coefficients	P
Constant	-5.138	0.000*
Age	0.009	0.268
First postoperative glucose values	0.356	0.000*
Surgery duration	0.661	0.003*
Blood loss	0.000	0.889
Intraoperative blood transfusion	0.448	0.224
Anemia	0.923	0.000*
Hypoproteinemia	1.887	0.000*

Note: \*P<0.05.

### Results

#### *Stress hyperglycemia incidence in patients with different surgery*

The **Table 1** shows stress hyperglycemia incidence for the three different surgical patients was statistically significant difference (P<0.05).

#### *The univariate analysis of stress hyperglycemia after hepatopancreatobiliary surgery*

Whether stress hyperglycemia occurs in patients after surgery was used as the dependent variable, and other variables as independent variables, and each variable was evaluated, and then univariate analysis was carried out (**Table 2**).

The above **Table 2** shows that among 10 variables, age, anemia, hypoproteinemia, intraoperative blood transfusion, the first postoperative glucose level, duration of surgery and blood loss content were associated with postoperative stress hyperglycemia (P<0.05).

#### *Multivariate logistic regression analysis after hepatopancreatobiliary surgery*

Screened seven single factors were evaluated by logistic regression analysis for pancreatic postoperative patients with stress hyperglycemia (**Table 3**).

The above table shows that regression coefficients of four independent variables of patients first blood glucose levels, duration of surgery, whether the anemia and the presence or absence of hypoproteinemia were statistically significant, indicating that they are stress hyperglycemia dangerous factors. Combined

with the variable reference level establishment and the results of OR and 95% confidence intervals, the first postoperative glucose values increased by 1 mmol/L, the occurrence of stress hyperglycemia risk increased by 1.440 times when other independent variables were fixed, 95% confidence interval was from 1.319 to 1.571; for operation time >2 h, occurrence of stress hyperglycemia risk was as 193.7 times as the surgical time ≤2 h, 95% confidence interval was from 1.250 to

3.002; for anemia, occurrence of stress hyperglycemia risk was as 2.516 times as the normal person, 95% confidence interval was from 1.559 to 4.060; hypoproteinemia risk was the 66.602 times as normal, 95% confidence interval was from 4.036 to 10.800.

### Discussions

The causes of stress hyperglycemia include the presence of excessive counter regulatory hormones (glucagon, growth hormone, catecholamine, and glucocorticoid, either endogenous or exogenous), high circulating or tissue levels of cytokine (in particular tumor necrosis factor- $\alpha$  [TN $\alpha$ ] and interleukin-1). This metabolic milieu results in failure of insulin to suppress hepatic gluconeogenesis despite hyperglycemia; in addition, insulin-mediated glucose uptake into skeletal muscle is impaired. Patients given excessive nutritional support, especially by the intravenous route, are particularly likely to encounter hyperglycemia.

#### *Incidence analysis of stress hyperglycemia for different surgical patients*

The results of this study show that stress hyperglycemia incidence for hepatopancreatobiliary postoperative patients was 34.28%, of which stress hyperglycemia incidence of pancreatic surgery, gallbladder resection and other biliary tract and liver surgery patients was 63.08%, 20.83% and 32.21%, respectively. Compared with other studies, the stress hyperglycemia incidence of pancreatic surgery patients was higher than acute stroke and acute myocardial infarction (42.3% and 50%, respectively) [8, 9]. Which may be associated with that insulin hormone being only one hormone to lower blood

sugar in the body and insulin secreted by pancreatic  $\beta$  cells, reduced insulin secretion by pancreatectomy or tissue damage [10]. However, stress hyperglycemia incidence of simple cholecystectomy and biliary tract and liver surgery patients is relatively low; most of bile duct stones patients had a certain degree of preoperative liver dysfunction, affecting gluconeogenesis and glycogen synthesis and decomposition process. And from 40% to 60% of the insulin clearance was in the liver due to decrease in insulin clearance, hyperinsulinemia, reduced gluconeogenesis and glycogenolysis which led to the lower occurrence of bile duct stones in patients with stress hyperglycemia. In addition, Podell et al [11] also reported that a positive correlation between the blood sugar level and disease severity. In this study, gallbladder resection and biliary tract and liver surgery patients were not severe and stress hyperglycemia incidence was relatively low.

### *Influencing factors of hepatopancreatobiliary postoperative patients with stress hyperglycemia*

This study found that the high first postoperative blood glucose, long duration of surgery, anemia and hypoproteinemia were stress hyperglycemia risk factors, suggesting that for the patients suffering from anemia and hypoproteinemia, long operation, first high postoperative blood sugar were prone to stress hyperglycemia, such patients should be paid attention to. The reasons may be: (1) postoperative patients transferred into the ICU immediately or 2 h, 4 h after elevated blood glucose was most obvious, so the patients with first time high blood sugar were more likely to occur stress hyperglycemia; (2) prolonged operative time enhanced the body's stress response [12], resulting in a serious matter and energy metabolism disorders in the body; (3) anemia patients can produce insulin resistance, studies have shown that recombinant human erythropoietin corrected anemia and may be an useful way to reverse cardiovascular disease and improve IR pathway [13]; (4) hypoproteinemia patients often had reduced protein synthesis, and protein composed of amino acids, many amino acid can be converted into glucose. If the decrease in protein synthesis, synthetic carbohydrate raw material would increase, patient's blood sugar was elevated.

In summary, hepatopancreatobiliary postoperative patients had a higher incidence of stress hyperglycemia (63.08%). The first elevated blood glucose, long duration of surgery; anemia and hypoproteinemia were the risk factors of stress hyperglycemia. Therefore, in order to effectively prevent or control stress hyperglycemia, we should actively correct the preoperative patient's anemia and hypoproteinemia during surgery, as much as possible to shorten the operation time, exactly and timely monitor postoperative blood glucose. If necessary, do a good job in blood management and improve the patient outcomes.

### **Acknowledgements**

We thank to the financial support by Hunan Province Nature Science Foundation (2011-SK3159), Hunan Provincial People's Hospital Renshu Surgery Research and Development Project 2011 (2011068), Research Fund for Doctoral Program of Higher Education (20120162110067) and Changsha Municipal Science and Technology Project (k120704-3~31, k1303034-31).

**Address correspondence to:** Dr. Siyuan Tang, School of Nursing Central South University, Tongzipo Road 172, Changsha, P.R. China. Tel: +86 731 82650235; E-mail: 978746044@qq.com

### **References**

- [1] McCowen KC, Malhotra A and Bistrian BR. Stress induced hyperglycemia. *Crit Care Clin* 2001; 17: 107-24.
- [2] Oswald GA, Smith CC, Betteridge DJ and Yudkin JS. Determinants and importance of stress hyperglycemia in nondiabetic patients with myocardial infarction. *Br Med J (Clin Res Ed)* 1986; 293: 917-22.
- [3] Malmberg K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenstrom A, Wedel H and Welin L; on behalf of the DIGAMI Study Group. A randomised trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction: effects on mortality at 1 year. *J Am Coll Cardiol* 1995; 26: 57-65.
- [4] Capes SE, Hunt D, Malmberg K and Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet* 2000; 355: 773-8.
- [5] Neri Serneri GG, Prisco D, Martini F, Gori AM, Brunelli T, Poggesi L and Rostagno C. Hypergly-

## Stress hyperglycemia and hepatopancreatobiliary surgery

- cemia, immunophlogosis, and myocardial infarction. *Diabetes Care* 2003; 11: 3129-3135.
- [6] Lerario AC, Coretti FM, Oliveira SF, Betti RT, Bastos Mdo S, Ferri Lde A, Garcia RM and Wajchenberg BL. [The prevalence of diabetes and stress hyperglycemia in the acute myocardial infarction patients]. *Arq Bras Endocrinol Metabol* 2008; 52: 465-72.
- [7] Gillespie DL, LaMorte WW, Josephs LG, Schneider T, Floch NR, Menzoian JO. Characteristics of patients at risk for perioperative myocardial infarction after infrainguinal bypass surgery: An exploratory study. *Ann Vasc Surg* 1995; 9: 155-62.
- [8] Rattanataweeboon P, Vilaichone W, Vanna-saeng S. Stress hyperglycemia in patients with sepsis. *J Med Assoc Thai* 2009; 92: S88-94.
- [9] Ishihara M. Acute hyperglycemia in patients with acute myocardial infarction. *Circ J* 2012; 76: 563-71.
- [10] Preitner F, Ibberson M, Franklin I, Binnert C, Pende M, Gjinovci A, Hansotia T, Drucker DJ, Wollheim C, Burcelin R and Thorens B. Glucocretins control insulin secretion at multiple levels as revealed in mice lacking GLP-1 and GIP receptors. *J Clin Invest* 2004; 13: 635-645.
- [11] Podell BK, Ackart DF, Kirk NM, Eck SP, Bell C and Basaraba RJ. Non-diabetic hyperglycemia exacerbates disease severity in *Mycobacterium tuberculosis* infected guinea pigs. *PLoS One* 2012; 7: e46824.
- [12] Vaccaro CA, Vaccarezza H, Rossi GL, Mentz R, Im VM, Quintana GO, Peralta N and Soriano ER. Body surface area: a new predictor factor for conversion and prolonged operative time in laparoscopic colorectal surgery. *Dis Colon Rectum* 2012; 55: 1153-9.
- [13] Jin HM and Pan Y. Angiotensin type-1 receptor blockade with losartan increases insulin sensitivity and improves glucose homeostasis in subjects with type 2 diabetes and nephropathy. *Nephrol Dial Transplant* 2007; 22: 1943-9.