Original Article

Stress Hyperglycemia - An Observational Study

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Abstract

Introduction: There are many studies which imply that poorly controlled blood glucose levels are associated with a higher in-hospital morbidity and mortality, unfavorable post-discharge outcomes and significant excess health care costs. Myocardial infarction (MI) following stress hyperglycemia (post hip fracture) is of common occurrence now-a-days.

Materials & Methods: From February 2013 to Dec 2013, we carried out a prospective observational analysis of 126 consecutive patients with no history of diabetes who suffered hip fractures. Fasting blood glucose (FBG) and glycosylated hemoglobin tests as well as electrocardiography, ultrasonic cardiography, and chest X-ray examinations were performed after admission. All selected hip fracture patients were divided into stress hyperglycemia and non-hyperglycemia groups according to their FBG, and the incidence of AMI was monitored.

Results: Among the patients enrolled, the frequency of stress hyperglycemia was 47.89% (75/157) and that of AMI was 9.31% (15/157), and the occurrence of AMI in the stress hyperglycemia group was higher than in the non-hyperglycemia group (12.46 vs. 6.41%, P, 0.05). In the stress hyperglycemia patients, FBG reached maximum levels at 2-3 days after hip fractures and then decreased gradually. The AMI incidence (62.67%) of the stress hyperglycemia group was highest in the initial 3 days after hip fracture, significantly coinciding with the FBG peak time (P>0.05). In all patients with AMI, non–ST-segment elevation myocardial infarction occurred more often than ST-segment elevation myocardial infarction (62.39% vs 37.61%).

Conclusion: Stress-induced hyperglycemia after hip fracture increased the risk of AMI.

Keywords: Acute myocardial infarction, Hyperglycemia, Stress

INTRODUCTION

Advancement in medical science prolonged the life span all over the world, but on the other hand has also increased the incidence of age related degenerative diseases like hip fractures in elderly persons.[1]

Szulc in 2009 in his study has confirmed a strong association between cardiovascular events and osteoporosis.[2]

Release of stress hormones following any stress full event is a phenomenon mediated through neuroendocrine hypothalamo pituitary-adrenal (HPA) axis which in turn triggers stress hyperglycemia.[3,4]

The American Diabetes Association defined stress hyperglycemia as any blood glucose concentration > (140 mg/dl) without evidence of previous diabetes.

HbA1c has been recommended over oral glucose tolerance test as the preferred diagnostic testing in hospitalized patients with stress hyperglycemia.[5]

Stress hyperglycemia induces a sequence of events like generation of reaction oxygen species, Lipid peroxidation, raised cardiovascular inflammatory markers, which induces death of cardiac muscle.[6,7]

Literature is scanty for assessing the risk of acute myocardial infarction, following hip fractures.[8,9] We conducted a clinical observation of the relationship between stress-induced hyperglycemia and AMI in non-diabetic patients who were hospitalized with acute hip fractures in our hospital.

MATERIALS & METHODS

Patient Selection

We performed an observational study at the TMMC&RC, Moradabad. Consecutive hip fracture patients (n = 126) were selected for the analysis during a one year period. The study protocol was approved by the Hospital ethics committee, and informed consent of all patients was obtained.

Inclusion Criteria

S.N.	Factors included in inclusion criteria
1	Hip fracture at least a day before admission
2	Blood glucose normal
3	No occurrence of deep vein thrombosis
4	Bone density examination

Exclusion Criteria

S.N.	Factors included in exclusion criteria
1	Hip fracture less than 24 hrs
2	Type-1 or 2 DM
3	Occurrence of deep vein thrombosis
4	Thyroid and Liver diseases

All routine biochemical, haematological, pathological and radiological examinations were done as per study/research protocol. In special investigations Electrocardiography, Doppler cardiography, bone mineral density test were done. Appropriate orthopaedic treatment started in the department of orthopaedics and cardiac medications were also continued.

Patients who met our inclusion criteria were recorded fasting blood glucose and ECGs was monitored at fixed time. If any possibility of suggestive of AMI, additional blood samples were drawn to examine creatine kinase (CK), CK-MB. AMI diagnosis criteria met at least two of following: 1) the CK-MB concentration elevated. 2) Persistent ST-T segment changes. 3) precordial chest pain lasting for at least 30 min.

Statistical Analyses

Variables were expressed in mean with ±SD. P value <0.05 was considered statistically significant.

RESULTS

126 patients who full fill our inclusion criteria were included in the study. Mean age of patients was 70.02± 8.60 yrs and 72 were women. Co-morbidity in decreasing order was hypertension (56.02%), (CAD) (47.80%), dyslipidemia (46.17%); triglyceride, (36.13%), Obesity (34.63%), smoking (22.16%) & low levels of HDL cholesterol 19.26%.

S.N.	Co-morbid factors	Percentage of co-morbid factors
1	Hypertension	(56.02%),
2	(CAD)	(47.80%),
3	Dyslipidemia	(46.17%);
4	Triglyceride	(36.13%)
5	Obesity	(34.63%),
6	Smoking	(22.16%).
7	Low level of HDL cholesterol	19.26%.

Stress hyperglycemia was seen in 58 patients. In the stress hyperglycemia group, FBG values reached a maximum 3 days post hip fracture and then started declining. Repeated blood glucose values were significantly different ($P < 0.05$) in hyperglycemic patients exposed to stress, while it was not the case with non-hyperglycemia patients, they did not change ($P > 0.01$).

Acute myocardial infarction in stress hyperglycemia group was significantly higher 20.46% as compared to non-hyperglycemia group 8.88%.

A regression analysis using a conditional method revealed that stress hyperglycemia is an independent risk factor for the development of AMI (relative risk [RR] 2.130 [95% CI 1.431-3.172]. At the end of 3 months follow-up, there were no differences in mortality in patients with versus without stress-induced hyperglycemia.

DISCUSSION

In our study, we found that stress hyperglycemia was present in 58 persons and AMI was diagnosed in 11 in patients after hip fractures. The incidence of AMI in the stress hyperglycemia group was, 20.46%. Comparing these values to study conducted by (10), the incidence of AMI in patients after hip fractures appears higher.

Increased incidence of AMI after hip fracture may be related to osteoporosis.[2,10]

Conditions like osteoporosis and cardiovascular diseases are linked with common factors (a) poor general health status, (b) lifestyle, (c) nutrition, (d) hormone secretion, (e) vitamin D deficiency, (f) C-reactive protein, (g) interleukin-6 etc.[11-15]

We found that particularly stress hyperglycemia plays a vital role, because the incidence of AMI in the stress hyperglycemia group was approximately 12% higher than in the non-hyperglycemia group. In patients with hip fractures, stress hyperglycemia was the sole significant independent risk factor for the development of AMI (95% CI 1.431-3.172). Acute fractures induce "stress response," which in turn leads to insulin resistance, resulting in hyperglycemia and the associated risk factors.[16]

Hyperglycemia induces platelet aggregation and increases plasma adrenaline and nor-adrenaline, which leads to plaque formation, the disturbances in micro-vascular system, and thrombogenesis.[17-27] Our present work indicates that for patients without a history of diabetes, stress-induced hyperglycemia plays a key role in the risk of developing AMI. Our present analysis revealed that most (62.67%) AMIs occurred within the first 3 days after hip fractures, which is in accordance with the literature.[2] In the stress hyperglycemia group, blood glucose peaked at 2-3 days after hip fracture and then declined gradually, indicating a coincidence of AMI with the peak time of FBG. The cause of a more frequent STEMI occurrence in stress-induced hyperglycemia might be that raised glucose levels contribute to platelet activation and thereby enhanced platelet-mediated thrombogenesis[28] which develops into completely occlusive thrombi.

In addition, our study showed stress hyperglycemia ranges of 6.1-9.7 mmol/L after hip fractures for the first time, and we recommend that stress induced hyperglycemias after hip fracture should be identified early.

A limitation of our study was that we did not investigate an effect of inflammatory factors and/or stress hormones on FBG levels, which lead to increased AMI risk. In addition, we did not compare the results of this study with patients suffering from diabetes, and we did not find differences between the stress hyperglycemia and no hyperglycemia groups regarding comorbid disorders and/or drug administrations, e.g. statin against hypertension. Therefore we cannot completely rule out that other factors also contributed to the incidence of myocardial infarctions. Moreover, patients were not accurately diagnosed for diabetes in the longer term, and because blood glucose levels largely fluctuate, we did not specifically treat the hyperglycemias. Up until now, there has been no clear agreement on whether it is necessary to control glucose levels in these patients. In addition, we only show the significance of hyperglycemia on the incidence of AMI during admission; we did not show clinical outcome data at follow up. However, this study underlines the importance of understanding the indication for adopting appropriate methods to identify stress-induced hyperglycemia in correlation with AMI after hip fracture. We recommend that in patients, even without previous diabetes, FBGs and ECGs should be monitored for at least first 7 days after hip fractures. This might be helpful for the endocrinologist, cardiologist, and orthopedic surgeon to timely detect AMIs.

CONCLUSION

We conclude that stress-induced hyperglycemia increased the risk of AMI in patients with hip fractures. Stress induced hyperglycemias after hip fracture should be identified early.

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