Hyperglycemia management in the acute coronary syndrome

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Abstract

Beyond the strong association between diabetes and coronary disease, there is a growing evidence that hyperglycaemia is responsible for adverse outcomes in the Acute Coronary Syndrome.

The better we understand the mechanisms behind this, the better we can treat these patients.

Recently, the American Heart Association published a scientific statement about this problem.

The authors suggest a possible intervention in hyperglycaemia in the patient with Acute Coronary Syndrome.

Key words: hyperglycaemia; Acute Coronary Syndrome.

INTRODUCTION

The presence of high glucose levels, Diabetes Mellitus or both contributes to more than three million deaths by cardiovascular pathology each year.

With the increased incidence of obesity, insulin resistance and metabolic syndrome, it is estimated that the prevalence of diabetes will double by the year 2030. This "diabetes epidemic" will, obviously, be responsible for the increase in cardiovascular pathology attributed to diabetes.[1]

The first step, for an adequate approach to this pathology, will be the correct and timely establishment of the diagnosis of Diabetes Mellitus, based on the referece diagnostic criteria, which will enable the need for action to be defined, in the scope of hyperglycemia (Table I).

Coronary arterial disease is the main cause of morbidity and mortality in patients with Diabetes Mellitus. These patients are at higher risk of acute myocardial infarction or heart failure, presenting a high risk in relation to non-diabetics, of dying after an attack of acute coronary syndrome. These differences may be related to the severity and extent of the coronary disease in diabetics, as well as left ventricular remodeling and the presence of significant ventricular dysrhythmias.[2]

The objective of this work is to provide basic notions in the approach to hyperglycemia, in the patient with Acute Coronary Syndrome, based on the most up-to-date knowledge in this area. Particular reference will be made to the possible physiological mechanisms involved, and the most appropriate course of action will be suggested, according to the current norms.

The problem of hyperglycemia in Acute Coronary Syndrome

The denomination acute coronary syndrome (ACS) includes unstable angina, acute myocardial infartion without ST elevation and acute myocardial infarction with ST elevation.

The evolution of the treatment and early healthcare significantly decreased the mortality rate in these patients, enabling the definition of objectives for stabilizing the residual cardiac function, with a possible improvement in the quality of life.

As the mortality and morbidity rates are being stabilized in patients with ACS, predictive factors of prognosis are sough that can be controlled, in order to positively influence the patient's evolution.

The association between hyperglycemia/diabetes and cardiovascular disease, as well as the growing evidence in relation to lack of glycemic control in ACS and significant morbidity, have led to intense investigation in this area.

Various studies demonstrate that the presence of hyperglycemia is common in the admission of patients with Acute Coronary Syndrome. It is also demonstrated that hyperglycemia in these patients is a strong predictor of mortality and of increased

TABLE I

Diagnosis criteria for Diabetes Mellitus (A.D.A. 2007)

Clinic interpretation of plasmatic glycemia	
Glycemia, mg/dL	**Clinical Interpretation**
Fasting	
< 100	Normal
100-125	Abnormal fasting glycemia /pre-diabetes
≥ 126	Diabetes Mellitus
Glucose tolerance test (2 hours after oral intake of 75 g glucose)	
< 140	Normal
140-199	Reduced tolerance to glucose/ pre diabetes
≥ 200	Diabetes Mellitus
Diagnosis criteria for Diabetes Mellitus[a]	
Diabetes symptoms (polyuria, polydipsia, non explained weight loss, + occasional plasmatic glycemia > 200 mg/dL	
or	
Fasting Glycemia > 126 mg/dL	
or	
Glycemia >200 mg/dL 2 hours after the glucose tolerance test with 75g of oral glucose	

a) One of these three criteria is enough to establish a diagnosis of Diabetes Mellitus. These parameters must be confirmed repeating the test on a subsequent day, in the absence of unequivocal hyperglycemia.

risk of hospital complications, whether in diabetic or non-diabetic patients.[3] However, there are many gaps in the knowledge of the mechanisms involved in the association between the high glucose levels and the unfavorable evolution in patients with acute coronary syndrome.

Some questions are of particular interest in the approach to this theme, for example: there is no current consensus on the glucose levels considered abnormal in the admission of these patients, and the best method for measuring and monitorign glucose levels. Also, the physiopathological process involved in the unfavorable association between hyperglycemia and the evolution of the ACS patient has not been fully defined.[3]

Hyperglycemia: marker of high risk or mediator of adverse effects?

Various physiological studies demonstrate that hyperglycemia may have a direct harmful effect on the myocardium, through a variety of mechanisms; some of these studies reveal a decrease in colateral circulation and increased infarction in the presence of severe hyperglycemia.[4,5]

In diabetic patients, postprandial hyperglycemia is associated with defects of myocardial perfusion, due to the microvascular dysfunction, a contition that improves with glycemic control. [6,7]

It is also demonstrated that high levels of glucose are associated with a prothrombotic condition, as well as an increase in markers of vascular inflammation and products of oxidation, which could induce tissue damage.[8-13]

In the particular case of ACS, hyperglycemia is associated with an increased concentration of free fatty acids, insulin resistance, and dysfunction of the use of glycose by the myocardium; thus, oxygen consumption increases, potentiation of ischemia, as well as the incidence of ventricular dysrhythmias.[14,15] Finally, hyperglycemia proved to be associated with immune response dysfunction (*Figure 1*).
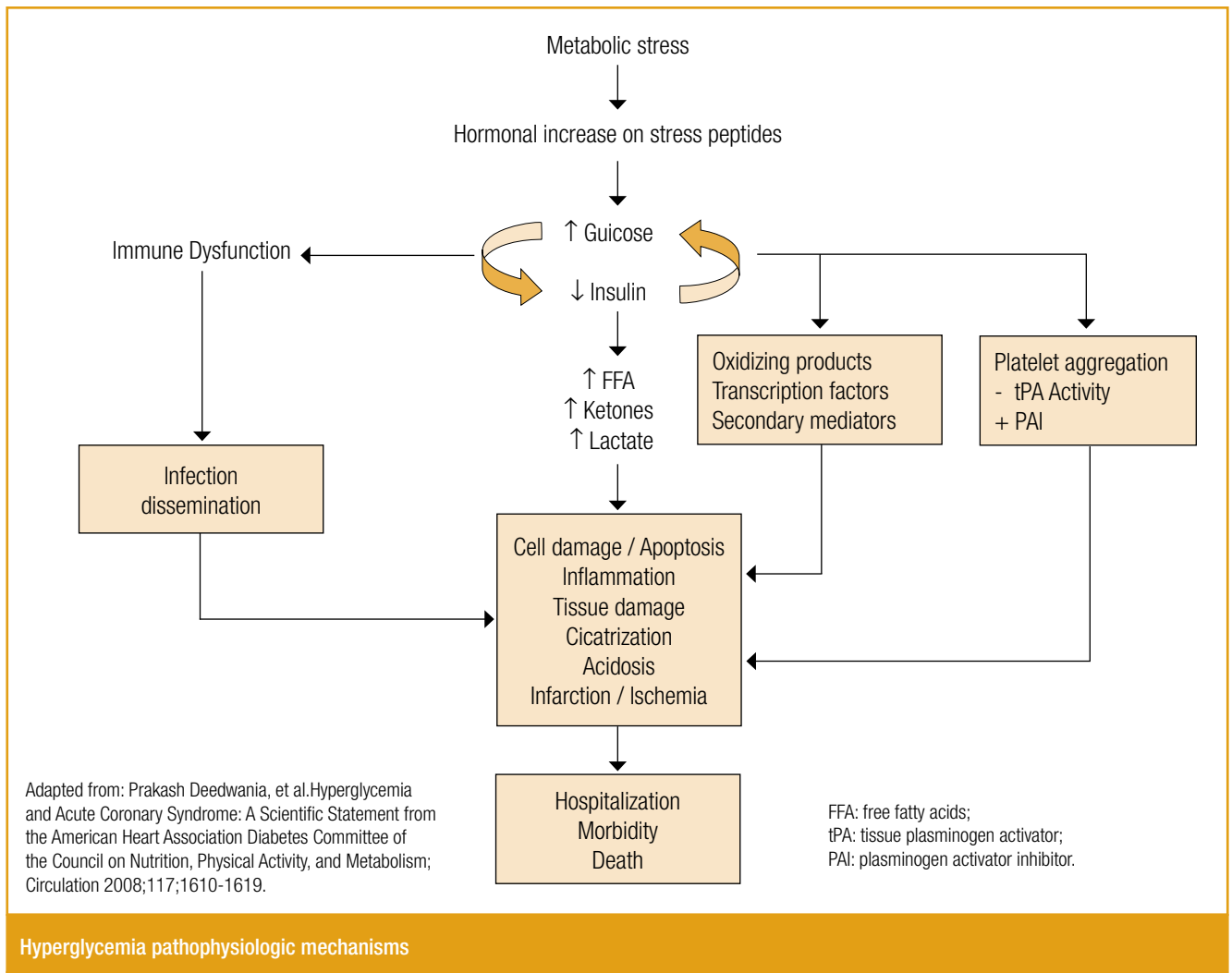
Metabolic stress

Hormonal increase on stress peptides

↑ Guicose
↓ Insulin

Immune Dysfunction

↑ FFA
↑ Ketones
↑ Lactate

Oxidizing products
Transcription factors
Secondary mediators

Platelet aggregation
- tPA Activity
+ PAI

Infection
dissemination

Cell damage / Apoptosis
Inflammation
Tissue damage
Cicatrization
Acidosis
Infarction / Ischemia

Adapted from: Prakash Deedwania, et al.Hyperglycemia
and Acute Coronary Syndrome: A Scientific Statement from
the American Heart Association Diabetes Committee of
the Council on Nutrition, Physical Activity, and Metabolism;
Circulation 2008;117;1610-1619.

Hospitalization
Morbidity
Death

FFA: free fatty acids;
tPA: tissue plasminogen activator;
PAI: plasminogen activator inhibitor.

Hyperglycemia pathophysiologic mechanisms

FIG. 1

Monitoring of glycemic controling during hospitalization of the ACS patient

Despite the usefulness of Hemoglobin A_{1C} (HbA_{1C}) in the outpatient, this parameter has limited useful-ness as a predictive factor of morbidity and mortality in ACS.[16] In reality, there is a simple laboratory test (like HbA_{1C}) that permits adequate monitoring of gly-cemic control during hospitalization. The best form of verifying glycemic control is regular medication with capillary glucose, in different times of the day, and linking it to the patient's nutritional state at a give time.

New technologies, such as continual glucose monitors, are currently being developed, and could simplify the function of monitoring glycemic control in the patient.

Treatment of hyperglycemia: Relationship between glycemic control and evolution of the ACS patient

Although there is little doubt as to the benefits of agressive and intensive control of hyperglycemia in the clincial evolution of the ACS patient, there re-mains, among health professionals, an underlying fear of using insulin therapy when indicated. Effectively, the adequate and timely use of insulin, with the most rigorous control possible of glucose levels, is the best treatment option for these patients.

The most relevant studies in this area demonstrate a significant association between hospitalization time, mortality and/or morbility vs. glycemic control.[17-22]

Faced with this evidence, the use of insulin is re-commended in the presence of hyperglycemia, from

the time the patient is admitted, and with adequate use during the hospitalization, according to the glucose levels in the ACS. Intensive therapy appears to be the most appropriate, with its benefits largely outweighing the risk of side effects (hypoglycemia).

The maximum benefit was found for an average average glucose level <110mg/dL; hyperglycemia should be controlled in patients with or without a history of diabetes (a definition of hyperglycemia is suggested as being a plasma glucose level on admission >140mg/dL). The protocols for use of insulin should be adapted according to the evolution of the glycemic values.

General recommendations for the approach of hyperglycemia in ACS (Adpted from the *American Heart Association, March 2008*)

Glucose level should be a part of the initial laboratory evaluation in all patients with suspected or confirmed ACS.

In patients admitted to an Intensive Care Unit (ICU) with ACS, glucose levels should be monitored closely. Glucose levels > 180mg/dL, regardless of prior diabetes history, should be treated agressively; although an optimum level of treatment has not yet been defined, a value of <110mg/dL is suggested, with an acceptable range of 90 to 140mg/dl.

Insulin, administered as an intravenous infusion, is currently the most effective method for controlling glucose among patients hospitalized in the ICU; care should be taken to avoid hypoglycemia.

Treatment should be instituted as soon as feasible, without compromising the administratation of urgent and therapeutic measures appropriate for ACS.

In patients hospitalized in the non-ICU setting, efforts should be directed at maintaining plasma glucose levels <180mg/dL with subcutaneous insulin regimens.

ACS patients with hyperglycemia, but without prior history of diabetes, should have further evaluation (preferably before hospital discharge) to determine the severity of their metabolic derangements; this evaluation may include fasting glucose and HbA_{1C} assessment and, in some cases, a postdischarge oral glucose tolerance test.

Before discharge, plans for optimal outpatient glucose control should be determined in those patients with established diabetes, newly diagnosed diabetes, or evidence of insuline resistance.

CONCLUSION

Hyperglycemia is very common in the context of ACS, and is often dealth with inappropriately, despite being clearly associated with unfavorable evolution in these patients. The concrete mechanism that measures this unfavorable association remains obscure, and doubts remain as to whether hyperglycemia is a marker or a mediator of high mortality, and the target value to be achieved in the treatment.

Future studies may answer these questions, enabling the care and evolution of ACS patients to be improved. ◼

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