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REVIEW

Treatment of hyperglycemia in patients with acute stroke[☆]



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KEYWORDS

Hyperglycemia;
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Acute stroke;
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Treatment

Abstract The proportion of diabetic patients who are hospitalized for stroke has been increasing in recent years, currently reaching almost a third of all cases of stroke. In addition, about half of patients with acute stroke present hyperglycemia in the first hours of the stroke.

Although hyperglycemia in the acute phase of stroke is associated with a poor prognosis, its treatment is currently a topic of debate. There is no evidence that the administration of intravenous insulin to these patients offers benefits in terms of the evolution of the stroke. New studies in development, such as the SHINE study (Stroke Hyperglycemia Insulin Network Effort), may contribute to clarifying the role of intensive control of glycemia during the acute phase of the stroke.

Ultimately, patients who have presented with stroke should be screened for diabetes.

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PALABRAS CLAVE

Hiperglucemia;
Diabetes;
Ictus agudo;
Insulina;
Diagnóstico;
Tratamiento

Tratamiento de la hiperglucemia en pacientes con ictus agudo

Resumen La proporción de pacientes diabéticos hospitalizados por ictus ha ido aumentando en los últimos años, alcanzando en la actualidad casi un tercio de todos los ictus. Además, prácticamente la mitad de los enfermos con ictus agudo pueden presentar hiperglucemia en las primeras horas del evento.

A pesar de que la hiperglucemia en la fase aguda del ictus se asocia a un peor pronóstico, su tratamiento es en la actualidad motivo de controversia. No existen evidencias de que la administración de insulina por vía intravenosa en estos pacientes proporcione beneficios en la

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evolución del ictus. Nuevos estudios en desarrollo, como el estudio Stroke Hyperglycemia Insulin Network Effort (SHINE), posiblemente contribuyan a aclarar el papel del control intensivo de la glucemia durante la fase aguda del ictus.

Finalmente, los pacientes que han presentado un ictus deberían ser sometidos a un cribado de diabetes.

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A 70-year-old man with a history of cholecystectomy and arterial hypertension for the last 10 years, undergoing treatment with enalapril 20 mg daily and with no known diabetes mellitus, was taken to hospital because when his wife woke him, his speech was incoherent and he lacked strength on the right side of the body. A cranial computed tomography was performed in the emergency department, which revealed an extensive infarction in the territory of the left middle cerebral artery. The laboratory tests on admission showed glycemia levels of 172 mg/dL.

What is the best strategy for treating hyperglycemia in such a patient, and what evidence is there on this subject?

The clinical problem

Stroke is a health problem of considerable importance, whose incidence is growing rapidly worldwide. In Spain, stroke is the main cause of death among women and the second, after ischemic heart disease, for men.¹ According to the most recent data from the Survey on Hospital Morbidity of the National Institute of Statistics, there were 118,308 admissions in 2013 for cerebrovascular disease.² In the last 15 years, the number of patients treated for cerebrovascular disorders in hospitals of the Spanish National Health System has increased more than 40%.³

Moreover, diabetes is a highly and increasingly prevalent disease in the adult population. In Spain alone, more than 5 million people (13.8% of the population) are affected by the disease, almost half of whom are unaware that they have it.⁴

Patients with diabetes have an increased risk of stroke, particularly ischemic.⁵ It is estimated that diabetes increases the risk of stroke 2–3 fold for men and 2–5 fold for women. A recent meta-analysis on more than 775,385 individuals has confirmed that the excess risk of stroke associated with diabetes is significantly greater in women than in men (27% more), regardless of the sex differences in other cardiovascular risk factors.⁶ The risk of ischemic stroke is increased by 3% for every year that a patient has diabetes.⁷

Therefore, the proportion of patients with diabetes who are hospitalized for stroke has been increasing in recent years, and currently represent a third of those hospitalized for stroke.⁸ The prognosis for stroke in patients with diabetes is also poorer. Hospital mortality (including long-term), risk of stroke recurrence, hospital stay and neurological and functional disability at discharge are all greater for patients with diabetes.^{9,10} Therefore, a greater

understanding of the approach to hyperglycemia for patients with acute stroke is essential for providing better care for these patients.

Hyperglycemia in the acute phase of stroke

Hyperglycemia is common in patients with acute stroke. In 2 studies, up to 40% and 50% of patients had hyperglycemia, respectively, many of whom had no history of diabetes mellitus.^{9,11} According to studies that continuously monitored glycemia levels, there are 2 phases of poststroke hyperglycemia: an early phase during the first 8 h, which occurs in 100% of patients with diabetes and in 50% of patients without diabetes; and a second later phase, 48 h after the stroke, which occurs in 78% of patients with diabetes and 27% of patients without diabetes.¹² Therefore, a high glucose concentration during the acute phase of a stroke does not help differentiate between "stress hyperglycemia" and an increase in glycemia levels in patients with prediabetes or established diabetes, whether or not it was previously known.

The stress reaction that induces hyperglycemia is produced by both the activation of hypothalamic–pituitary–adrenal axis, which results in the secretion of high quantities of glucocorticoids (cortisol), and by the activation of the sympathetic autonomic nervous system. The increase in stress hormone levels stimulates the production of glucose by glycogenolysis, gluconeogenesis, proteolysis and lipolysis. The increase in adrenaline also contributes to insulin resistance and hyperinsulinemia.^{13,14} Moreover, the damage to certain areas of the brain, such as the insular and opercular parts of the right hemisphere, promotes hyperglycemia, possibly by disinhibiting the sympathetic flow.¹⁵

The reactive increase in glucose levels is not trivial, but rather, as shown in numerous studies, there is an association between the hyperglycemia of an ischemic stroke at admission and a poorer prognosis. This prognosis is affected by a poorer response to fibrinolytic treatment and a larger volume of the infarction area (measured by magnetic resonance imaging), among other reasons.^{10,11,14,16}

The Glycemia in Acute Stroke (GLIAS) study performed in Spain, which included 476 patients with cerebral infarction of less than 24 h of evolution, determined that the threshold level of capillary glycemia that resulted in a poorer evolution was 155 mg/dL. Patients who reach this level within the first 48 h of the cerebral infarction have a 2.7-fold greater risk of death or dependence at 3 months, regardless of age, the

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