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Diabetes and stroke:

is there an early connection?

The prevalence of type 1 diabetes mellitus (T1DM) represents 0.2% of the general population in Spain. Incidence in children under 14 years of age reaches 18.80 cases per 100,000 inhabitants, making T1DM one of the most frequent chronic conditions in childhood. In children, most patients are diagnosed after the appearance of hyperglycemia symptoms (polyuria, polydipsia, polyphagia, etc.), and diabetic ketoacidosis (DKA) may be present in one third of initial diabetic presentations(1).

In general, **diabetes mellitus (DM) per se increases stroke risk** by 1.5 to 3 times (2). However, neurological complications such as cerebral edema or stroke are very rare in the pediatric population in the absence of severe diabetic ketoacidosis (DKA) or chronically poor glycemic control. Ischemic or hemorrhagic strokes may account for up to 10% of intracranial complications of DKA (1).

Furthermore, DKA may increase the risk of neurovascular injury through mechanisms such as hyperosmolarity, hypoxia, and increased prothrombotic state. Nevertheless, hyperglycemia—even without ketoacidosis—independently increases the risk of pediatric stroke (1).

Our objective is to raise awareness about the relationship between diabetes and pediatric stroke, its mechanisms, and the importance of prevention and early diagnosis.

DIABETES IN CHILDHOOD

T1DM is characterized by destruction of insulin-producing pancreatic beta cells, usually through an immune-mediated mechanism. In type 2 diabetes mellitus (T2DM), insulin resistance is present with relative insulin deficiency (3).

From a pathophysiological perspective, diabetes increases cardiovascular risk through inflammatory effects that alter vascular structure and function, accelerating atherosclerosis and thrombogenesis (2, 3). Vascular complications of diabetes are classified according to vessel size: **microvascular** (small vessels): retina, kidneys, and nerves. **Macrovascular** (large vessels): myocardial infarction, stroke, peripheral arterial disease (3).

Hyperglycemia activates the immune system, triggering the production of proinflammatory proteins which, together with endothelial dysfunction, increase stroke risk by promoting thrombogenic plaque formation (2, 3).

T1DM appears to increase risk more than T2DM, probably due to longer disease duration (4).

PEDIATRIC STROKE

Stroke is a cerebrovascular disease. It may be hemorrhagic (due to rupture of a blood vessel) or ischemic (due to reduced cerebral blood flow, preventing adequate oxygen and nutrient delivery). Up to 85% of strokes are ischemic (4).

Common causes of pediatric arterial ischemic stroke include cerebral arteriopathies (50–80% of cases), congenital or acquired heart disease, hypercoagulable states such as sickle cell disease or thrombophilia, and certain infections (5).

The most frequent causes of hemorrhagic stroke are cerebral vascular anomalies (present in up to 40–90% of cases), including arteriovenous malformations, cavernous malformations, and aneurysms. Less common causes include thrombocytopenia or brain tumors; arterial hypertension is less frequent in children than in adults (5).

In adults, diabetes—along with hypertension and hypercholesterolemia—is a major stroke risk factor (2).

Patients with diabetes are at higher risk for ischemic rather than hemorrhagic strokes, with worse functional outcomes, greater recurrence risk, and higher mortality.[2] The frequency of hemorrhagic stroke is similar in diabetic and non-diabetic patients (around 15%) (4).

Ischemic strokes are classified according to vessel size. In patients with diabetes, small-vessel strokes (such as lacunar infarcts) are more common than large-vessel strokes. Fortunately, children and young patients have greater recovery capacity due to higher neuronal plasticity and fewer comorbidities (2).

DIABETES AND PEDIATRIC STROKE: UNDERSTANDING THE EARLY CONNECTION

In diabetic populations, hyperglycemia and insulin resistance increase stroke risk. Diabetes is also a risk factor for cardiac diseases such as atrial fibrillation, heart failure, and coronary artery disease, which further increase stroke risk. Microalbuminuria and metabolic syndrome increase this risk even more (4).

Chronic hyperglycemia promotes atherosclerosis by inducing endothelial dysfunction and »

DIABETES INCREASES CARDIOVASCULAR RISK THROUGH INFLAMMATORY EFFECTS THAT ALTER THE STRUCTURE AND FUNCTION OF BLOOD VESSELS, ACCELERATING ATHEROSCLEROSIS AND THROMBOGENESIS

» cellular damage, increasing oxidative stress and thrombotic risk through platelet dysfunction and coagulation cascade dysregulation (2, 3). Diabetes alters lipid metabolism and damages blood vessels. Lack of insulin action on adipose tissue leads to free fatty acid release, contributing to vascular injury and increased cardiac and cerebral risk (3, 4).

Hyperglycemia also promotes fatty plaque formation in arteries, narrowing vessels and potentially blocking blood flow. This may lead to clot formation affecting any organ, including the brain. Studies indicate that these vascular changes begin during the first two decades of life in patients with T1DM. Cardiovascular remodeling appears early after diagnosis and is linked to chronic hyperglycemia, endothelial dysfunction, and inflammation (6).

Inflammation attracts immune cells that destabilize plaques and increase rupture risk. Diabetes also alters platelet and coagulation function, increasing the risk of thrombus formation and stroke (3).

Finally, we would like to mention that in cases of diabetic onset presenting with severe ketoacidosis, there may be a risk of neurological deterioration which, although it is usually due to cerebral edema, should also prompt consideration of stroke in the differential diagnosis because of the prothrombotic tendency observed in these children (7).

Clinically, stroke warning signs are usually sudden: limb weakness or numbness, facial droop, severe headache, speech difficulty, or diplopia. However, pediatric stroke may present subtly, with behavioral changes, seizures, or altered consciousness. Clinical suspicion should promptly activate diagnostic and treatment protocols (7).

Among the diagnostic tests for pediatric stroke, brain magnetic resonance imaging is the method of choice to avoid radiation exposure. However, in children younger than 8 years of age, sedation or anesthesia may be necessary, as the patient must remain immobile for a prolonged period to ensure optimal image acquisition. Brain imaging should be performed as soon as possible after the event (5).

In some cases, cerebral arteriovenous malformations responsible for hemorrhagic stroke are not evident on initial imaging studies following an acute hemorrhage. Therefore, when vascular imaging is normal or inconclusive in the acute phase, studies should be repeated 2–8 weeks later (after reabsorption of the intraparenchymal hematoma) (5).

As part of the etiological workup of pediatric stroke, additional complementary tests include echocardiography, electrocardiogram, Holter monitoring, blood tests, and toxicology screening (5).

IN THE DIAGNOSTIC WORKUP OF PEDIATRIC STROKE, BRAIN MAGNETIC RESONANCE IMAGING IS THE METHOD OF CHOICE TO AVOID RADIATION. HOWEVER, IN CHILDREN UNDER 8 YEARS OF AGE, SEDATION OR ANESTHESIA MAY BE REQUIRED

MANAGEMENT AND PREVENTION

Ischemic stroke is potentially treatable in children through thrombolysis, using medications designed to dissolve or reduce the size of the thrombus. In addition, a vascular intervention known as thrombectomy can be performed. This procedure consists of catheterization through the groin or wrist to remove the clot. However, the most important strategy in these patients is the prevention of such events.

To achieve this, several strategies can help identify early those children at risk of stroke. These include monitoring and controlling vascular risk factors, evaluating subclinical markers of vascular damage, periodic clinical risk stratification during follow-up visits, and promoting education and healthy lifestyles from an early age (6).

In children with diabetes, strict control of risk factors such as hyperglycemia, hypertension, dyslipidemia, and microalbuminuria is essential, as they increase the risk of cardiovascular disease and, consequently, stroke (2).

Multiple studies have demonstrated the protective role of insulin during acute stroke, as it has anti-inflammatory and antithrombotic properties that contribute to maintaining blood flow (3).

On the other hand, hyperglycemia has a neurotoxic effect that may increase infarct size or make it more susceptible to hemorrhagic transformation (4). Although reducing chronic hyperglycemia in diabetes appears to provide benefits, rapid glucose lowering during acute stroke does not seem to improve functional outcomes. Treatment of hyperglycemia is recommended to achieve target levels between 140 and 180 mg/dL (2). »

» One of the main protective factors for reducing cardiovascular risk is physical activity, which also helps establish collateral circulation to maintain cerebral blood flow. Performing more than 4 hours of exercise per week in patients with diabetes reduces stroke risk by nearly 50%.[2] However, the most effective strategy to prevent stroke in children with diabetes is achieving optimal blood pressure control (4).

To implement all these strategies effectively, a multidisciplinary team—including pediatricians, nursing staff, endocrinologists, neurologists, and cardiologists—is essential, along with family collaboration, to prevent and detect vascular risk factors at an early stage. D

CONCLUSIONS

In children with diabetes, chronic hyperglycemia and diabetic ketoacidosis are risk factors for stroke development.

Understanding cerebrovascular risk factors in these patients may facilitate early treatment and, in some cases, prevention. Family involvement is fundamental in the care and management of these children.

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