Major sugar substitute found to impair brain blood vessel cell function, posing potential stroke risk

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Erythritol may impair cellular functions essential to maintaining brain blood vessel health, according to researchers at the University of Colorado Boulder. Findings suggest that erythritol increases oxidative stress, disrupts nitric oxide signaling, raises vasoconstrictive peptide production, and diminishes clot-dissolving capacity in human brain microvascular endothelial cells.

Erythritol has become a fixture in the ingredient lists of protein bars, low-calorie beverages, and diabetic-friendly baked goods. Its appeal lies in its sweetness-to-calorie ratio, roughly 60–80% as sweet as sucrose with a tiny fraction of the energy yield, and its negligible effect on blood glucose. Erythritol is also synthesized endogenously from glucose and fructose via the pentose phosphate pathway, leaving baseline levels subject to both dietary and metabolic influences.

Concerns about erythritol's safety have escalated following epidemiological studies linking higher plasma concentrations with increased cardiovascular and cerebrovascular events. Positive associations between circulating erythritol and incidence of heart attack and stroke have been observed in U.S. and European cohorts, independent of known cardiometabolic risk factors. A causal mechanism for the link has remained elusive.

In the study, "The Non-Nutritive Sweetener Erythritol Adversely Affects Brain Microvascular Endothelial Cell Function," published in the *Journal of Applied Physiology*, researchers designed in vitro experiments to test the cellular consequences of erythritol exposure on cerebral endothelial function.

Human cerebral microvascular endothelial cells were cultured and exposed to an amount of erythritol equivalent to consuming a typical beverage. Experimental conditions included five biological replicates per group.

Cellular assays measured oxidative stress, antioxidant protein expression, nitric oxide bioavailability, endothelin production, and fibrinolytic capacity. Capillary electrophoresis immunoassay and ELISA were used to quantify expression of superoxide dismutase-1 (SOD-1), catalase, endothelial nitric oxide synthase (eNOS), phosphorylated eNOS, endothelin-1 (ET-1), and tissue-type plasminogen activator (t-PA).

Cells exposed to erythritol exhibited a substantial increase in oxidative stress. Reactive oxygen species levels rose by approximately 75% relative to untreated controls. Antioxidant defense markers were also elevated, with SOD-1 expression increasing by approximately 45% and catalase by approximately 25%.

Nitric oxide production declined by nearly 20% in response to erythritol. Although total eNOS expression remained unchanged, phosphorylation at the Ser1177 site, which is associated with enzymatic activation, fell by approximately 33%. In contrast, phosphorylation at the inhibitory Thr495 site increased by approximately 39%.

In another test, t-PA release in response to thrombin stimulation was blunted in erythritol-treated cells, indicating reduced fibrinolytic responsiveness.

The researchers conclude that erythritol exposure disrupts multiple mechanisms vital to maintaining cerebral endothelial health. Although results are limited to acute in vitro conditions, the findings align with prior epidemiological associations between erythritol and elevated stroke risk.

The authors recommend further investigation using long-term and in vivo models, citing the need for clinical studies to clarify whether repeated dietary exposure to erythritol carries cerebrovascular consequences.

Publication details

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