In Vitro Evidence that Sulfite and Thiosulfate Induce Brain Bioenergetic Dysfunction in Rat Brain

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INTRODUCTION: Sulfite oxidase (SO) deficiency is caused by the isolated deficiency of the enzyme SO itself or by a deficiency in the synthetic pathway of its molybdenum cofactor. These disorders are biochemically characterized by tissue accumulation and high urinary excretion of sulfite, thiosulfate and S-sulfocysteine. Clinically, affected patients present encephalopathy and neonatal seizures, whose pathophysiology is poorly known. In the present study, we investigated the in vitro effects of sulfite and thiosulfate on important parameters of energy metabolism in rat brain. MATERIAL AND METHODS: CO₂ production from glucose, the activities of the respiratory chain complexes I to IV, creatine kinase and Na⁺,K⁺-ATPase were determined in the presence or absence of sulfite or thiosulfate (1-500 µM) in cerebral cortex of young rats. RESULTS AND DISCUSSION: It was observed that sulfite inhibited complex IV of the respiratory chain, indicating that this compound impairs the electron transfer flow, whereas thiosulfate did not affect any of the complex activities. Moreover, sulfite and thiosulfate inhibited the activity of total creatine kinase (tCK) and its mitochondrial and cytosolic isoforms, suggesting that these compounds impair brain cellular energy buffering and transfer. Furthermore, melatonin, trolox (soluble analogue of α-tocopherol), glutathione and the nitric oxide inhibitor Nω-nitro-L-arginine methyl ester attenuated or fully prevented the inhibition of tCK induced by sulfite and thiosulfate, suggesting the involvement of reactive oxygen and nitrogen species in these effects. In contrast, CO₂ production from glucose and synaptic Na⁺,K⁺-ATPase activity were not altered by sulfite and thiosulfate. CONCLUSION: It may be presumed that impairment of energy production and transfer induced by sulfite and thiosulfate is involved in the neurological damage found in patients affected by SO deficiency.

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