

α -硫辛酸对缺氧应激肝癌细胞线粒体呼吸率和产能代谢的影响

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通过实验阐明抗氧化剂 α -硫辛酸(alpha-lipoic acid, α -LA)对肝癌细胞内活性氧具清除作用,并发现其对肝癌细胞和正常肝细胞增殖有不同作用影响。在缺氧条件下,研究使用抗氧化剂干预对肝癌细胞和正常肝细胞缺氧耐受性、线粒体活性和产能代谢的影响及差异。以SMMC-7721人肝癌细胞和L02正常肝细胞作为研究对象,在 α -硫辛酸干预条件下检测细胞生长曲线和细胞内ROS;分别在单纯缺氧及加 α -硫辛酸缺氧条件下,检测细胞存活率、细胞内ROS、细胞耗氧率、细胞生成ATP和癌基因c-myc mRNA的表达。实验结果说明:缺氧情况下,肝癌细胞通过增加糖酵解途径的产能方式诱导ATP能量代偿能力提高。使用抗氧化剂 α -硫辛酸干预清除细胞内过剩ROS,能降低肝癌细胞线粒体呼吸率,并能通过下调c-myc 表达抑制肝癌细胞的增殖及降低其缺氧耐受性。

The Effect of α -Lipoic Acid on Mitochondrial Respiratory Rate and Energy Metabolism in Hepatoma Cells in Response to Hypoxia Stress

This study investigated the ability of the antioxidant, alpha-lipoic acid, to scavenge the reactive oxygen species (ROS) in hepatoma cells, and assessed how the effects of alpha-lipoic acid on cell proliferation differed between SMMC-7721 human hepatoma cells and L02 immortalized normal liver cells. The effect of the antioxidant on cell survival ratio, mitochondrial activity and energy metabolism was explored further under the condition of hypoxia. Effects of the antioxidant for cancer cells and normal cells were compared to see if they differed. Cell growth and the level of ROS in cells were analysed in response to different concentrations of alpha-lipoic acid treatment. The survival ratio, ROS level in cells, consumption of O₂, generation of ATP and mRNA levels of c-myc oncogene were each detected under hypoxic condition, respectively in response to 5 mmol/L alpha-lipoic acid. The results suggest that hepatoma cells compensatively increase ATP generation though increasing the glycolysis pathway in response to hypoxia, the antioxidant, alpha-lipoic acid, scavenge the excess ROS in cells and decrease the mitochondria respiratory rate in hepatoma cells, and alpha-lipoic acid inhibit the proliferation of hepatoma cells and decrease their ability to endure hypoxia by downregulating the expression of c-myc.

关键词

Alpha-硫辛酸(Alpha-lipoic acid); 缺氧(Hypoxia); 糖酵解(Glycolysis); 肝癌(Hepatoma); 活性氧(Reactive oxygen species)