3-Bromopyruvate antagonizes effects of lactate and pyruvate, synergizes with citrate and exerts novel anti-glioma effects.

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Abstract
Oxidative stress-energy depletion therapy using oxidative stress induced by D-amino acid oxidase (DAO) and energy depletion induced by 3-bromopyruvate (3BP) was reported recently (El Sayed et al., Cancer Gene Ther., 19, 1-18, 2012). Even in the presence of oxygen, cancer cells oxidize glucose preferentially to produce lactate (Warburg effect) which seems vital for cancer microenvironment and progression. 3BP is a closely related structure to lactate and pyruvate and may antagonize their effects as a novel mechanism of its action. Pyruvate exerts a potent H2O2 scavenging effect to exogenous H2O2(2), while lactate had no scavenging effect. 3BP induced H2O2(2) production. Pyruvate protected against H2O2(2)-induced C6 glioma cell death, 3BP-induced C6 glioma cell death but not against DAO/D-serine-induced cell death, while lactate had no protecting effect. Lactate and pyruvate protected against 3BP-induced C6 glioma cell death and energy depletion which were overcome with higher doses of 3BP. Lactate and pyruvate enhanced migratory power of C6 glioma cells. 3BP induced a caspase-3-dependent cell death in C6 glioma. 3BP was powerful in decreasing viability of human glioblastoma multiforme cells using 3BP with citrate depleted ATP, clonogenic power and migratory power of C6 glioma cells. 3BP induced a caspase-3-dependent cell death in C6 glioma cells and spheroids. Glycolysis subjected to double inhibition exerted novel anti-glioma effects.

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