AMINOACETONE INDUCES COPPER-MEDIATED OXIDATIVE DAMAGE TO INSULIN-PRODUCING BETA CELLS

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Aminoacetone (AA) has been implicated as a contributing source of methylglyoxal (MG) in *diabetes mellitus*, together with triose phosphates and acetone. Considering that: (i) MG has been reported to trigger apoptosis and/or necrosis in insulin-producing cells (RINm5f), (ii) AA can cause ROS-mediated oxidative injury to these cells, as we have previously shown, (iii) iron and copper overload occur in diabetes, here we study the contribution of copper and iron ions to the AA-driven damage to RINm5f cells. Cytotoxicity of AA (0.5-2.0 mM)/metal was monitored by the MTT assay at 24h after treatment. Surprisingly, iron addition (30-960 µM) did not cause noticeable damage, whereas copper (50-300 µM) significantly increased cell death (70% with 1 mM/0.3 mM Cu^{2+}). SOD (50 U/mL) addition provided partial protection, whereas catalase (5.0 µM) allowed total protection to the RINm5f cells challenged with AA/Cu^{2+}. Addition of *N*-acetylcysteine (5.0 mM) resulted in increased cell death, probably due to recycling of Cu^{2+}/Cu^{1+} by the thiol and hydroxyl radical generation, through reaction of H_2O_2 with cuprous ions. Although the physiological concentrations of AA in tissues of diabetics are unknown, the model studies described here reinforce the hypothesis that overload of AA and "free" transition metals may contribute to pancreatic ß-cell death in diabetics and point to new therapeutic alternatives to diabetes.

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