REACTIVE SPECIES PRODUCTION INDUCED BY METHYLMERCURY IN ENDOTHELIAL CELLS IN VITRO

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Epidemiologic studies suggest that exposure to methylmercury (MeHg), a widespread environmental contaminant, is linked with increased risk of cardiovascular disease, such as hypertension and atherosclerosis. Oxidative stress represents a main cause of the endothelial dysfunction observed in cardiovascular disease. Despite the studies showing that MeHg induces oxidative damage in several organs and systems, the effects and mechanisms of action of this toxicant in endothelial cells are unknown. The present study aimed to evaluate the effects of MeHg on cultured endothelial cells, focusing on possible mechanisms involved in MeHg-induced endothelial dysfunction. Bovine aortic endothelial cells (BAECs) were exposed to MeHg up to 24h. Reactive species generation (dichlorofluorescein and dihydroethidium assays), NADH dehydrogenase and glutathione peroxidase activities, nitric oxide (NO) generation and levels of glutathione (GSH) were measured. MeHg significantly induced reactive species generation after 1 hour, although this event was more pronounced after 6 hours. The levels of superoxide anion increased only after 6 hours and the pre-treatment with apocynin (an NADPH oxidase inhibitor) completely prevented this phenomenon. The NADH dehydrogenase activity was not modified after 6 hours of treatment. In addition, the nitric oxide (NO) production was enhanced after MeHg treatment. The levels of GSH decreased after 6 hours of treatment, but the activity of glutathione peroxidase decreased only after 24h. Taken together, our results show that MeHg promotes the generation of reactive species in endothelial cells, especially superoxide and NO. Moreover, we showed that NADPH oxidase is important for the MeHg-induced superoxide production in this cell type. Superoxide and NO react to form peroxynitrite, a highly reactive specie, which can promote endothelial oxidative damage. We hypothesized that the oxidative effects of MeHg could be responsible, at least in part, for MeHg induced endothelial dysfunction, which is involved in cardiovascular diseases.

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