Cadmium Exposure Induces Prostaglandin E₂ Release from Cultured Human Astrocytes through Cyclooxygenase 2 Up-regulation

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Background: Cadmium is linked to the pathogenesis of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. After ingestion or inhalation, cadmium is able to impair the blood brain barrier and enters the brain. Prostaglandins E₂ (PGE₂) is a major proinflammatory mediator synthesized by cyclooxygenase-2 (COX-2) and microsomal prostaglandin E synthase-1 (mPGES-1). The increment in PGE₂ production could stimulate amyloid protein synthesis, leading to Alzheimer's disease. In vitro experiments showed that cadmium is toxic to neurons and astrocytes via oxidative stress. Cadmium stimulates PGE₂ production in macrophages and osteoblasts. A previous study in rat C6 glioma cells showed that cadmium induced expression of cyclooxygenase-2 (COX-2). Moreover, cadmium also increased IL-6 and IL-8 production in human astrocytes.

Method: The upregulation of cytokines could trigger the production of PGE₂. U-87 MG human astrocytoma cells was exposed to cadmium chloride (CdCl₂) and expression of COX-2 and mPGES-1 mRNA was measured by real time PCR. PGE₂ release was measured by ELISAs.

Results: CdCl₂ at 1 µM upregulated COX-2 mRNA expression by 5 folds compared to untreated cells at 3 and 6 hours post-exposure while 10 µM CdCl₂ by 7 and 13 folds at 3 and 6 hours, respectively. At 6 hours, levels of PGE₂ in culture supernatant in cadmium-treated cells were 3 folds higher than untreated cells. Pretreatment with celecoxib, a specific COX-2 inhibitor, reduced PGE₂ levels similar to untreated cells.

Conclusion: Cadmium mediates PGE₂ production in astrocytes through the upregulation of COX-2 expression. The inhibition of COX2 could have beneficial effects on cadmium-induced neuroinflammation.