Cadmium Exposure Induces Prostaglandin E\textsubscript{2} 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 E\textsubscript{2} (PGE\textsubscript{2}) is a major proinflammatory mediator synthesized by cyclooxygenase-2 (COX-2) and microsomal prostaglandin E synthase-1 (mPGES-1). The increment in PGE\textsubscript{2} 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 PGE\textsubscript{2} 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 PGE\textsubscript{2}. U-87 MG human astrocytoma cells was exposed to cadmium chloride (CdCl\textsubscript{2}) and expression of COX-2 and mPGES-1 mRNA was measured by real time PCR. PGE\textsubscript{2} release was measured by ELISAs.

Results: CdCl\textsubscript{2} 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 CdCl\textsubscript{2} by 7 and 13 folds at 3 and 6 hours, respectively. At 6 hours, levels of PGE\textsubscript{2} in culture supernatant in cadmium-treated cells were 3 folds higher than untreated cells. Pretreatment with celecoxib, a specific COX-2 inhibitor, reduced PGE\textsubscript{2} levels similar to untreated cells.

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