Molecular targets of aluminum toxicity: Cholinergic system, NADPH oxidase and mitochondrial dysfunction

Natasa Petronijević¹, Svetlana Vučetić-Arsić², Vesna Selaković³, Ankica Jelenković⁴, Tatjana Nikolić¹, Milica Velimirović¹, Tihomir Stojković¹ and Nevena V Radonjić¹

¹University of Belgrade, Serbia
²Special Hospital for Addictions, Serbia
³Military Medical Academy, Serbia
⁴Institute for Biological Research "Siniša Stanković", Serbia

Association of aluminum (Al) and some neurodegenerative disorders, including Alzheimer’s disease (AD), is implicated in 1965 when Al was recognized as neurotoxin. Since then, the role of Al as a pathogenetic factor in AD was suggested by many epidemiological studies. The exact mechanism responsible for changes induced by Al is not known. We have analyzed the effects of ingested Al on the acetylcholinesterase (AChE), NADPH oxidase (NOX2), respiratory chain enzymes and oxidative stress parameters in Mongolian gerbils brain. Also, the protective effects of intrahippocampal application of green tea leaf extract and glucose-6-phosphate dehydrogenase on aluminium-induced brain toxicity were studied. Adult gerbils were acutely (LD₅₀), or subacutely (LD₁₀) exposed to aluminum chloride by gavage and sacrificed 2, 6 or 24 hours after acute and 21 days after sub-acute treatment. Intrahipocampally solutions were injected into the CA1 region using a stereotaxic frame for small animals. The expressions of amyloid and tau protein, as well as, membrane-bound (gp91phox, p22phox) and cytosolic (p40phox, p47phox, p67phox) NOX2 subunits, the activity of AChE and oxidative stress parameters were determined in specific brain structures. Changes of AChE and COX activities, as well as, oxidative stress parameters were seen as the earliest effects of Al treatment. The changes of the expression of NOX subunits were seen six hour after acute poisoning. After subacute Al ingestion the oxidative stress was pronounced. Decreased gp91phox and increased p67phox expressions were seen in cortex while in the hippocampus the decrease of p67phox was noticed. Green tea leaf extract and glucose-6-phosphate dehydrogenase have shown protective effects.

Biography

Natasa Petronijević, MD, PhD has finished her PhD thesis in 2001 at the School of Medicine, University of Belgrade, Serbia. She is a specialist of Clinical Biochemistry and Laboratory Medicine. She is a Project Leader of scientific projects financed by Serbian Government Ministry of Science and a reviewer in several respectable international journals. She is a Course Director of Medical Biochemistry and Director of PhD studies of Neuroscience at the School of Medicine, University of Belgrade. She is a President of Section for Clinical biochemistry, Serbian Medical Society. She has published more than 35 papers in reputed journals.

natasapetronijevic@yahoo.com, natasa.petronijevic@med.bg.ac.rs

Notes: