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Impact of Stress and Protein Malnutrition on the Potential Role of Epigallocatechin-3-Gallate in Providing Protection from Nephrotoxicity and Hepatotoxicity Induced by Aluminum in Rats

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Abstract : Background: Aluminium (Al) is very abundant metal in the earth's crust. It is a constituent of cooking utensils, medicines, cosmetics, some foods and food additives. Salts of Al are widely used in the treatment of drinking water for purification purposes. Excessive and prolonged exposure to Al causes oxidative stress and impairment of many physiological functions. Its accumulation in liver and kidney causes hepatotoxicity and nephrotoxicity. Social isolation (SI) or Protein malnutrition (PM) also increases oxidative stress and may enhance the toxicity of Al as well as the degeneration in liver and kidney. Epigallocatechin-3-gallate (EGCG) is the most abundant catechin in green tea and has strong antioxidant as well as anti-inflammatory activities and can protect against oxidative stress-induced degenerations. Objective: To study the influence of stress or PM on Al-induced nephrotoxicity and hepatotoxicity in rats, as well as on the potential role of EGCG in providing protection. Methods: Rats received daily AlCl3 (70 mg/kg, IP) for three weeks (Al-toxicity groups) except one normal control group received saline. Al-toxicity groups were divided into four treated and four untreated groups; treated rats received EGCG (10 mg/kg, IP) together with AlCl3. One group of both treated and untreated rats served as control for each of them, and the others were subjected to either stress (mild using isolation or high using electric shock) or to PM (10% casein diet). Specimens of liver and kidney were used for assessment of levels of inflammatory mediators as TNF-α, IL6β, nuclear factor kappa B (NF-κB), oxidative stress (MDA, SOD, TAC, NO), Caspase-3 and for DNA fragmentation as well as for histopathological examinations. Biochemical changes were also measured in the serum as total lipids, cholesterol, triglycerides, glucose, proteins, bilirubin, creatinine and urea as well as the level of Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and lactate deshydrogenase (LDH). Results: Nephrotoxicity and hepatotoxicity induced by Al were enhanced in rats exposed to stress and to PM. The influence of stress was more pronounced than PM. Al-toxicity was indicated by the increase in liver and kidney MDA, NO, TNF-α, IL-6β, NF-κB, caspase-3, DNA fragmentation and in ALT, AST, ALP, LDH and total lipids, cholesterol, triglycerides, glucose, proteins, bilirubin, creatinine and urea levels, together with the decrease in total proteins, SOD, TAC. EGCG provided protection against hazards of Al as indicated by the decrease in MDA, NO, TNF-α, IL-6β, NF-κB, caspase-3 and DNA fragmentation as well as in levels of ALT, AST, ALP, LDH and total lipids, cholesterol, triglycerides, glucose, proteins, bilirubin, creatinine and urea in liver and kidney, together with the increase in total proteins, SOD, TAC and confirmed by histopathological examinations. It provided more pronounced protection in high stressful conditions than in mild one than in PM. Conclusion: Stress have a bad impact on Al-induced nephrotoxicity and hepatotoxicity more than PM. Thus it can clarify and maximize the role of EGCG in providing protection. Consequently, administration of EGCG is advised with excessive Al-exposure to avoid nephrotoxicity and hepatotoxicity especially in populations more subjected to stress or PM.

Keywords : aluminum, stress, protein malnutrition, nephrotoxicity, hepatotoxicity, epigallocatechin-3-gallate, rats
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