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Short-term and long-term effects of gadolinium and gadoteric acid exposure on rat kidney and liver functions

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Abstract

Background: There are currently concerns about the safety of gadolinium-based contrast agents (GBCA), as they can release gadolinium [Gd (III)], known to be toxic. Free Gd (III) deposition at different organs, as kidney and liver, has been reported [1,2]. We found that Gd (III) promotes inflammation and fibrosis in proximal tubular cells [3]. GBCA with macrocyclic structure, as gadoteric acid (Gd-DOTA), are considered more stable. **Objective:** To evaluate the short-term and the long-term effects of Gd (III) and Gd-DOTA exposure on biomarkers of renal and hepatic functions, using an animal model. **Methods:** In both short-term (48h) and long-term (20 weeks) studies, eight weeks-old male Wistar rats were divided in 3 groups *(n*=10 each) exposed to: a single dose (0.1 mmol/kg) of Gd (III), of Gd-DOTA (0.1 mmol/kg) or vehicle (control). At the end of protocols, blood was collected and the levels of creatinine, urea, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were evaluated using routine automated assays; cystatin C was measured by ELISA. **Results:** In the short-term study (48h), Gd (III) group presented significantly higher values of AST and ALT, and lower urea levels than the control group; Gd-DOTA group presented higher AST values, compared to the control group. Twenty-weeks after exposure, higher values of AST, ALT, and creatinine, than Gd-DOTA and control groups and, lower cystatin levels, compared to the control group, were found for the Gd (III) group. **Conclusions:** Single exposure to free Gd (III) induced short-term and long-term changes in liver biomarkers; the exposure to Gd-DOTA was associated with fewer short-term disturbances in transaminases, and with no long-term influence in their values. Exposure to Gd-DOTA had little influence in traditional kidney biomarkers. Despite the significantly safer profile for Gd-DOTA, further studies are necessary, testing other biomarkers, to clarify the short-term and the long-term impact of this GBCA.

Keywords: enantioselectivity; dietary supplements; chromatographic; nephrotoxicity; hepatotoxicity

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