Scientific Letters

Poster Communication 5

Single exposure to gadolinium or gadoteric acid – influence on metal elements levels in blood, kidney and brain

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Abstract

Background: In gadolinium-based contrast agents (GBCA), used in magnetic resonance imaging, gadolinium [Gd (III)] is chelated to prevent its release and toxicity [1]. Gadoteric acid (Gd-DOTA), a macrocyclic GBCA, presents one of the most stable structures [1]. Nevertheless, endogenous metal cations compete with Gd (III) for the ligand and may replace it; when this transmetallation occurs, Gd (III) is released from its chelate and can either be excreted by the kidneys or be deposited in several organs, such as the kidney and brain [1–3]. Both transmetallation and active cell membrane metal transporters appear to contribute to tissue Gd (III) deposition [3]. **Objective:** To evaluate the short- and long-term effects of a single exposure to Gd (III) or Gd-DOTA on metal elements homeostasis, by evaluating their values on the blood, kidney and brain. **Methods:** Male Wistar rats (ORBEA #7-2022; 28-Nov-2022) were divided in 3 groups *(n*=10 each) and exposed to a single dose (0.1 mmol/kg) of Gd (III), Gd-DOTA or vehicle (control); 2 days and 20 weeks after exposure, metal elements were evaluated on blood, brain and kidney by inductively coupled plasma-mass spectrometry (ICP-MS). **Results:** In blood, 2 days after exposure, Gd (III) group showed significantly higher manganese (Mn) than the control group, and increased copper (Cu) values compared to Gd-DOTA and controls; 20 weeks after, significantly higher zinc (Zn) levels were found in the Gd (III) group compared to the Gd-DOTA group. In the brain, 2 days after exposure, Gd-DOTA showed lower Mn values than the control group. In the kidney, 20 weeks after exposure, for the Gd (III) group, the levels of Cu, Zn and molybdenum (Mo) were significantly higher than for controls; no statistically significant differences were observed in short-term effects. **Conclusions:** Exposure to a single dose of Gd (III) interferes with metal homeostasis, as shown by the significant variations in blood levels of some metals, both at short- (Cu and Mn) and long-term (Zn) effects; and in the kidney, by metal alterations in the long-term effects (Cu, Zn and Mo). Exposure to a single dose of Gd-DOTA did not show a significant impact on blood, kidney and brain values of the metal elements studied, except for the short-term effect on the brain's Mn, which was significantly decreased. Further studies are warranted to evaluate its true safety, especially on its effect on the brain, and in cases of repeated exposures to this GBCA and/or in case of pre-existing renal function impairment.

Keywords: tissue deposition; transmetallation; zinc; copper; manganese; molybdenum

Funding/Acknowledgments

This work was supported by FCT - Fundação para a Ciência e Tecnologia, I.P., in the scope of the project UID/04378/2025 (DOI identifier 10.54499/UID/04378/2025), and UID/PRR/04378/2025 (DOI identifier 10.54499/UID/PRR/04378/2025), of the Research Unit on Applied Molecular Biosciences – UCIBIO and the project LA/P/0140/2020 (DOI identifier 10.54499/LA/P/0140/2020) of the Associate Laboratory Institute for Health and Bioeconomy - i4HB.

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