Abstract citation ID: gfae069.1773

#1613

Gadolinium and gadoteric acid's short-term impact on kidney function and lipid profile

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Background and Aims: Concerns regarding the safety of gadolinium-based contrast agents (GBCA), which are often employed in medical imaging, have been raised in light of reports of free gadolinium's [Gd (III)] cytotoxicity. It appears that GBCAs having macrocyclic structures, like gadoteric acid (Gd-DOTA), are more stable and less toxic.

Previous work from our group found that Gd (III) promotes inflammation and fibrosis in proximal tubular cells cultures. A disturbance of lipid metabolism was also reported, accompanied by the build-up of lipid droplets, lipid peroxidation and the overexpression of genes linked to lipogenesis and lipolysis.

The aim of this study was to evaluate the short-term effects of Gd (III) and of Gd-DOTA on renal function and lipid metabolism biomarkers, using an animal model.

Method: Male Wistar rats were exposed to a single dose of Gd (III) or Gd-DOTA (groups A and B, respectively); a control group was also included (C). Blood was collected after 48h of exposure to compounds. We evaluated circulating levels of renal function biomarkers—creatinine and cystatin—using a routine automated assay and ELISA, respectively. The lipid profile was also determined including triglycerides (TG), total cholesterol, HDL-cholesterol, LDL-cholesterol, and oxidized LDL (oxLDL) levels.

Results: Gd (III) group (A) presented significantly higher circulating cholesterol ($P=0.006$) and LDL-cholesterol ($P<0.001$) and lower TG ($P<0.001$) levels than the control group (C); a non-significant increment in cystatin was also observed for group A. The Gd-DOTA group (B) only presented lower TG levels ($P=0.002$) compared to the control group (C), being similar to those presented by group A. Both exposed groups (A and B) presented non-significantly higher oxLDL levels compared to the control group.

Conclusion: Single exposition to free Gd (III) induced prompt changes in lipid profile, with little short-term influence in traditional kidney biomarkers. The exposition to Gd-DOTA was associated with lower disturbance in lipids and lipoproteins (only lower TG levels) and imperceptible renal changes. Despite the significantly safer profile for Gd-DOTA, further studies are necessary, testing different biomarkers, to clarify the short-term, and even the long-term impacts, of these molecules.

Acknowledgements: This work was financed by FCT through the project 2022.08400.PTDC; FCT, in the scope of the project UIDP/04378/2020 and UIDB/04378/2020 of the Research Unit on Applied Molecular Biosciences—UCIBIO and the project LA/P/0140/2020 of the Associate Laboratory Institute for Health and Bioeconomy—i4HB.