Study raises questions about the safety of MRI contrast agent

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An article published today in the Springer journal *BioMetals* raises serious questions about the safety of the gadolinium-based contrast agents that are used in about 30 percent of magnetic resonance imaging (MRI) scans. In their literature review, researchers from MedInsight Research Institute and Israel's Ariel University analyzed studies detailing the known and proposed mechanisms of retained gadolinium toxicity. According to lead author Moshe Rogosnitzky, "Although gadolinium is bound to chelating agents designed to flush out the rare metal following an MRI, it has been found to deposit in the brain, bone, and other organs."

Rogosnitzky said that this finding contradicts the longstanding belief that patients with normal kidney function are not at risk for gadolinium accretion. In 2007, the U.S. Food and Drug Administration (FDA) ordered a black box warning for gadolinium-based contrast agents following the discovery that patients with kidney disease were developing nephrogenic systemic fibrosis (NSF) due to the inability to clear gadolinium from their bodies. In July 2015, the FDA announced it was evaluating the risk of brain-deposits in patients who undergo repeated exposure to gadolinium-based contrast agents. "At the time, FDA claimed that available information did not identify any adverse health effects. In the face of the information contained in our study, we believe this position is no longer tenable," said Rogosnitzky.

Study author and toxicologist Dr. Stacy Branch underscored the urgent need for the FDA to take action. "Given the ever-growing toxicological

and gadolinium tissue retention data, it is vital that the FDA promptly leads efforts, including retrospective and prospective clinical studies, to better define the connection between GBCA-exposure and adverse health events," she said. "This is needed to guide the choice of preventive methods, achieve accurate diagnoses, implement effective treatment approaches, and spark research for the design of safer contrast agents and imaging protocols."

Rogosnitzky, who heads the Center for Drug Repurposing at Ariel University, called upon the scientific community to quickly develop treatments for gadolinium overload. "Our literature review did not reveal a single suitable drug to swiftly remove gadolinium from the body," he said. "In one study, the authors estimated it might take up to 156 years to remove a patient's stored gadolinium using a particular drug." Rogosnitzky believes that a good first step is to study existing chelator drugs used for other metal toxicities in order to assess their possible utility in gadolinium accumulation.

The published article sounds the alarm about the gap in scientific knowledge about treatment for gadolinium toxicity. "With the ominous discovery that gadolinium is retained in healthy patients, there is a critical shortage of scientific information regarding how to assess gadolinium toxicity, and perhaps most importantly, how to treat it," Rogosnitzky said.

More information: Moshe Rogosnitzky et al. Gadolinium-based contrast agent toxicity: a review of known and proposed mechanisms, *BioMetals* (2016). DOI: 10.1007/s10534-016-9931-7

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