Manganese Based Contrast Agent (MBCA): Likely to Replace GBCA

Gadolinium based contrast agents (GBCA) are an integral part of MRI imaging suite as these induce enhancement on MRI images to improve diagnostic accuracy. Gadolinium ion has seven unpaired electrons and it shortens spin-lattice relaxation time (T1) of voxels in which they are present and this gives brighter signals to T1 weighted images. GBCAs are well tolerated by the patients; however, the previous decade has seen safety concerns associated with these agents. Importantly in 2007 an association between GBCA and nephrogenic systemic fibrosis (NSF) was reported in patients with impaired renal function. Based on reported data, FDA issued a contraindication to use of GBCAs in patients with glomerulation filtration rate less than 30 ml/min/1.73 m^2. However, current American College of Radiology (ACR) guidelines discourage use of GBCA in patients with GFR <40 ml/min/1.73 m^2. However, in 2016, 4 cases of NSF were reported in patients with normal renal function as well. Furthermore, there is evidence of further deterioration of impaired renal status in some patients which requires hemodialysis. In last 6 years, GBCA related safety concerns have been raised in patients with normal renal function. This is based on various authentic reports revealing long term retention of gadolinium in central nervous system and skin of patients who had had contrast enhanced MRI. It is assumed that NSF and CNS retention is caused by release of gadolinium from GBCA.

In 2015 researchers introduced a manganese-based contrast agent (MBCA) manganese-N-picolyl-N,N ,N -trans-1,2-cyclohexenediaminetriacetate (Mn-Py-C3A) which is resistant to manganese dissociation from molecule. Mn-PyC3A also possesses an aromatic pyridine ring that promotes partial hepatobiliary clearance in contrast to GBCA. Hepatobiliary clearance in addition to renal route enhances safety profile of MBCA in patients with impaired renal function. Furthermore, initial studies on animals have shown rapid blood clearance, mixed renal and hepatobiliary clearance and almost complete excretion of manganese 24 hour after injection. This essentially rules out retention of injected manganese as observed with GBCA. Even if there is a tracer of manganese that is released or stayed in the body, as long as that amount is quite small, it would not be a problem as it would either be incorporated into body's pool of manganese that is needed to survive or be eliminated. The body has good mechanisms for regulating how much manganese it needs. A recent trial upon rodents comparing GBCA and Mn-PyC3A (published in Investigative Radiology, November 2019, Vol. 54:11, pp. 697-703) showed that Mn-PyC3A achieved greater contrast-to-noise ratios in breast and liver lesions and significantly lower left-over manganese at day 1 and 7 than Gadolinium.

Manganese based contrast agent (MBCA) Mn-PyC3A due to its comparable image quality and better safety profile in preclinical studies has real clinical significance. It is quite possible that this would also behave in a similar fashion in humans and radiology fraternity is eagerly waiting to see it in clinical use. We expect that MBCA due to its comparable image enhancement and safer profile would finally replace GBCA.

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