Advisory on Linear Gadolinium-Based Contrast Agents

Background

In July 2017, the Pharmacovigilance and Risk Assessment Committee of the European Medicines Agency (EMA) suspended the intravenous administration of certain linear type, MRI gadolinium-based contrast agents (GBCA) after a safety review.

Intravenous administration of gadolinium-based contrast agents are widely used for enhancement of MRI studies. Safety concerns first emerged when patients who previously underwent contrast-enhanced MRI scans were found to have residual gadolinium in the globus pallidi. Since the substantia nigra, which is affected in Parkinson’s disease, controls voluntary movement via neural pathways to the globus pallidi, there were postulations that the gadolinium deposits could cause Parkinsonian symptoms. Residual GBCAs are also known to be deposited in the bone and skin.

The EMA also additionally recommended that macrocyclic GBCAs “can continue to be used in their current indications but in the lowest doses that enhance images sufficiently and only when unenhanced body scans are not suitable”. This is because macrocyclic GBCAs have significantly less gadolinium retention in the brain compared to the linear GBCAs.

Advisory

After a review of the available evidence by a workgroup commissioned by the College of Radiologists, the College is of the opinion that there is no definite evidence of Parkinson’s disease or other neurological diseases linked to linear GBCAs so far. These agents have also been used for many years with clear benefit to many patients without any major long term side effects, except for the potentially fatal nephrogenic systemic fibrosis which can occur in a very small cohort of patients with severe renal failure. Patients without any known risk factors for nephrogenic systemic fibrosis should, therefore, not be denied the use of linear or other known types of GBCAs if there are clear medical indications for their use. In light of this, while the College is cautious about the potential long term effects, it will not be issuing any advisory to restrict the use of linear GBCAs in Singapore at this point in time. This is also a similar stand taken by the Food and Drug Administration in USA.

Further Comments

It has also been noted in a survey with the major radiological centres in Singapore that all the public institutions and most of the private radiology centres have already voluntarily stopped using linear GBCAs except in rare cases where there are no alternatives (eg: Primovist and Multihance for liver imaging) or where systemic absorption is very low (intra-articular injections). A few radiology centres in the private sector are using linear GBCAs in limited cases and they are also in the process of replacing their current linear GBCA stock for the macrocyclic ones in their inventory.

As the College does not have its own resources for testing, it is unlikely it will conduct any GBCA safety studies in Singapore. The College will be heavily dependent on evidence and advisories from the available literature, vendors, and other regulatory or radiology bodies. The College remains vigilant and will review this issue again should any new evidence surface.


