POLICY STATEMENT REGARDING THE USE OF GADOLINIUM BASED CONTRAST AGENTS IN RESEARCH

11/20/2023

A rare but potentially serious adverse reaction has been observed in patients who received gadolinium (Gd) based contrast agents (GBCAs) during MRI examinations, a reaction called nephrogenic systemic fibrosis (NSF). NSF may cause skin thickening, joint pain and/or swelling, and in rare cases can lead to lung and heart problems and cause death. Patients with relatively severe kidney disease are at increased risk of developing NSF. NSF has never been reported in patients with normal kidney function. The American College of Radiology divides the GBCAs into three categories according to the risk of development of NSF:

Class I – Highest risk

1) Gadopentetate dimeglumine (Magnevist)
2) Gadodiamide (Omniscan)
3) Gadoversetamide (OptiMARK)

Class II – Low risk (no or few cases of NSF attributed to these agents separate from other agents)

1) Gadobenate dimeglumine (MultiHance)
2) Gadobutrol (Gadavist)
3) Gadoterate meglumine (Dotarem)
4) Gadoteridol (ProHance)

Class III – Unclear risk (much less data available compared with other agents)

Gadoxetate disodium (Eovist)

Additionally, it has been observed that some patients who have received multiple GBCA administrations have evidence of Gd retention in some tissues. The implications of this finding are uncertain, as no clear disease or clinical syndrome has been associated with Gd deposition.

Because of this potentially serious risk to some research participants, the Duke University Health System Institutional Review Board (DUHS IRB) has determined the following policy related to the use of gadolinium based contrast agents in research.

For research protocols utilizing a Class II GBCA

All adult participants who will undergo a research MRI that includes the intravenous administration of a Class II GBCA must have their serum creatinine estimated within 7 days before the MRI examination in order for an estimated glomerular filtration rate (eGFR in ml/min/1.73m^2) to be calculated using the MDRD formula*.

Only those adult participants whose eGFR is >/= 30 ml/min/1.73m^2 are eligible for MRI with Class II GBCA administration. All but one case of NSF have been reported in patients with eGFR < 30 ml/min.

For adult participants with eGFR < 30 ml/min/1.73m^2 or participants on dialysis (regardless of type of dialysis), the administration of Class I or III GBCAs for research is not allowed unless justified to and approved by the DUHS IRB. Class II agents would be preferred in this situation but would also still require justification for administration to research participants.

For research protocols utilizing a Class I or Class III GBCA

In general, the intravenous administration of Class I agents for human subjects research is not allowed. Investigators who believe they have a compelling reason for human intravenous administration of Class I agents must justify this to the DUHS IRB and be approved by the Duke IRB for exemption.

All adult participants who will undergo a research MRI that includes the intravenous administration of a Class I or Class III GBCA must have their serum creatinine quantified within 7 days before the MRI examination in order for an estimated glomerular filtration rate (eGFR in ml/min/1.73m^2) to be calculated using the MDRD formula*.

Only those adult participants whose eGFR is >/= 45 ml/min/1.73m^2 are eligible for MRI with intravenous administration of a Class I or III GBCA. No cases of NSF have been reported in patients with eGFR >/= 45 ml/min. For adult participants with eGFR < 45 ml/min/1.73m^2 or participants on dialysis (regardless of type of dialysis), the administration of Class I or III GBCAs for research is not allowed.

For research protocols using any GBCA

In all research usage of gadolinium based contrast, the amount and type of GBCA is to be entered in the patient's medical record. Only up to the standard FDA-approved dose of GBCA may be administered unless special justification is made to the Duke IRB and an exemption is granted.

Further, all consent forms for research including gadolinium based contrast agents must contain language regarding the risk of NSF. The IRB-approved standard language for use in consent forms may be found at the DUHS IRB web site.

Special populations:

Pediatric participants

For children (less than 18 years old) scheduled by research protocol to undergo a research MRI that includes the use of a gadolinium based contrast agent, only those for whom the MRI results will offer the prospect of direct benefit to the child will be permitted to receive the MRI with contrast, and then only if they meet the Duke Pediatric Radiology clinical standards for receiving gadolinium. Only Class II and III agents may be administered intravenously to pediatric participants. These agents should not be administered to pediatric participants with eGFR < 60 unless justification has been provided to and approved by the DUHS IRB. If the IRB approves gadolinium use in children participating in a research study, the consent form should include the applicable standard language pertaining to children, available on the DUHS IRB web site.

People of child-bearing potential

All GBCAs are considered Pregnancy Category C medications. Please refer to the Duke IRB Pregnancy Testing Policy.

* (nephron.com) or mdrd.com or http://www.kidney.org/professionals/KDOQI/gfr_calculator.cfm

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