U.S. Food and Drug Administration
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Drug Safety Communications

FDA evaluating the risk of brain deposits with repeated use of gadolinium-based contrast agents for magnetic resonance imaging (MRI)

Safety Announcement

[7-27-2015] The U.S. Food and Drug Administration (FDA) is investigating the risk of brain deposits following repeated use of gadolinium-based contrast agents (GBCAs) for magnetic resonance imaging (MRI). MRIs help detect abnormalities of body organs, blood vessels, and other tissues. Recent publications in the medical literature have reported that deposits of GBCAs (See Table 1) remain in the brains of some patients who undergo four or more contrast MRI scans, long after the last administration.[1-21] It is unknown whether these gadolinium deposits are harmful or can lead to adverse health effects.

FDA, including its National Center for Toxicological Research (NCTR), will study this possible safety risk further. We are working with the research community and industry to understand the mechanism of gadolinium retention and to determine if there are any potential adverse health effects. Based on the need for additional information, at this time, we are not requiring manufacturers to make changes to the labels of GBCA products.

To reduce the potential for gadolinium accumulation, health care professionals should consider limiting GBCA use to clinical circumstances in which the additional information provided by the contrast is necessary. Health care professionals are also urged to reassess the necessity of repetitive GBCA MRIs in established treatment protocols.

Patients, parents, and caregivers should talk to their health care professionals if they have any questions about the use of GBCAs with MRIs. This issue affects only GBCAs; it does not apply to other types of scanning agents used for other imaging procedures, such as those that are iodine-based or radioisotopes.

After being administered, GBCAs are mostly eliminated from the body through the kidneys. However, trace amounts of gadolinium may stay in the body long-term. Recent studies conducted in people and animals have confirmed that gadolinium can remain in the brain, even in individuals with normal kidney function.[1-21] Available information does not identify any adverse health effects.

We urge health care professionals, patients, and parents/caregivers to report possible side effects involving GBCAs to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Table 1. FDA Approved GBCAs

Brand name	Generic name
Ablavar	gadofosveset trisodium
Dotarem	gadoterate meglumine
Eovist	gadoxetate disodium
Gadavist	gadobutrol
Magnevist	gadopentetate dimeglumine
MultiHance	gadobenate dimeglumine
Omniscan	gadodiamide
OptiMARK	gadoversetamide injection
ProHance	gadoteridol

Data Summary

In published studies, investigators reviewed noncontrast magnetic resonance imaging (MRI) scans of patients who had received several gadolinium-based contrast agent (GBCA) MRIs as part of management for cancer, multiple sclerosis, or other illnesses.[1-21] The noncontrast MRIs demonstrated findings highly suggestive that gadolinium contrast was retained in various structures in the brain. To date, no signs or symptoms of adverse health effects and no pathological changes have been associated with these gadolinium deposits in the brain. In some of these studies, examination of brain tissue at autopsy confirmed the presence of gadolinium deposits. In these studies, researchers found that GBCAs more prone to dissociation into free gadolinium, which is when gadolinium separates from the molecule it is bound to, demonstrated greater brain deposition than GBCAs less prone to dissociation. A study in rats performed by a GBCA manufacturer showed greater gadolinium deposition throughout the brain in rats given a linear GBCA that is known to have greater dissociation of gadolinium, compared to a macrocyclic GBCA. No histopathological changes were observed in the animal brains. Gadolinium may also deposit in other body structures such as bone and skin.

We have also received reports submitted to the FDA Adverse Event Reporting System (FAERS) database and other reports from patients describing pain and other symptoms following either single or multiple administrations of GBCAs. To date, we have been unable to discern a commonality of features among these reports or reasonably link the reported symptoms to gadolinium.

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