NEW DRUG REVIEW

Gadoxetate Disodium for Contrast Magnetic Resonance Imaging of the Liver

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Contrast-enhanced magnetic resonance imaging (MRI) has diagnostic applications in several patient groups with potential lesions of the liver. These include patients with cirrhosis or chronic liver disease, who require screening for hepatocellular carcinoma (HCC), as well as those with primary sclerosing cholangitis, who are at risk for cholangiocarcinoma. These patients are effectively monitored through this type of imaging. Patients with known malignancies that have a propensity for liver metastasis, such as a melanoma, can also be monitored with contrast-enhanced MRI. Finally, patients with incidental findings from other imaging modalities, such as ultrasound, may require further evaluation via contrast-enhanced MRI.

Contrast agents can be categorized by their chemical composition and by their mechanism of action within the body. Extracellular agents behave much like the contrast agents used for computed tomography (CT) scanning. These agents highlight the extracellular space of the liver and include the original gadolinium-based contrast agent, Magnevist (gadopentetate dimeglumine). Liver-specific agents are either absorbed by the hepatocyte cells themselves or may be taken up by the reticuloendothelial or Kupffer cells in the liver, as is the case with iron-oxide–based agents.

The newly approved contrast agent gadoxetate disodium (Eovist, Bayer HealthCare Pharmaceuticals) is a gadolinium-based formulation, which has both extracellular and hepatocyte-specific properties. After injection, approximately 50% of Eovist is renally excreted, whereas the other 50% is actively transported into the liver cells and then excreted via the biliary system. With the cellular uptake of a gadolinium-based contrast agent, the liver will appear very bright on a T1-weighted MRI, whereas nonliver cells (such as malignant metastases) will not take up the agent and will appear darker. Enhancement of the normal liver parenchyma on a T1-weighted sequence peaks at approximately 20 minutes after injection and persists for up to 2 hours, providing a wide window of opportunity to image during the hepatocyte phase.

Eovist is also characterized by a high level of relaxivity, which determines how bright the contrast agent appears on a T1-weighted MRI. This elevated relaxivity allows for similar imaging results with a smaller dose of Eovist (0.025 mmol/kg body weight), as compared to other gadolinium-based agents. Eovist is also administered via intravenous bolus, which allows for dynamic-phase, contrast-enhanced imaging, followed by T1-weighted hepatocyte-phase imaging 20 minutes later, as part of the same procedure.

In terms of clinical utility, Eovist is particularly suited to the characterization of focal liver lesions, such as focal nodular hyperplasia (FNH). FNH is a type of liver tumor that was once thought to be rare but, with the advent of dynamic CT and MRI, was ultimately found to be fairly common and is incidentally seen in many patients, including those under surveillance for cancer metastasis or recurrence. Unlike older, extracellular gadolinium-based agents, which do not provide confident differentiation of FNH from other tumors in many cases, Eovist will typically be taken up by FNH because FNH lesions retain some hepatocyte function. Uptake of Eovist, which is revealed in hepatocyte-phase T1-weighted imaging, allows for a more confident diagnosis of FNH versus a malignant tumor such as metastasis or HCC. Because metastatic liver lesions lack hepatocytes, high contrast is achieved between enhanced normal liver and metastases during the hepatocyte phase. In most cases, lesions of HCC will also appear darker than background liver on T1-weighted hepatocyte-phase images, providing potential utility for detection of HCC in patients at risk.

Eovist is currently covered by the same black-box warning as all other gadolinium-based contrast agents, and rates of adverse reactions are very similar to those seen with other agents in the same class. Whether the smaller dose and high percentage of biliary excretion unique to Eovist will ultimately lead to fewer renal-failure–related complications remains to be seen.

Suggested Reading

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