Are Gadolinium-Based Contrast Media Safe Alternatives to Iodinated Contrast Agents for the Safe Performance of Spinal Injection Procedures?

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**Myth:** Gadolinium-based contrast media are as safe to use as standard iodinated contrast agents for spinal interventions.

**Fact:** The safety of gadolinium-based contrast media is unclear. These agents appear to be safe if spine procedures are performed accurately, but the published cohort studies are limited in size. Serious adverse effects are known to occur if gadolinium-based contrast media are injected into the intrathecal space at small doses.

Contrast media are used during image-guided spinal procedures in order to demonstrate where subsequent injected medication would presumably flow. Injection of contrast media, therefore, serves as a safeguard against unwanted injection into subdural, intradural, intrathecal, intravascular, or other non-target tissues. However, some patients are allergic to the iodinated contrast media that are most commonly used in clinical practice. Whereas some patients are truly allergic to iodinated contrast media, others may misinterpret physiologic reactions to corticosteroids (such as facial flushing) as allergic reactions. The latter patients need to be recognized lest they be falsely regarded as allergic to contrast media. For patients with known allergies to iodinated non-ionic contrast media, many providers use gadolinium-based contrast media (GBCM) as an alternative. However, when used in fluoroscopically-guided procedures, a GBCM is less radiodense, and therefore produces a dispersal pattern that is less distinct than that provided by iodinated contrast media. The temptation arises to inject more GBCM in order to obtain more information about the contrast dye pattern. This practice may lead to serious adverse effects.

Severe, life-threatening anaphylactoid reactions to intravenous (IV) GBCM are rare but possible [1,2]. Nephrogenic systemic fibrosis has been reported after intravenous administration of IV gadolinium in patients with renal compromise, particularly Stage 4 or 5 chronic kidney disease. However, this complication has only been reported in association with large doses of IV GBCM (> 0.2 mL/kg) [3], and this complication has not been reported since the institution of strict guidelines for IV GBCM use in patients with renal compromise. A growing body of evidence also documents that IV GBCM during MRI studies is associated with deposition of GBCM in the brain even in patients with relatively normal renal function [4,5], but the clinical significance of this phenomenon is unknown.

For spinal injection procedures, GBCM may be safe when injected into target spaces, but complications are possible if GBCM is injected intrathecally. Studies have reported encephalitis, chemical meningitis, and seizures with residual optic nerve involvement following intrathecal administration of 6-20 mL doses of gadolinium [6-8]. MRI myelography is used for the evaluation of cerebrospinal fluid leaks, in which case, the intrathecal space is intentionally accessed; <1 mL of gadolinium administration is considered to be safe during these procedures [9-12].

There are no reports in the literature of complications following fluoroscopically-guided transfemoral epidural steroid injections, medial branch blocks, or sacroiliac joint injections performed using GBCM. No complications were encountered in a study of 92 patients allergic to iodinated contrast media who underwent 127 procedures performed with GBCM [13]. The doses used ranged from 1.5 to 7.5 mL for discography, 1 to 5 mL for epidural steroid injection, 0.2 to 1 mL per level for nerve blocks, 0.2 to 0.5 mL per level for zygapophysial joint blocks, and 0.5 mL for intercostal blocks. No complications occurred in 38 patients who had interlaminar epidural steroid injections in an interventional radiology department, using 1 – 3
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mL of non-diluted GBCM [14]. In five cases, imaging was augmented with digital subtraction imaging to improve visualization of injected gadolinium.

Of particular concern is the use of GBCM during interlaminar epidural steroid injections, as the risk of potential intrathecal injection is higher with this injection than any other fluoroscopically-guided spinal injection procedure. In the conduct of interlaminar epidural injections, there is a 0.5% risk of unintended dural puncture despite fluoroscopic guidance and loss of resistance technique [14]. Since publication of the most recent FactFinder on the use of GBCM during spinal injections [15], a new case of an adverse event has come to light. A 73 year-old woman underwent an L4-L5 interlaminar epidural steroid injection, during which 1.5 mL of gadobutrol was injected. She was discharged in good condition; however, 2 hours later, she began vomiting, presented to the emergency room, demonstrated seizure activity, and required intubation due to impaired consciousness and respiratory compromise. Both a CT and an MRI of the brain were obtained, which demonstrated contrast material in the subarachnoid space, suggesting that the gadobutrol had been injected into the intrathecal space. The patient was extubated approximately 24 hours later and made a full neurologic recovery. The FDA recommends that “health care professionals should limit GBCM use to circumstances in which additional information provided by the contrast agent is necessary” [18]. As such, an alternative to using GBCM is to avoid the use of any contrast media. Whereas this might be reasonable for procedures with low risk/consequences of vascular uptake, subdural or intrathecal needle placement, such as intra-articular injections and medial branch nerve blocks, precautions should be implemented for procedures in which needle malposition is more likely or potentially more hazardous, such as transforaminal injections or interlaminar epidural injections, particularly in the cervical or thoracic spine. If prior contrast allergy was not severe (i.e. anaphylaxis), another alternative to GBCM use is to prescribe an oral corticosteroid/diphenhydramine pre-procedure prep for patients who are allergic to iodinated contrast media. While there is no evidence-based consensus protocol, typical dosing might include 50 mg of prednisone at 24 hours, 12 hours, and 1 hour prior to procedure with 25 mg of diphenhydramine at 12 hours and 1 hour prior to procedure. More fundamentally, the physician should consider recommending against the procedure if the risks outweigh the benefits for the individual patient.

**Recommendations**

As with every medication used, the spine interventionalist should have a thorough knowledge of the body of literature related to GBCM [16]. Physicians should use the lowest volume of GBCM necessary. This should not exceed 1 mL per session for injections in which the epidural space is accessed and the intrathecal space could potentially be entered. It must also be noted that GBCM preparations have differing molar equivalents, which influence radiopacity [17]; for example, 1 mL of gadobutrol will likely provide adequate visualization for a TFESI when digital subtraction imaging is used, while 1 mL of 0.5 molar GBCM may not. Greater molar equivalent agents, however, do create risk of toxicity at lower volumes of injection. Most importantly, the procedure should be aborted if intrathecal uptake is suspected. Safeguard measures include: administration of a local anesthetic test dose; use of a non-particulate steroid for an epidural steroid injection; fluoroscopic guidance of the needle to the ideal target using at least two planes to visualize location, with live fluoroscopic digital subtraction imaging when available (pulsed mode turned off), repeated negative aspirations, and administration of small aliquots (<0.5mL) of GBCM with subsequent fluoroscopic imaging before additional GBCM injection.

**References**

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