



## Are gadolinium-based contrast media safe alternatives to iodinated contrast agents for the safe performance of spinal injection procedures?

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### ABSTRACT

This FactFinder presents a brief summary of the evidence regarding the safety of gadolinium-based contrast media (GBCM) for spinal interventions.

**Myth:** Gadolinium-based contrast media (GBCM) are as safe as standard iodinated contrast agents for spinal interventions.

**Fact:** Evidence suggests that unintentional intrathecal administration of GBCM carries risks of encephalopathy and other complications. A Practice Advisory, supported by IPSIS and multiple specialty societies, does not recommend the use of GBCM for epidural steroid injections, particularly through the interlaminar approach [1]. If GBCM is essential for the procedure, conducting a thorough shared decision-making discussion with the patient is critical to carefully weigh the risks and benefits.

Contrast media are used during image-guided spinal procedures to demonstrate where subsequently injected medication would presumably flow. In addition to appropriate technique and use of multiplanar imaging, injection of contrast media safeguards against intravascular injection or injection into the subdural, intradural, intrathecal spaces or other non-target tissues. However, some patients are allergic to the iodinated contrast media (ICM) most commonly used in clinical practice. Whereas some patients are truly allergic to ICM, others may

misinterpret physiologic reactions to corticosteroids (such as facial flushing) as allergic reactions. The latter patients must be recognized lest they be falsely regarded as allergic to contrast media. Many providers consider GBCM an alternative to iodinated non-ionic contrast media for patients with known allergies.

GBCM are not FDA-approved for use in the intrathecal and epidural spaces [2], and the FDA recommends that "health care professionals should limit GBCM use to circumstances in which additional information provided by the contrast agent is necessary" [3]. Under fluoroscopy, GBCM are less radiodense than ICM and produce a comparatively less distinct dispersal pattern. The temptation may arise to inject more GBCM to obtain more information about the contrast pattern, which may further increase the risk of neurotoxicity and associated complications. Additionally, GBCM preparations have differing molar equivalents, which influence radiopacity [4]. For example, 1 mL of gadobutrol (1 mol/L) will likely provide adequate visualization for a TFESI when digital subtraction imaging is used, while 1 mL of 0.5 M GBCM may not [4]. Greater molar equivalent agents, however, do create a risk of

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toxicity at lower volumes of injection.

If prior contrast allergy was not severe (i.e., anaphylaxis), another alternative to GBCM use is to prescribe an oral corticosteroid/diphenhydramine pre-procedure preparation for patients allergic to ICM. While there is no evidence-based consensus protocol, typical dosing might include 50 mg of prednisone at 24 h, 12 h, and 1 h before the procedure, with 25 mg of diphenhydramine at 12 h and 1 h before the procedure [5]. It should be noted that despite premedication, there is still a risk for a breakthrough contrast reaction that could be similar in severity to prior reactions [2]. Additionally, it has been suggested that changing the ICM to another ICM type/formulation is potentially more effective than premedication in decreasing the risk of a hypersensitivity reaction [1, 6–8]. Further information regarding the treatment of hypersensitivity reactions can be found in the Manual on Contrast Media by the American College of Radiology [5].

Severe, life-threatening anaphylactoid reactions to intravenous (IV) GBCM are rare but possible [9,10]. Nephrogenic systemic fibrosis (NSF) has been reported after IV administration of gadolinium in patients with significant 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) [11], and this complication has not been reported since the institution of strict guidelines for IV GBCM use in patients with renal compromise. To our knowledge, there are no documented cases involving NSF with intramuscular, intraarticular, or spinal administration of GBCM.

A growing body of evidence also documents that IV GBCM during MRI studies is associated with the deposition of GBCM in the brain, even in patients with relatively normal renal function [12,13], but the clinical significance of this phenomenon is unknown.

A literature search conducted did not identify any direct reports of complications following fluoroscopically-guided transforaminal 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 ICM who underwent 127 procedures performed with GBCM [14]. The doses ranged from 1.5 to 7.5 mL for discography, 1–5 mL for epidural steroid injection, 0.2–1 mL per level for nerve blocks, 0.2–0.5 mL per level for zygapophysial joint blocks, and 0.5 mL for intercostal blocks. One retrospective study looked at patient outcomes following epidural injections using GBCM [15]. Upon review of the fluoroscopic images saved during 672 injections, 14 procedures using a transforaminal approach were found to have complications that were deemed to be associated with either confirmed or possible intrathecal spread. Most reactions involved severe pain, but one patient presented with multifocal stroke 2 weeks post-injection. However, due to the study's retrospective nature, the authors noted the difficulty with attributing causation directly to fluoroscopic injections using GBCM.

One particular concern is the use of GBCM during interlaminar epidural steroid injections, as the risk of inadvertent intrathecal injection is higher with this injection than with any other spinal injection procedure [16]. 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 [17]. Studies have reported encephalitis, chemical meningitis, and seizures with residual optic nerve involvement following intrathecal administration of 6–20 mL doses of gadolinium [18–20]. MRI myelography is used to evaluate cerebrospinal fluid leaks, in which case, the intrathecal space is intentionally accessed;  $<1$  mL of gadolinium administration is considered safe during these procedures [21–24].

There have been several case reports of complications associated with GBCM administration via an interlaminar approach for spinal injections [25].

- A 73-year-old woman underwent an L4-L5 interlaminar epidural steroid injection, during which 1.5 mL of gadobutrol was injected

[16]. The patient had seizure-like activity but was eventually discharged with a full neurological recovery.

- A 67-year-old female was inadvertently injected intrathecally with 4.0 mL of gadodiamide (Omniscan) while undergoing an L5-S1 interlaminar injection [26]. A subsequent CT of the head revealed diffuse cerebral edema with uncal herniation. The patient was eventually discharged in good medical and neurological condition.
- A 61-year-old male initially underwent an L4-L5 interlaminar injection that was complicated by inadvertent intrathecal injection. During a successful second attempt at the L5-S1 interspace, the patient received 4.0 mL of gadolinium (Omniscan) [19]. The patient was diagnosed with gadolinium encephalopathy, and after 10 days in the hospital, the patient was discharged home but continues to have seizure-like activity controlled by phenytoin.
- A 67-year-old female with lumbar stenosis secondary to ligamentum hypertrophy underwent a minimally invasive lumbar decompression (MILD) procedure that resulted in death attributed to unintentional intrathecal GBCM administration [27]. During the MILD procedure, the epidural space was targeted with an 18 gauge Tuohy needle, and 5 mL gadoteridol was injected to identify the epidural space. Presumably, an unintentional intrathecal injection occurred. Subsequent events included seizure activity, multisystem organ failure, and eventual coma. Advanced brain imaging demonstrated an accumulation of GBCM in the intrathecal fluid as well as infarcts suggestive of anoxic brain injury. This patient died 18 days after the MILD procedure.

## Recommendations

It is essential for interventional pain physicians to possess a comprehensive understanding of the current literature regarding GBCM to ensure informed and safe clinical practice [1].

- **The use of GBCM in the performance of spinal epidural injections using an interlaminar approach is not recommended.**
- For transforaminal epidural injections, GBCM is also not recommended, although this recommendation is less strong given the current level of evidence. When the use of GBCM is necessary, physicians should limit the volume to the minimum required, ensuring it does not exceed 1 mL per session for injections involving the epidural space, where there is a risk of intrathecal entry. Additionally, it's crucial to engage the patient in a shared decision-making process to thoroughly discuss the risks and benefits associated with GBCM use.
- For interventional procedures with a low risk of intrathecal access, such as medial branch blocks, the low risk of GBCM should be discussed with the patient.
- In the setting of an ICM allergy, certain procedures may be safely performed without using contrast media. All interventional spine procedures are elective, and the physician must be mindful that not performing the procedure may be the best available option.
- If performing an interventional spine procedure with GBCM and intrathecal injection is suspected, the procedure should be aborted. Additional GBCM should not be administered.
- If the decision to use GBCM is made, safeguard measures should include the use of a non-particulate steroid for a transforaminal epidural steroid injection, fluoroscopic guidance of the needle to the ideal target using at least two planes for precise localization, real-time fluoroscopic digital subtraction imaging when available, repeated negative aspirations, and administration of small aliquots ( $<0.5$  mL) of GBCM with subsequent fluoroscopic imaging before any additional injection. However, these measures are **not applicable to interlaminar injections**, as GBCM is not recommended for use in such procedures.
- Spine interventions using GBCM carry a risk of severe complications from inadvertent intrathecal injection. For certain procedures, like

ILESI, this risk is high enough that GBCM is not recommended. In other cases, while the use of GBCM is still not recommended, if considered under exceptional circumstances, the risks must be thoroughly evaluated and clearly communicated with the patient.

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