

Gadolinium Use in Spine Pain Management Procedures for Patients with Contrast Allergies: Results in 527 Procedures

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Abstract

Introduction To review the safety and efficacy of gadolinium in spine pain management procedures in patients at high risk for a contrast reaction and who are not suitable candidates for the use of standard non-ionic contrast.

Methods We reviewed records over a 61-month period of all image-guided spinal pain management procedures where patients had allergies making them unsuitable candidates for standard non-ionic contrast and where gadolinium was used to confirm needle tip placement prior to injection of medication.

Results Three hundred and four outpatients underwent 527 procedures. A spinal needle was used in all but 41 procedures. Gadolinium was visualized using portable C-arm fluoroscopy in vivo allowing for confirmation of needle tip location. The gadolinium dose ranged from 0.2 to 10 ml per level. The highest dose received by one patient was 15.83 ml intradiscally during a three-level discogram. Three hundred and one patients were discharged without

complication or known delayed complications. One patient had documented intrathecal injection but without sequelae and 2 patients who underwent cervical procedures experienced seizures requiring admission to the intensive care unit. Both the latter patients were discharged without any further complications.

Conclusion Based on our experience we recommend using gadolinium judiciously for needle tip confirmation. We feel more confident using gadolinium in the lumbar spine and in cervical nerve blocks. Gadolinium should probably not be used as an injectate volume expander. The indications for gadolinium use in cervical needle-guided spine procedures are less clear and use of a blunt-tipped needle should be considered.

Keywords Contrast · Contrast allergies · Discography · Epidural injection · Facet injections · Gadolinium · Nerve root blocks · Pain management

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Introduction

The use of epidural injections for the treatment of back pain was first described by Evans in 1930 [1]. Since then a growing body of evidence has documented the need for fluoroscopic confirmation of needle placement [2, 3] using X-ray-attenuating contrast. Most commonly, this involves non-ionic contrast. However, there is a small but significant group of patients who exhibit allergic symptoms to contrast. Previously contrast reactions have been documented in the setting of vascular injections. A vascular injection is a recognized complication of spinal pain management procedures [2]. Vascular injections should be avoided as they may result in injection of particulate steroid and local anesthetic into the systemic circulation with possible

embolic effects and arrhythmias, respectively. In one series by Katayama and coworkers, adverse drug reaction with the intravenous use of non-ionic contrast was noted in 1.2–3.13% of cases, of which 0.02–0.04% were severe [4]. Thus there is a group of patients, albeit a small one, who should not be receiving iodinated contrast be it ionic or non-ionic. Another common potential complication of epidural injections is inadvertent intrathecal injections. This carries a risk of spinal anesthesia with subsequent hypotension in patients who may have limited cardiovascular reserve; also adhesive arachnoiditis can be induced by some classes of steroids [5, 6].

Very little has been published in the literature regarding the use of gadolinium-based contrast agent in the intrathecal space [7–9] as there are few clinical applications, and there has been no work on the use of gadolinium-based contrast agent in the epidural space. In the limited series published thus far, low-dose intrathecal gadolinium-based contrast agent has not been associated with any significant adverse effects. As needle misplacement is the commonest complication of percutaneous spinal injections, it is essential to use a safe contrast medium to determine the exact position of the needle tip in all patients. We therefore present our collective findings on the use of gadolinium-based contrast agent as an effective contrast agent in percutaneous outpatient image-guided spine procedures, demonstrating it as a safe alternative in most patients who are otherwise not candidates for contrast use.

Materials and Methods

We performed a retrospective search of our computerized data system for records of percutaneous outpatient spinal interventions carried out from 2001 to January 2006 (61 months). The search included all interlaminar and foraminal epidural steroid injections, nerve blocks, facet and pars injections, intercostal blocks, and discograms in the lumbar, thoracic, and cervical spine where gadolinium-based contrast agent was used. Gadolinium-based contrast agent was used for confirmation of the needle tip location in cases where contraindications existed to the routine use of Iohexol 240 (Omnipaque, Nycomed, Edison, NJ, USA). Contraindications to iodinated contrast were defined as a documented history of adverse reactions following injection of iodinated contrast medium, patients in or with a history of renal failure, or diabetics with increased creatinine levels as determined by the reference ranges at the local laboratory, and patients on Glucophage or Glucovance who had taken their medication in the 48 hr leading up to the procedure.

All procedures were performed on an outpatient basis utilizing portable C-arm fluoroscopy (OEC 9600 or OEC

9800, General Electric, Milwaukee, WI, USA). The patients signed informed consent for the procedure and were given the alternatives of rescheduling the procedure after steroid premedication, the use of saline or air in place of contrast, or aborting the procedure. All cases were performed as part of routine clinical care and not as part of a research study. As is the clinical routine in our facility, all patients were observed for at least 30 min after procedure and given standard instructions to call the radiologist on call in the event of an adverse reaction. The procedures were performed under sterile conditions with the patient fasting for between 1 and 4 hr prior to the start. Under fluoroscopic guidance a Quincke (various manufacturers) 22G or 25G needle or, in some cases in the cervical spine, a Whitacre (various manufacturers) 22G needle, was guided into position. The gadolinium-based contrast agent was drawn into a syringe (5 or 10 ml) from a container that had been open for less than 24 hr and stored in a dark cupboard at temperatures between 15 and 30°C, as per the manufacturer's recommendations. A test injection of gadolinium-based contrast agent was then performed to confirm the correct location of the needle and to exclude vascular or intrathecal injection. The procedure was performed, at the discretion of the operator, using local anesthesia but without conscious sedation. All patients were outpatients and the procedure was performed using a portable C-arm (GE 9600 or 9800, General Electric, Milwaukee, WI, USA) for guidance in an outpatient suite. Following successful needle localization the patients were administered with, depending on the procedure type, the epidural or perineural therapeutic dose of steroid and anesthetic. Cervical epidural injections had only steroid administered and discograms had only intradiscal anesthetic administered after the pain response was determined. The patients were observed following the procedure. At the start of the observation period, the patients were walked off the procedure table back to the waiting area. During the walk back to the observation area their gait was observed to ensure that they could walk steadily. The patient then sat in the observation area for 20–45 min. Prior to discharge, the patient's pain was re-evaluated, and they were questioned as to any symptoms they had subsequent to the procedure that were not present previously. They were then given instructions with contact numbers to ring if necessary.

Results

We identified 304 patients who underwent 527 procedures by 14 practitioners in three states using gadolinium. The 304 patients in whom gadolinium was used were consecutive though they were interspersed with many patients without contraindications to routine use of Iohexol 240

who had pain management procedures. Table 1 provides a breakdown of the type of procedures and contrast amounts. A Quincke needle was used in all but 41 procedures. These 41 procedures were all cervical interlaminar injections where a Whitacre needle was used. All patients were outpatients and all except 2 were discharged without complication after 20–45 min. No delayed complications were reported to the operators by patients or the referring physicians. In all but 22 procedures gadodiamide (Omniscan; Nycomed Amersham, Oslo, Norway) was used. In the remaining 22 procedures gadopentetate (Magnevist; Schering, Germany) was utilized.

While gadolinium-based contrast agent was less conspicuous than Omnipaque, there was sufficient visualization of the contrast material (Figs. 1–3). For epidural steroid injections the dose of gadolinium-based contrast agent ranged from 1 ml to 10 ml, for nerve blocks from 0.2 to 1 ml per level, for facet injections from 0.2 to 0.5 ml per level, and for discograms from 1.5 to 7.5 ml per level. The highest dose received by one patient was 15.83 ml intradiscally during a three-level discogram.

Three hundred and one patients were discharged without complication after 20–45 min, with follow-up instructions. One patient had documented intrathecal injection but without sequelae. This patient had an attempted interlaminar injection at L5-S1. Once it was noted with the initial

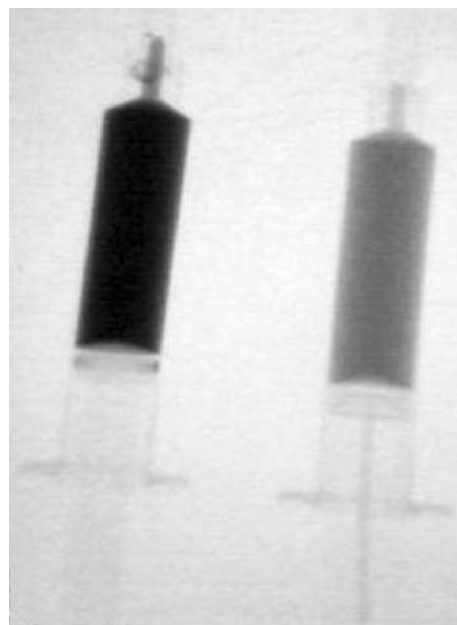


Fig. 1 Visualization of Iohexol and gadolinium-based contrast agent using fluoroscopy. Five milliliters of Iohexol/Omnipaque 240 (left) and Gadolinium/Omniscan (right) were drawn into a 5 ml syringe and a snapshot image obtained using a portable C-arm (GE 9600) at 0.6 mA and 46kV

Table 1 Procedure type, location, and contrast amounts

Procedure		No. of patients	No. of procedures	Gadolinium amounts (ml per level)
Grand total		305	527	
Discogram	Total	52	182	
Lumbar		46	157	0.3–7.5
Thoracic		4	13	0.9–1.8
Cervical		6	12	0.5–0.6
Epidural injection (interlaminar)	Total	171	204	
Cervical		44	54	0.2–5.0
Thoracic		6	6	1.0–2.0
Lumbar		113	142	0.2–10.0
Caudal		2	2	2–5
Facet injection	Total	11	25	
Cervical		2	6	0.2–0.2
Lumbar		9	19	0.2–0.5
Pars injection	Total	2	3	0.2–0.6
Intercostal injection	Total	1	3	0.5
Cervical nerve blocks	Total	12	14	0.2–1.0
Thoracic nerve blocks	Total	2	2	0.5–0.8
Lumbar transforaminal injection	Total	76	94	0.2–5.0

test injection of 3 ml of gadolinium that the needle had breached the intrathecal space, the procedure was converted to a transforaminal injection. The patient was discharged after the usual follow-up (approximately 30 min) without complications and reported no adverse events to us or their primary physician.

Another patient who had a strong positive history of multiple allergies (the patient claimed to be allergic to “anything red” as well as having had a previous contrast reaction), undergoing a two-level cervical discogram, initially tolerated the procedure well. She received a total of 1.4 ml of diluted Omniscan solution. There was no evidence of intrathecal injection. After 10 min in the recovery area, she complained of nausea followed by vomiting. The patient then broke out in a cold sweat, becoming progressively incoherent and hallucinatory. She was seen by an urgent care physician who proceeded to treat her for a contrast reaction. The patient then had two grand mal seizures. On transfer to the intensive care unit she was intubated. An MRI examination documented intrathecal gadolinium-based contrast agent (Fig. 4). She was treated symptomatically, had no further seizures, had an uneventful recovery, and was discharged home on day 3 without any residual complications. Follow-up at 10 days revealed a complete return to baseline functioning.

On the same day as the reaction above, another patient undergoing a cervical epidural injection with a 25G Quincke needle using 5 ml of Omniscan (from a different

Fig. 2 Cervical interlaminar epidurography using **A** gadolinium-based contrast agent and **B** Iohexol 240

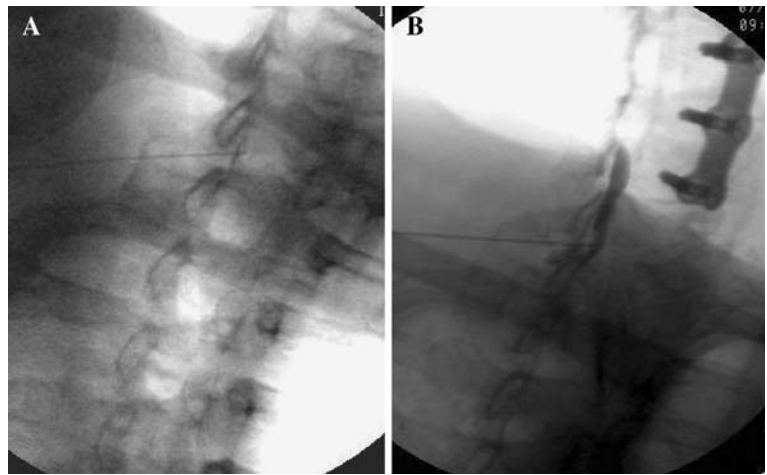
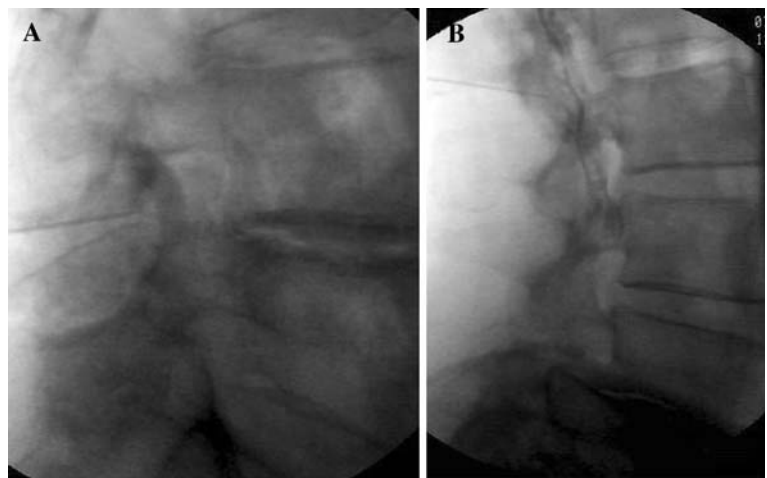


Fig. 3 Lumbar interlaminar epidurography using **A** gadolinium-based contrast agent and **B** Iohexol 240



bottle but the same batch as the above) started complaining of headache which rapidly became more severe approximately 10 min after the procedure and was soon followed by vomiting. After another 5–10 min, the patient had a grand mal seizure. A CT scan (Fig. 5) confirmed the presence of intrathecal contrast and gas. The patient was admitted to the intensive care unit where she experienced a ventricular tachycardia which responded well to medication. The patient's family admitted that the patient had suffered diarrhea and gastrointestinal upset recently, and an electrolyte evaluation revealed hypokalemia. The electrolyte imbalance was corrected and the patient was discharged on day 3 with amnesia to the actual event but no other sequelae. Follow-up at 10 days revealed no lasting effects.

Discussion

Degenerative back disease is a growing health care problem as more patients achieve older age. Furthermore, there is a growing trend toward using percutaneous image-

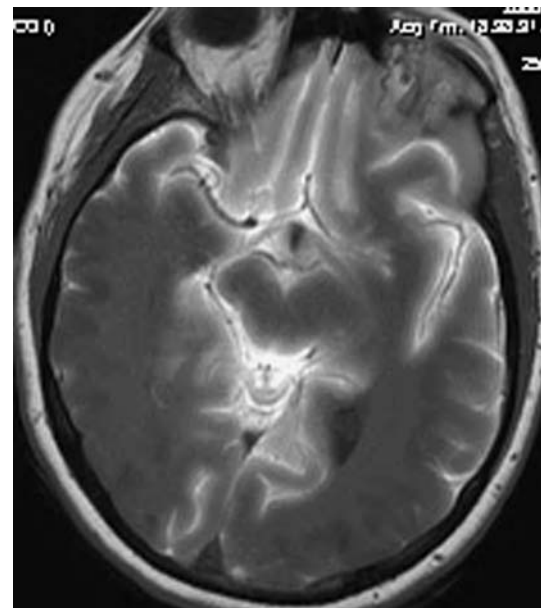


Fig. 4 T1 weighted axial MR image of the brain showing intrathecal gadolinium-based contrast agent

guided spine interventions to alleviate or palliate pain [10, 11], and as a prelude to surgery—both in determining whether surgery is necessary and in determining the operative levels [12, 13]. Yet to date there is no paper in the medical literature to guide physicians in the use of gadolinium-based contrast agent in the event a patient is considered an unsuitable candidate for iodinated contrast in image-guided spinal procedures. As part of the informed consent process required for such procedures, one of the basic tenets is to give the patient a complete overview of the risks and benefits. This paper addresses that gap in the literature.

There is a significant body of evidence attesting to the safety of gadolinium-based contrast agents injected intravenously, with doses as high as 60 ml being injected for CT angiography [14] and MR studies [15–17]. To date there have been no reported overdoses of Omniscan [18]. Mild to moderate side effects occurred in less than 1% of patients when administered intravenously [19–25]. Nausea or vomiting and headache are the most common side effects, with a frequency ranging from 0.26% to 0.42% [21]. Other rare reactions reported after the intravenous administration of gadolinium-based contrast agents include paresthesias, dizziness, focal convulsions, urticaria, mucosal reactions, generalized flushing, cardiovascular reactions (e.g., tachycardia, arrhythmia), generalized seizures, laryngospasm, and anaphylactic shock [19–25]. Severe life-threatening allergic reactions to intravenous administration of

gadolinium-based contrast agent have a reported frequency of 0.0003–0.01%. A study in an animal model that used intrathecal low doses of gadolinium-based contrast agent did not reveal such alterations [26]. A large multicenter study of 95 patients showed no deleterious effects of up to 5 ml of a gadolinium-based contrast agent (Magnevist; Schering, Berlin, Germany) injected into the lumbar subarachnoid space [8]. Other studies demonstrated the safety of gadolinium-based contrast agent injected directly into the ventricles [27] and for cisternography [9] without complications in small cohorts. The US Food and Drug Administration approves the use of gadolinium for joint injections (e.g., facets). Technically, the use of gadolinium-based agents for epidural injections and disk injections is in a gray area as some would view the disk as a joint (if a joint is defined as the area between two bones) and the epidural space in that region as analogous to the joint capsule. Our two adverse events both resolved without sequelae but required intensive care admissions. Both were cervical spine procedures: one a discogram and the other an interlaminar epidural. While there was no documentation of intrathecal injection in either, we postulate that an annular tear must have been present in the cervical discs injected and that somehow with the maneuvers involved the contrast made its way into the intrathecal space. Alternately, it is conceivable that somehow the needle entered the subarachnoid space. The dose of contrast used in that examination was well within the safe dose documented in previous studies. Furthermore, in discography the contrast mixture does include antibiotics, which have been demonstrated to result in seizures when instilled in the subarachnoid space. That patient did, additionally, have a strong allergic history. In the second patient, we postulate that the spinal needle used did somehow nick the dura and thus contrast made its way into the intrathecal space. This would be in keeping with the intrathecal gas seen on CT (Fig. 5). A confounding variable in both these procedures was that they happened within 1 hr of one another in the same clinic, to a very experienced radiologist using the same batch of Omniscan. The possibility that the batch was somehow defective can therefore not be excluded. It is of note that the one patient who also had a lumbar intrathecal injection had no adverse event.

While this study did not include a formal control group, as suggested by Johnson [28], the practice of epidural spinal injections is now so widely entrenched in routine clinical medicine that there is no need for a formal control group. The risks and complications of image-guided spinal procedures using iodinated contrast have been published by members of our group as well as others and have been well documented [2, 10, 11]. The authors of this paper (excluding the authors' partners/colleagues) together perform approximately 60 such procedures per day using



Fig. 5 Non-contrast axial CT scan of the brain showing intraventricular gadolinium-based contrast agent

Omnipaque. Extrapolating that to the thousands of physiatrists and pain specialists in the United States, innumerable of these procedures are performed daily. Therefore, the “control” is the routine standard of care. Furthermore, our injection techniques are identical to those used in the original paper by our colleagues in 5,334 cases [2] and which are currently the standard of care with a known and accepted safety profile.

We chose to include all image-guided pain management procedures in this study as the potential for intrathecal or intravenous administration exists with them all. Previous series of gadolinium-based contrast agent discography used gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) at low concentrations for MR discography [29, 30]. For these unusual applications of discography, such low doses suffice. However, for routine discography and other percutaneous spine interventions such low doses would not attenuate the X-ray beam sufficiently to be visualized and therefore higher doses would have to be used. A small case series [31] did use gadolinium-based contrast agent for lumbar discography and subsequent CT but did not specify the dose; no patient showed no complications. The entity of nephrogenic systemic fibrosis (NSF) has recently found interest as a contraindication to gadolinium use. We do not believe that this applies to these patients as the doses of gadolinium that are described in the literature leading to NSF are at least 3 to 9 times higher than those used in this study [32]. However, we did not perform any procedures on patients on dialysis, and therefore our data may be limited in this respect.

The importance of defining the exact position of the needle tip can not be understated and accurate positioning is difficult to achieve without some form of contrast injection [3]. The main danger in imprecise needle position is intrathecal administration of injectate, which may result in steroid-induced adhesive arachnoiditis and anesthetic-induced spinal anesthesia, which can cause hypotension [5, 6]. Vascular injection may result in particulate steroid material entering and embolizing in the circulation and resulting in arrhythmias due to vascular local anesthesia [33]. The only method of confirming a nonvascular location is via a contrast injection, as saline and/or air would not opacify the small perispinal vessels [2]. Ultimately, even if blind needle placement does not result in an adverse event, it has been shown that a blind approach does not result in correct placement of therapeutic material [2, 3, 34, 35] in up to 30% of instances. While this may not hurt the patient, it would not benefit them either and would result in an essentially ineffective procedure for which the patient is charged a fee. Therefore, contrast injection in the performance of image-guided spinal interventions is a necessity and not a luxury.

Conclusion

Based on our experience we recommend using gadolinium-based contrast agent judiciously for needle tip confirmation. We are more confident using gadolinium-based contrast agent in the lumbar spine and in cervical nerve blocks. Gadolinium-based contrast agent should probably not be used as an injectate volume expander. The indications for gadolinium-based contrast agent use in cervical epidural injections are less clear and use of a blunt-tipped needle should be considered.

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