

Intrathecal Iohexol: Rare Complications Clinicians Should Recognize

Intrathecal administration (into the cerebral spinal fluid (CSF)) of contrast agents are routinely used to enhance visualization to reveal detailed pictures of the spinal cord, nerve roots, and surrounding structures. Additionally, there have been reports of accidental administrations to the area. Compared with older ionic and oil-based agents, nonionic contrast agents such as iohexol have markedly improved safety profile with common adverse effects of headache, musculoskeletal pain, nausea, and vomiting. However, serious neurologic complications have been described.

Why did Iohexol replace older agents?

Earlier contrast agents such as iophendylate (Pantopaque) and metrizamide (Amipaque) were associated with high rates of seizures and encephalopathy. Animal studies consistently demonstrated severe inflammatory reactions, prolonged cerebrospinal fluid (CSF) retention, and direct neuronal injury related to the lipophilicity of these agents. In contrast, iohexol, a nonionic water-soluble contrast medium, demonstrated reduced neurotoxicity in both animal and human studies, with minimal meningeal irritation and rapid CSF clearance.^{2,4}

Pharmacokinetics

Human and animal pharmacokinetic studies demonstrate that intrathecal iohexol is rapidly absorbed from the CSF into systemic circulation, with peak serum concentrations occurring within 2–3 hours and approximately 80–85% eliminated renally within 24 hours.^{5,10} These rapid peak concentrations suggest that neurologic symptoms may occur within hours of administration, although multiple case reports describe delayed presentations with altered mental status more than 24 hours post-procedure.

Limitations in Safety: Continued Neurological Complications

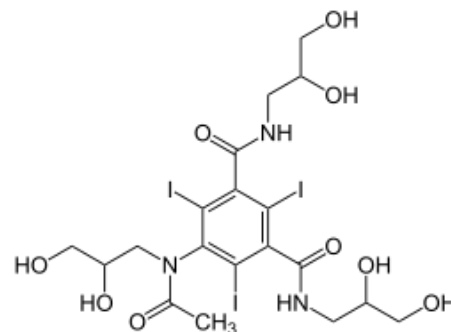
Despite its favorable safety profile, rare but serious complications have been reported. This includes seizures, status epilepticus, aseptic meningitis or meningoencephalitis, transient spinal shock, and diffuse cerebral edema. Notably, many cases describe delayed neurologic deterioration 24–72 hours after myelography, often following an initially uneventful course. Neuroimaging frequently reveals diffuse cerebral edema, while CSF cultures remain negative. Most patients recover with supportive care. Proposed mechanisms of neurotoxicity include blood–brain barrier disruption, osmotic shifts, and direct neuronal membrane toxicity.^{1, 7,8,9,11,12}

Management Options

There are no standardized treatment guidelines for suspected intrathecal iohexol neurotoxicity. Recommended management includes prompt neurologic assessment, urgent CT or MRI of the brain in patients with altered mental status, and ICU admission for moderate to severe symptoms. Utilization of CSF lavage, or drainage, has not been routinely reported in iohexol case series, likely due to its intended use in myelography and rapid CSF clearance. Published iohexol cases describe recovery with supportive management alone, including osmotherapy, corticosteroids for vasogenic edema, antiseizure therapy, and ICU monitoring.^{7,8} Conversely, CSF lavage has been primarily described in cases of accidental intrathecal exposure to ionic contrast agents, where immediate ventriculolumbar lavage or external ventricular drainage was used to rapidly remove a highly neurotoxic substance.^{6,13} While not routinely recommended, CSF removal may be considered in exceptional cases of immediately recognized nonionic contrast overdose, though evidence supporting this approach remains limited.

References:

1. Donaghy, M., Fletcher, N. A., & Schott, G. D. (1985). Encephalopathy after iohexol myelography. *The Lancet*, 2. Drobeck, H. P., et al. (1986). Subarachnoid administration of iohexol in primates. *Acta Radiologica Diagnostica*. 3. Drory, V. E., et al. (1990). EEG recordings following intrathecal iohexol administration. 4. Holder, J. C., et al. (1984). Iohexol lumbar myelography: clinical study. *AJNR*. 5. Holtz, E., et al. (1983). Absorption after subarachnoid and subdural administration of iohexol. *AJNR*. 6. Hudson, K., et al. (2017). Management of accidental intrathecal ionic contrast exposure. 7. Kelley, B. C., et al. (2011). Malignant cerebral edema following CT myelogram. *Radiology Research and Practice*. 8. Khodor, S., & Blumenthal, S. (2018). Vasogenic cerebral edema following CT myelogram. *Case Reports in Neurological Medicine*. 9. Lohana, A. C., et al. (2020). Intrathecal iodinated contrast-induced spinal shock. *BMJ Case Reports*. 10. Olsson, B., et al. (1985). Absorption of iohexol from CSF to blood. *Neuroradiology*. 11. Romesburg, J., & Ragozzino, M. (2009). Aseptic meningitis after iohexol myelography. *AJNR*. 12. Rosenberg, H., & Grant, M. (2004). Ascending tonic-clonic syndrome after intrathecal iohexol. *Journal of Clinical Anesthesia*. 13. Schwab, S., et al. (1996). Ventriculolumbar lavage after accidental intrathecal ionic contrast. *Journal of Neurology*.



Iohexol Chemical Structure

Did you know?

There was a long standing myth that shellfish allergies increased the risk of adverse reactions to iodinated contrast dye.

This misconception stemmed from the presence of iodine in shellfish, but has since been debunked. Shellfish allergies are protein-mediated, not iodine-related, and do not require routine premedication or contrast avoidance.

Misbah Khatib, PharmD
Clinical Toxicology Fellow

 @MPCToxTidbits