

# CASE SERIES ON IOHEXOL INDUCED FEBRILE REACTIONS, TACHYCARDIA, CHILLS, AND EMESIS

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## **ABSTRACT:**

A medication called Iohexol is used prior to imaging or radio imaging treatments. Iohexol is a prescription drug that includes iodine and is categorized as a contrast medium or dye. It works in these imaging examinations by making body fluids and tissues stand out more, by opacification of blood vessels is how it works. Anaesthesia, fever, chills, rash, dyspnoea, emesis, cardiac arrhythmia, and anaphylactic reactions are examples of serious adverse drug reactions of Iohexol. Patients in this case series have reported chills, tachycardia, fibrillation, emesis, when using it for CT-SCAN. In this case series, we have discussed the reactions to contrast agents. Most of these reactions occur in the first 20 minutes following the administration of contrast. Positive patient outcomes, therefore, depend on their early detection and treatment. The radiology personnel and the hospital emergency response team together with pharmacist must step in when there are serious reactions.

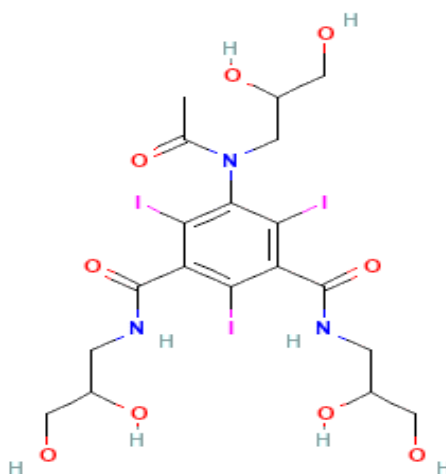
**KEY WORDS: Iohexol, Computed Tomography Scan (CT-SCAN), Opacification, Hyperthermia, Anaphylactic reactions, Dyspnoea.**

## SUMMARY

### Case series on Iohexol Induced Febrile Reactions Tachycardia, Chills, And Emesis

## INTRODUCTION:

Iohexol, N,N'-Bis(2,3-dihydroxypropyl)-5-[N-(2,3-dihydroxypropyl)-acetamido]-2,4,6-triiodoisophthalamide is a non-ionic, water-soluble radiographic contrast medium with a molecular weight of 821.14 (iodine content of 46.36%). Tri iodinated molecule is insoluble in an aqueous solution.



**Fig 1:Chemical structure of Iohexol**

This drug is used before imaging or radio imaging procedures (like Computed Tomography scans). Iohexol is an iodine containing contrast medium which functions by enhancing the contrast of bodily fluids and other parts in the imaging studies <sup>[1]</sup>

#### Product Overview:

- The volume and concentration of Iohexol to be injected is determined by the equipment and technique used, as well as the degree and extent of contrast necessary in the areas(s) under inspection.
- The least amount of dose required for sufficient visualization should be administered. Maximum concentration is not required in most of the procedures. Based on the clinical trial data till date, the recommended dose for adult myelographic examination is 360mg of Iodine or a concentration of 300mgI/ml<sup>[2]</sup>.
- Iohexol which is rather hypertonic to CSF, is advised for adult lumbar or direct cervical injection examinations of the thoracic ,cervical, and lumbar regions at a concentration of 300mgI/mL.
- Anesthesia , premedication tranquilizers or sedatives are typically not required. Patients should drink plenty of water both before and after receiving contrast <sup>[3]</sup>

- Patients who are prone to seizures ought to continue taking anticonvulsants.
- Concurrent medications shouldn't be physically mixed with contrast agents because several radiopaque contrast agents are incompatible in vitro with a variety of other medications, including certain antihistamines <sup>[4]</sup>.

## Mechanism of Action

Iodine-containing body structures can be distinguished from non-iodine-containing body structures by means of organic iodine compounds that absorb x-rays as they travel through the body. The entire amount (concentration and volume) of the iodinated contrast agent in the x-ray's path directly relates to the degree of opacity these compounds create. The subarachnoid spaces of the head and spinal canal can be seen after intrathecal administration due to the dispersion of iohexol in the CSF. Iohexol causes the vessels along its path of flow to become opaque after intravascular administration, enabling interior features to be seen until a considerable hemodilution takes place. <sup>[5]</sup>.

### Pharmacokinetics

- In conventional radiography, Iohexol will continue to offer acceptable diagnostic contrast for at least half an hour after intrathecal injection. Iohexol gradually diffuses throughout the CSF before being absorbed into the bloodstream. (6) Iohexol exhibits limited potential to bind to serum or plasma proteins after it enters the systemic circulation. Conventional myelography will no longer be able to use diagnostic-quality contrast for around an hour after injection. If a computed tomographic (CT) myelography is the next step, it is advisable to wait a few hours for the contrast level to drop <sup>[7]</sup>.
- Computerized tomography reveals the presence of contrast medium in the thoracic region in approximately one hour, in the cervical region in approximately two hours, and in the basal cisterns in three to four hours following administration into the lumbar subarachnoid space. Volume of distribution 350-349ml/kg.
- Iohexol is excreted by the kidneys after being taken into the bloodstream from the cerebrospinal fluid (CSF). There is no discernible biotransformation, deiodination, or metabolism.
- 87-89% of IV injected Iohexol is excreted unchanged through the kidneys within 24hours in patients with normal renal functions. Elimination Half-life was 2 hours <sup>[8]</sup>.

## Adverse drug reactions

Numerous clinical investigations have demonstrated that hematomas and ecchymoses have been associated with Iohexol <sup>[10]</sup>.

**Table 1: Adverse drug Reactions of Iohexol <sup>[11]</sup>**

<b>Responses to Iohexol</b>	<b>Adverse drug reactions</b>
Hemodynamic Responses	Thrombophlebitis, Vein cramps
Cardiovascular Reactions	Cardiac Arrhythmias, Reflex Tachycardia, Hypertension, Cyanosis, Chest discomfort, Peripheral Vasodilation, Shock, Cardiac arrest.
Renal Responses	Transitory Proteinuria, Oliguria, Anuria
Allergic Reactions	Asthma attacks, nasal and conjunctival symptoms, urticaria with or without pruritus, pleomorphic rashes, sneezing, lacrimation, and infrequently anaphylactic reactions
Respiratory Responses	Bronchospasm, Dyspnoea, and pulmonary or laryngeal oedema
Other Effects	Flushing, discomfort, warmth, metallic taste, nausea, vomiting, headache, anxiety, pallor, weakness, sweating, localized oedema, particularly in the face, neutropenia, and dizziness are some other effects

Rarely, rigors can come on suddenly or gradually, and they can occasionally be followed by hyperpyrexia

In this case series three cases were described in which all the cases represented **Iohexol Induced Febrile Reactions Tachycardia, Chills, And Emesis.**

### **CASES REPORTS:**

We present three cases admitted for different clinical scenarios who underwent Contrast injected computed Tomography (CT) scans that resulted in the development of CT contrast - induced febrile reactions, breathlessness, high pulse rate, anxiety, etc.

#### **Case: 1**

A 32-year-old male patient was admitted in general medicine ward with chief complaints of intermittent fever, decreased appetite for 1 week, weight loss and was on Tab Escitalopram 20mg 0-0-1 for his recognized anxiety condition. Vitals were normal and was diagnosed with pyrexia with unknown origin. He had a CECT scan of his abdomen and pelvis, which revealed several solid liver lesions, splenomegaly with a dilated portal vein system. His ESR was elevated, his C-reactive protein test resulted in 176.8 mg/L (0-6mg/L), and his haemoglobin level was found to be low. Antipyretic medicines and Optineuron (Vitamin B Complex injection) in 100ml NS was administered to the patient. Additionally, he was taking antibiotics like Inj. Ceftriaxone, which helped to lower his fever. The patient developed high grade fever, chills, and emesis following contrast induced computed tomography. Inj. Pheniramine Maleate 2ml IV stat, Inj. Acetaminophen 1g IV, and Ondansetron 4mg IV were administered. On a review it was concluded that the above mentioned reactions were induced by Iohexol.

**Case: 2**

A 41-year-old female patient is a known case of type 2 diabetes mellitus and hypertension admitted to general medicine ward with complaints of burning micturition for 2 months, fever, and abdominal pain while urinating, was diagnosed to have urinary tract infection hypertension and diabetes. The patient was advised to undergo CT Scan following which she developed dyspnoea, elevated Heart Rate, anxiety, and increase in body temperature. She was administered with Hydrocortisone 100mg IV stat, Inj. Acetaminophen 1g stat IV right away. After the investigation it was determined the above results were induced by CT Contrast.

**Case: 3**

A 55-year-old male patient was diagnosed to have Urinary tract infection with pyelonephritis with complaint of Fever, chills, abdominal pain and severe vomiting. The patient was advised for contrast KUB (Kidney, Ureter, Bladder) of CT SCAN following which he developed high grade fever, palpitations and dyspnoea. On examination, Temperature was 102 °F, Pulse rate was 110bpm, Respiratory rate was 30 bpm. On review by clinical pharmacist, it was determined that the above-mentioned reactions were induced by Iohexol. Hence Inj. Hydrocortisone stat was given right away. It verified the palpitations and dyspnoea was brought on by Iohexol.

**Adverse drug reactions were recorded and causality assessment was done by clinical pharmacist.**

**DISCUSSION:**

It has been noted that the incidence of adverse drug reactions to non-ionic iodinated contrast media is rare. Certain studies have revealed that Iohexol has shown the evidence of chills, hyperthermic, neurotoxicity in patient following coronary angiogram with Iohexol in an end-stage renal disease. According to *Sridhar et al.*, Iohexol was used during CT-SCAN in which the patient's experienced chills, Hyperthermia and dyspnoea<sup>[12]</sup>. *Mortele et al.*, studies explains the evidence of adverse events such as urticaria, facial or laryngeal oedema, bronchospasm, severe nausea/vomiting<sup>[13]</sup>. Similarly, *Wang et al.*, reported acute allergic like reactions occurred in patients related to IV administered non-iodinated contrast media. From these case reports, adverse drug reactions to the non-iodinated CT-contrast were managed therapeutically and significant clinical recovery was achieved<sup>[14]</sup>.

Rehydration therapy with water can be administered as a pharmacist intervention to offset the effects of dehydration, both before and after CT-SCAN. Antihistamines and systemic corticosteroids used as preventative measures may stop mild to moderate hypersensitivity reactions in their tracks. Monitor the patient's cardiac rhythm, blood pressure and oxygenated saturation. Contrast media reactions can be prevented by test dose for intended contrast or use of an alternative.

## CONCLUSION:

This case series confirm that Iohexol induces chills, febrile reactions, tachycardia, palpitations. More prospective studies are required to consolidate the drug action. Reactions to contrast media range from mild reactions to life threatening severe reactions. Most acute reactions occur within 1 hour of contrast administration with majority occurring within first 20 minutes. Therefore, it is important to be aware of these reactions, to monitor the patient closely and manage the reactions when they do occur.

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