IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Adverse Drug Reaction of Iohexol a Case Report

Ms. Vaishnavi Ajit Gawari, Prof. Kiran. K. Bibave, Mr. Suresh J. Chaudhary
Mr Prasad Chokhande, Dr. P. N. Sable
SSP Shikshan Sanstha Siddhi College of Pharmacy, Chikhali, Pune, India

Abstract: *Iohexol is a medicinal product used for the diagnosis of any abnormalities associated with blood vessels and also used in CTSCAN. It acts by the mechanism of opacification of blood vessels. Major ADR's includes Hypersensitivity Reactions such as Chills, hyperthermia, rash, dyspnoea etc., but they are very uncommon and sometimes negligible (<1%) In a Tertiary-care hospital, it is used for CT-SCAN which the patients have experienced Chills & Hyperthermia. 33 years old female patient came to the hospital for CT Brain venography, Inj. iohexol(350 mg I/ml) was administered. Patient developed fever after few hours. In this case series, we have discussed the incidence, management and analysis of fever an ADR of Iohexol with the help of healthcare professional intervention.*

Keywords: Iohexol, CT-SCAN, Venography, Fever, healthcare professional intervention, Opacification

I. INTRODUCTION

1.1 Adverse drug reactions:

The term "adverse drug reaction" (ADR) refers to an unpleasant and inadvertent reaction that happens at the dosage of a medication that is typically used for illness prophylaxis, diagnosis, or therapy.

Traditionally, ADRs have been classified into two types:

Type A reactions – sometimes referred to as augmented reactions – which are 'dose-dependent' and predictable on the basis of the pharmacology of the drug

1) Excess pharmacological effect

It is the most common adverse drug reaction which may occur due to excessive pharmacological effect of the drug. Excessive pharmacological effect generally appears due to over dosage of a drug.

This is particularly troublesome with cardioactive., hypotensive, hypogiycemia and central nervous system depressive agents.

Eg Paracetamol can cause hepatic Toxicity in case of liver disease

Hepatocytes metabolize paracetamol via microsomal cytochrome P450 (CYP450) into non-toxic byproducts. This metabolism pathway via CYP450, specifically cytochrome P450 2E1 (CYP2E1), produces reactive oxygen species, originally thought to be the ultimate cause of liver injury in paracetamol overdose.

2) secondary pharmacological effect

No drugs have a single pharmacological effect. Any effects which are associated with a drug besides the desired effects are called as Secondary Effects

Drugs have several pharmacological actions at usual therapeutic dose but it is Prescribed solely for one of these be.

Eg . Bronchospasm with propranolol (due to effect on undesirable beta2 blocking effect) Thus for propranolol, Bradycardia is primary pharmacological adverse effects Bronchospasm is a secondary pharmacological adverse effect.

3) Toxicity following sudden withdrawal of drug

For example, alcohol is a depressant, so if you suddenly stop consuming alcohol, you might experience symptoms of overstimulation such as anxiety or restlessness.

Tolerance occurs after prolong use of variety of drugs of narcotic analgesics, ethyl alcohol, some hypotensive agents (clonidine) and corticosteroids drugs. Sudden Withdrawal of such drugs shows severe adverse effects.

Type B reactions – bizarre reactions – which are idiosyncratic and not predictable on the basis of the pharmacology.

1) Idiosyncrasy

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Eg Barbiturate instead of inducing depression ,leads to excitement and mental confusion in some individuals.Barbiturates enhance GABA-mediated chloride currents by binding to the GABA-A receptor–ionophore complex and increasing the duration of ionophore opening

Idiosyncratic adverse drug reactions result from mechanisms that are not currently understood. This type of adverse drug reaction is largely unpredictable. Examples of such adverse drug reactions include rashes, jaundice, anemia, a decrease in the white blood cell count, kidney damage, and nerve injury that may impair vision or hearing. These reactions tend to be more serious but typically occur in a very small number of people. Affected people may have genetic differences in the way their body metabolizes or responds to drugs.

2) allergic drug reactions

Eg anaphylaxis to Amoxicillin

Unfortunately, the pathogenesis of allergic reactions to antibiotics in general and amoxicillin in particular is not well characterized; in addition to IgE and T cell-mediated mechanisms it has been suggested that certain antibiotics can bind non-covalently to antigen-interacting structures, such as the T cell receptor

Allergic drug reactions are not dose-related but require prior exposure to a drug. Allergic reactions develop when the body's immune system develops an inappropriate reaction to a drug (sometimes referred to as sensitization). After a person is sensitized, later exposures to the drug produce one of several different types of allergic reaction. Sometimes doctors do skin tests to help predict allergic drug reactions.

3) Genetically determined Toxicity

• Patients of selected genetic makeup are at substantially greater than average risk for some specific drug toxicities.

E.g.:- glucose-G-phosphate dehydrogenase is involved in degradation of glucose for producing energy.

1.2 What are the benefits of ADRs repoting:

• Improvement on the quality of care offered to patients
• Reduction of medicine related problems leading to better treatment outcome
• Improved patient confidence in professional practice.
• Access to feedback information on medicine related problems reported within the country and internationally
• Satisfaction for the fulfillment of a moral and professional obligation

Seriousness

1.3 ADR Detection Methods and Reporting:

Detection Method of ADRs :

1) Pre-marketing studies
2) Post-marketing surveillance
3) Assessing Causality
4) Communicating ADRs
5) Postal Survey Method.

Spontaneous reporting of Adverse Drug Reactions:

The Spontaneous reporting structure is the voluntary and the most common way through which the regulatory bodies collect ADR information for medicines once they are on the market.

Individual Case Safety Report (ICSR):

A document providing the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary reporter to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual patient at a particular point of time.

Preventability of ADRs: Complete preventability of ADR is not possible, but some of the ADR can be preventable if that ADR can give at least one answer of Schumock and Thornton Scale.

Predictability of ADRs: Patients who have had the drug on previous occasion(s): If the drug was previously well-tolerated at the same dose and route of administration, the ADR is NOT PREDICTABLE; there was a history of allergy

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

or previous reaction to the drug, the ADR is PREDICTABLE. Patients who have never had the drug previously: Incidence of the ADR reported in product information or other literature determines its predictability.

Causality Assessment of ADRs Based on Algorithm:

The degree of association of an adverse of an adverse reaction with a drug is done with the help of Naranjo's algorithm.

Severity of ADRs:

After the causality assessment has been done, the severity of the ADR is analyzes using adapted Hart wig severity scale

The Scale is classified as:

1. Mild: A reaction that does not required treatment or hospital stay.

2. Moderate: A reaction that requires treatment and or prolongs hospitalization by at least one day.

3. Severe: A reaction that is potentially life threatening or contributes to the death of patient is permanently disabling requires intensive medical care or results in a congenital anomaly cancer or unintentional overdose.

To study the onset of ADRs:

1. Acute: Acute events are those which are observed within 60 minutes after the administration of medication.

2. Sub-Acute: These occur within 1-24 hours from the time f administration of medication.

3. Latent: These reaction take 2 more days to become apparent.

1.4 Adverse Drug Reaction Probability Scale(Naranjo scale):

The Naranjo algorithm, Naranjo Scale, or Naranjo Nomogram is a questionnaire designed by Naranjo et al. for determining the likelihood of whether an ADR (adverse drug reaction) is actually due to the drug rather than the result of other factors. Probability is assigned via a score termed definite, probable, possible or doubtful. Values obtained from this algorithm are often used in peer reviews to verify the validity of author's conclusions regarding adverse drug reactions. It is also called the Naranjo Scale or Naranjo Score.

The ADR Probability Scale consists of 10 questions that are answered as either Yes, No, or "Do not know". Different point

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
	Total Score:			

Scoring

1) ≥ 9 = definite ADR
2) 5-8 = probable ADR
3) 1-4 = possible ADR
4) 0 = doubtful ADR

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

CT Brain Venography:

CT cerebral venography (also known as a CTV head or CT venogram) is a contrast-enhanced examination with an acquisition delay providing an accurate detailed depiction of the cerebral venous system.

A CT venogram is obtained in a number of clinical scenarios where anatomy and patency of the cerebral veins is required. CT venography yields detailed images of the intracranial venous circulation with consistently high quality. It is a rapid, useful method for diagnosis of dural sinus thrombosis and for preoperative mapping of venous structures in patients with neoplasm.

II. AIM AND OBJECTIVES

Aims:

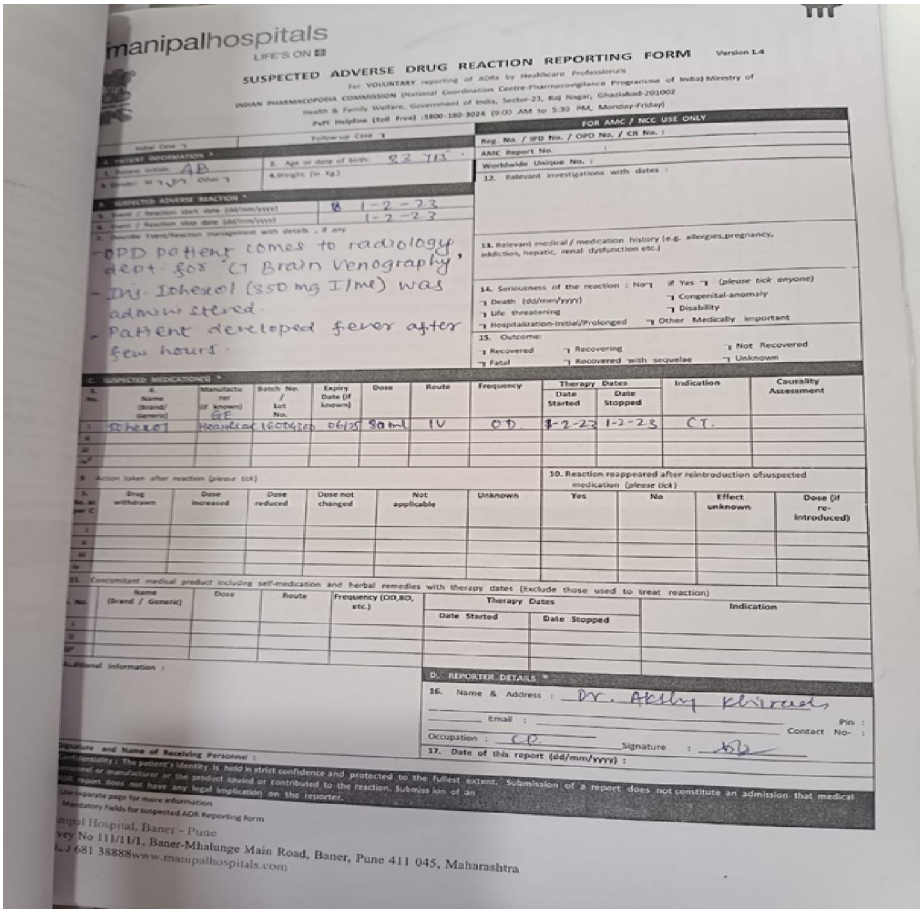
- Aim of these case report observational study of adverse drug reaction
- It focus on the Adverse drug reaction of Inj, Iohexol

Objectives:

- To monitor ADR in Indian population.
- To generate independent, evidence based recommendations on the safe of medicines.

Primary objective:

- To Study the adverse drug reaction due to iohexol Injection.



IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

III. STUDY MATERIAL & METHOD

STUDY CRITERIA:

Inclusions:

- Patient's name, age, gender.
- Drug Prescribed.
- Dosage of Drugs Prescribed & dosage form.
- Route of Administration.

Exclusions:

- Incomplete information regarding patient

3.1 Materials and Methods:

Study Title:-

To study adverse drug reaction due to Iohexol injection.

The Present study was conducted at Manipal Hospital, Baner during the period of 22 april, 2023 to 28 april, 2023.

Study Design

observational study

Source of study population :-

OPD patient visited to Manipal Hospital, Baner.

Sample Size:-

Number of Patient admitted for Adverse drugs Reaction in Manipal Hospital ,Baner meeting inclusion and exclusion criteria during eight day's study period .

Inclusion: -

Patient's name, age, gender.

Drug Prescribed.

Dosage of Drugs Prescribed & dosage form.

Route of Administration.

Exclusion:-

Incomplete information regarding patient

IV. CASE STUDY

Patient demographics: OPD patient came in radiology department for CT brain venography, Inj. Iohexol 350mg/ml was administered by intravenous route ,patient developed fever after few hours.

4.1 Patient Information:

Patient Initials –AB

Age – 33 yrs

Sex – Female

Hospital/Clinic – Manipal Hospital Baner , Pune

Therapy Dates :

Date Started – 01/02/2023

Date Stopped – 01/02/2023

Indication – CT

Suspected Medication Details -

Drug - Inj.Iohexol

Batch No.-16004300

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Reaction start date:1/2/23
Reaction stop date :1/2/23
Dose – 350mg/ml
Route – Intravenous (IV)
Expiry date – 06/25
Frequency - OD
Indication – Fever
Reporter Details
Name – Dr. Akshay Khirade
Address- Clinical Pharmacologist ,Manipal Hospitals.
Contact – 9604020940
Occupation- Clinical Pharmacologist

V. SUSPECTED MEDICATION

Iohexol is a contrast agent for intrathecal administration used in myelography and contrast enhancement for computerized tomography.

History

Omnipaque (Iohexol) was approved for medical use in 1985. It is on the World Health Organization's List of Essential Medicines.(1)

124 reports was analyzed of adverse reactions related to contrast agents between 2006 and 2021. Our findings revealed that ADR combinations occurred more frequently after the use of iodinated contrast agents (72.08%) than gadolinium contrast agents (27.92%).

Iomeprol, Iopromide, Ioversol, Iodixanol, and Iohexol are the examples of iodine contrast media [2]. Conversely, Gadobutrol, Gadobenic acid, Gadoteridol, and Gadoteric acid are the examples of Gadolinium contrast media (2)

WHY IOHEXOL IS PREFERRED CONTRAST MEDIA

The development of non-ionic contrast mediums, e.g. iohexol, iopamidol, has considerably reduced the risk of complications during or following angiography.

Iohexol is a safe, nonionic, low osmolar contrast agent (MW 821 Da). It is eliminated exclusively by the kidneys, where it is filtered but not secreted, metabolized, or reabsorbed. It has less than 2% binding to protein. Therefore it makes an ideal marker of GFR and a good alternative to radiotracers.

Iohexol is emerging as an excellent alternative to inulin and radioisotopes for clearance studies.

Iohexol and iothalamate have similar kinetic profiles, but iohexol has a lower allergic potential.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Brand Names
Omnipaque, Oraltag
Generic Name
Iohexol
Background:
Iohexol is an effective non-ionic, water-soluble contrast agent which is used in myelography, arthrography, nephroangiography, arteriography, and other radiographic procedures. Its low systemic toxicity is the combined result of low chemotoxicity and low osmolality.

5.1 Drug Categories: contrast media or dyes
Dose strengths:
Adult & Pediatrics:
180mg/mL
240mg/mL
300mg/mL
Route of Administration:
Intrathecal
Volume of distribution
350-849 mL/kg
Route of elimination
Iohexol is absorbed from cerebrospinal fluid (CSF) into the bloodstream and is eliminated by renal excretion. No significant metabolism, deiodination, or biotransformation occurs.
Omnipaque 140/300/350
Ventriculography: 40 mL, range of 30-60 mL; may be repeated as needed, not to exceed 250 mL
Pharmacodynamics
Iohexol is an effective non-ionic, water-soluble contrast agent which is used in myelography, arthrography, nephroangiography, arteriography, and other radiographic procedures. Its low systemic toxicity is the combined result of low chemotoxicity and low osmolality.
Mechanism of action :Allows for radiographic visualization through the opacification of vessels and anatomical structures in the path of flow of the contrast media
Pharmacokinetics
Protein binding: Minimal
Excretion: Urine (80-90%)
Duration: 30 min following intrathecal administration, 60 min following IV administration; 15-120 seconds in serum
Organic iodine compounds block x-rays as they pass through the body, thereby allowing body structures containing iodine to be delineated in contrast to those structures that do not contain iodine. The degree of opacity produced by these compounds is directly proportional to the total amount (concentration and volume) of the iodinated contrast agent in the path of the x-rays.
Half-life
Intrathecal half-life is 3.4 hours (mean). Intravascular is approximately 2 hours (with normal renal function).
Clearance
109 mL/min [Adult p
Toxicity:
Non-ionic radiocontrast agents like iohexol are cytotoxic to renal cells. The toxic effects include apoptosis, cellular energy failure, disruption of calcium homeostasis, and disturbance of tubular cell polarity, and are thought to be linked to oxidative stress.
Additional Information
Our Omnipaque (iohexol injection) Side Effects Drug Center provides a comprehensive view of available drug information on the potential side effects when taking this medication.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Description for Omnipaque

Iohexol,N,N′ -Bis(2,3-dihydroxypropyl)-5-[N-(2,3-dihydroxypropyl)-acetamido]-2,4,6-triiodoisophthalamide, is a nonionic, water-soluble radiographic contrast medium with a molecular weight of 821.14 (iodine content 46.36%). In aqueous solution each triiodinated molecule remains undissociated. The chemical structure is:(1)

Precautions

Before taking iohexol, tell your doctor or pharmacist if you are allergic to it; or to other contrast media; or to iodine; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details.

Before using this medication, tell your doctor or pharmacist your medical history, especially of: asthma, hay fever, kidney disease.

Before having surgery, tell your doctor or dentist about all the products you use (including prescription drugs, nonprescription drugs, and herbal products).

During pregnancy, this medication should be used only when clearly needed. Discuss the risks and benefits with your doctor.

When taken by mouth, this medication is unlikely to pass into breast milk. Consult your doctor before breastfeeding.

Indication

Iohexol ia used in myelography, arthrography, nephroangiography, arteriography, and other radiographic procedures.

Uses:

This medication is used before X-ray imaging tests (such as CT scans). Iohexol contains iodine and belongs to a class of drugs known as contrast media or dyes. It works by adding contrast to body parts and fluids in these imaging tests. Iohexol improves the images obtained during a CT scan, so your doctor can more easily diagnose your condition**.**

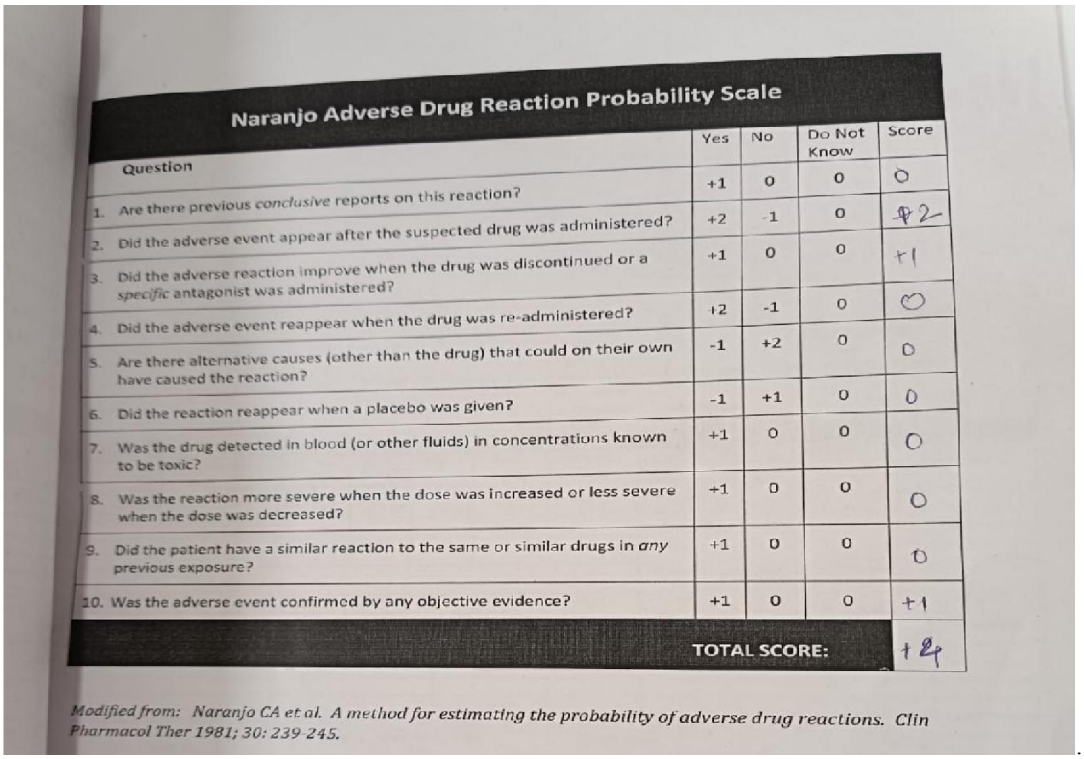
Drug interactions:

- **Acetazolamide:** The therapeutic efficacy of Acetazolamide can be decreased when used in combination with Iohexol.
- **Bupropion:** The risk or severity of seizure can be increased when Bupropion is combined with Iohexol.
- **Butalbital:** The therapeutic efficacy of Butalbital can be decreased when used in combination with Iohexol.
- **Cannabidiol:** The therapeutic efficacy of Cannabidiol can be decreased when used in combination with Iohexol

Adverse Effects:

- Frequency Not Defined
- Headache
- Mild to moderate pain including backache, neckache and stiffness
- Nausea, and vomiting
- Neuralgia
- Rash
- Erythema
- Pruritus
- Urticaria
- Skin discoloration
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis (SJS/TEN)
- Acute generalized exanthematous pustulosis (AGEP)
- Drug reaction with eosinophilia and systemic symptoms (DRESS)

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024



Naranjo Adverse Drug Reaction Probability Scale

Question	Yes	No	Do Not Know	Score
1. Are there previous *conclusive* reports on this reaction?	+1	0	0	0
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
			TOTAL SCORE:	+4

Modified from: Naranjo CA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30: 239-245.

Total total score:4

Scoring

1) ≥ 9 = definite ADR
2) 5-8 = probable ADR
3) 1-4 = possible ADR
4) 0 = doubtful ADR

VI. RESULT

The score on the Naranjo scale for the case report of adverse drug reactions (ADRs) of Inj. Iohexol (350mg/ml) OPD (Outpatient Department) patients is 4, it suggests a possible causal relationship between the medications and the observed ADRs. the need of ADR reporting in tertiary care hospitals to help in assessing the benefit risk ratio of drugs. From this study, it had been concluded that incidence of ADR occur due to the contrast media used in radiology department.

VIII. DISCUSSION

Omnipaque (iohexol injection) is a radiographic contrast medium indicated for intrathecal administration in adults including Venography and in contrast enhancement for computerized tomography (myelography, cisternography, ventriculography). Common side effects of Omnipaque include:headache,mild to moderate pain including backache, neck ache and stiffness, nerve pain, nausea,vomiting, hives, stomach upset or pain, visual hallucinations, and neurological changes.

33 years old female patient came to the hospital for CT Brain venography, Inj. iohexol(350 mg I/ml) was administered .Patient developed fever after few hours. In present study Naranjo scale was measured 4, it states that the type of adverse drug reaction is possible adverse drug reaction type. The study shows that the patient developed fever after the inj iohexol prescribed so it states that there is causality assessment in between adverse drug reaction and suspected medications

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

IX. CONCLUSION

The given case report concluded that the patient with CT venography prescribed with inj. iohexol developed a adverse drug reaction like fever after few hour .It states that there is causality assessment between suspected medication and adverse drug reaction. The score of Naranjo scale was 4, is states that the adverse drug reaction type is possible adverse drug reaction type.

Healthcare professionals should be aware of the potential for ADRs and be prepared to manage them appropriately, including promptly recognizing and discontinuing the offending medication if necessary. Overall, this case report highlights the importance of pharmacovigilance in monitoring patients for adverse drug reactions, spontaneous reporting particularly when introducing new medications or observing unexpected symptoms. It also emphasizes the need for further research and investigation to better understand the specific risk factors and mechanisms underlying adverse reactions to medications like Iohexol.

Further investigation, may be warranted to confirm the specific drug allergy and determine whether Inj. Iohexol should be avoided in the future. Healthcare professionals should also consider documenting and reporting this adverse drug reaction to relevant pharmacovigilance systems, contributing to the overall understanding and monitoring of drug safety profiles. Further investigation is needed.

REFERENCES

[1]. https://www.who.int/docs/default-source/medicines/safety-of-medicines--adverse-drug-reactions-

[2]. Aronson JK. Ferner RE. Clarification of terminology in drug safety. *Drug Saf.* 2005;28:851–70.

[3]. European Directive 2010/84/EU of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

[4]. Bates DW. Leape LL. Petrycki S. Incidence and preventability of adverse drug events in hospitalized adults. *J Gen Intern Med.* 1993;8:289–94.

[5]. Lazarou J. Pomeranz BH. Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA.* 1998;279:1200-1204.

[6]. Pirmohamed M. James S. Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ.* 2004;329:15–9.

[7]. World Health Organization. *International Drug Monitoring: The Role of National Centres.* Geneva: World Health Organization; 1972. (Technical Report Series No. 498).

[8]. Waller P. *An Introduction to Pharmacovigilance.* Southampton, UK: Blackwell Publishing; 2010

[9]. Kalaiselvan V, Mishra P, Singh GN. Helpline facility to assist reporting of adverse drug reactions in India. *WHO South East Asia J Public Health.* 2014;3:194.

[10]. Kalaiselvan V, Prasad T, Bisht A, Singh S, Singh GN. Adverse drug reactions reporting culture in pharmacovigilance programme of India. *Indian J Med Res.* 2014;140:563–

[11]. https://reference.medscape.com/drug/omnipaque-oraltag-iohexol-343760

[12]. https://go.drugbank.com/drugs/DB01362#:~:text=Iohexol%20is%20an%20effective%20non,low%20chemotoxicity%20and%20low%20osmolality.

[13]. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, et al. A method for estimating the probability of adverse drug reactions. Clin Pharacol Ther. 1981;30:239–45.