Original Article

A Case Series On Contrast Hypersensitivity Reaction During Coronary Angiography: Prompt Recognition And Treatment Is Life Saving

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Abstract

Background: Acute adverse drug reactions (ADRs) of contrast media are defined as abnormal symptoms occurring within 60 minutes following the administration of contrast media during cardiac catheterization. The symptoms range from minor ones like headaches, nausea, and vomiting to serious ones like cardiac arrhythmias, pulmonary collapse, laryngeal oedema, and other potentially fatal symptoms. Previous allergic reactions to contrast material, asthma, and allergies are factors associated with an increased risk of developing an adverse reaction.
Here we have described ten cases that have developed severe hypersensitivity to contrast agents during coronary angiography/angioplasty procedure.
Methods: This study was conducted at Department of Cardiology at Christian Medical College and Hospital (CMC&H), Ludhiana. A total of 10 patients who underwent angiography were taken from the Department of Cardiology at Christian Medical College and Hospital, Ludhiana over a 6-year period. An informed consent form (ICF) was provided to the patient prior to taking his/her personal details.
Results: Over a six-year period, 10 (0.18%) patients out of 5405 who underwent coronary angiography developed severe contrast reactions. These were 8 males and 2 female patients. Eight (80%) patients developed severe anaphylactic reaction during the procedure and two (20%) patient developed severe anaphylactic reaction within 2 hrs of the procedure. Contrast agent used was Visipaque in 4
(80%) patients and Omnipaque in 2 (20%) patient. Two patients subsequently underwent repeat invasive procedure in view of recurrent angina.
Conclusion: Life threatening severe contrast hypersensitivity reactions can occur rarely during invasive cardiovascular procedures. High index of suspicion of contrast hypersensitivity should be kept in mind with development of sudden onset of hypotension during the procedure. Prompt treatment with intravenous steroids
and adrenaline can be lifesaving. In patients, where deemed essential, repeat procedure can be done after pre-treating the patient with oral steroids.

Keywords: Contrast Hypersensitivity, ADR, Coronary Angiography, Non- ionic contrast, case series

Introduction

Contrast-enhanced angiography is a very useful tool for the diagnosis and evaluation of vascular diseases. Since their initial introduction in the 1930s, contrast media (CM) have grown in importance as a diagnostic tool. Nonetheless, there have been reports of CM reactions that fall into two categories: chemotoxic and allergic/pseudoallergic. The onset time, clinical symptoms, severity, pathogenesis,

diagnostic techniques, and management strategies of both reactions vary. Because they are less common, late adverse reactions to CM could be easily missed.[1]
Acute adverse drug reactions (ADRs) of contrast media are defined as abnormal symptoms occurring within 60 minutes following the administration of contrast media during cardiac catheterization. The symptoms range from minor ones like headaches, nausea, and vomiting to serious ones like cardiac arrhythmias, pulmonary collapse, laryngeal oedema, and other potentially fatal symptoms.[2,3]

Mild acute general adverse reactions include nausea, vomiting, mild urticaria, pallor, and pain in the injected extremity. Moderate adverse reactions include severe vomiting, extensive urticaria, laryngeal edema, dyspnea, and rigors. Severe reactions include pulmonary edema, cardiac arrhythmias, cardiac arrest, circulatory
collapse, and unconsciousness.[4] The kinin system and the direct or indirect activation of mast cells and basophils by the contrast agent or non-specifically activated complements as anaphylatoxin are thought to be responsible for the pathophysiology of the anaphylactoid reaction (C3a, C5a). Conversely, the contrast media's hyperosmoticity and hydrophobicity may result in a chemotoxic response.[5]

These reactions may be the consequence of several factors working in concordance with predisposed individuals, The factors include conditions such as age, sex, allergies, cardiovascular conditions, past reactions to these drugs, and characteristics of the contrast examination.[6] Pre-treatment of patients who have such risk factors with a corticosteroid and diphenhyramine decreases the chance of allergic reactions, including anaphylaxis, renal failure, or a possible life-threatening emergency.[7]
Here we have described ten cases that have developed severe hypersensitivity to contrast agents during coronary angiography procedure.

Methods:

This study was conducted at Department of Cardiology at Christian Medical College and Hospital (CMC&H), Ludhiana. A total of 10 patients who underwent angiography were taken from the Department of Cardiology at Christian Medical College and Hospital, Ludhiana over a 6-year period. These patients developed anaphylactic reaction to contrast agent used in coronary angiography. An informed consent form (ICF) was provided to the patient prior to taking his/her personal details. The format of ICF is shown in Annexure I. The study did not require approval from research and ethical committee as it was a case series.
The causality assessment was done by applying the Naranjo causality assessment scale. The Adverse Drug Reaction (ADR) Probability Scale was developed in 1991 by Naranjo. It consists of a series of 10 questions with responses of “yes”, “no” and “don’t know” where different point values (-1, 0, +1 or +2) are assigned to each answer. The reaction is deemed definite if the score is 9 or above, probable if it is 5 to 8, possible if it is 1 to 4, and doubtful if it is 0 or lower. The total scores range from -4 to +13.[8] The details of the Naranjo probability scale is shown in Annexure II.

Study design: This was a Descriptive case study.

Inclusion criteria: Patients diagnosed with anaphylactic reaction with contrast agent were considered.

Exclusion criteria:
1. Patients with underlying condition of hypersensitivity/allergic reactions.
2. Patients who refused to give the consent.

Statistical Analysis

The results were analysed using descriptive statistics and presented as percentage and proportions. Other than this as case series does not have any control group, no further statistics are required for analysis.

Results:

A total of 10 (0.18%) patients out of 5405 patients who underwent coronary angiography developed severe contrast reactions. There were a total of 8 male and 2 female patients. Mean age of the patients was 55.2±9.2. Eight (80%) patients developed severe anaphylactic reaction during the procedure and two (w0%) patients developed severe anaphylactic reaction within 2 hours of the procedure. All patients required intravenous hydrocortisone and adrenaline injection. Contrast agent used was Visipaque in 8 (80%) patients and Omnipaque in 2 (20%) patient. There was no mortality reported among the patients. Two patients subsequently underwent repeat invasive procedure in view of recurrent angina. Procedures were done after giving oral steroids and anti-histamines.
All adverse drug reactions reported secondary to contrast hypersensitivity were scrutinized as per the type of Contrast used: Ionic /Non ionic, Dose of the Contrast , whether the reaction was Early or Late and finally the causal relationship of the allergic reaction to the contrast.

10 cases were included in the Study. The Salient Features of these cases are shown in Table 1:

Table1- Comprehensive patient review

Pt.no	Age	Gender	Indication	Contrast used	Symptoms observed	Treatment given	Causality assessment
1	61	M	Coronary Artery Disease	Visipaque	Hypotension, itching	IV Hydrocortisone & Oral Prednisolone	Probable
2	49	M	Ant Wall STEMI	Omnipaque	Hypotension	IV Hydrocortisone & Oral Prednisolone	Probable
3	68	F	Acute Coronary Syndrome	Visipaque	Bronchospasm and hypotension	IV Hydrocortisone	Probable
4	48	M	Ant Wall MI	Omnipaque	Hypotension	IV Hydrocortisone & Oral Prednisolone	Probable
5	53	M	Ant Wall MI	Visipaque	Hypotension and generalized swelling	Inj Pheniramine and IV Hydrocortisone	Probable
6	64	M	Acute Coronary Syndrome	Visipaque	Hypotension, urticarial	IV Hydrocortisone & Oral Prednisolone	Probable
7	54	F	Ant Wall NSTEMI	Visipaque	Hypotension, itching	Inj Pheniramine and IV Hydrocortisone	Probable
8	61	M	Ant wall STEMI	Visipaque	Bronchospasm, generalized swelling	IV Hydrocortisone & Oral Prednisolone	Probable
9	67	M	Ant Wall MI	Visipaque	Hypotension, bronchospasm	IV Hydrocortisone	Probable
10	60	M	Coronary Artery Disease	Visipaque	Hypotension and generalized swelling	IV Hydrocortisone & Oral Prednisolone	Probable

Discussion

An increasing number of patients need coronary angiography due to the economy's rapid development and improvements in people's standards of living. Cardiac angiography and PCI (Percutaneous Cutaneous Angiography) are central to the evaluation and treatment of CAD (Coronary Artery Disease). These procedures rely on contrast media to accurately evaluate anatomy of the coronary vessels. Contrast agents can be iodinated or noniodinated.[9] High-osmolar contrast is associated with a 15% incidence of adverse events, whereas low-osmolar contrast is associated with a 3% incidence. Adverse reactions related to non-ionic contrast media are estimated at 5-10%.[10,11]
Adverse event is defined as any “untoward medical occurrence that may occur due to treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with treatment”.

It becomes an adverse drug reaction (ADR) whenever a causal link between the drug and the adverse event is established.[12]
Iodine contrast media (ICM)-related anaphylactic shock (AS) is the most serious adverse reaction that occurs in imaging examinations.[13] In anaphylaxis, systemic vasodilatation, reduced venous return, and volume loss due to increased vascular permeability lead to a diminished cardiac output, which contribute to coronary hypoperfusion and subsequent myocardial damage.[14]
In a study conducted by **Huang Z** et al, among of the 417,938 patients in whom ICM was used, 34 with Anaphylactic shock (AS) were monitored. The prevalence of AS was 0.008%. Among the 34 patients, 6 (0.001%) died from fatal anaphylactic reactions accompanying shock, 26 (76.5%) had hypotension as the first presentation of AS. It was inferred that Hypotension was more frequent in AS related to CM, and unconsciousness at the initial onset of AS implied a poor prognosis.[13]
Bhaskaran A confirmed a rare presentation of intraprocedural type II Kounis syndrome likely due to radioiodine contrast.[15]
Patients with cardiovascular diseases (especially when treated with beta-blockers) or oncologic comorbidities are at higher risk of developing hypersensitivity reactions to ICM.[14]
Acute severe life-threatening or fatal reactions to ICM are often unpredictable, and prompt recognition and immediate intervention are required.[16]

Premedication with corticosteroids and antihistamines is efficient in preventing ADRs.[17] Although emergent treatments for the ADRs usually work, some severe and fatal reactions, most of which occur within 20 min of the contrast medium injection, are too sudden and changeable to deal with.[18]

In a study conducted by He et al, a tool was developed on the base of TRUST trial(The Safety and toleRability of UltraviSt in Patients Undergoing Cardiac Catheterization, ClinicalTrials.gov identifier: NCT01206257), a simple risk score model was applied by clinicians at bedside to evaluate the risk of developing ADRs, so that action can be taken before unexpected reactions occur.
Age: if not 50–69 years, score =1;
Contrast media dose <100, score =1;
Preprocedural hydration: if not, score =2;
Premedication: if not, score = 1.

The risk score formula was RS (risk score) = 1 (age not 50–69) + 1 (CM dose <100) + 2 (preprocedural hydration: not) + 1 (premedication: not). Furthermore, patients were characterized with different risk scores into graduated risk levels according to the predicted probability of ADRs: low risk, score 0–2 (predicted probability: 0.09%); moderate risk, score 3–4 (predicted probability: 0.36%); high risk, score ≥5 (predicted probability: 1.78%).[3]
Based on above model, it was concluded that Age, contrast media dose, prehydration, and premedication are the basic factors of the model, as indicated by proper efficacy and accuracy.
Corticosteroids and H1/H2-receptor blocker were the common treatment for patients with adverse drug reactions. For patients who were evaluated to be high risk of ADRs, prophylactic premedication prior to administration of CM is proposed to be most effective in reducing the occurrence of mild or moderate ADRs. Absence of pre-medication as seen in the present study would therefore increase risk of ADRs.[3]

Iso-osmolar contrast media (like Visipaque) can help reduce major adverse cardiac and renal events (MARCE) in high risk patients.[3]
In this case series, patients developed severe hypotension which reverted with intravenous Fluids and Steroids . One case developed Severe Brochospasm which also responded to Steroids. Over the last 6 years, we observed only 10 cases which responded to Steroids and the patients subsequently underwent further interventions.

Conclusion

Life threatening severe contrast hypersensitivity reaction can occur rarely during invasive cardiovascular procedures and a high index of suspicion should be kept in mind with development of sudden onset of hypotension during the procedure. Prompt treatment with intravenous steroids and adrenaline can be life saving. In patients, wherever deemed essential, repeat procedures can be done after pre-treating the patient with oral steroids.

Conflict of interest

There is no conflict of interest.

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Nil

Patient consent

The consent was obtained from patients for reporting and publication. All information regarding patient's identity remains confidential.

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ANNEXURE-I

INFORMED CONSENT FORM

Title of study: **"CONTRAST HYPERSENSITIVITY REACTION DURING CORONARY ANGIOGRAPHY: PROMPT RECOGNITION AND TREATMENT IS LIFE SAVING"**

I, ……, do hereby consent to participate in the study entitled "CONTRAST HYPERSENSITIVITY REACTION DURING CORONARY ANGIOGRAPHY: PROMPT RECOGNITION AND TREATMENT IS LIFE SAVING."
I understand that:

1) The information collected about me from my participation of the study will be kept confidential and it will only be looked after by the concerned responsible individual for relevant academic/research purpose.
2) The nature and purpose of the study and its potential risks / benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail in a language that I comprehend and I have understood the contents to my satisfaction. I confirm that I had opportunity to ask questions.
3) Taking part in this case report is voluntary. I may choose not to take part or you may change your mind at any time. However, once the case report is written and published, it will not be possible for me to withdraw it.
4) I will not receive any financial benefits from the publication of this case and allowing your information to be used in this case report will not involve any additional costs to you.
5) The physician has fully explained to me the nature and purpose of a case report, the options and possibility of withdrawal.
I agree to take part in the above study.

_____ Date:
(Signature / Left Thumb Impression) Place:
Name of the Participant: ……
Son / Daughter / Spouse of: ……

Investigator
Signature: ……..
Date:
Name :……..
Place: ……..……
Phone ……..
Witness
Signature …….
Date: ....……
Name: ……
Place:

ANNEXURE II

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:			