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Research Article

CONTRAST INDUCED ALLERGIC REACTIONS AFTER CORONARY ANGIOGRAM PERFORMED USING NONIONIC CONTRAST MEDIUM

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A R T I C L E I N F O

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Coronary angiogram, Contrast induced reactions, Contrast material, Iopromide, premedication.

A B S T R A C T

Background information: The aim of the study is to identify and prevent the contrast-induced reactions during and after the coronary angiogram.
Materials & methods: 100 patients were included in our study. The patients who met the study criteria were enrolled into the study. Other relevant data was collected from the patient's profile form and by interviewing the patient. All the data was collected, entered in an Excel sheet and the statistical analysis was done in SPSS 16.0 Software by an appropriate statistical method chi-square significant p-value < 0.005(confidence interval 95%).
Results: The overall rate of reactions includes; 16 less severe reactions (33%) - grade 3 reactions, 12 moderate reactions (25%) – grade 2 reactions, 20 mild reactions (41.7%)– grade1 reactions. There is no significance difference in the grades having p-value 0.368(> 0.005). When compared, patients without premedication has higher incidence of reactions than in patients who took the premedication prior to the procedure which show significance p-value < 0.0012.
Conclusion: Our study unfolds that the use of iopromide is safe, less severe reactions were observed compared to the studies of ionic contrast material. Premedication is beneficial to the patients which reduce the occurrence of reactions predominantly in patients with risk. Mild to moderate reactions are common with the use of iopromide dye; careful assessment must be made in the prevention of reaction by providing symptomatic treatment.

INTRODUCTION

Coronary angiogram is the gold standard test for coronary artery disease. Common signs and symptoms that indicate to take the test are chest pain shortness of breath, palpitations, etc. Common angiograms can look at the arteries near the heart (coronary angiogram), brain (cerebral angiogram), lungs (pulmonary angiogram), head & neck (carotid angiogram), legs or arms (peripheral angiogram) and the aorta (aortogram) can be used[1].

The method of angiogram includes in which a thin tube (catheter) is inserted in the blood vessels in the groin (femoral artery or vein) or just above the elbow (brachial or radial artery) [2].Then iodine dye (contrast material) is injected into the blood vessels through a catheter to make the area show clearly visible on the X-ray pictures. It can find a bulge in the blood vessel (aneurysm), it can show narrowing or blockage in a blood vessel that affects blood flow. The indications [3] are Itis done to detect problems with blood vessels that affect blood flows such as a tear in blood vessels (which can blockage or internal bleeding), aneurysms (a weakness in the

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Blood Vessel wall) & Narrowed Areas

- It detects the changes in the blood vessels of injured or damaged organs.
- Show the pattern of blood flow to a tumor, it not only shows how much the tumor has spread but also guide treatment.
- Identify the source of bleeding, such as an ulcer.
- Check for the presence of atherosclerosis in the coronary arteries.
- Give an idea about the surgery on diseased blood vessels throughout the body.

Iopromide is the most commonly used contrast agent for coronary angiogram as there are comparatively less adverse reactions reported with this agent. Iopromide is a low osmolar nonionic X-ray CM for intravascular administration. It functions as a contrast agent by opacifying blood vessels in the path of flow of a contrast agent, permitting radiographic visualization of internal structure. Several cutaneous adverse reactions may develop from 1hr to several weeks after intravascular administration of contrast dye.[4]

Contrast media (dye) can cause within minutes after administration due to ingestion of iopromide dye, this cause mild to severe ADR'S. There was a higher incidence of ADRs

among women and for the age group ranging between 18 and 30 years. Patients who have experienced any reaction to contrast media or known allergic to iopromide are more prone to developing an ADR compared to the patients without these risk factors.

The incidence of ADRs was not altered by the use of premedication. In routine clinical practice, safety of iopromide can be compared to the safety of other contrast agents from the same group through published safety profiles. Adverse drug reaction rates were affected by age, gender, and risk factors (especially previous CM reactions or allergies), but not by premedication[5].

Review of Literature

Mortelé KJ, Oliva MR**,** Universal use of the nonionic iodinated contrast medium for CT; The ADRs induced by non-ionic iodinated contrast media are mainly mild ones, while moderate or severe ADRs are relatively rare, suggesting that enhanced CT examination with non-ionic iodinated contrast media is highly safe, and severe adverse events will seldom occur under appropriate care.

Michael A.Bettmann[1] Angiographic contrast agents, in the study this article reviews these side effects, examines their cause & considers the advantages of the newer media. These have satisfactory physical properties, reasonable cost & acceptable safe as indicated.

Dewachter P[1] Immediate allergy to iodinated contrast agents and prevention of reactions*;* this study reviews that allergic hypersensitivity to a given ICM imposes its definitive avoidance but not the avoidance of all iodinated drugs. Asthma and treatment with beta-blockers are not risk factors of immediate allergic reactions to ICM, but may increase their severity.

MATERIALS AND METHODS

Study design

It is a prospective observational study on the contrast induced reactions that occur during the coronary angiogram performed after injecting an iodinated contrast material.

Study Criteria

Inclusion Criteria

i. Patients with Coronary artery disease of both the genders
ii. Patients with Angina
iii. Patients with Single vessel disease(SVD)
iv. Patients with ST elevation myocardial infraction

Exclusion Criteria

i. Patients with the history of myocardial infarction.
ii. Patients below 18 years of age
iii. Patients who are already allergic to the contrast dye.
iv. Patients with atrial fibrillation.

- ✓ Patients who are admitted in to the inpatient ward of cardiology department of Sri Krishna Institute of Medical Sciences and who meet the study criteria are enrolled into the study.
- ✓ Relevant data such as demographic details, disease history, diagnosis, drug name, dose, route, frequency, duration of therapy, total pills per day, laboratory data, allergy status will be collected from medical records of the patient and by patient interview where ever required is collected and documented.
- ✓ Iopromide is the contrast media that is used in our study which is a nonionic contrast medium. Dose of the contrast media was given according to the weight of the patient i.e. 3-4ml/kg body weight.
- ✓ Changes to drug therapy, if any will be noted on the daily basis & documented.
- ✓ A suitable data collection form is designed for use in the study.
- ✓ To monitor the patient about the allergic reactions that may occur.
- ✓ Symptomatic treatment is given to avoid expected reactions to the contrast media.
- ✓ Premedication used in our study are Pheniramine maleate 25mg IV stat, Hydrocortisone 100mg Stat, Ampicillin IV for the premedication group and Montelukast is used for known sensitive patients like asthma, COPD.

Complete follow up was done within 2-3 weeks by interviewing during their review or by phone calls.

Source of Data

All the Relevant and Necessary Data Will be Collected From

1. Treatment charts.
2. Echo, ECG, Cath reports.
3. Interviewing the patient & patients care takers.
4. Interviewing nurse, cardiologist.
5. Any other relevant sources.

Naranjo Scale

Adverse Drug Reaction (ADR) Probability Scale: This scale was introduced to help standardize assessment of causality for all adverse drug reactions[6].This scale was used to assess the causality of the ADR in the study. It consists of 10 questions, answered as either Yes, No, or "Do not know". Different point values (-1, 0, +1 or +2) are assigned to each answer. A simplified version of the 10 questions, answers the question accordingly +1, 0,-1

The scores if > 9 = definite
ADR 5-8 = probable
ADR 1-4 = possible
ADR 0 = doubtful ADR

Statistical Analysis

All the raw data was collected, entered in Excel sheet 2007 in windows 10 version, the statistical analysis was done in SPSS 16.0 Software by an appropriate statistical method chi-square for knowing the significant pvalue < 0.005(confidence interval 95%).

RESULTS

Over the 6 months period of this study, we have collected 100 patients data, who underwent the cardiac catheterization based on the criteria (symptoms, ECG, Echo, and TMT).

Initially 112 patients were included in this study; 12 patients were excluded as they do not fit the criteria of the study. Among 12 patients, 8 patients were not willing to go through the test and four patients have no proper follow up.

Table 5.1 Mean of the patients from the study

The mean of the male patients is 58.44 ± 11.904 years.
The mean of the female patient is 54.92 ± 11.56 years.
The average mean of the total patients is 57.19 ± 11.812 years

Table 5.1 Mean of the patients included in the study

	Male	Female	Total
Mean	58.44	54.92	57.19
Standard deviation	11.904	11.56	11.812

Figure 1: Shows the age factor of the patients. Most patients who have undergone angiogram are between 41 to 60 years of age.

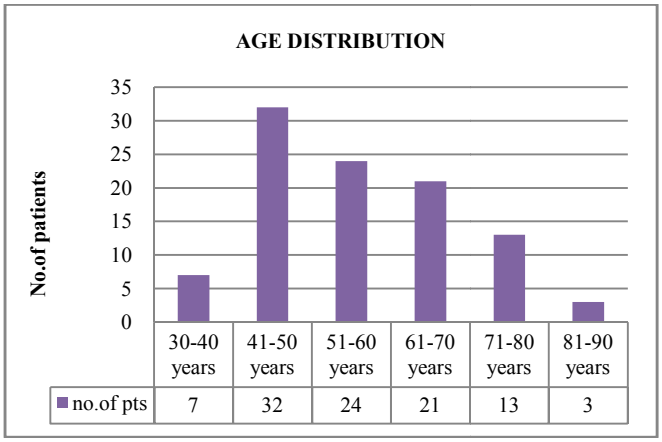


Figure 1 Age distribution of the patients from the study

Table 5.2 shows the patient characteristics based on gender. Among 100 patients 61 are male and 39 are female who have undergone angiogram. There might be higher chances of males to undergo the test than females indicating 22% higher prevalence of undergoing the test in the male patients.

Table 5. 2 (GENDER)

Gender	No of patients	Percentage
Male	61	61%
Female	39	39%
Total	100	100%

Figure 3 shows the patient characteristics i.e. past medical history, based on this we will give premedication to the subject prior to the test. There might be chances of contrast induced reactions due to risk factors (DM, Asthma, COPD, and CKD).

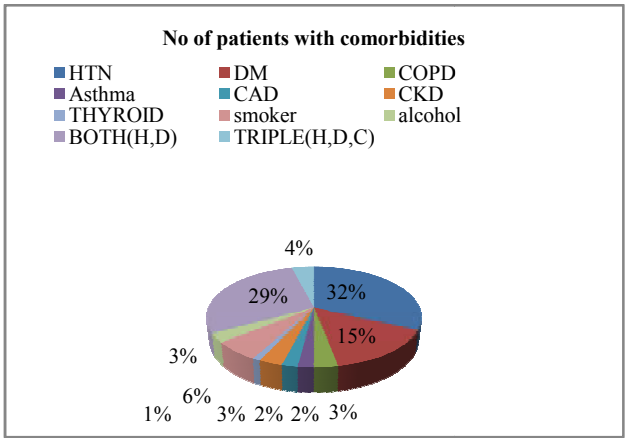


Figure 2 Patient comorbidities

Figure 3 This graph represents, incidence of the reaction. A total of 48 reactions were observed in 39 patients in a total number of 100 patients. 20 reactions in 15 patients were observed (grade 1 reactions). Grade 1 reactions are mild reactions, no hospitalization is required. Reactions in the patient were observed for 20 to 30 minutes or within 1 to 2 days.

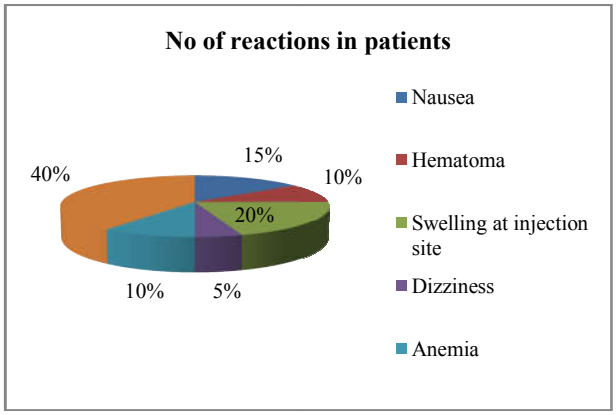


Figure 3 Grade 1 Reactions

Table 5.3 shows moderate reactions which doesn't require hospitalization but treatment is required. Among 48 reactions in 39 patients, 8 patients were observed grade 2 reactions. Grade 2 reactions are termed as moderate reactions that are not life threatening although they might be a progress of reactions but often require treatment. These reactions are closely monitored until they are resolved completely. Anti histamines (diphenhydramine) is given.

Table 5.3 Grade 2 reactions

Grade 2 reactions	No of reactions in patients	Percentage	Duration of reaction
Rigors	2	4.2%	1day
Vomiting	1	2.1%	1-2days
Hypotension	8	16.7%	1-4days
Fever & chills	1	2.1%	2-3days
Total	12	25%	

Table 5.4 shows severe reaction is life threatening which requires hospitalization and also treatment until they resolve. Mostly observed reactions in grade 3 were CIN (contrast induced nephropathy). Elevated serum creatinine level (grade3 reaction) was present in 16 patients. Treatment was given to the patients i.e. IV fluids (Nacl-0.9%, NaHCO3-166meq/L), furosemide or mannitol. Duration of reaction is 2-4 days and no incidence of reoccurrence.

Table 5.4 Grade 3 reactions

Grade 3 reactions	No of patients	Percentage	Duration of reaction
CIN	16	33.3%	2- 4 days

Table 5.5 shows that among 100 patients, 48 reactions were observed and these are categorized into grade 1, 2, and 3. By using Chi square test the observed and expected values were determined. Grade 1 observed value is 20 & expected value is 16, Grade 2 observed value is 12 and expected value is 16, Grade 3 observed value is 16 and expected value is 16.

Table 5.5 Chi square goodness of fit

Grade	1	2	3	4
Patients	20	12	16	0

Here, there is no significant difference between the grade1, grade 2, grade 3 reactions having p value - 0.368(> 0.005, 95%

confidence interval). By conventional criteria, there is no difference.

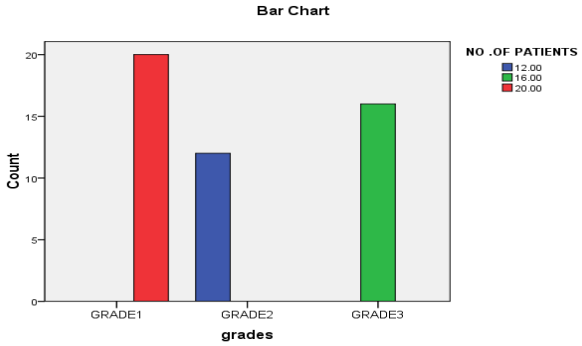


Figure 4

The premedication is beneficial to the patient which is given prior to the procedure. Among 100 patients included in the study, we categorized into 4 groups according to premedication.

a. Reactions were observed in patients who took premedication prior to the procedure i.e. 15 patients (15%)
b. Reactions were observed in patients who did not take the premedication prior to the procedure i.e. 24 patients (24%)
c. No reactions were observed in patients who took premedication prior to the procedure i.e. 38 patients (38%)
d. No reactions were observed in patients who did not take premedication prior to the procedure i.e. 23 patients (23%).

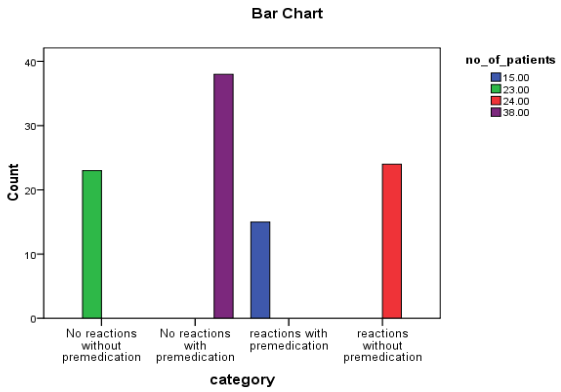
Table 5.12 shows that using the chi-square test in four groups & number of patients involved in the groups gives the expected & observed value i.e. A - observed value 15, B- observed value 24, C- observed value is 38, D- observed value is 23.

Table 5.6 Chi square (test of independence)

	Reactions	**Without reactions**	**Total**
Premedication	15	38	53
Without premedication	24	23	47
Total	39	61	100

Here, there is statistical significance difference between the 4 groups by using chi-square test, the following having p value 0.012(95% confidence interval). By conventional criteria, this difference is considered to be statistically significant.

Figure 5: The graphical representation shows that premedication is beneficial to the patients who are undergoing angiogram. This shows a peak at C indicating that the premedication is beneficial to the patient prior to the procedure which reduces the reactions on set.



DISCUSSION

The results observed from the taken sample size and subjects are, the prevalence of cardiac disorders is greater in male subjects than female i.e. 61% in males and 39% in females. Considering the age factor, the prevalence of cardiac disorders is more in the age group of above 40 years. Subjects in the age group 30-40years are 7, in 41-50 years are 29, in 51- 60 years are 27, in 61-70 years are 21, in 71-80 years are 13, and in 81-90 years are 3. In Grade I reactions - 20 reactions in 15 patients i.e. (3 subjects) 6.3% had nausea, (2 subjects) 4.2% had hematoma, (8 subjects), 16.7% got fever, (4 subjects) 8.3% suffered from a swelling at injection site, (1 subject) 2.1% had dizziness, (2 subjects), 4.2% had anemia. From Grade II reactions - 12 reactions in 8 patients, (2 subjects) 4.2% got rigors, (1 subject) 2.1% had emesis, (8 subjects) 16.7% had hypotension, (1 subject) 2.1% had fever & chills. From Grade III reactions (16 subjects) 33.3% had contrast induced nephropathy (CIN). According to our study the Naranjo scale score is 4, i.e. possible ADR. The chance of ADR is possible. We suggest a modified grading system on the basis of previously published severity categorizations[7, 8].

There are no deaths in our study. All the subjects in this study have co-morbidities. In this study we observed for adverse reactions after coronary angiogram with Non-ionic contrast media. We know that non-ionic contrast media are safer than that of Iodinated contrast material i.e. less ADRs compared to iodinated contrast material[9]. Nausea and vomiting are less common with Non-ionic low osmolal contrast media (LOCM). Some reactions are immediate, takes place within an hour of injection of contrast media. These reactions can be mild, moderate and severe. Patients with co-morbidities especially asthma and weak immune system, premedication is given to avoid the risk of ADRs. So the subjects given premedication are compared with those who have undergone angiogram without premedication. Reactions despite premedication are 15% without premedication are 24%. It is clear that premedication helps reducing the risk of reactions. Symptomatic treatment was given to the patients with reactions. The usage of steroid premedication is less clear, espoused by some authors as effective and others as useless in preventing recurrent reactions. Contrast induced nephropathy (CIN) is common with any contrast media but comparably less in non-ionic contrast media. In this study we have noted the increase in serum creatinine concentrations in some patients who have undergone coronary angiogram. This indicates the CIN in the subjects. In our opinion, those patients requiring urgent procedures before renal function can be measured should also be considered high risk. As there are many

subjects with co morbidities like diabetes and hypertension which is likely risk factors for CIN, this will justify the increased percentage of CIN in this study. The use of LOCM has been reported to reduce the incidence of adverse reactions as compared with HOCM.

CONCLUSION

According to this study the use of iopromide is safe and less severe reactions were observed compared to the previous studies of ionic contrast material. Premedication was beneficial to the patients, as it helped to reduce the occurrence of reactions predominantly in patients with risk. There are limited evidence that shows a single drug i.e. antihistamines may prevent certain reactions, drug combinations should be prescribed for the patients as premedication who are at the risk of reactions. Non-ionic contrast materials are better tolerated and the reactions are less severe. We conclude that non-ionic contrast material is widely used as it causes less severe reaction compared to HOCM. Mild to moderate reactions are common with the use of iopromide dye; careful assessment must be made in the prevention of reaction by giving symptomatic treatment. Patients have recovered from the reaction within a short period. Grade-1 reactions are more common compared to other reactions. There was no reoccurrence of reactions seen in the patients who have undergone the coronary angiogram.

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