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Original Investigation

A Study of Management of Adverse Reaction to Iodinated Contrast Media used in Computed Tomography at UCMS-TH

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ABSTRACT

INTRODUCTION: Iodinated contrast media is used in computed tomography imaging to enhance the visibility of blood vessels and tissues. They have distinct clinical effectiveness and toxicity profiles. Although low osmolar contrast media have made iodinated contrast media safer in recent years, adverse reactions can sometimes occur. The management of adverse reactions to iodinated contrast media is an important aspect of patient care during computed tomography examinations. The purpose of this study was to evaluate the management of adverse reactions to iodinated contrast media during contrast-enhanced computed tomography examinations at Universal College of Medical Sciences and Teaching Hospital, Bhairahawa, Nepal. **MATERIALS AND METHODS:** A prospective, observational study was conducted on 323 patients at Department of Radiodiagnosis and Medical Imaging, Universal College of Medical Sciences and Teaching Hospital, Bhairahawa, Nepal, from December 15, 2022 to May 15, 2023. All data was obtained from the Department of Radiodiagnosis and Medical Imaging, as per the study inclusion criteria. The data were analyzed with statistical package for the social sciences version 20. **RESULTS:** The mean age of study participants was 48.49±19.78 years. There were 34.67% male and 65.33% female patients involved in this study. Universal College of Medical Sciences and Teaching Hospital favoured a more strict approach, to determine the normal renal function and withhold metformin before iodinated contrast media exposure. 36.84% of patients had a history of previous adverse reactions, before undergoing contrast-enhanced computed tomography scans. Following iodinated contrast media administration, 94.74% experienced nausea and vomiting which was followed by mild urticaria (88.54%) and dyspnea (19.81%). Premedication protocol was predominantly implemented with antihistamine, pheniramine (73.1%), and corticosteroid, hydrocortisone (26.9%). Mild urticaria was treated with pheniramine (87.1%), nausea and vomiting was treated with metoclopramide (83.01%), dyspnea was treated by epinephrine, hydrocortisone and oxygen (9.38%). **CONCLUSIONS:** Universal College of Medical Sciences and Teaching Hospital has established a standard protocol for the management of adverse reactions experienced by patients during iodinated contrast media administration. Premedication with antihistamines and corticosteroids was recommended for high-risk patients.

Keywords: Computed tomography, drugs, iodinated contrast media

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INTRODUCTION

Iodinated contrast media (ICM) is commonly used in computed tomography (CT) imaging to enhance the visibility of blood vessels and tissues [1]. They have distinct clinical effectiveness and toxicity profiles [2-5]. Although the introduction of low osmolar contrast media (LOCM) has made iodinated contrast media safer in recent years, unpleasant responses can still occur. It is expected that 0.2% to 0.7% of LOCM patients would experience adverse effects [6-10]. Adverse effects to ICM can be classified as either immediate (occurring within an hour after CM administration) or delayed (occurring between one hour to one week after CM administration). Erythema, pruritus, urticaria, and angioedema are all signs of an allergic reaction to contrast media, but more serious reactions include hypotension, loss of consciousness and possibly fatal

bronchospasm and airway blockage [11]. Risk factors for adverse reactions to ICM include previous history of reaction, chronic urticaria, multiple exposures, large dose, increased rate of administration, intra-arterial administration, female sex, age, asthma, heart disease, dehydration, renal disease, anxiety, thyroid disorders, and diabetes. Nephrotoxic agents like non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate, aminoglycosides, and biguanides are also capable of acting synergistically with contrast media and causing renal failure. Patients treated simultaneously with these drugs should be carefully considered [12,13]. Biguanides induce lactic acidosis especially in patients with renal impairment when administered with iodinated contrast media. To avoid this complication, the CM manual recommends, withholding of metformin 48 hours before and 48 hours after administration of contrast media.

In patients without renal impairment or other comorbidities, there is no need to discontinue taking the metformin before receiving contrast media [14]. The American College of Radiology (ACR) and the European Society of Urogenital Radiology (ESUR) has recommended considering premedication guidelines to avoid adverse effects of ICM in patients receiving intravenous contrast media. Premedication includes antihistamines (Pheniramine or Diphenyhydramine either orally or intramuscularly) 1 hour before and corticosteroids like hydrocortisone intravenously, 1 hour before or oral methylprednisone [15-17]. Adverse reactions to iodinated contrast media may necessitate symptomatic treatment with antihistamines, corticosteroids, and other medications such as atropine, diazepam, midazolam, oxygen, and beta-2 agonists [18]. The purpose of this study was to evaluate the management of adverse reactions to ICM during contrast-enhanced CT examinations at Universal College of Medical Sciences and Teaching Hospital (UCMS-TH), Bhairahawa, Nepal.

MATERIALS AND METHODS

Study design and setting

This was a hospital-based, prospective, observational study. The study was conducted in Department of Radiodiagnosis and Medical Imaging, Universal College of Medical Sciences and Teaching Hospital, Bhairahawa, Nepal from December 15, 2022 to May 15, 2023.

Participants, sample size and sampling technique:

Participants who experienced adverse reactions to iodinated contrast media during contrast enhanced CT scans were included in this study. Convenience sampling technique was used to collect data. The sample size was calculated using following formula, n = z2pq/d2. Where, z = 1.96 at 95% confidence interval, p (prevalence) = 70% prevalence of adverse reactions across Korean and oversea hospital [12], q = 1-p and d = allowable error at 5%. By placing these values in the above-mentioned formula, hence, the sample size was approximately 322.69. Therefore, a total of 323 participants were included in this study. The inclusion criteria for the patients included: All patients who received IV iodinated contrast media, regardless of their age & gender, and experienced certain adverse effects; Serum creatinine in a range of 0.6-1.3 mg/dl; and patients who had given written consent. Patients with Serum creatinine > 1.3 mg/dl, and those who were under metformin medication (≥1500 mg/day) were excluded from this study.

Data collection procedure and study variables:

Data were collected on the basis of the severity of adverse reactions of participants after receiving iodinated contrast media while performing contrast-enhanced CT scans. This was an observational design where baseline variables of patients included: Age, gender, and types of adverse reactions. Data was gathered through face to face interview using a semi-structured questionnaire. The questionnaire was validated with expert's opinion from clinical faculties. Four hours mandatory fasting along renal function test was to be done before undergoing a contrast-enhanced CT scan.

Statistical analysis and data management:

Data were recorded in MS Excel and analyzed with SPSS version 20. Continuous data were expressed as mean ± standard deviation and categorical data were expressed as frequency and percentage.

Ethical consideration:

Ethical approval was taken from Institutional Review Committee (IRC) of Universal College of Medical Sciences and Teaching Hospital, with the reference number UCMS/IRC/226/22.

RESULTS

Table 1 shows a total of 323 patients who experienced adverse reactions to ICM out of which, 112 (34.67%) were male and 211 (65.33%) were female. The mean age of participating patients was 48.49±19.78 years. Majority of patients belonged to the age group of 41-60 years with a frequency of 103 (31.89%) followed by the age group of 61-80 years, 94 (29.1%) and 21-40 years, 85 (26.32%). The most common adverse reactions experienced after ICM administration was nausea and

Table 1 | Socio-demographic and medical status of the participants (n = 323)

Characteristics	Frequency	Percentage
Gender		
Male	112	34.67
Female	211	65.33
Age groups (years)		
< 20	32	9.90
21-40	85	26.32
41-60	103	31.89
61-80	94	29.10
> 81	9	2.79
Diseases		
Diabetes (type 2)	97	30.03
Renal Function		
Serum creatinine mg/dl)		
0.8	46	14.24
0.9	74	22.91
1.0	54	16.72
1.1	97	30.03
1.2	31	9.60
1.3	21	6.50
Risk factors for ICM administration		
History of previous adverse reactions to ICM	119	36.84

Table 2 | Types of adverse reactions experienced after ICM administration (n=323)

Types of Adverse Reactions	Frequency	Percentage
Mild Urticaria (includes-allergic reactions, skin rashes, erythema, itching and burning sensation)	286	88.54
Nausea and Vomiting	306	94.74
Dyspnea	64	19.81

Table 3 | Distribution of duration of withholding metformin among diabetics (n=97)

Duration	Frequency	Percentage
One day before	34	35.1
One day before and One day after	63	64.9

Table 4 | Management of patients with a history of previous adverse reactions to ICM **(n=119)**

Premedication	Frequency	Percentage
Antihistamines (pheniramine 25 mg Oral tablet)	87	73.1
Corticosteroids (hydrocortisone 100 mg IV injection))	32	26.9

vomiting in 306 (94.74%) patients, followed by mild urticaria in 286 (88.54%) patients and dyspnea in 64 (19.81%) patients, as shown in Table 2. Among 97 diabetics patients, 34 (35.1%) patients had been advised to stop metformin one day before ICM administration and 63 (64.9%) patients had been advised to stop metformin one day before & one day after ICM administration, as shown in Table 3. In Table 4, out of 119 participants, most 87 (73.1%) of the participants were premedicated with antihistamine (pheniramine) followed by 32 (26.9%) patients premedicated with corticosteroids (hydrocortisone). The most commonly prescribed anti-histaminic drug for mild urticaria was pheniramine 249 (87.1%) followed by metoclopramide 254 (83.01%) for vomiting, and epinephrine with hydrocortisone 53 (82.81%) for dyspnoea, as shown in Table 5

Table 5 | Management of adverse reactions after ICM administration (n=323)

Treatment	Frequency	Percentage
Mild Urticaria (n=286)		
Pheniramine 22.7 mg (IV injection)	249	87.1
Pheniramine 22.7 mg & hydrocortisone 100 mg (IV injection)	30	10.5
Pheniramine 25 mg (oral tablet)	7	2.4
Nausea & Vomiting (n=306)		
Metoclopramide 5 mg (IV injection)	254	83.01
Ondansetron 4 mg (oral tablet)	52	16.99
Dyspnea (n=64)		
Epinephrine 0.5 mg IM	5	7.81
Epinephrine 0.5 mg and hydrocortisone 100 mg IV	53	82.81
Epinephrine 0.5 mg, hydrocortisone 100 mg and oxygen 60 mmHg	6	9.38

DISCUSSION

We evaluated the management of adverse reactions associated with low osmolar iodinated contrast in CT imaging. This study found adverse reactions to iodinated contrast media in all age groups, though the incidence was significantly higher between the ages of 41 to 60 years. The mean age of participants was 48.49±19.78 years, which is similar to the findings of Patel et al. [2] and Mukhopadhyay et al. [1] where the mean age was 50.71±11.85 years and 47.02±15.37 years, respectively. This study had 34.67% males and 65.33% females, which is in contrast to the findings of Mukhopadhyay et al. [1], where 76% were males and 24% were females. Majority of the patients (30.03%) in this study had a serum creatinine level of 1.1 mg/dl on renal function test done prior to contrast administration. The renal function laboratory reference value of serum creatinine range was evaluated on the basis of UCMS hospital, which was 0.6-1.3 mg/dl. The findings of risk factors in this study were associated with a history of previous adverse reactions to low osmolar iodinated contrast media (36.84%), which is significantly higher than the findings of Pradubpongsa P et al. [19], in which 11.6% of patients had a history of previous reaction.

In this study, 30.03% of the patients with diabetes mellitus were using metformin, which is a substantial risk factor, however it was found lower than the findings of Han et al. (94.8%) [12], but higher than Pradubpongsa et al. (13.3%) [19]. Since, metformin is known to cause lactic acidosis following iodinated contrast delivery [14], participants in this trial were instructed to discontinue its usage prior to obtaining a contrast-enhanced CT scan. Similar to Han et al. [12], the median length of metformin withdrawal for 35.1% of the participants was one day before and for 64.9% of the participants it was one day after. Based on blood creatinine/eGFR levels, McCartney MM et al. [20] recommended withholding for 48 hours. The majority of adverse reaction after ICM administration was nausea and vomiting (94.74%), followed by mild urticaria (88.54%) and dyspnea (19.81%), which is consistent to the findings of the study done by Han et al. [12] and Karim NA et al. [21], where hypersensitivity reactions (98.3%) was more common adverse reactions followed by asthma (84.5%), and hypertension (79.3%), respectively, followed by nausea (63.11%) and dyspnea (0.61%) respectively. Our study had a less prevalence of adverse reactions than Han et al. [12] but slightly more than Karim NA et al. [21]. Premedication with antihistamine (pheniramine 25 mg oral tablet, 73.1%) and corticosteroids (hydrocortisone 100 mg IV injection, 26.9%) was used to treat participants who had a history of adverse reactions to ICM, in a manner similar to the studies done by Han et al. [12], Maddox TG et al. [6], and Schrijvers R et al. [15]. In this study, the management of adverse reactions to iodinated contrast media during contrast-enhanced computed tomography scans revealed a few significant differences in the management approach when compared to other standard guidelines. Premedication was given to only 36.84% of patients prior to the scans, which reduced the risk associated with the practice. The ACR recommends premedication with corticosteroids and antihistamines for high-risk individuals, whereas the ESR recommends premedication for all patients receiving intravenous iodinated contrast media. The use of premedication is intended to reduce the likelihood of adverse reactions, particularly in patients who have previously experienced an allergic reaction or who have risk factors for an allergic reaction. According to our findings, antihistamines and corticosteroids were primarily used to manage adverse reactions. The ACR and ESR guidelines prescribe epinephrine as the first-line treatment for adverse reactions. The severity of adverse reactions encountered in our study may have contributed to the variability in the management approach. In spite of the fact that the present guidelines are intended to provide uniformity in the management of patients, there is some variability observed due to factors such as institutional protocols and differences in patient populations.

CONCLUSIONS

The prevalence of adverse reactions after iodinated contrast media in our study is less as compared to other similar setting studies and was well managed with the use of antihistamines, corticosteroids, and anti-emetics.

ADDITIONAL INFORMATION AND DECLARATIONS

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Data Availability: Data will be available upon request to corresponding authors after valid reason.

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