IMMEDIATE REACTIONS TO INTRAVENOUS INJECTION OF IODINATED CONTRAST MEDIA IN A TERTIARY HEALTH FACILITY IN LAGOS, NIGERIA

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SUMMARY

OBJECTIVE

Adverse reactions to iodinated contrast media constitute a major challenge in radiography practice. This study was aimed at establishing the prevalence of such reactions in our environment so as to plan for more effective management.

MATERIALS & METHODS

A total of 750 patients were approached for this study, but only One hundred and fifty patients participated. They were those referred for Intravenous Urography (IVU) and Computed Tomography (CT) Scans involving intravenous injection of Urografin 76%, at the Lagos University Teaching Hospital (LUTH) Lagos, Nigeria. A semi-structured questionnaire was used to capture the patient's demography, experience during the procedure and adverse reactions observed.

Data were analyzed using a soft ware package EPI Info 3.5.1 and results were tested at 5% level of significance.

RESULTS

A very high prevalence of immediate adverse reaction of 92.7% was revealed. Use of ionic, high - osmolar contrasts agent, level of anxiety, suspected poor storage condition and handling by the importing vendors accounted for this high degree. History of allergy had no significance, while rapid injection rate was associated with increased prevalence. Most adverse reactions occurred within 5mins of injection of the contrast medium.

Nausea (63%), and Dizziness (50.4%) were the most two adverse reactions that manifested.

CONCLUSION

Majority of patients in this study suffered adverse reactions due to the use of ionic contrast agent. Non ionic contrast agents should replace ionic contrasts, in spite of the high cost. However, adequate precautionary measures should be put in place if the use of ionic contrast agent is inevitable.

KEY WORDS

Acute adverse reaction, contrast media, radiographic procedures, risk factors.

INTRODUCTION

Historically, the use of iodinated contrast media in radiological examinations had its origin in the use of iodine in the treatment of syphilis in the 1920s, where it was noted that the urinary bladder became radio-opaque following the concentration of iodine within the lumen (Speck et al., 1983). Today, iodinated contrast media are among the most commonly prescribed drugs in the history of modern medicine. According to Katzbery (2008), approximately 80 million doses were administered in 2002 worldwide, corresponding to approximately 8million liters. Christensen (2005) in a similar study noted that over 75 million episodes of contrast media were administered annually for purposes of diagnosis and treatment of diseases. These statistics may have doubled presently due to the increasing utilization of iodinated contrast media, especially in computed tomography studies and related interventional angiographic procedures. The use of iodinated contrast media is therefore very common and on the increase (Dickson & Kam, 2008). However, the use of contrast media has been associated with adverse reactions (Beatriz & Clarice, 2007, Manouchehrs, 2012) and efforts have been made to reduce such effects to the barest minimum. These efforts started with the first production of a safe and reliable intravenous contrast agent for urography called the uroselectan in the 1950s (Speck et al.), to the present manufacture of low-osmolar, non-ionic brands such as hypaque, ultravist, scanlux among others. Currently, some patients may still manifest adverse reactions during radiological examinations involving iodinated contrast agents.

The patho-physiology of adverse reaction to contrast media remains poorly understood as the pattern of severity differs from one individual to the other (Rawlins, 1981). Several studies have shown that adverse reactions due to iodinated contrast media are, though present in a few percentage of population, are inevitable (Speck et al., 1983, Beatriz & Clarice, 2007, Manouchehrs, 2012) and can be serious (Dijkmans et al., 2005). Serious or fatal reactions to contrast media are therefore real, unpredictable, but fortunately rare (Katayama et al., 1990).

The use of ionic, high - osmolar contrast media is still popular in the developing economies and so the associated adverse reactions; due to the increasing cost of healthcare services, especially radiographic procedures in the environment.

Literature on adverse reactions and the predisposing factors are not in lack in the developed countries where most of the clinical trials of the contrast media species are carried out (Manouchehrs, 2012, Katayama et al., 1990). Knowledge of the type, nature and extent of these reactions have been relied upon to formulate protocols for screening for risk-factors, administration of the contrast media and management of contrast-related adverse reactions in such places. However, this is the contrary in the developing countries such as Nigeria where reactions to contrast media are presently poorly reported and documented. Many risk factors, including race, have been associated with adverse reactions to iodinated contrast media (Manouchehr, 2012, Morcos, 2005, Panitan et al., 2013, ACR, 2010). The incidence of iodinated contrast media (ICM) reactions among patients of Indian origin or Mediterranean region in the United Kingdom was significantly higher when compared with the indigenous white population in a study by Ansell, et al (1980). The incidence in the African population is currently not known to the researchers, and is expected to be different. This study is therefore aimed at documenting and establishing the prevalence of such adverse reactions in our environment for effective management.

MATERIALS AND METHODS

This study involved one hundred and fifty patients that underwent contrast enhanced Intravenous Urography (IVU) and Computed Tomography(CT) scan at the Lagos University Teaching Hospital, Idi-Araba, Lagos, South West, Nigeria. The study included only procedures that involved urografin 76% (Sodium Amidotrizoate/Meglumine Amidotrizoate); an ionic, high osmolar contrast media. This is the contrast of choice in this centre during the period of this study due to cost and availability.

The study subjects were recruited by convenience sampling from the usual pool of patients already screened and booked for the two studies. Eligible subjects were approached and details of the study requirements explained to them. Those that consented were recruited to participate.

DATA CLLECTION

This was a prospective clinical surveillance study aimed at documenting immediate adverse reactions that were associated with the administration of a high osmolar, ionic contrast media – Urografin 76% in a Nigerian health facility. The surveillance started from the onset of intravenous contrast injection to an hour post-administration. The study is quantitative and exploratory-descriptive in approach. It is part of a PhD thesis work on ‘Studies on the Reactions to Common Intravenous Contrast Media among Patients in Lagos; South West, Nigeria’. Data collection instrument included a detailed, semi-structured questionnaire on patients’ demography

and clinical history which was partly filled by the subjects before contrast administration. The first segment of the questionnaire contained the demographic data and other background possible risk factors such as history of allergy, previous reaction to contrast media, and presence of respiratory disease such as asthma, among others. The second section which contained such information as the contrast agent used, volume applied, rate of injection, premedication, presence of reaction noticed, severity and effect on the procedure was filled by the researchers. An intravenous iodinated contrast media (ICM) incident data form was used by the researchers to document details of the noted adverse reactions. Further information was sourced from patients' medical records from hospital database and case notes.

Data collected were analyzed and presented using the descriptive statistics of mean, standard deviation and percentages. Chi-square test was used to establish the association between severity of contrast-related adverse reactions and variables using soft ware package, EPI info 3.5.1. The results were tested at 5% level of significance and illustrated in tables and histogram for easy appreciation.

ETHICAL CONSIDERATION

This study relied on the pool of booked cases for intravenous urography and computed tomography procedures. Permission was however obtained from the head of department and director of radiography services before carrying out this research, since the research was based on the normal departmental protocol for routine conduct of these procedures. Individual consent was also sought and obtained from each participant.

RESULT

A total of 750 patients were approached for the study but only 150 consented to participate within the period of this research. Seventy nine (52.7%) participants were males while females constituted seventy one (47.3%). The ages ranged from 1 to 80 years, with a mean age of 38yrs (Fig.1). The study involved intravenous urography (IVU) and computed tomography (CT) scans. Forty five (30%) participants had IVU, while 105 (70%) underwent CT scan. The prevalence of adverse reactions among the study population was very high. One hundred and thirty nine of the participants (92.7%) experienced one form of adverse reaction or the other. Most of the reactions (51.8%) occurred within five (5) minutes of onset of contrast injection (Table 1). About 44.6% of the reactions manifested between 5-10 minutes while 3.6% took place between 11-20 minutes. The adverse reactions mostly observed were nausea, which involved 63% of the participants. Other reactions noted were, dizziness (50.4%), headache (15.1%), vomiting (14.4%) and skin rashes which occurred in only one person (0.7%); Table 2. All the noted adverse reactions resolved within one hour of contrast administration. About fifty three percent (52.5%) of the observed reactions did not last beyond 10minutes, while about 36.0% lasted between 10 – 20minutes. Only nine patients (6.5%) experienced the effect beyond 30 minutes but not up to an hour post injection, as seen in Table 3. In this study, slightly more than half of the respondents

(50.6%) had history of allergy, of which 44.9% were allergic to dust; seafood (17.9%), exhaust fumes (12.8%), while 16.6% were collectively allergic to other drugs or products (Table 4). No statistical significant relationship was established between history of allergy and prevalence (p =0.1553).

Gender was a predisposing factor to adverse reactions in this study. Seventy seven (55.4%) of the respondents that experienced adverse reactions were males, while sixty two (44.6%) were females. There was a significant statistical difference between the respondents' sex and prevalence of adverse reaction (p = 0.0325).

Anxiety was also noted as a risk factor for adverse reaction. Eighty four patients (56.0%) expressed worry over the outcome of the examination, effect of the investigation, equipment or pain due to injection. Fifty (36.0%) patients of those that experienced adverse reactions were administered with medication to curb them. Twenty (40%) of them received phenergan, nine (18%) had some other forms of treatment; whereas one (2%) received IV infusion. All the patients that had adverse reactions and/or offered medication got relief within one hour of injection.

The volume of contrast media administered affected the prevalence of adverse reactions and so the rate of injection. Most of the reactions were associated with rapid injection rate.

Majority of the reactions did not have negative effect on the procedures being carried out as eighty eight (63.3%) recorded no disruption in the process. Delay was recorded in 40 (28.8%) procedures due to administration of emergency drugs to curb the reaction, or waiting for reaction to subside. Six (4.3%) of the examinations were rebooked, while four (2.9%) procedures were terminated.

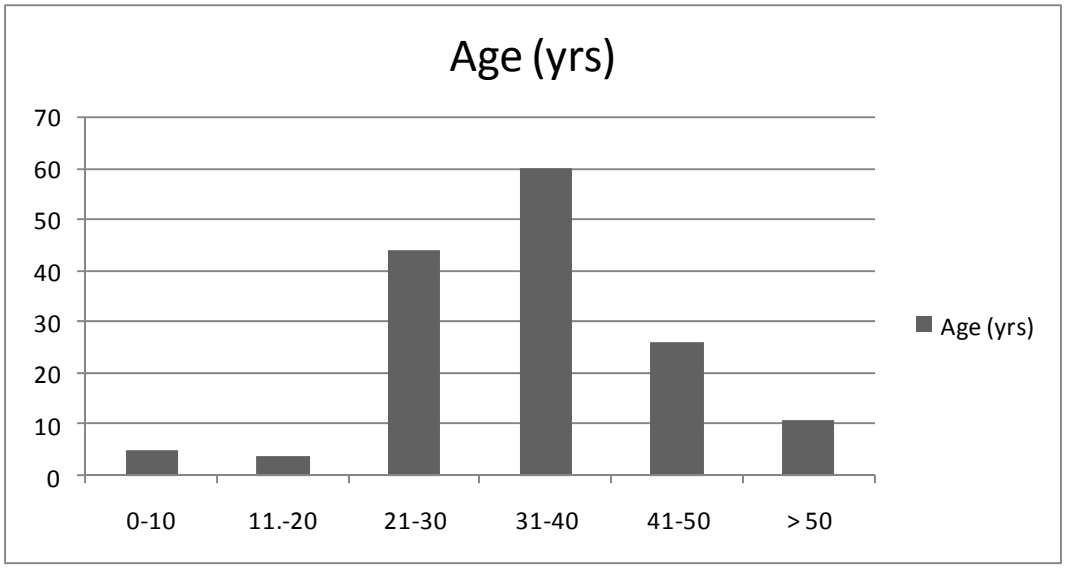

Figure 1- AGE DISTRIBUTION OF THE RESPONDENTS

Table 1: ONSET OF REACTION TO CONTRAST

Onset of reaction	Frequency	Percent%
0-5 minutes after injection	**72**	**51.8**
6-10 minutes after	**62**	**44.6**
11-20 minutes after	**5**	**3.6**
Total	**139**	**100.0**

51.8% of the respondents who had reactions noticed the reactions within 5 minutes following contrast injections. 44.6% noticed the reactions between 5-10 minutes post injection.

Table 2: REACTIONS TO CONTRAST

Reactions	Frequency	Percent (%)
Nausea	**88**	**63.3**
Vomiting	**20**	**14.4**
Dizziness	**70**	**50.4**
Skin rashes	**1**	**0.7**
Headache	**21**	**15.1**
Redness/swelling	**18**	**12.9**
Others	**8**	**5.8**

Nausea (63.3%) and Dizziness (50.4%) were the most noticed reactions. Others were headache (15.1%), vomiting (14.4%), and redness/swelling (12.9%)

Table 3: DURATION OF REACTIONS

Duration of reaction	Frequency	Percent (%)
Less than 10 minutes	**73**	**52.5**
10-20 minutes	**50**	**36.0**
20-30 minutes	**7**	**5.0**
30 minutes -1 hour	**9**	**6.5**

Total 139 100.0	**139**	**100.0**

Most of the reactions (52.5%) lasted less than 10 minutes while 36.0% resolved within 10 – 20 minutes.

Table 4. RESPONDENTS HISTORY OF ALLERGY & ALLERGENS IMPLICATED

Variable	**Frequency**	**Percent (%)**
Respondents with history of allergy	76	50.6
Allergic	76	50.6
Not allergic	74	49.3
Total	150	100.0
Allergen		
Dust	35	44.9
Seafood	**14**	**17.9**
Pollen	**6**	**7.7**
Exhaust fumes	**10**	**12.8**
Drugs	**10**	**12.8**
Others	**3**	**3.8**

50.6% of the respondents had history of allergy and allergens were dust (44.9%), seafood (17.9%), exhaust fumes (12.8%), drugs (12.8%), and pollens (7.7%).

Table 5: ASSOCIATION BETWEEN AGE AND PREVALENCE OF ADVERSE REACTION.

Prevalence of adverse reaction			
Age (yrs)	**Yes**	**No**	**TOTAL**
1-10	4(80.0%)	1(20.0%)	5
11-20	4(100.0%)	-	4
21-30	41(93.2%)	3(6.8%)	44

31-40	54(90.0%)	6(10.0%)	60
41-50	26(100.0%)	-	26
>50	10(90.9%)	1(9.1%)	11
TOTAL	**139**	**9**	**150**

P =0.5606

There was no statistical significant difference between the respondents' age and prevalence of adverse reaction.

DISCUSSION

This study was among patients that underwent intravenous urography (45; 30%) or computed tomography (105; 70%) contrast-enhanced radiological procedures at Lagos University Teaching Hospital, between April – July 2013. In spite of the 750 patients approached for this study, only 150 consented and were recruited. The low response rate is surprising but could be attributed to wrong perception of research as an experimental procedure, where the participant is regarded as a 'guinea pig.' The contrast media studied was urografin 76%; an ionic high osmolar contrast agent. The continued use of ionic contrast media in this center instead of the non-ionic version was attributed to cost and availability as all radiological contrast agents are imported.

A very high prevalence of adverse reaction of about 92.7% was recorded. Though, ionic high osmolar contrast media are associated with high incidence of adverse reactions, the finding in this study, is extremely at variance with the American College of Radiology's (2010) agreed range of about 5% - 15% for ionic contrast agents. Other prevalence levels according to literature are far lower and are Caucasian based (Katayama et al., 1990, Manouchehrs, 2012).

The reason for this high prevalence could be due to race. Other suspected factors such as environment and socio-economic instability with associated increased threshold of anxiety and uncertainty requires further investigation. The effect of handling and warehousing condition on quality of the imported contrast agents is not within the scope of this study. However, it is suspected that proper and ethical handling of the products before reaching the point of utilization is not guaranteed as the importations are basically in the hands of business vendors whose primary objective is profit. The research equally documented all degrees of acute adverse reactions ranging from the mildest to the most severe noted. This could have contributed to the high incidence.

Seventy two (51.8%) patients experienced adverse reactions within 5 minutes of contrast medium injection, while sixty two (44.6%) noticed reactions within 5-10minutes of injection. This showed that the manifestation of adverse reactions was chiefly immediate, with only 3.6% of the reactions manifesting after 10 minutes of contrast administration. These findings are in

line with the studies carried out by Katayama et al., (1990), Thomsen et al., (2000), and Morcos et al., (2001) on the acute nature of most contrast induced adverse reactions. They noted that adverse reactions due to iodinated contrast media are majorly acute in nature and mostly transient.

Of the reactions recorded, nausea and dizziness constituted the most prevalent, affecting 63.3% and 50.4% of the participants respectively. Other reactions recorded were headache (15.1%), vomiting (14.4%) and redness/swelling (12.9%). Only one person presented with rashes on the skin, and this was the most severe reactions recorded. This concurs with literature that severe reactions to contrast agents are exceedingly rare (Katayama et al., 1990, Laser et al., 1997)

The duration of all the adverse reactions noted in this study did not exceed one hour from onset of injection. Seventy three (52.5%) adverse incidents lasted less than 10 minutes while 36.0% of them disappeared between 10-20 minutes post contrast administration. Only nine (9) patients (6.5%) had symptoms associated with the contrast injection between 30mins – 1 hour of the contrast administration. This result is in tandem with that of Wang et al., (2008) which noted that most contrast-induced reactions are short-lived and not severe.

Thomsen et al., (2000) in a previous study cited history of allergy as a predisposing factor to adverse reaction to contrast media. In this study, slightly more than half of the respondents (50.6%) had history of allergy, of which 44% were allergic to dust, while 12.8% were allergic to one drug or the other. The finding in this study was not statistically significant ($p = 0.1553$) and did not substantiate the relationship between allergy and prevalence, as previously cited by Thomsen et al., and other researchers (Katayama et al., 1990, Morcos et al., 2001).

The mean age of the participants was 38yrs, with the largest group falling within age of 31-40yrs (40%). There was no statistical significant difference between the respondents' age groups and prevalence of adverse reactions (Table 5). This is contrary to a previous study by Wang et al. (1998) which noted that adverse reactions increase with age.

Contrary to a study by Modi et al., (2012) gender was noted as a predisposing factor to adverse reactions due to intravenous contrast media in this work. Seventy seven (55.4%) respondents that experienced adverse reactions were males, while sixty two (44.6%) were females. There was a significant statistical difference between the respondents' sex and prevalence of adverse reaction ($p = 0.0325$). This finding is in accord with another study carried out by Lang, et al. (1995) on gender as a risk factor for adverse reactions.

Eighty four (56.0%) patients expressed worry over the outcome of the examination, safety of the investigation, equipment or pain due to injection, which contributed to raised anxiety, in spite of full explanation of the procedure and reassurances of care. In line with a previous study by Morcos et al, (2001) anxiety was associated with increased prevalence in this work. It was shown that those who expressed fear or anxiety before the procedure (56.0%) manifested more adverse reactions than their counterparts that did not (44.0%).

In compliance with established practice (Morcos et al., 2001), the department maintained an emergency and intervention unit for contrast-related procedures. In this study, fifty (36.0%) patients that experienced adverse reactions received one form of medication or the other to curb them, with only one (2%) person having an IV infusion. All the patients that had adverse reactions got relief after medication. This supports Morcos et al, that prompt recognition and treatment of adverse reaction to contrast media will be invaluable in blunting such a reaction and preventing it from becoming severe. The administration of medication to some identified adverse reactions yielded successful progression of the procedures to completion. Eighty eight (63.3%) cases associated with adverse reactions recorded no disruption. Only forty (28.8%) cases had their procedures delayed due to administration of emergency drugs to curb the reactions, or waiting for reaction to subside. Five cases could not proceed and were terminated.

In line with a related work of Maddox, (2002), volume of contrast media injected and rate of injection were directly associated with the incidence of adverse reactions in this study.

CONCLUSION

The incidence of adverse reactions to ICM was very high among patients that underwent ionic contrast-related radiological procedures in Lagos University Teaching Hospital, Lagos, Nigeria, within the study period. The high incidence noted in this present study appears to highlight the significant risk to patients posed by the continued use of ionic contrast media in the country. The findings are quite contrary to the existing literature and seem not to be easily explained by the factor of race. The quality of the batch of contrast media supplied to the centre for the period covered by this research calls for further scrutiny, in terms of active composition, storage, handling and shelf-life.

The findings of this study with respect to sex, volume of contrast administered and injection rate as factors that affect prevalence of adverse reaction to contrasts media are in line with existing literature but differ in the history of allergy being a risk factor for adverse reaction. There is therefore urgent need for a multicentre study on prevalence of adverse reactions to the different types of iodinated contrast media among Nigerians. However, the use of ionic high-osmolar contrast media in the country should be discouraged since most developed countries have banned such substances.

LIMITATIONS OF STUDY

This study would have been better with a larger sample size but for poor response to participation within the period covered by this research.

AREAS FOR FURTHER RESEARCH

In view of the high incidence of adverse reactions in this study, a multicentre study involving a larger sample size and longer period is recommended in order to establish a more reflective

prevalence rate among the Nigerian population. This study should also cover both ionic and non-ionic contrast agents.

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