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ORIGINAL ARTICLE

RISK OF CONTRAST INDUCED NEPHROPATHY WITH INTRAVENOUS ADMINISTRATION

Gururaj Sharma[1], Jayaprakash[2]

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ABSTRACT: With the increasing use of iodinated contrast media for CT Scan and other radiologic procedures, contrast induced nephropathy (CIN) has emerged as an important delayed adverse effect due the intravascular administration of contrast media. **OBJECTIVES:** To study the incidence of CIN in patients undergoing intravenous contrast enhanced CT (CECT) scans and to assess the safety of iodinated, low osmolar contrast media (LOCM) in such patients. **MATERIALS AND METHODS:** We conducted a study in 182 patients who received intravenous low osmolar contrast media to assess the risk of CIN in patients undergoing diagnostic CECT. All the patients had a baseline serum creatinine (SeCr) value done prior to the procedure, and were then followed up with a repeat SeCr at 48 to 72hrs, and where necessary, on day 5 to 7 after the procedure. **RESULTS:** Thirty eight patients (20.9%) showed no change in their baseline SeCr value at 48 hrs. after contrast administration, while 13 patients (7.1%) showed a slight decrease, and 131 patients (72%) showed an increase in SeCr. None of the patients showed a greater than 0.5mg/dL increase in the SeCr, while 3 patients (1.6%) showed a 25% increase in the 48 hrs. SeCr from baseline value. **CONCLUSION:** The incidence of CIN varied from 0 to 1.6% depending on the definition used. Contrast induced nephropathy is a rare complication of intravenous administration of contrast media. LOCMs can be safely used in the general population who do not have pre-existing renal impairment or other major risk factors.

KEYWORDS: Contrast induced nephropathy (CIN), Contrast media, Low-osmolar contrast media (LOCM), Nephropathy.

INTRODUCTION: There has been a continued increase in the number of Computed Tomography (CT) Scans that are being performed for diagnostic purposes. A significant number of these cases will also undergo contrast enhanced CT (CECT) study, which involves the intravascular injection of iodinated contrast. While the use of intravenous contrast material is known to improve the accuracy of the CT study, there are known risks involved. Contrast induced nephropathy (CIN) is a potential delayed adverse effect due to the intravenously injected contrast material, and has been gaining increasing attention in recent years. It has emerged as the third most common cause of acute renal failure after diabetes and nephrotoxic drugs.[1,2]

Most of the earlier data on contrast induced nephropathy have been derived from intra-arterial administration of contrast and percutaneous coronary interventions which have shown a higher incidence of CIN.[3,4] However, these cannot be easily extrapolated to radiology, where most of the contrast administration is via the intravenous route. Hence, we decided to conduct a study is to assess the incidence of CIN in patients undergoing contrast enhanced CT scans who were administered low osmolar contrast material intravenously.

OBJECTIVES: The aim of this study was to document the incidence of CIN in patients undergoing contrast enhanced CT Scans (CECT) with low osmolar contrast media (LOCM) and thereby, to assess the safety of LOCM in such patients.

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MATERIALS AND METHODS: This was a prospective study carried out in our institution between January 2012 and December 2014. Requisite approval from our Institutional Ethics Committee was obtained prior to carrying out this study. A total of 182 patients who were referred for CT scan of the chest, abdomen or CT angiography were included in this study, since this subset of patients received the largest volume of contrast per study (70 to 100mls).

All patients had a baseline serum creatinine (SeCr) which was done on the previous day or on the day of the CT scan. All the patients received 70 to 100mls of low osmolar contrast iopromide (Ultravist 370, Bayer Zydus Pharmaceuticals, Ltd), depending on the type of study and body weight of the patient. SeCr was then repeated 48 to 72 hrs. After CECT to determine whether the patient had developed impaired renal function. If the SeCr did not show any rise over the baseline value, then no further follow up was done. Where the 48-hour SeCr showed a rising trend, a follow up value was obtained between day 5 and 7, and subsequently every alternate day until it reached baseline value.

RESULTS: There were a total of 126 males (Age range of 20 to 85 yrs. and 56 females (Age range of 21 to 75 yrs.) in this study (Table 1). Of the 182 patients, 122(67%) did not have any other co-morbid conditions, while 60 patients (33%) had associated co-morbidity (Table 2), such as diabetes mellitus in 38 (21%) patients and hypertension in 4(2%) patients. There were 18 (10%) patients who had both diabetes and hypertension.

Table 3 shows the absolute change in serum creatinine at 48 hours after administration of contrast media. While 38 patients (20.9%) showed no change in the 48-hour SeCr, 131 patients (72%) showed an increase, and 13 patients (7.1%) showed a decrease in the 48-hour SeCr. The pre-procedural baseline Se Creatinine ranged from 0.6 to 2.0mg/dL with a mean of 0.99mg/dL (SD=0.34), while the 48-hour SeCr ranged from 0.6 to 2.1mg/dL with a mean of 1.08mg/dL (SD=0.34).

The percentage variation in serum creatinine is shown in Table 4. Thirty eight patients (20.9%) showed no change in the 48-hour SeCr when compared to their baseline value, while 13 patients (7.1%) showed a slight (less than 10%) decrease. The remaining 131 patients showed an increase in their 48-hour SeCr. Of these, 46 patients (25.2%) showed less than 10% increase, 71 patients (39.0%) showed 11 to 20% increase and 14 patients (7.7%) showed a 21 to 30% increase. The last group includes 11 patients with 22% increase and 3 patients with 25% increase.

There is no statistically significant difference ($p<0.05$) in the 48-hour fluctuation of serum creatinine between males and females and between young (<50yrs.) and old (>50yrs). However, there is a statistically significant difference ($p < 0.001$) in the 48-hour fluctuation of serum creatinine between patients with co-morbidity (DM, HT or both) and those with no co-morbidity (Table 5).

DISCUSSION: CIN is defined as an acute impairment in renal function after the introduction of intravenous contrast in the absence of any other known causes. The most common definition of CIN today is an absolute increase of 0.5mg/dL or greater, or an increase of 25% or more, in serum creatinine from baseline value, at 48 hrs following the exposure to CM.[2,5]

Based on this definition, we did not encounter any patient with a more than 0.5mg/dL increase in the SeCr above baseline value. However 3 patients (1.6%) showed a 25% increase in the SeCr above baseline at 48 hrs after contrast administration. Thus the incidence of CIN in our study group varied from 0 – 1.6%, depending on the definition used.

Several studies have shown that the incidence of CIN is low in the general population receiving intravenous injection of low osmolar contrast media. Rankin and Eng (1982) reported no

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incidence of CIN in their study of 220 patients who received intravenous LOCM.[6] Similarly, Newhouse et al (1994) in their study of 200 patients.[7] have also reported nil incidence of CIN, while Moore et al (1992) reported CIN in three (1.2%) of 250 subjects receiving intravenous LOCM.[8]

In a retrospective study of 594 patients who received intravenous LOCM, Kragha K.O. (2014) reported 2 patients (0.3%) with a 0.5mg/dL or greater increase in 48-hour SeCr, and 40 patients (6.7%) who had a 25% or greater increase in SeCr, giving an incidence of 0.3 to 6.7% depending on the definition used.[9] The author further opined that the definition of CIN as a 25% increase in serum creatinine may be too permissive; rather a 50% increase may be more appropriate.

Our study revealed 3 patients who had a 25% increase in their 48-hour serum creatinine. This includes 1 patient with an increase in SeCr from 0.8mg/dL to 1.0mg/dL, which was not considered clinically relevant. Two patients showed an increase from 1.2 mg/dL to 1.5mg/d in the 48-hour SeCr; however, a follow up SeCr done on the 5th day revealed a significant fall/return to baseline in all three patients, without the institution of any specific therapeutic measures.

The incidence of contrast-induced nephropathy varies markedly, depending on the definition used, type of radiology procedure, the dose and type of contrast agent administered, and differing patient populations.[10] The incidence of CIN in the general population undergoing intravenous injection for diagnostic CT procedures is reported to be 0 to 2.3%.[10,11] However, in several other patient subsets, the incidence is known to be higher depending on the presence of associated risk factors.

Preexisting renal insufficiency is the single greatest risk factor that predisposes to increased risk of CIN. In one comprehensive review, an estimated 60% of patients with contrast-induced nephropathy had preexisting renal insufficiency.[12] Several studies have suggested that the risk of developing CIN is negligible if the SeCr is <2.0mgs/dL, and that the the risk starts increasing markedly above this value.[13,14]

In addition to preexisting renal disease, a variety of risk factors have been implicated, including diabetes mellitus, dehydration, multiple myeloma, large doses of contrast medium, peripheral vascular disease, hypertension, proteinuria, concurrent use of nephrotoxic drugs, and elderly patients.[15] However these have not been rigorously confirmed to be independent risk factors.

CIN has also been reported to be higher after intra-arterial injections as in percutaneous coronary interventions, affecting upto 14.5% of patients.[16] This has been attributed to the fact that intra-arterial injection results in higher renal concentrations of contrast when compared with intravenous administration as in CT Scan or IV Urography.[3,10]

Contrast-induced nephropathy most commonly manifests as a nonoliguric and asymptomatic transient decline in renal function. The serum creatinine level begins to rise within 24 hrs. of contrast administration, usually peaks within 3–5 days, and returns to baseline within 10–14 days,[5,10] It is unusual for patients to develop permanent renal dysfunction. When chronic renal failure develops, it is usually in the setting of multiple risk factors.[5,14]

Methods to minimise the incidence of CIN include a careful consideration whether the contrast examination is absolutely needed, especially in high-risk patients; using the minimal effective dose; and eliminating potentially nephrotoxic drugs (e.g. NSAIDs, aminoglycoside antibiotics, cisplatin, cyclosporin A, and amphotericin B) at least 24 hrs before the study. Patients should be well hydrated by allowing adequate fluid intake up to 2 hours prior to the procedure (although the patient remains remains nil by mouth for solids).

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Several pharmacological agents such as N-acetylcysteine, theophylline, ascorbic acid, fenaldopam, endothelin-1 have been tried in trials for the prophylaxis of contrast induced nephropathy. However, most studies and meta-analysis have shown conflicting reports and these agents are not currently recommended for the prevention of contrast induced nephropathy.[5,14]

CONCLUSION: We conclude that the risk of contrast induced nephropathy with intravenous administration of contrast material for diagnostic CT scan is very low, and that currently used low osmolar contrast media are safe for intravascular use in the general population. However, the risks are slightly higher in patients with certain co-morbid conditions such as pre-existing renal failure and diabetes, and caution is advocated in such patients. Preventive measures that include adequate hydration with oral or i/v fluids may help. Judicious use of other imaging modalities in patients at high risk should be considered wherever possible.

	No. of Patients	Percentage
Males	126	69%
Females	52	31%
TOTAL	**182**	**100%**

Table 1: Number of Patients with Gender Distribution

Co-morbidity	No. of Patients	Percentage
Diabetes Mellitus (DM)	38	21%
Hypertension (HT)	4	2%
Both (DM + HT)	18	10%
No co-morbidity	122	67%
TOTAL	**182**	**100%**

Table 2: Number of Patients with Co-Morbidity

Change in SeCr (mg/dL)	No. of Patients	Percentage
-2	3	1.6%
-1	10	5.5%
0	38	20.9%
+1	90	49.5%
+2	33	18.1%
+3	8	4.4%
TOTAL	**182**	**100%**

Table 3: Frequency of Absolute Change in 48-Hrs Secr Value after Contrast Administration

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Change in SeCr (% age)	No. of Patients	Percentage
-10 - -1%	13	7.1%
0 %	38	20.9%
1 – 10%	46	25.3%
11 – 20%	71	39.0%
21 – 30%	14	7.7%
TOTAL	**182**	**100%**

Table 4: Frequency of Percentage Change in 48-Hrs Secr after Contrast Administration

Change in SeCr (% age)	Co-morbidity		TOTAL
	Absent	Present	
≤ 0%	46	5	51
1 – 10 %	29	17	46
11 – 20%	45	26	71
>20%	2	12	14
TOTAL	**122**	**60**	**182**

Table 5: Percentage Change in Secr in Patients Without and With Co-Morbid Conditions (Dm, Ht or Both)

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AUTHORS:
1. Gururaj Sharma
2. Jayaprakash

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Radiodiagnosis, A. J. Institute of Medical Sciences, Mangalore.
2. Former PG Student, Department of Radiodiagnosis, A. J. Institute of Medical Sciences, Mangalore.

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NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Gururaj Sharma,
Department of Radiodiagnosis,
A. J. Institute of Medical Sciences,
Kuntikana, Mangalore-575004,
Karnataka.
E-mail: gururajsharma@yahoo.com

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