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IMPORTANCE OF N-ACETYLYCYSTEINE IN PREVENTION OF CONTRAST INDUCED NEPHROPATHY

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Abstract:

Aim: *To determine the role of N-acetylcysteine in the prevention of CIN in high-risk patients undergoing coronary angiography.*

Study design: *A retrospective, observational study.*

Place and Duration: *The study was conducted in the nephrology department of Lahore General Hospital Lahore for one year duration from March 2019 to March 2020.*

Methods: *We reviewed the medical records of 120 patients over the age of 30 who underwent coronary angiography. All these patients were divided into two groups. Group A was given N-acetylcysteine, and patients in Group B were not given N-acetylcysteine. Acute Nephropathy caused by contrast was defined as an increase of at least 0.5 mg / dL serum creatinine from baseline to 48 hours after administration of the contrast agent. All data was collected in a previously designed form. The age was compared between the two groups using an independent t-test, and other parameters were analyzed using a Chi-square test.*

Results: *There was a statistically significant difference between the two groups (group without N-acetylcysteine 17% and group N-acetylcysteine 3%, p = 0.029).*

Conclusion: *Iopromidol, a nonionic, low osmolality contrast agent can induce acute contrast induced nephropathy in high risk patients which can be prevented by prophylactic oral administration of the antioxidant N-acetylcysteine, keeping all patients well hyrated/euvolemic.*

Key words: *contrast induced nephropathy, N-acetylcysteine, Iopromidol.*

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INTRODUCTION:

Contrast-induced nephropathy has become the third leading cause of acute renal failure acquired in hospital, with increased use of contrast agents in diagnostic and intervention procedures, accounting for 12% of all causes[1-2]. Although newer, less nephrotoxic contrast agents have been used in high-risk patients in recent years, there is a significant risk of morbidity and death[3-4]. Risk factors for contrast-induced nephropathy (CIN) are pre-existing renal failure, diabetes, hypertension, congestive heart failure, dehydration, and low-impact circulation volume, and myocardial infarction, use of aortic balloon pump, contrast volume and osmolarity[5-6]. Contrast nephropathy between 5% and 30% has been reported in patients with diabetes. Contrast agents reduce renal function by altering renal hemodynamics and directly toxic to tubular epithelial cells. Evidence has accumulated that reactive oxygen species play a role in kidney damage caused by contrast agents[7].

Many agents tested to prevent CIN include saline hydration, low dopamine doses, endothelin, prostaglandin E, naphthylcysteine, ascorbic acid, bicarbonate. Research is ongoing to confirm the effectiveness of these drugs in the prevention of CIN and is still being studied because of their lower statistical significance[8-9]. This Nasetylcysteine gave good results in reducing CIN. Therefore, the reason for this study was to assess the effect of N-acetylcysteine on reducing the incidence of CIN in high-risk patients who underwent coronary artery surgery in our population because this drug was inexpensive, well-tolerated, and had no side effects. Important[10].

TOOLS AND METHODS:

The study was conducted in the nephrology department of Lahore General Hospital Lahore for one-year duration from March 2019 to March 2020. 120 patients of both sexes were examined and over 30 coronary angiographies were performed. Primary and secondary diseases (isolated diabetes, chronic renal failure for another reason and diabetic nephropathy), renal parameters in the initial and final procedure, volume status during the procedure, type and volume of the agent, contrast used, sodium bicarbonate before and after the intravenous fluid was collected and administration of N-acetylcysteine were determined. All these patients were given a low osmolality non-ionic contrast agent, iopamidol 370 (370 mg iodine and 75.5 g iopamidol / 100 ml per milliliter) at a dose of 100 ml and all were well wetted / euvolemic. Of these, 62 patients received N-acetylcysteine at a standard dose of 600 mg twice daily orally one day before and one day after administration of the contrast medium for a total of two days, designated as Group A and 58 other patients who did not receive N-acetylcysteine designated as Group B. Acute contrast-induced nephropathy was defined as an increase in serum creatinine of at least 0.5 mg / dL from baseline up to 48 hours after administration of the contrast agent. All data was collected in a previously designed proforma. In statistical analysis, age was compared between two groups using an independent t-test, and other parameters were analyzed using a chi-square test.

RESULTS:

One hundred and twenty high-risk patients in Group A and Group B were evaluated in this study. The demographics are shown in the table below.

Demographic Data

Characteristics	Group A (n=62)		Group B(n=58)		pvalue
Age(years), mean±SD	54±9.3		56±11.3		0.47
Gender	M	41	M	38	0.5
	F	21	F	20	
Isolated diabetes mellitus	29		30		0.36
Diabetic nephropathy	22		15		0.24
Renal insufficiency due to other cause	11		13		0.82
Baseline s/creatinine (mg/dl) mean±SD	1.3±0.5		1.5±0.8		0.3
Renal failure after contrast	2		10		0.029

The results showed that there was no statistically significant difference between the two groups in terms of age, sex, renal parameters (baseline serum creatinine) and their primary and secondary diseases because the p-value was not <0.5. However, serum creatinine increased by 0.5 mg / dL or more (acute contrast nephropathy) from baseline after angiography in 12 of 120 patients, including 10 from group B (group without N-acetylsysteine 17%) and 2 in group A (Patients from the N-acetylcysteine group 3%, p = 0.029), which was statistically significant. The CIN rate / frequency was 17% in the non-acetylcysteine group, 3% in the standard dose of the N-acetylcysteine group when an absolute increase in ceatin concentration (> 0.5 mg / dl) (p-0.029) was used as the case definition. A greater increase in creatinine was observed in patients without acetylcysteine than in patients

treated with N-acetylcysteine. Especially N-acetylcysteine seems to help prevent CIN in patients with isolated diabetes mellitus, isolated kidney failure as well as diabetic nephropathy.

DISCUSSION:

Contrast-induced nephropathy (CIN) is an increasingly common cause of treatment-related renal failure and increases mortality regardless of other risk factors. The main risk factors for CIN are chronic renal failure, diabetes mellitus (especially when accompanied by renal failure), ionic contrast and the use of high doses of contrast agents. Therefore, strategies for reducing the incidence of CIN include not only identifying risk factors but also changing these risk factors, choosing contrast agents that are unlikely to cause CIN, and administering therapeutic agents. This further reduces the risk of CIN. In our study, the prophylactic administration of a standard dose of 600 mg nasetylcysteine two days before and one day after administration of low-osmolality non-ionic contrast agent in coronary angiography reduces the risk of contrast-induced nephropathy ($p = 0.029$)[11]. In a previous study, meta-analysis results from 13 randomized tests showed that prophylactic administration of N-acetylcysteine in coronary angiography prevented a statistically significant reduction in contrast-induced nephropathy ($p = 0.006$). In another study, intravenous / oral naphthylcysteine prevents CIN with a dose-dependent effect in patients treated with primary angioplasty and may improve hospital outcomes ($p <0.001$)[12]. Recent studies have shown that prophylactic acetylcysteine administration significantly prevented CIN in radiological procedures ($p <0.001$). An important finding of this study is that oral prophylactic administration of the acetylcysteine antioxidant reduces the incidence of CIN. The incidence of reduced renal function induced by the contrast agent ranges from 0 to 90%, depending on the presence of risk factors. Indirect contrast reductions in renal function have been reported in diabetic patients of 9-40% in mild to moderate chronic renal failure and 50-90 percent in patients with severe chronic renal failure. There was also diabetes in this study. It is believed that non-diabetic patients with diabetes with renal insufficiency are at high risk of decreased renal function due to renal function[13].

As suggested in previous studies, we have found that the acute reduction in renal failure caused by contrast is an increase in serum creatinine of at least 0.5 mg per deciliter, up to 48 hours after administration of the contrast agent. This increase can be important because it can extend your stay in hospital. To avoid bias resulting from the use of different types of contrast media or the use of different volumes, all patients in this study used 100 mL volumes of non-ionic, low osmolality ions (same amount), but one group was given N-acetylcysteine and the other group was not taken on acetylcysteine , both patients maintained a well hydrated / euvolemic group. The use of such agents is associated with a lower incidence of acute decrease in renal function with a lower frequency than the use of high osmolality ionic agents. Contrast-induced nephropathy is caused by impaired renal hemodynamics and direct toxic effects on epithelial cell channels. Toxic kidney damage may contribute to the formation of reactive oxygen species or reduced antioxidant activity. Early use of acetylcysteine prevents the reduction of renal failure in patients with acetaminophen poisoning with liver failure. A recent non-randomized study suggests that acetylcysteine may improve kidney function in patients with hepatorenal syndrome. It can therefore prevent contrast-induced nephropathy by improving renal hemodynamics and preventing direct damage to oxidative tissue[14]. As a result, prophylactic oral administration of the acetylcysteine antioxidant is done at a dose of 600 mg twice a day before and on the day of administration of the contrast agent, with continuous hydration and the use of a low-osmolality nonionic agent[15]. More research is needed to determine the role of the above-mentioned factors. In addition, the use of bicarbonate as hydration and ascorbic acid as an antioxidant is used to prevent CIN, but its effect has not been fully established and is still trace.

CONCLUSION:

Iopromidol, a nonionic, low osmolality contrast agent can induce acute contrast induced nephropathy in high risk patients which can be prevented by prophylactic oral administration of the antioxidant N-acetylcysteine, keeping all patients well hyrated/euvolemic.

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