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IMPORTANCE OF N- ACETYLCYSTEINE IN INHIBITION OF CONTRAST INDUCED NEPHROPATHY

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Abstract:
Aim: *To determine the role of N-acetylcysteine in the prevention of Contrast induced nephropathy in high-risk patients undergoing coronary angiography*
Study design: *A Retrospective, observational study.*
Place and Duration: *In the Nephrology and Cardiology department of Mayo Hospital Lahore for one-year duration from March 2019 to March 2020.*
Methodology: *Medical records of 120 patients, both sex and age> 30 years, undergoing coronary angiography were reviewed. All patients were divided into two groups. Group A received N-acetylcysteine and patients in group B did not receive N-acetylcysteine. 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 contrast medium administration. All data was collected on a pre-designed proforma. Age was compared between the two groups using an independent t-test, and the remaining parameters were analyzed using the Chi-square test.*
Results: *There was a statistically significant difference between the two groups (group without N-acetylsysteine 17% and N-acetylcysteine group 3%, p = 0.029).*
Conclusion: *Iopromidol, a low osmolality non-ionic 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 hydrated / euvolemic.*
Key words: *contrast induced nephropathy, N-acetylcysteine, Iopromidol.*

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INTRODUCTION:

With the increase in the use of contrast agents in diagnostic and interventional procedures, contrast-induced nephropathy has become the third most common cause of inpatient acute renal failure, accounting for 12% of all causes. It carries a significant risk of morbidity and death, despite the use of newer and less nephrotoxic contrast agents in high-risk patients in the last year.

Risk factors for contrast induced nephropathy (CIN) include pre-existing renal failure, diabetes mellitus, hypertension, congestive heart failure, dehydration, low effective circulation volume, myocardial infarction, aortic balloon pump use, contrast medium volume, and contrast agent osmolarity. The incidence of contrast agent nephropathy among diabetic patients ranges from 5% to 30%.

Contrast agents reduce renal function by altering renal hemodynamics and exert a direct toxic effect on renal tubular epithelial cells. There is increasing evidence that reactive oxygen species play a role in contrast agent-induced kidney damage.

Many anti-CIN agents have been tried, including saline rehydration, low-dose dopamine, endothelin, prostaglandin E, N-acetylcysteine, ascorbic acid, and bicarbonate. Studies are underway to test the effectiveness of these drugs in preventing CIN and are still being explored due to their lower statists importance. In these, N-acetylcysteine has shown good results in reducing CIN. Thus, the rationale for this study was to assess the effect of N-acetylcysteine on reducing the incidence of CIN in high-risk patients who have not undergone coronary surgery in our population, because this drug is inexpensive, well-tolerated and devoid of significant side effects.

MATERIAL AND METHODS:

The study was conducted in the Nephrology and Cardiology department of Mayo Hospital Lahore for one-year duration from March 2019 to March 2020. The medical records of 120 patients over 30 years of age undergoing coronary angiography were reviewed. Data on their primary and secondary diseases (isolated diabetes mellitus, chronic renal failure from other causes and diabetic nephropathy), baseline and postoperative renal parameters, volume status during surgery, type and volume of contrast medium used, administration of sodium bicarbonate, intravenous fluid and N-acetylcysteine before and after treatment were collected. All of these patients received a low osmolality non-ionic contrast agent, Iopamidol 370 (370 mg iodine per milliliter and 75.5 g iopamidol / 100 ml) at a dose of 100 ml at the time of surgery and all were well hydrated / euvolemic.

Of these, 62 patients received N-acetylcysteine at the standard dose of 600 mg twice daily orally one day before and one day after contrast agent administration for a total of two days designated as Group A, and the remaining 58 patients who did not receive N-acetylcysteine labeled 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 contrast medium administration. All data was collected on a pre-designed proforma. In the statistical analysis, the age between the two groups was compared with the independent t-test, and the remaining parameters were analyzed with the chi-square test.

RESULTS:

One hundred and twenty high-risk patients from Group A and Group B were reviewed in this study. Demographics are presented 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 as the p-value was not <0.5.

However, serum creatinine increased by 0.5 mg / dL or more (acute contrast induced nephropathy) from baseline after angiography in 12 of 120 patients, including 10 patients in group B (17% non-N-acetylsysteine group) and 2 from group A (Patients in the N-acetylcysteine group 3%, p = 0.029), which was statistically significant.
The CIN rate / frequency was 17% in the non-acetylcysteine group and 3% in the standard N-acetylcysteine dose group when the absolute increase in creatinine concentration was used as the case definition (> 0.5 mg / dL) (p-0.029). Greater increases in creatinine were observed in patients without acetylcysteine than in patients treated with N-acetylcysteine. In particular, N-acetylcysteine appears to help prevent CIN in patients with isolated diabetes mellitus, isolated renal failure, and also 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 include chronic renal failure, diabetes mellitus (especially when accompanied by renal failure), ion contrast, and the use of high doses of contrast media. Thus, strategies for reducing the incidence of CIN include not only identifying risk factors, but also modifying these factors, selecting contrast agents that are less likely to induce CIN, and administering therapeutic agents that further reduce the risk of CIN.

In our study, prophylactic administration of N-acetylcysteine at a standard dose of 600 mg twice daily before and one day after the administration of a low osmolality non-ionic contrast agent in coronary angiography reduces a significant risk of contrast-induced nephropathy (p = 0.029).

In one of the previous studies, a meta-analysis of 13 randomized traces showed that prophylactic administration of N-acetylcysteine in coronary angiography prevents a statistically significant reduction in contrast-induced nephropathy (p = 0.006). In another study, intravenous / oral N-acetylcysteine prevented CIN with a dose-dependent effect in patients treated with primary angioplasty and may improve hospital outcomes (p <0.001). In one recent study, the results showed that prophylactic administration of acetylcysteine significantly prevents CIN in radiological procedures (p <0.001).

An important finding from this study is that prophylactic oral administration of the antioxidant acetylcysteine reduced the incidence of CIN. The rate of contrast-induced deterioration in renal function varies from 0 to 90% depending on the presence of risk factors. The frequency of contrast agent-induced deterioration of renal function in patients with diabetes has been reported to be 9-40% in mild to moderate chronic renal failure and 50-90% in patients with severe chronic renal failure. This study included diabetic and nondiabetic patients with chronic renal failure because diabetic patients are considered to be at high risk of contrast mediated renal impairment.

As recommended in previous studies, we defined the acute reduction in renal failure induced by contrast as an increase in serum creatinine of at least 0.5 mg per deciliter up to 48 hours after administration of the contrast medium. This increase may be important as it may extend hospitalization time. To avoid the bias of using different types of contrast media or administering different volumes, all patients in this study used 100 ml of a low osmolality non-ionic contrast agent (with the same amount), but N-acetylcysteine in one group and no acetylcysteine was used in the other group. which kept the patients of both groups well hydrated / euvolaemic. The use of such agents is associated with a lower incidence of acute deterioration of renal function than the use of ionic agents with high osmolality.

How can the beneficial effects of acetylcysteine be explained? Contrast-induced nephropathy is caused by changes in renal hemodynamics and a direct toxic effect on tubular epithelial cells. Toxic kidney damage may contribute to the formation of reactive oxygen species or reduced antioxidant activity. Early administration of acetylcysteine prevents the reduction of renal failure in patients with acetaminophen poisoning with hepatic insufficiency. A recent non-randomized study suggests that acetylcysteine may improve kidney function in patients with hepatorenal syndrome. Therefore, it may be able to prevent contrast induced nephropathy both by improving renal hemodynamics and by preventing direct damage to oxidative tissue.

CONCLUSION:

In summary, prophylactic oral administration of the antioxidant acetylcysteine at a dose of 600 mg twice daily on the day before and on the day of contrast administration, while maintaining hydration and using a non-ionic low osmolality agent is an effective means of preventing contrast induced kidney damage. More research is needed to determine the role of the above-mentioned factors. Also, today, bicarbonate as a moisturizer and ascorbic acid as an antioxidant are

used to prevent CIN, but their effects are not fully established and are still being tracked.

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