Role of N-Acetylcysteine in Prevention of Contrast Induced Nephropathy

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ABSTRACT

Objective: To determine the role of N-acetylcysteine in the prevention of CIN in high risk patients who underwent coronary angiography

Study design: Retrospective, observational study.

Methods: Medical records of 120 patients of both gender and age >30years who underwent coronary angiography, were reviewed from January 2010 to November 2010. All these patients divided into two groups. Group A received N-acetylcysteine and Group B patients did not received N-acetylcysteine. Acute contrast induced nephropathy was defined as an increase in the serum creatinine concentration of at least 0.5mg/dl from base line upto 48 hours after administration of contrast agent. All data was collected on a predesigned proforma. Age was compared between two groups by independent t test and others parameters were analyzed by Chi-square test.

Results: There was statistically significant difference between two groups (non N-acetylsysteine group17% and N-acetylcysteine group 3%,p=0.029).

Conclusion: Iopromidol, a non ionic, 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.

INTRODUCTION

With the increasing use of contrast media in diagnostic and interventional procedures, nephropathy induced by contrast media has become the third leading cause of hospital acquired acute renal failure accounting 12%of all causes. It is associated with significant risk of morbidity and death, despite the use of newer and less nephrotoxic contrast agent in high risk patients in recent year.

Risk factors for contrast induced nephropathy(CIN) are pre existing renal failure, diabetes mellitus, hypertension, congestive cardiac failure, dehydration, low effective circulatory volume, myocardial infarction, use of in aortic ballon pump, volume of contrast and osmolarity of contrast media. The incidence of contrast medium nephropathy among diabetic patients has been reported to be 5%-30%.

Contrast agents reduces renal functions by altering renal hemodynamics and by exerting direct toxic effects on tubular epithelial cells. There is accumulating evidence that reactive oxygen species have a role in the renal damage caused by contrast agent.

Many agents are tried for prevention of CIN include saline hydration, low dose dopamine, endothelin, prostaglandin E, N-acetylcysteine, ascorbic acid, bicarbonate. Studies are carried out to check the efficacy of the these drugs for preventing CIN and still under study because of less satatistical significance. In these N-acetylcysteine showed good results to reduce CIN.

So, the rationale of this study was to evaluate the effect of N-acetylcysteine for reducing the incidence of CIN in high risk patients who undrevent coronary procedures in our population because this drug is inexpensive, well tolerated and devoid of significant side effect.

MATERIAL AND METHODS

The study was conducted at nephrology ward with the collaboration of coronary care unit of Shaikh Zayed hospital Lahore, from January 2010 to November 2010. Medical records of 120 patients of both gender and age >30Years who undrewent coronary angiography, were reviewed. Data regarding their primary and secondary illnesses (isolated diabetes mellitus, Chronic renal insufficiency due to other cause and diabetic nephropathy), renal parameters at base line and post procedure, volume status at time of procedure, type and volume of...
contrast agent used, administration of sodium bicarbonate, intravenous fluid and N-acetylcysteine before and after the procedure were collected. All these patients had received a non ionic, low osmolality contrast agent, iopamidol 370(370mg of iodine per milliliter and 75.5g iopamidol/100ml) in a dose of 100ml and at time of procedure and all these were well hydrated/euvolemic.

Out of these, 62 patients had received N-acetylcysteine in a standard dose of 600mg twice daily orally one day before and one day after administration of the contrast agent for a total of two days, designated as Group A and other 58 patients who did not received N-acetylcysteine designated as Group B.

Acute contrast induced nephropathy was defined as an increase in the serum creatinine concentration of at least 0.5mg/dl from base line upto 48 hours after administration of contrast agent. All data was collected on a predesigned proforma. In statistical analysis, Age was compared between two groups by independent t test and other parameters were analyzed by chi-square test.

RESULT

One hundred and twenty high risk patients of group A and group B were reviewed in this study. The demographic data shown in table below.

Demographic Data

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

The results showed that there was no statistically significant difference between two groups in terms of age, sex, renal parameters (baseline serum creatinine concentration), and their primary and secondary illnesses because p value was not <0.5.

However, the serum creatinine concentration increased 0.5mg/dl or more( acute contrast induced nephropathy) from baseline after angiography in 12 out of 120 patients of which 10 of the group B patients (non N-acetylsysteine group17%) and 2 in group A (N-acetylcysteine group patients3%, p=0.029) which was statistically significant.

The rate/frequency of CIN was17% in the non-acetylcysteine group3% in the standard dose of N-acetylcysteine group when as absolute rise in creatinine concentration (>0.5mg/dl) was used as the case definition (p=0.029). A greater increase in the creatinine concentration was observed in non-acetylcysteine patients then in patients treated with N-acetylcysteine. Notably N-acetylcysteine seemed to be helped prevent CIN in patients with isolated diabetes mellitus, isolated renal insufficiency, as well as Diabetic nephropathy.

DISCUSSION

Contrast induced nephropathy (CIN) represents an increasing common cause of treatment related renal failure and increases mortality independent of other risk factors1,2. Major risk factors for CIN include chronic renal insufficiency, diabetes mellitus (especially when accompanied by renal insufficiency), ionic contrast and use of large doses of contrast media3,4,5. So, thus strategies for reducing the incidence of CIN include not just risk factor identification, but modification of these risk factors, choice of contrast media less likely to cause CIN, and administration of therapeutic agents that further reduce the risk of CIN.

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

In one previous study, the results of meta analysis of 13 randomized trial showed that prophylactic administration of N-acetylcysteine in coronary angiographies prevents the statistically significant reduction in contrast induced nephropathy (p=0.006).6 In another study, intravenous/ oral N-acetylcysteine prevents the CIN with a dose dependant effect in patients treated with primary angioplasty and may improve hospital outcome (p<0.001).7 In one recent study results showed that prophylactic administration of acetylcysteine significantly prevents the CIN in radiological procedures (p<0.001).8

The important finding of this study is that prophylactic oral administration of antioxidant acetylcysteine reduced the incidence of CIN. The incidence of contrast agent induced reduction in renal function varies from 0 to 90%, depending on the presence of risk factors9. The incidence of contrast agent induced reduction in renal function among
patients with diabetes has been reported to be 9-40% in mild to moderate chronic renal insufficiency and 50 to 90 percent in patients with severe chronic renal insufficiency]. The present study included diabetic as well as non diabetic patient with chronic renal insufficiency, since diabetic patients are thought to be at high risk for contrast agent induced reduction in renal function.

As recommended in earlier studies, we defined an acute cintrast induced reduction in renal failure as an increase in the serum creatinine concentration of at least 0.5mg per deciliter upto 48 hours after administration of contrast agent. Such an increase may be important, because it can increase the duration of hospitalization[13,4]. To avoid any bias due to the use of different types of contrast agents or the administration of different volumes, 100ml volume of non ionic ,low osmolality (with same amount) of contrast agent was used to all patients in this study but N-acetylcystein was given to one group and other was not taken acetylcysteine keeping both groups patients well hydrated/euvolemic. The use of such agents is associated with a lower incidence of acute reduction in renal function than the use of ionic, high osmolality agents[14].

How can the beneficial effect of acetylcysteine be explained? Contrast induced nephropathy is due to alteration in renal hemodynamics and direct toxic effects on tubular epithelial cells. The toxic renal damage may contribute to the formation of reactive oxygen species or to reduced antioxidant activity[2,7,8]. Early administration of acetylcysteine prevents a reduction in renal failure inpatients with acetaminophen poisoning who have liver failure[15]. A recent nonrandomized study suggested that acetylcysteine may improve renal function in patients with hepatorenal syndrome[16]. Therefore, it may be capable of preventing a contrast agent induced nephropathy both by improving renal hemodynamics and by preventing direct oxidative tissue damage.

In conclusion, prophylactic oral administration of the antioxidant acetylcysteine at a dose of 600mg twice daily on the day before and on the day of administration of the contrast agent, along with maintained hydration and use of non ionic low osmolality agent is an effective means of preventing contrast induced renal damage. Further studies needs to be required for establishing role of above mentioned agents. Also now use of bicarbonate as a hydration and ascorbic acid as an antioxidant is now being used for preventing CIN but their effect is not fully established and still under trair.

REFERENCES