Radiocontrast Nephropathy: Is it dose related or not?

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Abstract

Objective: To assess the safety of high dose non-ionic contrast media during a single radiological procedure in patients with pre-existing renal impairment.

Methods: One hundred eighteen patients, with serum Creatinine greater than 1.3 mg/dl who were undergoing coronary angiography or percutaneous transluminal coronary angiography (PTCA) were included in the study. All patients received the nonionic dye ULTRAVIST (Iopromide). Serum creatinine were measured before, 48 hours and 1 week after the administration of contrast agent. An acute contrast induced reduction in renal function was defined as an increase in Serum Creatinine concentration of >=0.5mg/dl, 48 hours after the administration of contrast agent. All patients with end stage renal disease or patients undergoing coronary bypass surgery within a week after coronary angiography or had any concomitant factors that could cause acute renal failure e.g., sepsis, hypotention, etc., were excluded. Patients receiving a dose of upto100 ml of contrast agent (low dose group) were separated from those who received greater than 100 ml of contrast agent (high dose group). Patients in both groups had similar characteristics in terms of sex, age, weight and underlying disease. Student's t-test was used for statistical analysis.

Results: The mean age of our patients was 62.3 ± 8.83 (range 40 - 84 years). There were 93 (78.8%) males and 25 (21.2%) females. The mean pre-contrast creatinine in the low contrast group was 1.97±0.92 and high dose group was 2.16±1.90 (p=0.48). The post-contrast Creatinine at 48 hours was 2.11±1.11 and 2.06±1.39 in the groups receiving low and high dose contrast agents respectively (p=0.830), while at 7 days post-contrast it was 2.17±1.28 and 1.95±1.43 respectively in the two groups (p=0.391). The contrast-induced reduction in renal function (rise in serum Cr >=0.5 mg/dl above base line) occurred in 14% (n=8) of patients in low dose and in 11% (n=7) in high dose contrast group (p=0.830, insignificant).

Conclusion: The results of our study confirm that high dose non-ionic contrast is not associated with increased risk of contrast-mediated nephrotoxicity in patients with pre-existing renal insufficiency undergoing cardiac angiography (p=0.830, insignificant) (JPMA 54:372;2004).

Introduction

Contrast induced nephropathy (CIN), is becoming a major cause of iatrogenic acute renal failure, especially with the increasing use of radio-contrast agents in both diagnostic and interventional procedures.1-5 CIN is the third most common cause of acute renal failure, and is associated with increased morbidity and in-hospital mortality.1,5,6 CIN typically presents as an acute rise in serum Creatinine levels, usually within 48 hours of exposure to contrast media.7 A theorized mechanism of CIN is renal medullary ischemia secondary to contrast induced vasoconstriction leading to renal tubule ischemia.7-9 Direct tubular toxicity also has been shown to play a role. These effects may be partly mediated by the generation of reactive oxygen species.9 Diabetes mellitus and pre-existing renal insufficiency are considered generally accepted risk factors.10 Congestive cardiac failure11, advanced age, extracellular volume depletion, multiple Myeloma and certain medications12 have been cited as additional risk factors. Several authors6,11-14 consider volume of contrast media as an independent risk factor for the development of CIN, whereas others15-18 find no evidence of dose related risk. In the view of this controversy, conventional wisdom mandates that the volume of contrast medium be limited wherever possible.

Several studies have reported decreased contrast medium toxicity of low Osmolality and non-ionic contrast media, particularly in patients with underlying risk factors for CIN.19,20 The incidence of CIN can be reduced by hydration, which continues to be the most effective method of prevention.7,8,20 Some recent studies have shown the effectiveness of certain antioxidants such as N-acetylcysteine in the prevention of CIN21 but other studies had showed no impact.22

Materials and Methods

We prospectively studied 118 patients, with serum Creatinine greater than 1.3 mg/dl who were undergoing coronary angiography or PTCA. Patients included had stable creatinine values since the last one month. We excluded patients undergoing dialysis, having urinary tract infection, urethral obstruction, acute renal failure and those who underwent coronary bypass procedures within a week after coronary angiography procedure. Patients who were hypotensive or on nephrotoxic drugs (ACE Inhibitors, NSAIDS, amino-glycosides, trimethoprim and diuretics) were also excluded from the study. All patients received the
nonionic dye ULTRAVIST (Iopromide). The dose selection was non-randomized. The mean dose of contrast agent administered was 112.64 ml ± 63.42 (range 20ml - 370 ml). All patients were hydrated with 0.9% saline 24 hours prior to the procedure. None of the patients received theophylline, mannitol or furosemide during the study. Serum creatinine was measured before, 48 hours after and 1 week after the administration of contrast agent. An acute contrast induced reduction in renal function was defined as an increase in serum creatinine concentration of >0.5mg/dl, 48 hours after the administration of contrast agent. The patients were also divided into two groups depending on the dose of the contrast agent administered. Patients receiving a dose of less than 100 ml of contrast agent (low dose group) were separated from those who received greater than 100 ml of contrast agent (high dose group).

The data were computed on SPSS data processor (SPSS version 10). The differences between the pre-contrast Serum Creatinine, post-contrast serum Creatinine at 48 hours and at 1 week in all overall study groups were analyzed. All the differences between serum creatinine concentrations were analyzed by Student's T-test. All statistical analyses were two-sided. A p-value of less than 0.05 was considered statistically significant.

**Results**

The mean age was 62.3 years ± 8.83 (range 40 - 84 years), with 93 (78.8%) males and 25 (21.2%) females. The mean weight of patients were similar at the start of the study in both groups. (High dose group, 72.98±11 kg, low dose group, 71.79±13 kg). Fifty four percent (n=64) patients enrolled in this study were diabetics, 76% (n=90) were hypertensive and 5% (n=6) had less than 40% left ventricular ejection fraction on echocardiographic examination. Fifty-three percent (n=62) of patients received high contrast dose (>100 ml) whereas 47% (n=56) received low contrast dose (<100 ml). The demographics of the patients in our study group are given in Table 1. In low dose group, the mean dose of contrast agent administered was 66 ±18ml, whereas in high dose group it was 151± 50ml.

### Table 1. General demographics of our study population

<table>
<thead>
<tr>
<th></th>
<th>High dose contrast group</th>
<th>Low dose contrast group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patient</td>
<td>62</td>
<td>56</td>
</tr>
<tr>
<td>· Male</td>
<td>48 (77%)</td>
<td>46 (74%)</td>
</tr>
<tr>
<td>· Female</td>
<td>14 (23%)</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>Mean Age</td>
<td>63±9 years</td>
<td>61±9 years</td>
</tr>
<tr>
<td>Mean weight</td>
<td>72.98±11 kg</td>
<td>71.79±13 kg</td>
</tr>
<tr>
<td>Mean contrast dose</td>
<td>151±50 ml</td>
<td>66±18 ml</td>
</tr>
<tr>
<td>Pre-contrast creatinine</td>
<td>2.16±1.90 mg/dl</td>
<td>1.97±0.92 mg/dl</td>
</tr>
<tr>
<td>Associated diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>· Diabetes</td>
<td>33 (55%)</td>
<td>31 (55%)</td>
</tr>
<tr>
<td>· Hypertension</td>
<td>46 (74%)</td>
<td>44 (78%)</td>
</tr>
<tr>
<td>· Congestive cardiac Failure</td>
<td>4 (6%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

### Table 2. Comparison of creatinine levels of patients receiving high dose and low dose of contrast.

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Pre-contrast creatinine mean ± SD</th>
<th>P value</th>
<th>Post contrast creatinine (48h) mean ± SD</th>
<th>P value</th>
<th>Post-contrast creatinine (7 days) mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 ml</td>
<td>1.97±0.92</td>
<td>0.487</td>
<td>2.11±1.11</td>
<td>0.830</td>
<td>2.17±1.28</td>
<td>0.391</td>
</tr>
<tr>
<td>n = 56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100 ml</td>
<td>2.16±1.90</td>
<td></td>
<td>2.06±1.39</td>
<td></td>
<td>1.95±1.43</td>
<td></td>
</tr>
<tr>
<td>n = 62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of serum Creatinine values before and after the administration of the contrast agent is given in Table 2. The mean pre-contrast creatinine in the low contrast group was 1.97±0.92mg/dl and high dose group was 2.16±1.90mg/dl (p=0.48). The post-contrast creatinine at 48 hours was 2.11±1.11mg/dl and 2.06±1.39mg/dl in the groups receiving low and high dose contrast agents respectively (p=0.830), while at 7 days post-contrast it was 2.17±1.28mg/dl and 1.95±1.43mg/dl respectively in the two groups (p=0.391).

The contrast-induced reduction in renal function (rise in serum Creatinine ≥0.5mg/dl above base line) occurred in 14% (n=8) patients in low dose and in 11% (n=7) in high dose contrast group (p=0.830, insignificant). None of these patients required dialysis.
Discussion

The reported incidence of contrast-mediated nephrotoxicity depends on its definition. Although changes in serum creatinine levels may be imperceptible in the face of moderately reduced Glomerular filtration rates (40-80 ml/min/1.73m²), an increase in serum creatinine (S. Cr) level remains the first biochemical sign of renal impairment and is the biochemical marker most readily available. Furthermore, the significance of any sub-clinical contrast-induced nephropathy is dubious.

Although Cigarroa RG et al have reported that contrast-mediated renal dysfunction occurs infrequently if the amount of contrast agent is limited in accordance with the degree of azotemia, the overall literature review however reveals disagreement as to whether the incidence of CN is reduced by limiting the amount of contrast agent in patients with pre-existing renal impairment.

In our study we did not find any difference in the S.Cr levels between patients receiving high or low doses of contrast agent both at 48 hours and at 1-week post contrast therapy.

Although the maximum volume of contrast that can be administered safely is unknown, our patients in high dose group received an average dose of 151 ml (±50) low osmolality contrast agent (ultravist) without any additional risk of developing contrast mediated decline in their renal function. Thus this volume appears safe.

It can be concluded that non-ionic contrast may be administered at considerably high dose than those routinely employed for most imaging applications. This has important implications in patients who require administration of large doses of contrast agent for multiple imaging procedures (e.g., CT examination of chest, abdomen, pelvis and brain) or for patients who must undergo contrast enhanced CT examinations over a short time (e.g., contrast enhanced CT followed by aortic angiography to evaluate for aortic dissection). In such patients, a delay in workup owing to concerns about contrast-mediated nephrotoxicity appears inappropriate. For patients who require extremely large doses of contrast agent during interventional procedures (e.g., evaluation for occlusion of a vascular malformation or coronary angiography), completion of the appropriate medical therapy should take precedence over concerns about dose-related contrast mediated nephropathy.

These conclusions however should not be generalized to patients with other risk factors for contrast-mediated nephrotoxicity or to patients who receive high-osmolality (ionic) contrast agent.

Conclusion

The results of our study confirm that high dose non-ionic contrast is not associated with increased risk of contrast-mediated nephrotoxicity in patients with pre-existing renal insufficiency who undergo cardiac angiography (p=0.830, insignificant).

References