Renal Consequences of Rapid High Dose Contrast CT

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A retrospective study of renal deterioration after high doses (80 g I) of intravenous contrast medium was done of 286 adult patients. The incidence, duration, and severity of deterioration was compared with those reported in a series of 377 similar patients after low dose contrast infusion (43 g I). No statistically significant difference between these groups was seen in nondiabetics with a preinfusion serum creatinine below 4.5 mg/dl. A prospective study of fractional excretions in 35 patients receiving high dose infusion demonstrated no additional subtle renal damage in 34 patients. One patient developed a transient rise in serum creatinine that was identical to the course of renal deterioration after 43 g of iodine. It is concluded that the severity and duration of renal deterioration was not affected by the dose of contrast material (43–80 g iodine).

The dose of intravenous contrast substance recommended for computed tomography (CT) has gradually risen from 21 g iodine in 1975 to 56 g in 1978 [1, 2]. During the past few years we found that an 80 g iodine dose of contrast medium appreciably improved the CT display of clinically useful information [3–7]. Although iodine doses of that degree are used in angiographic procedures [8], their use in intravenous infusion for CT of the head is not yet widespread.

Our study was undertaken to evaluate the incidence and severity of renal dysfunction after rapid intravenous administration of an 80 g iodine dose of contrast medium. The study was in two parts: (1) a prospective study of 35 patients who were closely monitored and (2) a retrospective study of 286 patients by chart review.

Materials and Methods

The prospective study of renal injury was performed on 35 adult, nondiabetic patients who underwent cranial CT during rapid intravenous infusion of diatrizoate meglumine containing 80 g iodine. Renal function was normal in 28 patients (serum creatinine less than 1.2 mg/dl) and seven had impaired renal function (serum creatinine 1.2–4.5 mg/dl).

On the day before CT and 1 and 3 days after contrast medium infusion, the following values were determined: hematocrit, hemoglobin, serum creatinine, sodium, potassium, chloride, carbon dioxide, calcium, alkaline phosphatase, serum protein fractions, cholesterol, triglycerides, bilirubin, SGOT, SGPT, and lactic dehydrogenase. In addition, 24 hr urine specimens were collected on all patients to determine urine volume, creatinine, protein, potassium, calcium, uric acid, and phosphate.

The retrospective study of 286 adult patients who had cranial CT scans during infusion of an 80 g iodine dose of contrast medium was done by chart review. Serum creatinine and blood urea values obtained within 7 days before and after contrast infusion as well as evidence indicating presence or absence of preexisting renal disease and/or diabetes mellitus were available in all patients. Of the 286 patients, 11 had diabetes; 275 did not.
The patients were divided into three categories: group I—preinfusion serum creatinine of less than 1.5 mg/dl (this group included normal subjects as well as those with unrecognized renal disease with only mildly reduced renal function); group II—preinfusion serum creatinine of 1.5–4.5 mg/dl; and group III—severe renal impairment manifested by serum creatinine levels in excess of 4.5 mg/dl before infusion.

Contrast-associated renal dysfunction was diagnosed when the previously stable creatinine increased at least 1.0 mg/dl, with or without oliguria, and no nephrotoxic factor other than meglumine diatrizoate was present. Only three patients with renal dysfunction were excluded because of multiplicity of nephrotoxic factors (nephrotoxic drugs, sepsis, or rapidly failing renal function).

About 570 ml of Reno-M-DIP (Squibb) was infused intravenously for contrast-enhanced CT brain scans. The first 270 ml (37.7 g iodine) was given by pressure infusion in 90–120 sec. About 30 ml was retained in the first bottle as a precaution against air embolism. A second bottle of 300 ml (42.3 g iodine) was administered by rapid drip over the next 5–7 min. The meal before examination was omitted and hydration maintained with surgical fluids.

**Results**

**Prospective Study**

Renal tubular function was unchanged in 34 of the 35 patients who were monitored before and after contrast medium infusion of 80 g iodine. Hematocrit, hemoglobin, cholesterol, triglycerides, bilirubin, and enzymes were unchanged in all patients. No uricosuric effect was noted. In the last patient acute renal deterioration developed. He was oliguric (urine volume averaging 40 ml/hr) for 48 hr after contrast infusion. His serum creatinine measurements before as well as 1, 2, 3, and 7 days after infusion were 3.3, 5.1, 6.3, 9.3, and 3.8 mg/dl, respectively. Dialysis was not performed. The tubular damage recorded by the rise in serum creatinine was reflected in the more sensitive measurements of fractional excretions.

It should be noted that this patient had been exposed to other nephrotoxic factors. He had been treated for bilateral pneumonia and sepsis with gentamicin (100 mg followed by 40 mg every 8 hr) for 1 week immediately before contrast infusion. He was also being treated for severe congestive heart failure. He had diffuse atherosclerotic vascular disease that was manifested by previous cerebral infarction and renal insufficiency (baseline of 3.3 mg/dl). It is likely that the contrast medium was at least partly responsible for the renal deterioration, but the sepsis, nephrotoxic drugs, congestive heart failure, and preexisting renal insufficiency cannot arbitrarily be exonerated.

**Retrospective Study**

Both pre- and postinfusion serum creatinine values were recorded on 286 patients. Results for the 275 nondiabetic patients are presented in table 1 and for the 11 diabetic patients in table 2. Eight of the 286 patients showed postinfusion renal deterioration (six nondiabetics and two diabetics). Six of these showed return of serum creatinine values to baseline levels within 14 days after infusion. Two nondiabetics with preexisting severe renal disease died of causes unrelated to the renal disease or the infusion of contrast medium. One of the eight who had been severely dehydrated experienced transient oliguria.

**Discussion**

It is widely accepted, without documentation, that the incidence of renal deterioration after infusion of modern contrast media is dose related. However, clinical studies do not support this position insofar as arterial injections are concerned. Doses as high as 103 g iodine have been used in arteriography [9, 10], but the effect of such high doses administered intravenously has not previously been evaluated.

Our retrospective study was patterned after that of VanZee et al. [11] who reported the incidence of renal damage after drip infusion of a "standard dose" of meglumine diatrizoate (43 g iodine) in hospitalized patients. The same criteria were used for patient selection, definition of renal failure, and classification of patients. In addition, meglumine diatrizoate (Reno-M-DIP) was used in both studies. Only the total amount of contrast medium and the rate of administration differed.

The incidence of renal deterioration in the week after a high dose (80 g iodine) was compared with that reported after a low dose (43 g iodine). In three groups of nondiabetics (table 1) there was no difference in the rate of renal deterioration at even the 10% level, based on the one-tailed Fisher exact possibility test. Upper limits of 95% confidence intervals for the rate of renal deterioration at the two dose levels of iodine were 3.9% and 3.1%, respectively, in group

**TABLE 1: Renal Deterioration in Nondiabetics After Diatrizoate Meglumine Infusions**

<table>
<thead>
<tr>
<th>Patient Group*</th>
<th>No. Patients (Deterioration/Group Total) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>43 g Iodine [11]</td>
</tr>
<tr>
<td>I</td>
<td>4/264 (1.5)</td>
</tr>
<tr>
<td>II</td>
<td>2/66 (3.0)</td>
</tr>
<tr>
<td>III</td>
<td>5/16 (31.0)</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>11/346 (3.2)</td>
</tr>
</tbody>
</table>

* Preinfusion serum creatinine levels for group I = <1.5 mg/dl; group II = 1.5–4.5 mg/dl; group III = >4.5 mg/dl.

**TABLE 2: Renal Deterioration in Diabetics After Contrast Media Infusions**

<table>
<thead>
<tr>
<th>Patient Group*</th>
<th>No. Patients (Deterioration/Group Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>43 g Iodine [11]</td>
</tr>
<tr>
<td>I</td>
<td>0/19</td>
</tr>
<tr>
<td>II</td>
<td>5/10</td>
</tr>
<tr>
<td>III</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>12/19</td>
</tr>
</tbody>
</table>

* Preinfusion serum creatinine levels for group I = <1.5 mg/dl; group II = 1.5–4.5 mg/dl; group III = >4.5 mg/dl.
I and 10.5% and 13.5%, respectively, in group II. In group III, the numbers were too small to justify definitive conclusions. Recent reports on small numbers of patients indicate an increased risk of renal deterioration in group III patients and diabetics in groups II and III (table 2) [11–13]. This information has compelled practitioners to limit the number of these patients to whom iodine contrast is administered and has therefore limited the reservoir of clinical material available for evaluation of renal deterioration. Fortunately most patients referred for cranial CT do not fit into these groups.

In our prospective study, the serum creatinine value was sufficient to detect renal deterioration. Additional subtle changes in fractional excretion electrolytes or creatinine were not seen in the absence of serum creatinine changes. The possibility of such subtle damage suggested by Older et al. [14] was not substantiated.

In summary, our studies offer no evidence that larger doses of intravenously administered contrast medium increase the risk or severity of permanent renal injury. In the eight patients in whom renal deterioration occurred after an 80 g dose, the clinical course and duration were identical to that reported after 43 g iodine infusion. In nondiabetic patients with serum creatinine of less than 4.5 mg/dl (271 patients in groups I and II) the rate of renal injury was unaffected by the contrast medium dose in the 43–80 g range. In patients with severe renal impairment and diabetes, limited clinical data indicate that caution should be used when administering any dose of contrast medium.

REFERENCES