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Low Osmolar Contrast Agents and Nephrotoxicity

TO THE EDITOR: New intravascular radiographic contrast agents, iopamidol, iohexol, and ioxaglate all have lower osmolality than do older agents (1). Several authors have claimed that the low osmolar contrast agents are less toxic to the kidneys than are the older agents (1, 2). However, we observed three episodes of decreasing renal function closely associated with the use of two of the new agents. All three patients had diabetes mellitus, fundiscopic evidence of diabetic retinopathy, and renal insufficiency before coronary angiography was done.

A 65-year-old woman was hospitalized with acute myocardial infarction. Both a history and physical examination showed diffuse atherosclerotic vascular disease and moderate congestive heart failure. Before angiography, her serum creatinine level was 1.9 mg/dL. She received 70 mL of iohexol. Her creatinine peaked on day 4, then returned toward the baseline value.

A 36-year-old woman was hospitalized with subendocardial myocardial infarction. She had received acute hemodialysis at two previous hospitalizations for temporary exacerbations of her chronic azotemia. She underwent cardiac catheterization and received 83 mL of iohexol. A serum creatinine level of 2.3 mg/dL before the study climbed to 7.3 by the third day of the study before returning to the baseline value.

A 61-year-old man developed renewed chest pain 6 years after undergoing coronary artery bypass surgery. His serum creatinine level was 1.5 mg/dL. He received 116 mL of iopamidol during coronary angiography. By the third day after the procedure, the creatinine level was 2.3 mg/dL and by the 19th day, when hemodialysis was initiated, the creatinine level was 8.4 mg/dL. The patient continues to receive maintenance hemodialysis.

Although the low osmolar contrast agents result in fewer subjective symptoms in patients than do the older agents, these three cases serve to demonstrate that the risk of contrast-associated nephrotoxicity is still present with these newer agents. We recently reviewed clinical studies between 1980 and 1985 that concerned the effect of these agents on renal function. In five studies in which comparisons were made between the effect of low osmolar contrast agents and higher osmolar contrast agents on measurements of glomerular filtration, no significant difference was found between the older and the newer agents (3). Furthermore, contrast nephrotoxicity was recently reported in five patients receiving ioxaglate and in one patient receiving iohexol. All of these patients had chronic renal insufficiency and most of them had diabetes mellitus (4). With the addition of our report, all of the low osmolar contrast agents available in the United States now have been associated with nephrotoxicity. The occurrence of contrast nephrotoxicity without pre-existing renal insufficiency is very limited with the high osmolar agents (5). Patients with azotemia, especially when diabetes mellitus is also present, appear to have a much higher incidence (5). We suspect that such patients are at a higher risk for contrast nephrotoxicity with low osmolar contrast agents as well. Any advantage in the nephrotoxicity profile that low osmolar contrast agents may have remains to be determined.

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Salsalate and Minimal-Change Nephrotic Syndrome

TO THE EDITOR: Acute interstitial nephritis and minimal-change glomerulopathy has been reported as adverse reactions with most of the nonsteroidal antiinflammatory drugs (1-3), although isolated nephrotic syndrome secondary to minimal-change glomerulopathy has been infrequently attributed to these kinds of drugs (4). However, the syndrome has never been associated with the nonsteroidal antiinflammatory agent, salsalate, as it is herein reported.

A 76-year-old man was hospitalized with a clinical and biologic nephrotic syndrome. Major biochemical abnormalities included a serum albumin level of 1.63 gm/dL and proteinuria, 11 g/24-h urine sample. Moderate renal insufficiency with a serum creatinine level of 2.6 mg/dL was present without any other abnormalities in the rest of the biochemical or immunologic analysis, including a urinary microscopic examination. He had been receiving salsalate, approximately 1.5 to 2 g/wk, for the last 2 years as treatment for lumbar pain attributed to degenerative changes in the spinal column. A renal biopsy specimen done by percutaneous puncture showed 13 glomeruli. No changes were detected by optic microscopy and an immunofluorescent analysis was negative for IgG, IgM, IgA, and complement factors. No electron-dense deposits were detected by electron microscopy and fusion of podocytes was the only remarkable finding by this technique. Fifteen days after discontinuation of salsalate treatment, the nephrotic syndrome was no longer present, with only a trace of proteinuria and a normal serum creatinine level. After discharge, the patient spontaneously resumed salsalate ingestion and 2 months later he again developed a nephrotic syndrome with a proteinuria of 37 g/L, which again disappeared after discontinuation of salsalate treatment. No changes in serum creatinine were detected, and no other immunologic or biochemical findings were remarkable during this second episode. The patient remains asymptomatic 6 months later.

Salsalate is a nonacetylated compound, a product of the sterification of two molecules of salicylic acid. After gut absorption, it is slowly hydrolized in two molecules of free salicylic acid, which is then able to produce, by inhibiting prostaglandin E_2 synthesis, a lymphokine excess (3). This excess induces an increase in the vascular permeability at the renal glomeruli. Minimal-change glomerulopathy and acute renal failure have been described infrequently by the association of ibuprofen and aspirin (5), but not with the isolated molecule of salicylic acid. The combination of aspirin with any other nonsteroidal inflammatory drug is not recommended, however, because of the expected greater rate of adverse reactions (3). Therefore, we believe that salsalate must be added to the list of nonsteroidal inflammatory drugs that can produce minimal-change nephrotic syndrome presumably by means of the two free salicylic acid molecules in which it is hydrolized.

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Lactic Acidosis and Bicarbonate Therapy

TO THE EDITOR: *Annals* has recently published an editorial by Stacpoole (1) opposing the use of bicarbonate for the treatment of lactic acidosis and an argument in rebuttal by Narins and Cohen (2) in support of its use. The arguments used by Narins and Cohen omit certain details.