An Evaluation of the Nephrotoxic Effects of Nonionic Low Osmolality Contrast Media Using Urinary Enzymes

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A prospective clinical study was conducted to examine the usefulness of urinary enzymes as a sensitive parameter for determining nephrotoxicity caused by LOCM. Forty-seven patients were intravenously injected with 100 ml of LOCM (Iohexol or Iopamidol) in radiographic studies. Serum creatinine and creatinine clearance (Ccr) were determined before and 7 days after LOCM infusion. Urinary excretion of N-acetyl-β-D-glucosaminidase (NAG) and γ-glutamyltransferase (γ-GTP) was determined before and 1, 2, 3 and 7 days after LOCM administration. To analyze the relationship between the nephrotoxic effect of LOCM and renal function, patients were divided into group L (Ccr<70 ml/min, n = 19) and group N (Ccr≥70 ml/min, n = 28). No significant changes were noted in serum creatinine or Ccr in either group. Urinary NAG and γ-GTP levels were significantly elevated on day 1 compared with the levels prior to LOCM infusion, but these returned to the base line after day 2. The increase ratio of urinary NAG in group L was significantly higher than that in group N on days 3 and 7. No statistical difference between groups L and N was observed regarding urinary γ-GTP increases on any of the days. In conclusion, urinary enzymes are sensitive and useful indicators for evaluating contrast media nephrotoxicity, which cannot be detected by serum creatinine or Ccr. Careful attention should be paid in radiographic studies to patients with renal dysfunction, even when LOCM is being employed.

Introduction

Contrast media-induced nephrotoxicity is a widely recognized clinical event. Recently, several nonionic low osmolality contrast media (LOCM) have been introduced in radiographic studies. The clinical benefit of LOCM in reducing vascular pain, nausea and vomiting is now widely accepted. The administration of LOCM to patients with renal dysfunction is generally recommended, based on results obtained from randomized clinical trials [1]. However, the superiority of LOCM over conventional ionic high osmolality contrast media (HOCM) with regard to nephrotoxic adverse effects has not been firmly established. One of the reasons for inconsistencies concerning the clinical benefit of LOCM is undoubtedly the lack of any sensitive, reliable markers for detecting nephrotoxicity caused by contrast media. Serum creatinine and creatinine clearance are common parameters for evaluating renal
function, but serum creatinine does not directly reflect renal damage and creatinine clearance is sometimes unreliable because of inaccurate urine collection, especially in elderly patients. The present prospective clinical study was conducted to examine the usefulness of urinary enzymes as sensitive parameters to determine LOCM nephrotoxicity.

Patients and methods

Thirty males and 17 females, aged 19 to 81 years (mean 63 years), were enrolled in the present study after their informed consent was obtained. These 47 patients were intravenously injected with 100 ml of LOCM (iohexol or iopamidol) for radiographic studies including computed tomography and intravenous urography. Nephrotoxic effects of contrast materials were evaluated by serum creatinine, 24-hour creatinine clearance (Ccr) and urinary excretion of N-acetyl-β-D-glucosaminidase (NAG) and g-glutamyltransferase (γ-GTP). Urine samples were obtained from patients as spot urine both before and 1, 2, 3 and 7 days after contrast media administration urinary NAG, γ-GTP and creatinine. Urinary enzyme activities were corrected with urinary creatinine concentration. The baseline for the excretion of urinary enzymes in each patient was defined as the mean value of 3 samples over 3 days prior to contrast media infusion. Serum creatinine levels and Ccr were determined both before and 7 days after contrast media infusion. To analyze the relationship between the nephrotoxic effect of contrast media and renal function, patients were divided into two groups based on Ccr, comprising group L (n = 19), in which Ccr was less than 70 ml/min, and group N (n = 28), in which Ccr was over 70 ml/min. Statistical analysis was performed using Student's t-test or Mann–Whitney U-test.

Results

Figure 1 shows the urinary excretion of NAG after contrast media infusion. The urinary NAG levels were significantly elevated on day 1 compared with the levels prior to contrast media infusion. The urinary NAG excretion returned to the base line after day 2. Urinary γ-GTP excretion demonstrated almost the same pattern as that of NAG (Fig. 2).

Figures 3 and 4 show the urinary enzyme levels of groups L and N. Data are presented as the increase ratio of urinary enzyme excretion to the base line excretion. The increase ratios of urinary NAG in group L on days 1, 2, 3 and 7 after contrast media administration were respectively 1.7, 1.4, 1.3 and 1.3 times the base line. On the other hand, those in group N on days 1, 2, 3 and 7 were respectively 1.4, 1.1, 1.9 and 0.9 times the base line (Fig. 3). There was no significant difference in NAG increase on day 1 (p = 0.111) or day 2 (p = 0.059) between the two groups. However, the increase ratio of urinary NAG in group L was significantly higher than that in group N on days 3