A COMPARISON BETWEEN IONIC AND NONIONIC CONTRAST NEPHROPATHY AMONG HIGH RISK PATIENTS CANDIDATE FOR CORONARY ANGIOGRAPHY

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Abstract

Among the causes of nephrotoxic acute renal failure, the increase use of contrast agents has caused the contrast nephropathy to come second after aminoglycosides. The aim of this study is comparison of nephrotoxicity of ionic (Urografin) and nonionic (Omnipaque, Ultravist) contrast agents in high risk patients candidate for coronary angiography. In this study 82 high risk patients who were candidate for coronary angiography in a 6 months period in the year 2004 in Golestan hospital of Ahwaz were randomly divided into two equall groups – ionic and nonionic contrast agents – and the prevalence of contrast nephropathy in each group was determined. Electrolyte changes (Na, K) of these patients were also assessed. Plasma level of BUN, Cr, Na and K were measured before and 24 to 48 h after angiography and it was accounted as contrast nephropathy if Cr level has raised at least 0.5 mg.

Among 41 patients who undergone angiography with nonionic agents (Omnipaque, Ultravist), 2 patients (5%) were affected by contrast nephropathy while this complication was seen in 6 patients (14.6%) among those who undergone angiography with ionic contrast agent (Urografin). No significant changes were seen in electrolyte concentration (Na, K) before and after angiography. Noting the fact that the predictive value of this finding is 0.132 ($P>0.05$), the statistical value of this is not proved. Therfore, there is no diffrence in nephrotoxicity between ionic and non-ionic contrast nephropathy in high risk patients. The most common risk factors of this complication were diabetes mellitus (DM) 50%, age≥65, 50% and chronic renal failure 25%. Relative risk (RR) of DM was 1.16, for old age 1.1 and it was 1.49 for chronic renal failure (CRF). The results of this study were similar to the results of American college of cardiology metaanalysis, Shwab study in USA and Esnalt study in France.

Introduction

One of the most important complications of use of contrast agents is acute renal failure which is often nonoliguric (1). Pathologic changes are limited to the proximal tubule and the characteristic finding is vacuolization of proximal tubule cells called osmotic nephrosis (1). Contrast nephropathy may results from hemodynamic changes, tubule obstruction, cellular injury or immunologic reaction to contrast agents (2).The increase use of contrast agents has caused increasing prevalence of contrast nephropathy in admitted patients from 5% to more than 30% (1,3,4,5,6). This difference in prevalence is because of differences between contrast agents and individuals who receive these agents. Today in the view of nephrotoxicity, contrast agents have placed second after aminoglycosides (6). Contrast nephropathy is defined as 0.5 to 1 mg raise of serum creatinine or 25 to 50% relative increase of serum creatinine which is raised during 24 to 72 hours and decrease to baseline within 7 to 10 days and most often is nonoliguric (2,4,6,7). Its prevalence increase in the presence of risk factors like old age, renal failure, diabetes mellitus and

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severe heart failure (1,2,4). Two kinds of contrast agents are used in angiography including ionic and nonionic. There is no consensus about reduction of nephrotoxicity by nonionic agents. However, they cause less allergic, cardiovascular and endothelial reaction than ionic contrast agents (1, 4,8,9,10,11,12,13). In one study at 2002 in France by Esnault it is recommended to use nonionic contrast agents with low osmolality in patients with renal failure (8) but in Schwab study no differences was found in nephrotoxicity between ionic and nonionic contrast agents (9). The Aspelin trial in 2003 has resulted that contrast nephropathy would be reduced in high risk patients if they undergone nonionic isoosmolar contrast agents in comparison with low osmolar agents (10).

Metaanalysis of American college of cardiology in 1993 had offered that although in clinical trials the nephrotoxicity of nonionic contrast agents is less than ionic agents but its significance is unclear (13). According to no consensus on reduction of nephrotoxicity by nonionic agents, the aim of this study is comparison between ionic and nonionic contrast nephropathy among high risk patients candidate for coronary angiography.

Results

In this study 82 high risk patients undergone angiography, 41 with ionic (Urografin) and another 41 with nonionic agents. In the second group 24 patients (59%) received Omnipaque and 17 patients (41%) received Ultravist. Overall these 82 patients constitute of 30 women (37%) and 52 men (63%).42 were diabetic (51%), 5 had heart failure (6%), 12 had CRF (15%) and 39 patients were older than 65 (47%).19 patients (23%) had more than 1 risk factor. In the nonionic group 2 patients (5%) were affected by contrast nephropathy, both were diabetic and one of them had CRF. In these patients average concentration of Na before and after angiography was 138 meq/dl and average concentration of K before and after procedure was 4.3 meq/dl. In group of Urografin (ionic contrast agent), overall 6 patients (14.6%) were affected by contrast nephropathy, 4 women and 2 men. From those 2 were diabetic (33%), 4 were older then 65 (66.6%) and one of them had CRF. The relative risk of contrast nephropathy by ionic agent with confidence index of 95% (CI 95% = 64%, 14%) was 3 and also it was 1.16, 1.1 and 1.49 for DM, old age and CRF respectively. In the ionic agent group, average concentration of Na and K before angiography was 138.5 and 4.1 and it was 137.8 and 4.1 after angiography. Overall 8 patients were affected by contrast nephropathy, in which concentration of Na was 139 before and after angiography. In 74 patients who remain unaffected by nephropathy, concentration of Na was 138.2 before procedure and 137.9 after angiography (P = 0.509) and therefore contrast nephropathy had no meaningful effect on Na concentration. In affected patients by contrast nephropathy the average concentration of K was 3.9 before angiography and 4.2 after angiography and this value in uncomplicated patients was 4 and 4.2 (P=0.76) and therefore there was no effect on concentration of K by contrast nephropathy too.

Overall the prevalence of DM in affected patients were 50% and one half of them (4 patients) were older than 65. 2 patients (25%) had CRF and sexual distribution was equal (4 women and 4 men). none of them had severe heart failure. In comparison of contrast nephropathy by ionic and nonionic contrast agents the predictive value was 0.132 (P>0.05) and also P. value of DM was 0.558, for severe heart failure 0.473, for old age 0.587 and for CRF it was 0.451.

Method

In this experimental clinical trial, all of the high risk patients candidate for coronary angiography at a six months period in the year 2004 in Golestan hospital of Ahwaz

were randomly divided into two groups – ionic and nonionic contrast agents.
It was accounted as high risk if there was any of these conditions : severe heart failure with EF ≤ 30%, renal failure with Cr ≥ 1.5 , DM and old age > 65 years old. Sampling of patients achieved randomly and number of sample were determined 82 with confidence index of 95% maximum difference from reference value of 10% by this

Formula:

$$N = \frac{Z^2_{1-\alpha/2} \cdot P^{1-p}}{d^2}$$

41 patients were randomly put in group of ionic contrast agents and another 41 patients in group of nonionic agents. In each group, urea, Cr, Na, K and FBS were measured before and 24 to 48 h after angiography and electrolyte changes and prevalence of acute renal failure in each group, defined as at least 0.5 mg rising of Cr from basal level, were assessed. Statistical calculations of this study were achieved by statistician based on chi square test and Pearson coefficient.

Discussion

Noting to the results of this study and P value of 0.132 (P>0.05) the statistical and clinical value of this study is not proved although contrast nephropathy is seen more frequent by ionic agent (14.6%) than nonionic agents (5%). The most common risk factor of this complication were DM with RR of 1.16, old age with RR of 1.1 and CRF with RR of 1.49. In the Rich study old age more than 70 and after that CRF and DM were offered as risk factors (14). In this study the change in concentration of Na (P=0.509) and K (P=0.076) in affected patients was subtle and it had no statistical meaning (P>0.05). Although in vitro studies have shown that cellular injury by nonionic agents is less (15) but clinical studies have no consensus on this matter and some have not shown any effect of nonionic agents in reduction of nephropathy (8,9,13,16). The results of this study were similar to results of American college of cardiology metaanalysis, study of Schwab et al. (9,13) and Esnault study (8) but differ with the results of metaanalysis of 45 clinical study that shows reduction of contrast nephropathy by nonionic agents in high risk patients, such as those with preexisting renal impairment (17). Controversy about prevalence of contrast nephropathy and ambiguous results are because of difference in patient's clinical situation, indistinct definition of acute renal failure after use of contrast agents and use of different criteria for definition of this condition. It seems that more expanded studies with careful supervision on patient's clinical condition and exact definition of ARF can solve this controversy. N- acetyl cystein) and other agents can be assessed in clinical trials.

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