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Full Length Research Paper

Influence of different doses of Iopromide on renal function of elderly patients

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This study aims to investigate influences of different doses of hypisotonic non-ionic contrast agent (Iopromide) on renal function of elderly patients. A total of 30 cases of elderly patients without a history of nephrosis and with normal renal function were divided into two groups according to the different doses of received contrast agent. Influences of Iopromide on renal function were observed by detecting blood urea nitrogen (BUN), serum creatinine (Scr) and creatinine clearance rate (Ccr) at the postoperative 2nd and 5th day. There was no significant difference for BUN, Scr and Ccr levels before angiography and at the 2nd and 5th days after operation between two groups of patients (P > 0.05). At the postoperative 2nd day, Scr of two groups of patients slightly increased and Ccr slightly reduced. At the 5th day, they restored to the levels before angiography. Based on the results, we believe one dosage of not more than 294 ml non-ionic contrast agent Iopromide is relatively safe for elderly patients.

Key words: Non-ionic contrast agent, contrast induced nephropathy, elderly patients.

INTRODUCTION

In recent years, the incidence rate of contrast induced nephropathy (CIN) increased yearly, with wide applications of angiography and catheter intervention operation in clinic. At present, CIN has become the third largest cause of acquired acute renal injury in hospital (Finn, 2006). It is currently thought that main risk factors of CIN occurrence include age, basic kidney disease and diabetes mellitus. For patients with creatinine clearance rate less than 20 ml/min/1.73 m^2, CIN risk after receiving contrast agent reaches over 14%. By comparison, the incidence rate of patients with normal renal function is only 7.5% (Rundback et al., 2011). At the same time, the type and dosage of contrast agent are closely related to CIN occurrence (From et al., 2010). Compared with the traditional ionic contrast agent, safety of the non-ionic contrast agent greatly increases. The study of Lin and Bonventre (2005) showed that there was no significant difference for the experiment result between the homotonic non-ionic contrast agent group and the placebo group, after the postoperative hydration therapy.

However, there are few reports on safety of using the non-ionic contrast agent for elderly patients (over 65 years old) at present. Especially on safety of using a higher-dose non-ionic contrast agent for elderly patients, the relevant literatures are very rare. Therefore, this study investigates influences of the non-ionic contrast agent on the renal function of elderly population by observing the renal function indicators before and after operation after two groups of elderly patients, respectively receive high-dose and low-dose non-ionic contrast agent Iopromide.

MATERIALS AND METHODS

Objects

A total of 30 cases of elderly patients receiving angiography, percutaneous transluminal coronary angioplasty (PTCA) and permanent pacemaker implantation from January, 2010 to December, 2010 in

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our department were selected. Among them, 12 cases received simple coronary angiography, 14 cases received PTCA and stent implantation, 1 case received brain angiography, 2 cases received renoarteriography, and 1 case received pacemaker implantation plus right ventriculography. All 30 cases were male patients, and their ages ranged from 68 to 89 years old. The average age was 78 ± 6.1 years old. Among them, there were 29 cases of patients with coronary heart disease (including 12 cases of patients with stable angina (one case was complicated with old non-Q-wave myocardial infarction) and 17 cases of patients with unstable angina (two cases were complicated with old non-Q-wave myocardial infarction, and 6 cases were complicated with old Q-wave myocardial infarction).

Among 30 cases, 21 cases were complicated with hypertension, rather than diabetes mellitus or chronic nephrosis. As admission of all patients, both serum creatinine and creatinine clearance rate were within the normal range. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of General Hospital of Chinese PLA General Hospital. Written informed consent was obtained from all participants.

Experimental

For all 30 cases of elderly patients, hypotonic non-ionic contrast agent Iopromide (Iopromide, trade name Ultravist, manufactured by Guangdong Shering Company) was used to carry out angiography or catheter intervention operation. According to the dose of contrast agent, they were divided into the high dose group and the low dose group. In the high dose group, there were 14 cases. The dosage of contrast agent ranged from 278 to 294 ml, and the average dosage was 286 ± 6 ml. In the low dose group, there were 16 cases. The dosage of contrast agent ranged from 86 to 97 ml, and the average dosage was 92 ± 4 ml. Before and after patients received the contrast agent, hydration therapy was conducted in order to prevent CIN occurrence. For the specific method, venoclysis was started at 2 h before receiving contrast agent, and each patient was encouraged to drink more than 500 ml water. For venoclysis, 0.9% normal saline was used and the rate was 1.0 ml/kg/h. For all cases, blood was drawn, respectively before operation, and at the 2nd and 5th days after operation, to detect blood urea nitrogen (BUN) and serum creatinine (Scr). Also, the clinical common Cockcroft and Gault formula was used to calculate serum creatinine clearance rate (Ccr). For the evaluation indicators of renal injury caused by the contrast agent, compared with before angiography, Scr increased by 44 μmol/L or 25%, and creatinine clearance rate (Ccr) reduced by 25% at the postoperative 2nd day (Mehran and Nikolsky, 2006).

Statistical analysis

After collecting data, EXCEL database was established. Statistical software SPSS11.0 was used to conduct statistical analysis for variables and conduct paired t-test, F-test and correlation analysis. In case of variance nonhomogeneity, rank sum test was used. If $P < 0.05$, a significant difference could be observed.

RESULTS

Change of renal function of patients at 2 days after receiving contrast agent

As shown in (Table 1), compared with before angiography, Scr of two groups of patients increased and Ccr reduced on the 2nd day after receiving contrast agent, and there were significant differences for changes of Scr and Ccr ($P < 0.05$). In addition, there was no significant difference for the change of BUN.

Change of renal function of patients at 5 days after receiving contrast agent

As shown in (Table 1), Scr and Ccr levels of two groups of patients at the postoperative 5th day restored to the preoperative levels, and there was no significant difference for BUN, Scr and Ccr between two groups of patients ($P > 0.05$).

Incidence situations of contrast induced nephropathy

At the 5th day after receiving contrast agent, Scr increased values of the two groups of patients were less than 44 μmol/L. Compared with before angiography, Ccr of one case (contrast agent dose was 290 ml) within 2 days after angiography reduced by over 25%. According to the diagnosis criterion that Ccr reduced by 25% after receiving contrast agent, the incidence rate of CIN within 2 days after receiving contrast agent was 3.3%. At the 5th day, Ccr of this patient restored to the level before receiving contrast agent.

Correlation analysis

According to the correlation analysis, there was no significant correlation between contrast agent dose and Ccr change (the low dose group $r = -0.34$, $P = 0.19$; the high dose group: $r = 0.16$, $P = 0.58$).

DISCUSSION

Contrast induced nephropathy (CIN) refers to a radiology-induced acute renal function after angiography (Mehran and Nikolsky, 2006). Generally, it is regarded as the diagnosis criterion that serum creatinine (Scr) increases by 44 μmol/L or Ccr reduces by 25% within 48 h, after patients received contrast agent. In recent years, the interventional medicine is gradually popularized in China, and more and more patients receive contrast agent in examination and treatment. Correspondingly, CIN incidence rate also apparently increases. Studies suggest that contrast agent is the second-largest reason of causing drug toxicity-induced acute renal failure, only following aminoglycoside antibiotics, while CIN has become the third common disease causing acute renal inadequacy, currently in hospitals (Li and He, 2011).

CIN incidence not only delays hospitalization time of patients and increases medical cost, but also apparently

Table 1. Renal function changes in the two groups before and after accepting Iopromide (mean ± SD).

Kidney function index	Low dose group (n=17)			High dose group (n=14)		
	Before angiography	Two days after angiography	Five days after angiography	After angiography	Two days after angiography	Five days after angiography
BUN (mmol/L)	6.1±1.4	6.9±1.0	6.1±1.8	6.6±1.5	6.9±2.5	6.1±1.6
Scr (μmol/L)	76.4±8.4	84.5±11.2*	77.8±16.4	79.7±10.8	90.3±15.0*	80.0±20.6
Ccr (ml/min)	68.4±7.5	61.8±9.5*	67.4±14.6	69.9±9.6	62.6±10.5*	68.8±19.9

(1) Versus before angiography, *P < 0.05; (2) All time point and indexes comparison between low dose group and high dose group, P > 0.05.

increases the fatality rate of patients (Senoo et al., 2010). A majority of studies think that the contrast agent-induced acute renal function damage is reversible and patients with CIN mostly restore to the normal status within about the postoperative 7th to 10th day. In this study, after one case of patient used 290 ml Iopromide, contrast induced nephropathy occurred within 2 days. At the 5th day, re-examination of renal function showed that all indicators restored to the levels before angiography, which was in line with the conclusion of the literature (Barrett et al., 1992). However, some reports showed that after CIN occurred, 25 to 30% patients would leave over different extents of renal inadequacy. The fatality rate of patients with CIN was 34%, while that of the control group without CIN in which patients had matched age and received contrast agent was only 7% (Levy et al., 1996). Therefore, clinicians shall pay attention to CIN harm.

At present, the pathogenesis of CIN is still unclear. It is generally thought that CIN is related to direct renal toxicity of contrast agent, secondary renal hemodynamics change and renal tubular injury, and reactive oxygen species mediate these injuries (Tumlin et al., 2006; Heyman et al., 1991; Fiaccadori et al., 2004). Studies suggest that CIN incidence rate is directly related to multiple risk factors. These factors include original renal inadequacy, diabetes mellitus, high-dose or short term repeatedly-used contrast agent, contrast agent permeability, cardiac insufficiency, peripheral angiopathy, liver function damage and elderly population. Compared with patients without risk factors, their incidence rate of acute renal inadequacy greatly increases after angio-graphy (Sgura et al., 2010). It is worth noting that both age and dosage of contrast agent are the independent indicators among CIN risk factors.

The study of Solomon (2005) showed that for a patient with chronic renal inadequacy, as each dosage of 100 ml contrast agent was increased, CIN risk would rise by 12%. However, there is no special safety research on contrast agent for elderly patients at present. Recently, two years back, researches on hypisotonic non-ionic contrast agent safety gradually increased with popularization of non-ionic contrast agent application. Currently, it is widely thought in clinic that for patients with more risk factors before operation, it is better to select non-ionic contrast agent as it will reduce the posto-perative incidence rate of CIN.

Non-ionic contrast agent has characteristics of water solubility and easy diffusion, and it is in a free state in blood. It neither binds with plasma protein and conducts dissociation, nor participates in body's metabolism, while the traditional ionic contrast agent containing Iodine, such as compound diatrzoatc meglumlne will decompose into cation and anion containing Iodine unrelated to contrast agent in solution. Therefore, its osmotic pressure is two times more than non-ionic contrast agent. Studies suggest that non-ionic contrast agent has a smaller influence to the hemodynamics of tissue and kidney than ionic contrast agent, and it has a smaller effect to renal tubule. So, kidney has a better tolerance to non-ionic contrast agent (O'Donnell et al., 2010).

The results of this study suggest that for the elderly patients without diabetes mellitus and basic renal inadequacy, after high-dose and low-dose non-ionic contrast agent Iopromide were administered, there was no significant difference for changes of Scr and Ccr between different doses of groups, which was not in line with the reports (Vassiliu et al., 2002; Asif et al., 2003). There was a certain dose-dependent relationship for the renal toxicity of contrast agent. We think that the renal toxicity of non-ionic contrast agent possibly has a certain critical value, and in this threshold range, contrast agent dose is nonlinearly related to renal function injury. But even so, it is still one of main measure of reducing CIN to strictly control the dosage of contrast agent (Nyman et al., 2008). Therefore, for elderly patients, if a higher-dose contrast agent is required for operation, we recommend applying the non-ionic contrast agent with a lower renal toxicity. For elderly patients with better preoperative basic renal function situations, it is appropriate to use a dosage of no more than 294 ml Iopromide. But because of the cases in our study were elderly male patients, whether the conclusions are also suitable for elderly female patients still requires further research.

Meanwhile, we think that besides appropriate contrast agent type, the other cause of low CIN incidence rate after two groups of elderly patients received contrast agent lies in hydration therapy. Hydration reduces the concentration and residence time of contrast agent in

renal tubule by increasing renal blood flow to reduce the damage of contrast agent to renal tubular epithelial cells, and it is an effective means of preventing CIN (Weisbord et al., 2008; Stacul et al., 2011).

Also, it is relatively safe to use the non-ionic contrast agent within a certain dose range for elderly patients without diabetes mellitus and renal function. However, even if there are no renal function damage, diabetes mellitus and nephrosis before angiography, within 2 days after receiving the non-ionic contrast agent, Scr will change transitorily, which is worth noting by clinicians. It is necessary for preventing CIN occurrence, to take comprehensive measures by strictly mastering the indications and dosage of angiography, correctly assessing risks of patients before operation, conducting adequate hydration therapy before and after receiving contrast agent. At the same time, it is beneficial for reducing CIN incidence rate for elderly patients, to select the safer non-ionic contrast agent.

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