

Original Article**Captopril for prevention of Contrast Induced Nephropathy in patients undergoing Coronary Angioplasty: A double blind placebo controlled clinical trial**

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ABSTRACT

Background: Contrast induced nephropathy is a potential cause of mortality and morbidity in patients undergoing angiography-angioplasty. Except for hydrating and probably low – isoosmolar contrast agents in high risk groups, other modalities have not provided benefit. We investigated preventive effects of captopril for contrast induced nephropathy during angiography-angioplasty.

Methods: In a double blind placebo controlled clinical trial, 88 patients were randomized to two groups: 42 patients received captopril (12.5 mg) every 8 hours from 2 hours before the procedure until 48 hours thereafter, and 46 patients received placebo in the same manner. Serum creatinine was measured before and 48 hours after angioplasty. The data were analyzed by SPSS software, using unpaired student t-test for comparing mean creatinine rise in both groups and paired student t-test for the changes in serum creatinine in each group.

Results: The mean creatinine rise in captopril group (0.214 mg/dl) and placebo group (0.226 mg/dl) were not significantly different. The incidence of acute renal failure (creatinine rise more than 0.5 mg/dl) in the captopril (11.9 %) and placebo group (10.8 %) were not significantly different.

Conclusion: Captopril does not effectively prevent contrast nephropathy, but it is not harmful for renal function and can be administered safely during angiography – angioplasty in patients with normal renal function. However, the effect of captopril in patients with high- risk characteristics remains to be clarified. Of note, we found a trend for less creatinine rise in diabetics who received captopril during the procedure in comparison to diabetics who received placebo.

Keywords: Angiography, Angioplasty, Contrast induced Nephropathy, Captopril, Angiotension Converting Enzyme Inhibitor, Creatinine

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Contrast induced nephropathy (CIN) in patients undergoing coronary angiography-angioplasty although is often mild and transient¹⁻⁵, but can lead to significant renal insufficiency, requiring dialysis with high and long-term in-hospital morbidity and mortality.

Those with baseline renal insufficiency (creatinine > 2 mg/dl) particularly with diabetic nephropathy are at much higher risk⁶. The reported incidence of CIN in different centers

varies in the range of 0–50%⁶. The variability is mainly due to different definitions, preventing protocols, risk factors and amount or type of contrast media.

The only accepted preventive method with proven benefits is hydrating the patient and avoiding non-steroidal anti inflammatory drugs (NSAIDS)⁷. Low or iso-osmolar contrast agents may also decrease nephropathy in high-risk patients⁸.

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The role of other modalities such as administering N-acetylcysteine, theophylline, atrial natriuretic peptide, nifedipine and prophylactic hemodialysis is uncertain. Considering renal arteriolar constriction as a proposed mechanism for CIN, vasodilator effect of captopril on renal efferent arterioles may theoretically prevent contrast nephropathy.

However, related studies and data are limited. Of course, decrease in glomerular filtration rate (GFR) due to captopril is a risk factor for CIN; this controversy has been mentioned in a few published clinical trials⁹⁻¹⁰.

Subjects and Methods

In a double blind placebo controlled clinical trial, 113 patients undergoing coronary angioplasty were enrolled from October until December 2004 in Chamran university hospital, Isfahan, Iran. Exclusion criteria were the amount of contrast used for each patient <100 or >300 mls^{5, 7}, calcium antagonists, ACE-I, theophyllin prescribed within 2 days before the procedure, and baseline creatinine greater than 2 mg/dl.

After performing routine laboratory tests including blood urea nitrogen and creatinine, and obtaining permission, all patients were randomized into two groups:

In group1(case), captopril (25 mg tablets, AlborzDaroo, Iran) was administered as 12.5 mg every 8 hours from 2 hours prior the procedure until 48 hours thereafter. Group 2(control) received placebo in the same protocol.

All the patients had received aspirin 100 mg/d and ticlopidin 250 mg/bid from one week prior to angioplasty, and normal saline 0.9% infusion (total volume of 1.5 liter) at a rate of 60 ml/hr from 12 hours before angioplasty until 12 hours after the procedure.

The contrast media used for all patients was meglumin compound (76%, DarooPakhsh, Iran) (370 mg/ 20 ml), available drug with very lower cost than other agents.

Totally, 25 patients were excluded because of out of range contrast volume, missing laboratory data, or using other brands of contrast

agents. In remaining 88 patients (42 patients in captopril group and 46 in placebo group), blood urea nitrogen and creatinine were reexamined 48 hours after the procedure.

The data were analyzed by SPSS software, using paired and unpaired t-student test for comparing creatinine changes in the same patients and in two groups, respectively.

This study was approved by Department of cardiology and internal medicine, Isfahan University of medical science.

Results

The mean of age, baseline creatinine, sex distribution, prevalence of diabetes and the volume of contrast agent was not significantly different in both groups (P value > 0.05) (Table 1).

Table 1. Demographic data and risk factors

	Captopril group	Placebo group	P value
Mean of age (years)	55.1±17	53.6±21	> 0.5
Female (%)	12 (29%)	13 (28%)	> 0.5
Diabetics (%)	10 (23.8%)	9 (19.56%)	> 0.5
Volume of contrast agent(ml)	225±120	223.3±130	> 0.5
Basal creatinine (mg/d)	0.98±0.43	1.05±0.39	> 0.5

The mean increase of serum creatinine in the captopril group (0.214 mg/dl, 21.8%) and in the placebo group (0.226 mg/dl, 21.5%) demonstrated no significant difference (P value > 0.05).

In each group, 5 patients had creatinine rising, more than 0.5 mg/dl (defined as acute renal failure^{1, 3, 9}) without statistically significant difference. None of the patients with acute renal failure developed creatinine level of more than 2 mg/dl and the serum creatinine declined to the baseline level within one week.

In the captopril group, 10 patients were diabetic with baseline creatinine of 1.147mg/dl which rose to 1.35mg/dl. In the placebo group, the baseline creatinine rose from 1.11 to 1.47 mg/dl in nine diabetic patients.

Discussion

As mentioned above, published data on the use of ACE-I for prevention of CIN are limited, with controversial and markedly different results and recommendation^{10, 11}. However, this issue is of great importance in clinical practice because of widespread captopril use in cardiovascular patients who undergo angiography-angioplasty.

Reliable data will make it possible to have a strong recommendation whether the ACE-I should be discontinued before a contrast study to prevent its potential harmful effects, or whether captopril should be prescribed before the contrast study to prevent CIN.

We enrolled low risk patients for CIN and studied the effect of captopril on the majority of patients undergoing angiography-angioplasty, but we found no difference in outcome. The clinical applicability of this finding is that captopril is not harmful, although it does not provide any benefit in preventing CIN and creatinine rise.

This finding is in sharp contrast with a Turkish study in which that captopril was hazardous in patients undergoing angiography and it increased the risk of CIN¹⁰.

Although we did not find the preventive effect of captopril, as it was found in a study

from India¹⁰, but we can conclude that if captopril administration is indicated for treatment of hypertension, heart failure or any other indication, it can be safely prescribed without fear of increased risk of CIN. However, this conclusion is limited to patients with normal renal function and low-risk characteristics as mentioned above.

The effect of captopril in high risk patients remains to be clarified. The high-risk patients are in minority of patients undergoing angiography-angioplasty, with high mortality and morbidity rate^{1, 6}.

Therefore, they require special attention to search for effective preventive modalities and performing clinical trials enrolling the high-risk patients. Diabetic patients with normal renal function known as low-risk for CIN^{1, 8, 9}, but in our study, diabetic patients who received captopril, had a trend toward smaller creatinine rise. However, because of small number of diabetics, no statistically significant correlation could be found in this subgroup.

Ultimately, we suggest clinical trials for evaluation of captopril in high-risk patients undergoing angiography/angioplasty with large number of diabetics in this regard with respect to our results

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