The effects of chronic usage of enzyme inhibitors and angiotensin receptor blockers on contrast-induced nephropathy in low-risk patients

Düşük riskli hastalarda anjiyotensin dönüştürücü enzim inhibitörleri ve anjiyotensin reseptör blokerlerinin kronik kullanımının kontrast madde nefropatisi üzerine etkileri

To the Editor,

I read the article entitled "The effects of chronic usage of enzyme inhibitors and angiotensin receptor blockers on contrast-induced nephropathy in low-risk patients" by Barış et al. (1) with great interest. Frankly, I appreciate the authors for their original study. Yet, I have some criticism about the presented study. The authors evaluated the effects of chronic usage of renin- angiotensin- aldosterone system (RAAS) blocker drugs on development of contrast-induced nephropathy (CIN) in low risk patients. They found that in patients with near normal renal functions who are undergoing elective coronary procedure, chronic usage of angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) was associated with the increased risk of CIN. Although the ACEI and ARB's act by different mechanism, their effects in the pathogenesis of CIN is similar. Therefore, why a distinction has been created between ACEI and ARB as a RAAS blockers heading? They reported that CIN was higher in ACEI than no RAAS blocker group, with no statistical significance. Although it did not reach statistical significance, patients treated with N-acetylcysteine (NAC) in the ARB group were slightly older and more likely to have baseline renal insufficiency. Also, preventive treatment has been used mostly in this group. Hence, I think that this result is not surprising. In fact, the role of NAC in the prevention of contrast induced nephropathy (CIN) is still controversial (2). In the no RAAS blocker group drug classes other than RAAS blockers, are not denoted in the text. Is there any comparision between the groups for anemia? Because anemia is a strong risk factor in the development of CIN (3). Serum creatinine (SCr) is a rather poor marker for glomerular filtration rate (GFR). SCr is determined by the interplay of creatinine production, GFR, and the kinetics of creatinine distribution among the body's fluid compartments. Owing to the exponential relationship between SCr and GFR, SCr is very insensitive in patients with normal pre-existing renal function (4, 5). In this state, GFR using is a reasonable approach. The authors reported that in the subgroup of patients with eGFR 30-60 mL/min there was no statistical significant difference for CIN between ACEI, ARB and no RAAS blocker groups. Contrast media (CM) dose is a risk factor that has not receive adequate attention. Regardless of CM type, the amount of CM a patient receives is a powerful predictor of CIN (6). Diabetes mellitus is a major risk factor and is synergistic with baseline GFR (7). Proteinuria is an important marker of pre-existing renal damage and a risk factor for CIN (3, 5). In a review by Zhang and colleagues they reported that chronic statin treatment (≥1 week) was reduced the risk of CIN ($p<0.05$) (8). There is no information in the text about the usage of statin in hyperlipidemic patients and additional drug usage such as tiazide diuretics and calcium channel blockers in the RAAS blocker group. In this study, daily maintenance doses of these drugs are not written in the text. The differences in daily maintenance doses of these drugs between groups might influence SCr and affect results of the study. RAAS blockers are potent drugs that we use frequently in daily practice. At this point, the question is "Is it really possible to stop the RAAS blockers in patients with near normal renal functions who are undergoing elective coronary procedure". If it is possible, then when? What is the authors' recommendation? In the Mehran score, a number of clinical variables related to hemodynamic stability, age, diabetes mellitus and estimated baseline GFR are summated yielding an integer score that is the directly related to the risk of CIN and hemodialysis. A score of ≤5 is associated with a risk of CIN ≤7.5% and a risk of dialysis of 0.04% (9). However, it is well known that this score is designed to predict CIN occurrence after percutaneous coronary intervention (PCI) with weighted coefficients for independent predictors of CIN. Therefore, I wonder the requirement of hemodialysis in patients who developed CIN and about the reason for using Mehran score in the presented study.

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Author`s Reply

To the Editor,

I would like to answer the comments about our article entitled ''The effects of chronic usage of angiotensin converting enzyme inhibitors and angiotensin receptor blockers on contrast induced nephropathy in low risk patients''.

Nowadays, there are a lot of debates about angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) for their mechanism, effects and cardiovascular outcomes. They can be called as rennin angiotensin aldosterone blockers (RAAS), but the data for these drugs is still controversial. In the literature these two drug groups were investigated as two different drugs (1-3). Actually, this distinction is valuable to learn about the difference between these drugs for contrast-induced nephropathy (CIN). In our study ARB group was older than others but it was not statistically significant (no RAAS, ACEI and ARB group respectively, 61.9±12.9; 64.1±12.0; 65.4±13.1; p=0.16). There was no significant difference between groups for baseline characteristics except hypertension.

The usage of N-acetylcysteine with fluid infusion was recommended in guideline as a class II recommendation but only N-acetylcysteine administration was not recommended (4). According to ethical rules, the patients whose baseline creatinine was ≥1.2 mg/dL, received preventive treatment. We used our protocol for CIN prevention including 0.9% isotonic infusion (1 mL/kg/h, upper limit 100 mL/h) and N-acetylcysteine 600 mg twice daily as our previous study (5).

We analyzed our study population for hemoglobin and hematocrit values before contrast administration. We found that all three groups were comparable for hemoglobin and hematocrit, there was no significant difference (Table 1).

In our study there were no significant difference between groups for hyperlipidemia and diabetes mellitus. The usage of anti-hyperlipidemic and anti-diabetic drugs was allowed according to clinical indications. In ACEI and ARB groups, we have data for molecule type and dosage. But the numbers were too small for statistical analyses.

Fortunately, no patients needed hemodialysis. Mehran risk score is an important parameter which can predict the risk of CIN in patients with elective coronary procedures and also with acute coronary syndromes (6). Mehran score was found one of the independent predictors of CIN in our study. The contrast type and dosage were not significantly different between three groups.

Finally, our study was not designed to investigate to stop or continue the RAAS blocker drugs before contrast administration. We did not comment this issue in our article. Maybe another study will be designed to clarify this important question.

Table 1. The comparison between groups for hemoglobin and hematocrit values

Variables	No RAAS (n=95)	ACEI (n=106)	ARB (n=94)	p
Hemoglobin	13.1±1.6	13.2±2.2	12.9±1.9	0.69
Hematocrit	38.8±4.7	39.1±6.4	38.1±5.5	0.47

Data are presented as mean±SD
ACEI - angiotensin coversting enzyme inhibitor, ARB - angiotensin receptor blocker, RAAS - renin-angiotensin-aldosterone system

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About contrast-induced nephropathy

Kontrast nefropatisi üzerine

To the Editor,

Congratulations to the authors for this very interesting and published valuable study in The Anatolian Journal Cardiology entitled "The effects of chronic usage of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on contrast-induced nephropathy in low-risk patients." by Barış et al. (1). We want to put emphasis on some issues that are important to us:

The onset of kidney injury is probably within minutes of exposure to contrast agents. However, clinical manifestations such as oliguria or an increase in the serum creatinine are generally observed within 24 to 48 hours after contrast exposure (2). The creatinine usually starts to decline within three to seven days. In the present study, the patients were followed for 48-72 hours after the procedure for the assessment of renal functions. Why did the authors not follow the patients more than 72 hours to see whether the creatinine values reached the basal values or the nephropathy became persistent? So, the question of "how