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Contrast Induced Nephropathy in Patients with Acute Coronary Syndrome

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Abstract

Introduction. Contrast-induced nephropathy (CIN) is associated with increased morbidity and mortality after percutaneous coronary intervention (PCI). On the other hand, CIN is a serious complication in patients with diabetes or renal impairment undergoing percutaneous coronary intervention (PCI). CIN after PCI may be associated with prolonged hospitalization, increased rates of kidney injury, and short- and long-term mortality. Factors that have been associated with CIN include: diabetes mellitus, congestive heart failure, recent acute myfocardial infarction, cardiogenic shock, and pre-existing renal impairment. In this study, we investigated contrast nephropathy development after coronary angiography (CAG) in patients presenting with acute coronary syndrome, who were hospitalized initially in the Coronary Care Unit and subsequenttly referred to the Internal Medicine Clinic in a tertiary care hospital.
Methods. We've analyzed 335 patients' records retrospectively in 1 year that were followed-up with acute coronary syndrome (ACS) in the Coronary Care Unit (CCU) and transferred to the Internal Medicine Clinic (IMC). The following parameters were evaluated: age, gender, chronic disease and drug history, biochemical values evaluated before hospitalization to CCU, ejection fraction (EF) and left atrium diameter (LA), with or without previous CAG; values of serum creatinine (sCr) levels before CAG and after 48 hours. Values of $p < 0.05$ were considered to be significant.
Results. 126 of 335 patients were female and 209 were male. The average age of patients was 64.2 years. 122 patients used angiotensin converting enzyme inhibitor (ACEI), 54 patients used furosemide. CIN development rate of CAG patients was 22.8% (n=54). There was no significant relationship with age, gender and chronic disease history in CIN patients. When laboratory findings were compared, there was no significant relationship except for potassium value before CAG. However, potassium values were significantly higher in CIN patients (p=0.001). When drug usage of patients was compared, 48.1% (n=26) of CIN patients used ACEI and there was a significant relationship between ACEI use and CIN development (p=0.026).
Conclusions. CIN development rate was 22.8% and it was relatively high when compared with literature data. Awareness about contrast nephropathy develepment risk and assessment of risk factors before the procedure should be increased in our Center.

Key words: nephropathy, acute coronary syndrome, angiography

Introduction

Contrast-induced nephropathy (CIN) is defined as either a 50% increase in serum creatinine level from baseline or 0.5 mg/dL and even more in absolute value, measured within 48 hours of intravenous contrast administration [1]. The development of acute renal failure (ARF) is a significant complication of intravascular contrast medium use and is associated with excess morbidity and mortality. An overall incidence of CIN in the general population is reported to be 0.6-2.3% [2]. We have assessed contrast nephropathy development after coronary angiography (CAG) in patients with acute coronary syndrome in the Coronary Care Unit and subsequently referred to the Internal Medicine Clinic in a tertiary care hospital.

Material and methods

Between January and December 2013, we analyzed 335 patients' records retrospectively that were followed-up with acute coronary syndrome in the Coronary Care Unit and subsequently were transferred to the Internal Medicine Clinic. After an evaluation according to inclusion and exclusion criteria, 335 patients were enrolled in our study. The parameters used and evaluated with statistical methods were: age, gender, history of chronic disease and drug usage, biochemical values evaluated before hospitalization to coronary care unit, ejection fraction (EF) and left atrium diameter (LA), with or

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without CAG; values of serum urea and creatinine levels before and 48 hours after CAG.

Statistical analyses

Compliance with the normal distribution for continuous variables was analyzed with the Shapiro-Wilk test. Descriptive statistics was used for defining continuous variables. Student's t-test was used to compare the two groups with independent and continuous variables showing normal distribution. Mann-Whitney U test was used for comparison of the two groups independent and continuous variables showing normal distribution. Wilcoxon Signed Rank test was used for comparison of not normally distributed dependent variables. Statistical significance was set at 0.05. Statistical analysis was performed by using the MedCalc Software Program, version 12.7.7 (MedCalc Software bvba, Ostend, Belgium).

Findings

A hundred and twenty-six of 335 patients were female and 209 were male. The average age of patients was 64.2 years. Fifty-two patients had congestive heart failure (CHF), 12 patients had malignancy, 79 patients had chronic renal failure (CRF), 108 patients had diabetes mellitus (DM) and 168 patients had hypertension (HT). 122 patients used angiotensin converting enzyme inhibitor (ACEI), 54 patients used furosemide. Three hundred and eleven patients were discharged, 6 of patients were transferred to another unit, 11 of patients were voluntarily discharged, 7 of patients died. Four of these deceased patients had CRF history and mortality might be related to CRF (p= 0.027). There was no significant relationship with the other parameters concerning mortality.

Table 1. Laboratory findings and mean EF values before CAG

	Average	Median	St Deviation	Minimum	Maximum	N
Glucose	131.5	107	70.9	11	441	335
HbA1C	7.3	6.6	2.2	1.5	12.5	33
Uric Acid	7.9	6.4	9.9	3	113	268
Total Cholesterol	185.5	182	51.5	14	350	274
HDL	40.4	38	15.5	18	207	274
LDL	122.7	113	62.8	12	400	272
Triglyceride	167.3	139.5	116	40	854	272
AST	83.3	37	116.2	4	851	329
ALT	30	21.5	93.1	3	1320	330
Albumin	3.8	3.8	0	1.7	17	269
Sodium	137.6	138	3.9	117	147	335
Potassium	4.5	4.4	0.7	0.9	7	335
Calcium	9.1	9.1	0.7	6.5	11.4	331
Phosphorus	3.6	3.5	1.1	1.3	100.8	263
LDH	424.9	337	268.3	5.3	1852	269
Troponin	7379.8	4.9	17732.1	0	50000	333
Hemoglobin	12.7	12.9	2.2	5.9	18.7	335
EF %	49.4	50	10.9	15	70	310
Urea	53.4	42	35.6	16	228	334
Creatinine	1.6	1.1	1.6	0.5	15	335

EF: Cardiac ejection fraction, LDH: Lactate dehydrogenase, ALT: Alanine aminotransferase, AST: Aspartate amino transferase, HDL: High-density lipoprotein, LDL: Low- density lipoprotein, CAG: Coronary angiography

Among these 335 patients that were transferred to the Internal Medicine Clinic from the Cardiology Coronary Care Unit with the diagnosis of acute coronary syndrome, CAG had been performed in 237 patients. Laboratory findings and mean EF values before CAG in these 237 patients with CAG are shown in table 1. CIN development rate in these 237 patients with CAG was 22.8% (n=54). Before and after CAG average creatinine values of patients with CIN were 1.2 mg/dL and 1.7 mg/dL, respectively. There was no significant relationship with age, gender and chronic disease history in CIN patients. When laboratory findings were compared, there was no significant relationship except for serum potassium values before CAG (Table 2). Serum potassium values were significantly higher in patients with CIN (with Mann-Whitney U test, p= 0.001). We evaluated the drug usage of patients. We found that 48.1% (n= 26) of CIN patients used ACEI and there was a significant relationship between ACEI use and CIN development (p= 0.026). A significant relationship was not found between the use furosemide and CIN development.

Table 2. Comparison of laboratory findings before and after CAG

	Nephropathy positive		Nephropathy negative		P value
	Avg±St Deviation	Med (min-max)	Avg±St Deviation	Med (min-max)	
Glucose	145.6±79.7	111.5(58-415)	130.3±66.5	109(47-440)	0.291**
HbA1C	7.1±2.6	6.8(1.5-11)	7.4±2	6.8(5.4-12.5)	0.913**
Urea (before CAG)	42.8±23.7	36(20-159)	43.4±28.9	36(16-228)	0.883*
Urea (after CAG)	63.6±34.1	60(20-185)	45±26.6	35(14-170)	<0.001**
Uric Acid	7.4±8.4	5.9(3.7-9.3)	7.2±9.2	6.2(3-9.4)	0.712**
Total Cholesterol	203.9±46.7	188(107-346)	191.2±51.6	186(14-350)	0.132*
HDL	40.4±9.4	39(24-74)	41.6±19.2	39(19-207)	0.876**
LDL	143.3±77	121(60-400)	128.5±60	115(35-400)	0.251**
Triglyceride	198.5±157.1	151(50-854)	173±107.2	146(40-719)	0.591**
AST	66.2±53	48.5(15-244)	100.7±132	48(11-851)	0.839**
ALT	24.1±13.3	20(3-82)	36.4±32	26(11-205)	0.065**
Albumin	3.8±0.4	3.9(2.9-4.6)	4±1.2	3.9(2.9-4.7)	0.385*
Sodium	136.9±3.3	137(129-146)	138.1±3.7	138(126-147)	0.030*
Potassium	4.7±0.5	4.6(3.8-6.4)	4.3±0.6	4.2(2.9-6.5)	<0.001**
Calcium	9.1±0.6	9.1(8-11)	9.2±0.6	9.2(6.5-11)	0.491**
Phosphorus	3.2±0.8	3.2(1.4-5.1)	3.4±0.8	4.3(1.3-6.2)	0.191*
LDH	423.5±321.6	320(5-1852)	457.8±279.7	362(165-1664)	0.287**
Troponin	3714.7±13214	7.6(0-50000)	11298±20930	9.24(0-50000)	0.521**
Hemoglobin	13.1±2.1	13.2(7.9-16.6)	13.4±1.8	13.6(7.2-18.7)	0.354*
EF %	50.1±8.8	50(28-63)	49.4±10.2	50(20-70)	0.679*
LA	36.5±5.7	37(22-47)	37.1±5.6	37(26-61)	0.521*

EF: Cardiac ejection fraction, LA: Left atrium diameter, LDH: Lactate dehydrogenase, ALT: Alanine aminotransferase, AST: Aspartate amino transferase, HDL: High-density lipoprotein, LDL: Low- density lipoprotein, CAG: Coronary angiography
*Student t-test, **Mann-Whitney U test

Discussion

Contrast-induced nephropathy is a growing issue in the field of interventional cardiology. CIN is one cause of acute renal injury, resulting in a decrease in the glomerular filtration rate (GFR), reduced excretion of nitrogenous waste, hypervolemia, and hyperkalemia. CIN is associated with significant increases in mortality. However, mortality in patients who develop CIN is rarely due to renal failure. Patients with CIN also have significantly higher hospital mortality than those without CIN. CIN is one of the important reasons of hospital-acquired acute kidney injury [3]. As a widely accepted method, either a 50% increase in serum creatinine level from baseline or 0.5 mg/dL and more increase in absolute value, measured within 48 hours of intravenous contrast administration can be considered as CIN [1,3-7]. We have diagnosed CIN according to this definition. Risk factors for CIN include pre-existing renal insufficiency, diabetes mellitus, older age, reduced left-ventricle systolic function, advanced heart failure, acute myocardial infarction, shock, concomitant use of nephrotoxic drugs, hypotension, dehydration, hypoalbuminemia, anemia, use of intra-aortic balloon pump, volume and type of contrast material (Table 3) [8]. In our study, the use of ACEIs and hyperkalemia were found to be associated with the development of CIN (p=0.026 and p<0.001, respectively) (Table 4). However, conflicting results exist regarding the effects of RAS blockers in the pathophysiology of CIN. Some studies reported RAAS blockers were preventive for CIN [9,10]. The study by Gupta *et al*. [10] included patients randomised to receive captopril (a sulfhydryl group containing angiotensin-converting enzyme inhibitor at a dose of 25 mg thrice a day for three days, starting one hour prior to angiography) while patients in the control group underwent angiography without receiving captopril. They reported that captopril reduced the risk of development of contrast-induced nephrotoxicity in diabetic patients by 79% [10]. They speculated that abnormalities of renal perfusion possibly mediated by RAS were responsible for development of CIN and administration of captopril offers protection against development of CIN. Holscher *et al.* [11] prospectively assessed predictors of CIN within 72 h and long-term outcomes of 412 consecutive patients with serum creatinine levels of 1.3 mg/dL to 3.5 mg/dL undergoing elective CAG. In their study, patients were randomly assigned to periprocedural hydration alone, hydration plus one-time hemodialysis or hydration plus N-acetylcysteine [11]. Multivariate logistic regression identified the predictors of CIN as prophylactic postprocedural hemodialysis (OR 2.86, 95% CI 1.07 to 7.69), use of angiotensin-converting enzyme inhibitors (OR 6.16, 95% CI 2.01 to 18.93), baseline glomerular filtration rate (OR 0.94, 95% CI 0.90 to 0.98) and the amount of contrast material (OR 1.01, 95% CI 1.00 to 1.01). In addition, they found that independent predictors for death during follow-up included left ventricular ejection fraction lower than 35% (HRR 4.01, 95% CI 2.22 to 7.26), serum phosphate (HRR 1.64, 95% CI 1.10 to 2.43) and hemoglobin (HRR 0.80, 95% CI 0.67 to 0.96) [11]. From their prospective trial, Holscher *et al*. [11] concluded that postprocedural he-

modialysis, use of angiotensin-converting enzyme inhibitors, reduced baseline glomerular filtration rate and amount of contrast media were independent predictors of CIN within 72 h after coronary procedure Assessing renal function after 30 days, rather than within 72 h, seemed to be more predictive for patients' long-term survival.

Table 3. Risk factors for renal impairment or development of CIN

• Diabetes mellitus	• Dehydration or volume contraction
• Renal disease or solitary kidney	• Age >70 years
• Sepsis or acute hypotension	• Previous chemotherapy
• Cardiovascular disease	• Organ transplant
• Human immunodeficiency syndrome	• Nephrotoxic drugs (amphotericin B, aminoglycosides, vancomycin, NSAIDs, chemotherapy agents such as cisplatin)
Hypercholesterolemia	Administration of >100 mL of contrast medium
Anemia	

Table 4. Comparison of drugs usage

	Drug Usage	Nephropathy			P value
		Developed	No Developed	Total	
Use of ACEI	Yes	58(%31.7)	26(%48.1)	84(%35.4)	0.026*
	No	125(%68.3)	28(%51.9)	153 (%64.6)	
	Total	183(%100)	54(%100)	237(%100)	
Use of Furosemid	Yes	16(%8.7)	5(%9.3)	21(%8.9)	1.00**
	No	167(%91.3)	49(%90.7)	216(%91.1)	
	Total	183(%100)	54(%100)	237(%100)	

ACEI: Angiotensin converting enzyme inhibitor, *Ki-Kare, **Fisher Exact test

Treatment with RAAS blockers does not usually cause renal dysfunction or hyperkalemia in patients with normal renal function. These complications can be observed in patients with high CV risk and generalized atheromatous disease such as, of course, renal atheromatosis and/or abnormal renal function. Blood pressure should be held steady before the procedure, as the patient will receive intense fluid intake. Avoid blood pressure levels 20 to 30 mmHg lower than normal and, do not administer contrast media if blood pressure is unacceptably low. ACEIs and ARBs are most frequently associated with CIN, especially in patients with depletion. Hyperkalemia was found to be associated with CIN in our study and may be due to the use of ACEI. On the other hand, there is limited information about the serum electrolyte levels in patients with CIN in the literature.

Conclusions

Coronary artery interventions are most frequently associated with CIN among the procedures in which intravenous contrast material is used. While in prospective studies CIN incidence is around 3.3%, in the subgroup of patients that has had myocardial infarction and required primary angioplasty, CIN incidence rises to 19% [12]. In our study, CIN development rate was 22.8% and this rate is considerably high. Our awareness about contrast nephropathy and assessment of risk factors before the process has to be optimized. Consequently, a thorough understanding and pathophysiology of CIN along with the drug interactions have to be studied in future by including a larger series of patients with high cardiovascular risk.

Conflict of interest statement. None declared.

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