To cite this article: Ozbeyaz NB, Gokalp G, Algul E, Aydinyilmaz F, Sahan HF, Felekoglu MA, Guliyev I, Iscen S. Hypomagnesemia and the risk of contrast-induced nephropathy in patients undergoing elective coronary angiography Turk J Clin Lab 2023; 1: 18-22

Original Article

Hypomagnesemia and the risk of contrast-induced nephropathy in patients undergoing elective coronary angiography

Elektif koroner anjiyografi yapılan hastalarda hipomagnezemi ve kontrast ilişkili nefropati riski ilişkisi

Nail Burak Ozbeyaz*[1], Gokalp Gokhan [1], Algul Engin [2], Aydinyilmaz Faruk [3], Sahan Haluk Furkan [2], Felekoglu Mehmet Ali [2], Guliyev İlkin [4], Iscen Sinan[2]

[1]Pursaklar State Hospital, Department of Cardiology Clinic Ankara, Turkey
[2]University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital
[3]Erzurum Education and Research Hospital, Erzurum, Turkey
[4]Medical Park Hospital Tokat, Turkey

Abstract

Aim: The present study aimed to assess the influence of hypomagnesemia (hypoMg) on the risk of developing contrast-induced nephropathy (CIN) after coronary angiography.

Material and Methods: This is a single-center prospective, observational study conducted at a tertiary referral hospital between December 31, 2016, and February 28, 2021. 223 patients who had undergone coronary angiography procedures and had preprocedural baseline Mg levels were enrolled in this study. CIN was defined as an increase of >0.5 mg/dl or >25 % in serum creatinine concentration over baseline within 48-72 h after administration. HypoMg was defined as Mg< 1.60 mg/dL.

Results: Of 223 patients enrolled, CIN occurred in 28 patients (12.6%). CIN occurred in 53.3 % of the patients with hypoMg and 8.9 % of those with non-hypoMg (P<0.01). Multivariate logistic regression analysis found that baseline Mg levels were independent predictors of CIN.

Conclusion: HypoMg was associated with an increased risk for CIN. These results suggest magnesium replacement in hypomagnesemia may be beneficially indicated before diagnostic/interventional studies using contrast media.

Keywords: Hypomagnesemia, Coronary Angiography, Contrast-Induced Nephropathy

Corresponding Author*: Nail Burak Ozbeyaz, Pursaklar State Hospital, Department of Cardiology Clinic Ankara, Turkey.
E-mail: drozbeyaz@gmail.com
Orcid: 0000-0002-7132-4286
Doi: 10.18663/tjcl.1183898
Received: 03.11. 2022 accepted: 25. 11. 2022

TJCL Volume 14 Number 1 p: 18-22

Öz

Amaç: Bu çalışma, hipomagnezeminin (hipoMg) elektif koroner anjiyografi sonrası kontrast kaynaklı nefropati (KKN) geliştirme riski üzerindeki etkisini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Bu çalışma, üçüncü basamak bir eğitim ve araştırma hastanesinde yürütülen tek merkezli ileriye dönük, gözlemsel bir çalışmadır. 31 Aralık 2018 ve 28 Şubat 2022 tarihleri arasında koroner anjiyografi işlemi geçirmiş ve işlem öncesi başlangıç Mg seviyeleri olan 223 tane hasta bu çalışmaya dahil edilmiştir. CIN, uygulamadan sonra 48-72 saat içinde başlangıca göre serum kreatinin konsantrasyonunda >0.5 mg/dl veya > %25 artış olarak tanımlanmıştır. HipoMg, Mg< 1.60 mg/dL olarak tanımlanmıştır.

Bulgular: Kaydedilen 223 hastanın 28'inde (%12.6) KKN meydana geldi. KKN, hipoMg'si olan hastaların %36.4'ünde ve hipoMg'si olmayanların %11,3'ünde meydana gelmiştir. (P=0,002). Çok değişkenli lojistik regresyon analizi, başlangıç Mg düzeylerinin KKN' nin bağımsız öngörücüleri olduğunu bulunmuştur.

Sonuç: HipoMg, artan KKN riski ile ilişkili olarak bulunmuştur. Bu sonuçlar, hipoMG'de magnezyum replasmanı yapılmasının, kontrast madde kullanılan tanısal/girişimsel işlemlerden önce fayda sağlayabileceğini düşündürmektedir.

Anahtar kelimeler: Hipomagnezemi, Koroner Anjiyografi, Kontrast Kaynaklı Nefropati

Introduction

Contrast-induced nephropathy (CIN) is a disorder from exposure to contrast media. The CIN implicates impairment of renal function (the elevation of serum creatinine by >0.5 mg/dl or >25 %) occurring within three days following the intravascular administration of contrast media, not attributable to other causes(1, 2). CIN is associated with increased morbidity and mortality, particularly in high-risk patients undergoing coronary angiography or percutaneous coronary intervention (PCI).

Animal studies have shown that apoptotic processes are faster in animals with low magnesium levels; therefore, cell death is more common in animals with low magnesium levels(3, 4). Cell damage due to oxygen radicals is also observed less in individuals with normal magnesium levels(5). The conclusion to be drawn from this is that it will be more challenging to repair and recycle any cell damage in individuals who already have low magnesium levels. Studies have also shown that magnesium has a nephroprotective effect in using many nephrotoxic drugs, and deterioration in renal functions is reversed more quickly in patients with adequate magnesium levels(6, 7). It achieves this effect by increasing renal blood supply both with the above-mentioned cellular activity and renal vasodilation(8).

The nephrotoxic efficacy of iodine-based contrast agents routinely used in coronary angiography procedures has been known for a long. Magnesium (Mg) has been shown to protect the kidney from contrast media-produced oxygen free radicals (9). In addition, it has been demonstrated that the prophylactic use of intravenous Mg significantly reduces CIN in primary PCI patients(5, 10). However, there is no report in the literature disclosing that hypoMg was a risk factor for CIN after coronary angiography. Thus, the current study aimed to assess the role of hypoMg in the development of CIN after elective coronary angiography.

Material And Methods

Study population

Between December 31, 2016, and February 28, 2018, a total of 223 patients who had undergone coronary angiography procedures and had preprocedural baseline Mg levels were enrolled in this study. HypoMg was defined as Mg< 1.60 mg/dL according to the reference values of the hospital biochemistry device. Among them, 137 were men and 86 women; the median age was 64 (34–89 years). Patients with chronic kidney disease (CKD) stage 5, end-stage kidney disease, active infection, allergic reaction to contrast material, incomplete patient data, those who have used nephrotoxic drugs in the last seven days (NSAID, etc.), contrast agent exposure in the past seven days, and unstable cardiac conditions were excluded. Patients with reduced renal function were hydrated with 0.9 % saline at 1 ml/kg/h for 12 h before and after catheterization. A nonionic, low-osmolality contrast agent (iohexol (300 mg iodine/ml; 672 mosml/kg of water; Kopaq; KOÇSEL İLAÇ SAN. VE TİC. A.Ş.; Türkiye and Omnipaque; GE Healthcare İnc. The USA) was used almost exclusively in our

laboratory.

Study variables

Serum creatinine concentrations were measured before and within 72 h of administration of contrast media in every patient, and further measurements were performed in all patients developing CIN. The serum Mg levels were collected before the coronary angiography. Renal function was assessed by the estimated glomerular filtration rate (eGFR) using the MDRD formula.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD), and categorical data are presented as absolute values and percentages. T-tests were used for parametric comparison. Chi-square tests were used for the comparison of categorical variables as required. A two-sided 95 % confidence interval (CI) was constructed around the odds ratio (OR) point estimate. Logistic regression analysis evaluated the independent association between Mg level, HypoMg, and CIN. All hypothesis testing was two-tailed. A p-value <.05 was considered statistically significant. Analysis was performed by using SPSS 23.0 statistical software.

Results

The baseline clinical characteristics of patients with CIN and non-CIN are summarized in Table 1. Of the 233 patients in this study, hypoMg was present in 15(%6.7) at baseline. Twenty-eight patients (12.6 %) experienced CIN after the procedure. These patients had a significantly higher incidence of hypoMg(%28.6).

Patients who developed CIN had a lower eGFR (Table 1). Compared to patients with or without CIN, patients with CIN also had lower Mg levels. As shown in Fig. 1, compared to patients without CIN, patients with CIN also had lower Mg levels (1.96± 0.15 vs. 1.73±0.08 P<.001).

Table 1. Baselines clinical characteristics.

	Non-CIN (n = 195)	CIN (n =28)	P value
Demographics			
Age(years)	63.6 ± 10.6	65.5 ± 10.0	.382
Male	118(60.5%)	19(67.9%)	.451
Hypertension (HTN)	122(62.6%)	17 (60.7%)	.856
Hyperlipidemia (HL)	70(35.9%)	11(39.3%)	.734
Diabetes mellitus (DM)	50(25.6%)	18(64.3%)	<.001
Congestive Heart Failure (CHF)	61(31.3%)	14(50%)	.044
Coronary artery disease (CAD)	41 (21%)	12(42.9%)	.026
Anemia	45(23.1%)	16(57.1%)	<.001
CKD(<60mL/min/1.73m2)	39(20%)	12(41.7%)	.027
Drugs			
Statın used	75(38.5%)	9(32.1%)	.590
Dıuretıc used	42 (21.5%)	9(32.9%)	.218
ACE/ARB used	106(54.4%)	12(42.9%)	.267
Amount of contrast agent ml	102.43±42.04	104.52±37.68	.534
Laboratory data			
Hgb(g/dl)	13.1±1.8	12.6±2.5	<.001
WBC (10^3 /µl)	9.41±3.16	9.43±3.38	.682
Platelets, mm3	270.25±78.04	273.59±92.84	.135
Creatinine (mg/dl)	1.02±0.91	1.36±1.17	.039
GFR(mL/min/1.73m2)	74.8±17.2	64.4±14.7	<.001
Glucose (mg/dl)	119.34±52.86	153.46±67.29	.019
LDL-C (mg/dl)	124.82±51.22	126.51±48.25	.890
LVEF (%)	54 ± 11	46 ± 12	<.001
HypoMg, n	7(%3.6)	8(%28.6)	.002
Magnesium(mg/dl)	1.96± 0.15	1.73±0.08	<.001

WBC: White blood cell, ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, CKD: Chronic kidney disease, LVEF: left ventricular ejection fraction, GFR: Glomerular filtration rate, LDL-C: low-density cholesterol, HypoMG: Hypomagnesemia

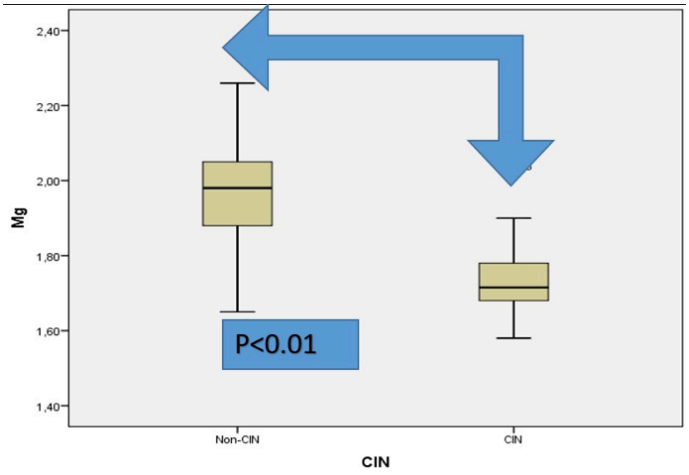

Figure 1. Compared with patients without CIN(Contrast-induced nephropathy), patients with CIN also had lower Mg levels (1.96± 0.15 vs. 1.73±0.08 P<.001).

Logistic regression models were built to assess whether hypoMg contributed to the CIN development. The variables included in the first step of these multivariate analyses were LVEF, presence of diabetes mellitus, AMI, prior MI, baseline eGFR, amount of contrast agent administered, hemoglobin, and Mg level. Multivariate logistic regression analysis revealed baseline Mg levels as independent predictors of CIN after coronary angiography. HypoMg was also an independent predictor of CIN (OR 2.90, 95 % CI 1.42–5.93, P=.004) when introduced into the multivariate model instead of the baseline Mg level.

Discussion

To our knowledge, this is the first study to describe that hypoMg was a risk factor for CIN after coronary angiography. CIN is an essential complication in using iodinated contrast media (1, 11). With an increasing number of diagnostic and therapeutic catheterizations each year, particularly among patients with severe conditions predisposing to CIN, the incidence of CIN will continuously increase.

The present study demonstrated that Mg level was related to the incidence of CIN during hospitalization. Of the 223 patients enrolled, CIN occurred in 28 patients (12.6%). HypoMg was defined as Mg< 1.60 mg/dL. CIN occurred in %53.3 of the patients with HypoMg and %8.9 of those with non-HypoMg (P=<0.001). The incidence of CIN in our study is higher than the results of previous studies(12, 13). Also, due to excluding incomplete patient data, we may have included high-risk patients (DM (30.5%), anemia(%27.4), CKD(%22.9), and CHF (33.6%)) in terms of CIN.

When risk factors were considered, many patients became hypomagnesemia from chronic diuretic therapy combined with low dietary magnesium intake. Patients with long-standing diabetes mellitus also acquire a renal tubular defect for magnesium and become hypomagnesemia. But our study demonstrated that baseline hypoMg was an independent risk factor for CIN in all patients. These associations remained when adjusted for all variables, including CKD, CHF, DM, and medications (Dıuretıc used, etc.).

Several plausible explanations exist for the increased CIN risk in patients with hypoMg. The renoprotective effect of magnesium is likely multifactorial. Besides its role as an antioxidant and coenzyme for compensatory sodium-potassium ATPase (Na+/K+-ATPase or Na+/K+-pump), magnesium has blocked the calcium channel (9). It counteracts vasoconstriction by endogenous catecholamines and potentiates the action of endogenous vasodilators(14-16). The infusion of Mg has increased renal blood flow via an endothelium-dependent release of nitric oxide and its ability as a calcium channel antagonist (17, 18).

Previously Mg has been shown to protect the kidney from contrast media-produced oxygen free radicals(9). In addition, it has been demonstrated that the prophylactic use of intravenous Mg significantly reduces CIN in primary PCI patients(10). These results suggest magnesium replacement in hypomagnesemia may be indicated before diagnostic/interventional studies using contrast media.

The present study has some limitations. Our study is single-center; thus, the results presented here can be biased due to some non-identified center characteristics. Secondly, this is an observational study, so we may have included high-risk patients (DM (30.5%), anemia (%27.4), CKD(%22.9), and CHF (33.6%)) due to excluding incomplete patient data. In addition, because of the observational nature of our study, a causal association between hypoMg and CIN was not completely established, the demonstration of which would further require randomized, controlled trials.

Conclusion

This study demonstrates that hypoMg is associated with an increased risk for CIN.

Disclosure Statement

The authors have no relevant financial or non-financial interests to disclose.

Peer-Review Externally

Peer Reviewed

Support Resources

No financial support was used by authors during this study.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the content of this article.

Ethical Declaration

Ethical permission was obtained from the University of Health Science, Diskapi Yildirim Beyazit Training and Research Hospital Clinical Research Ethics Committee for this study with the date 18.04.2022 and number 135/07, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: N.B.O, S.I, Design: N.B.O, S.I, E.A. ,.Data Collection or Processing: N.B.O, S.I, E.A., F.A, I.G., Analysis or Interpretation: N.B.O, G.G., Literature Search: N.B.O, S.I, E.A., H.F.Ş., I.G, M.A.F, Writing: N.B.O, S.I., G.G

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