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Impact Of Dapagliflozin To Prevent Contrast Induced Nephropathy After Heart Catheterization And Percutaneous Coronary Intervention

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ORIGINAL ARTICLE

Impact of Dapagliflozin to Prevent Contrast Induced Nephropathy After Heart Catheterization and Percutaneous Coronary Intervention

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Abstract

Background: **Contrast-induced nephropathy (CIN) is a potential complication that can occur afterward heart catheterization and percutaneous coronary intervention (PCI), particularly in cases with comorbid conditions like diabetes and chronic kidney disease. CIN is characterized by a rapid loss in kidney function after treatment with contrast agents during these procedures. It is linked with higher morbidity, mortality, and healthcare expenditures. Therefore, finding effective preventive measures for CIN is crucial.**

Aim and objectives: **To determine the role of Dapagliflozin in CIN following cardiac catheterization and PCI.**

Patients and methods: **Prospective research was performed at the Department of Cardiology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. The research involved 400 cases separated into three groups.**

Results: **There was statistically nonsubstantial distinction the examined groups concerning sex or age. There was statistically substantial relation between development of CIN and all of procedure and between eGFR baseline and follow-up.**

Conclusion: **Dapagliflozin for the prevention of CIN during cardiac catheterization and PCI was well tolerated and achieved the desired results. Based on the results of our research, SGLT2 inhibitors may offer protection against CIN, particularly in individuals with co-morbidities like diabetes. Comorbid heart failure, higher baseline serum creatinine and non-use of dapagliflozin significantly independently increase risk of CIN.**

Keywords: Contrast induced nephropathy, Heart catheterization, Percutaneous coronary intervention

1. Introduction

The use of iodinated contrast media (CM) during left cardiac catheterization and PCI has expanded into the field of interventional cardiology. CM containing iodine are thought to be safe for people with normal renal function, but may pose a concern for those with chronic renal failure or diabetes. Acute kidney damage (AKI) is a prominent source of morbidity and death in hospitals, and Contrast-induced nephropathy (CIN) continues to be a major contributor.[1] CIN is defined as an elevation of serum creatinine of more than 25 % or greater than or equal to 0.5 mg/dl (44 μmol/l) from baseline within 48 h of intravenous contrast administration after excluding other factors that may cause nephropathy, such as nephrotoxins, hypotension, urinary obstruction, or atheromatous emboli. It is self-limited in most instances, with Scr levels peaking in 3–5 days and gradually returning to baseline levels within 7–10 days.[2]

Sodium-glucose co-transporter type 2 inhibitors (SGLT2i) are the latest generation of diabetes medications.[3]

Despite the fact that SGLT2i were initially utilized only as antidiabetics due to their glycosuric influence, newer studies have shown that these drugs may independently decrease cardiovascular events, particularly in cases with heart failure. This benefit was seen in both diabetic and non-diabetic cases. A

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reno-protective impact is only one of the multiple consequences that have been noted. SGLT2i has direct nephroprotective effects, including suppression of inflammation and fibrosis, besides the indirect benefits mediated by intrarenal hemodynamic alterations. Reduced glomerulosclerosis and tubulointerstitial fibrosis are direct results of SGLT2i's ability to inhibit ROS generation.[4]

These results raise the possibility that SGLT2i might help minimize or avoid the nephrotoxic effects of CM, leading one to believe that their usage might reduce the frequency of nephropathy following cardiac catheterization and angioplasty.[5]

2. Patients and methods

This randomized controlled trial was performed in at Department of Cardiology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. This research involved 400 patients who presented, between June 2022 and April 2023 for coronary angiography or percutaneous coronary intervention, were separated into three groups: group I involved 226 patients receiving dapagliflozin 10 mg, group II 124 patients receiving dapagliflozin 5 mg and group III 50 patients received placebo. Inclusion Criteria: glomerular filtration rate (GFR) greater than or equal to 30 ml/min/1.73 m^2 [CKD stage G1-G3], Cardiac Catheterization and PCI. Written informed approval. Exclusion Criteria: Active malignancy, Active urogenital infection, Diabetes mellitus, Cardiogenic shock and eGFR less than 29 ml/min/1.73 m^2. All patients underwent a thorough history taking (age, sex, smoking status, and comorbidities), clinical examination, 12-lead standard ECG: to identify evidence of any ischemic changes, chamber enlargement, abnormal axis deviation, rate and rhythm disturbances and Q-T prolongation, resting transthoracic echocardiography (TTE): assessment of LV systolic function and find anomalies in wall motion. EDD, ESD, PWD, IVSD, FS, and LVEF were evaluated by biplane Simpson's method or M-mode using standard echocardiographic views using a Philips Echo machine equipped with a transthoracic 5-1 MHz transducer, and the results were completed blindly by two echo experts for all subjects, laboratory tests: complete blood count (CBC), serum creatinine level, and GFR by (CKD-EPI Creatinine (2021) equation).[6]

2.1. Coronary angiography

To identify their coronary anatomy, site of lesions, amount and type of Dye used, and duration of procedure, PCI was done by experienced operators in conventional manner using femoral or radial approach with fixing of the lesion with DES.

2.2. Statistical analysis

The statistical analysis application SPSS v26 was utilized (IBM Inc., Chicago, IL, USA). Quantitative data from the three groups were compared using the unpaired Student's *t*-test. Mean and standard deviation were supplied for quantitative variables (SD). When appropriate, the Chi-square test or Fisher's exact test was used to analyze qualitative variables. The results are shown as frequency and percentage (%). The edge for factual importance was a two-followed *P* worth of 0.05.

2.3. Data collection

The clinical history, clinical examination, laboratory, and echocardiographic data were collected in an anonymized coded sheets.

2.4. Data analysis

Univariated and multivariated analysis of the patients data submitted to compare in hospital and before discharge follow up by serum creatinine and urea (Table 1).

3. Results

There was a variation that was insignificant in terms of statistics amongst the examined groups concerning gender or age (Table 2).

There was a variation that was insignificant in terms of statistics amongst the examined groups concerning baseline estimated glomerular filtration. There was a considerable variance, according to the statistics amongst the examined groups concerning follow-up estimated glomerular filtration. On doing posthoc test, the distinction is substantial amongst group I and each of groups II and III (highest level among group I). Within group I, there is nonsignificant increase in eGFR, while within groups II and III, there is nonsubstantial decrease in eGFR (Fig. 1, Table 3).

There was a variation that was insignificant in terms of statistics amongst the examined groups concerning baseline serum creatinine. There was a considerable variance, according to the statistics among the examined groups concerning follow-up serum creatinine. On doing pairwise contrast, the distinction was substantial among group I and each of groups II and III (lowest level among group I)

Table 1. Comparison amongst the examined groups concerning baseline data.

	Group I $N = 226$ (%)	Group II $N = 124$ (%)	Group III $N = 50$ (%)	χ^2	*P*
Sex					
Female	65 (28.8 %)	30 (24.2 %)	19 (38 %)	3.351	0.187
Male	161 (71.2 %)	94 (75.8 %)	31 (62 %)		
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**F**	***P***
Age (y)	55.81 ± 9.91	56.62 ± 8.9	56.24 ± 10.22	0.288	0.75

F One way ANOVA test χ^2Chi square test.

Table 2. Comparison amongst the examined groups concerning glomerular filtration rate baseline and on follow–up.

	Group I $N = 226$	Group II $N = 124$	Group III $N = 50$	F	*P*
	Mean ± SD	Mean ± SD	Mean ± SD		
Baseline	88.01 ± 18.15	84.62 ± 22.41	84.26 ± 21.39	1.508	0.223
Follow–up	89.67 ± 18.96	82.64 ± 18.5	76.92 ± 22.32	11.543	<0.001**
LSD	$P_1 < 0.001$**	P_2 0.077	$P_3 < 0.001$**		
Pt	0.084	0.139	0.117		

LSD Fisher least significant difference test ***P* less than or equal to 0.001 is statistically highly significant p1 difference between group I and group II p2 difference between group II and III p3 difference between group I and group III Pt paired sample *t*-test.

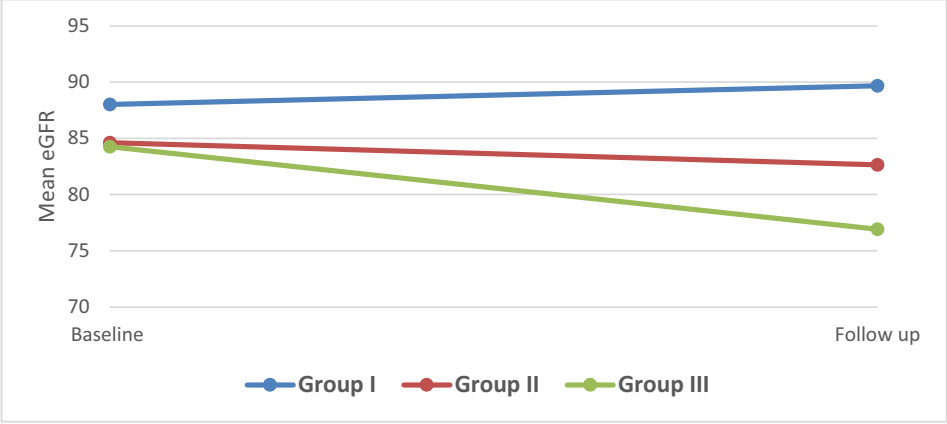

Fig. 1. Multiple line graph showing change in glomerular filtration rate among examined patients.

Table 3. Comparison among the examined groups as regards serum creatinine baseline and on follow-up.

	Group I $N = 226$ (%)	Group II $N = 124$ (%)	Group III $N = 50$ (%)	F	*P*
	Mean ± SD	Mean ± SD	Mean ± SD		
Baseline	0.92 ± 0.23	0.97 ± 0.29	0.9 ± 0.25	1.678	0.188
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**KW**	***P***
Follow-up	1 (0.8–1)	1 (0.9–1.1)	1 (0.9–1.13)	18.776	<0.001**
Pairwise	$P_1 < 0.001$**	P_2 0.703	P_3 0.002*		
P (Wx)	0.048*	0.005*	<0.001**		

KW, Kruskal Wallis test IQR interquartile range **P* less than 0.05 is statistically significant Wx p for Wilcoxon signed rank test.

Within each group, there was a substantial rise in serum creatinine (Table 4).

There was a considerable variance, according to the statistics among the examined groups concerning incidence of CIN. On comparing each two groups, variance was substantial among control group and each other group (6 % within control group vs. 0.4 % within group I and 0 % within group II developed CIN) (Fig. 2, Table 5).

There was statistically substantial correlation among development of CIN and all of procedure (all those with CIN underwent PCI), type of dye (all patients with CIN had sodium-meglumine-iox-ithalamate), vessels affected and amount of dye (CIN

Table 4. Comparative analysis of contrast-induced nephropathy amongst the groups that were examined.

	Group I $N = 226$ (%)	Group II $N = 124$ (%)	Group III $N = 50$ (%)	χ^2	P
CIN					
Absent	225 (99.6 %)	124 (100 %)	47 (94 %)	MC	<0.001**
Present	1 (0.4 %)	0	3 (6 %)		
P	$P_1 > 0.999$	P_2 0.023*	P_3 0.019*		

MC, Monte Carlo test.

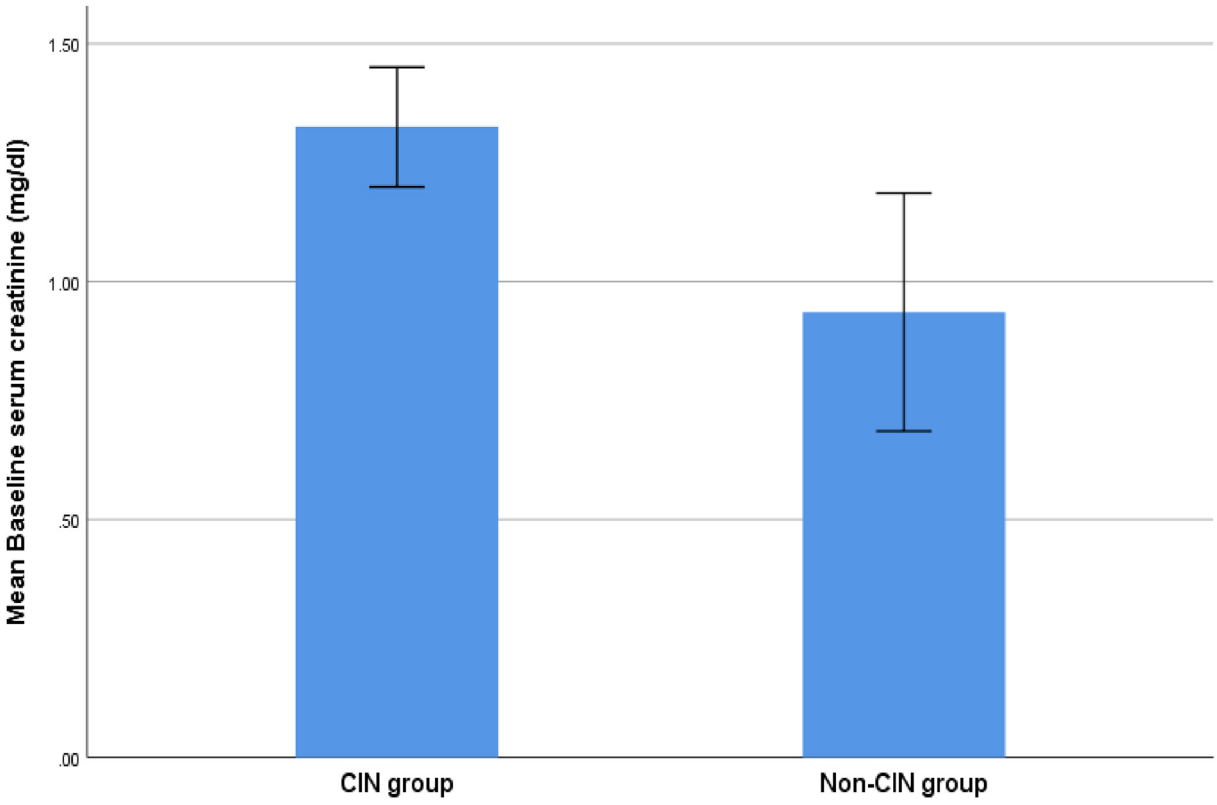

Fig. 2. Simple bar chart showing relation between contrast-induced nephropathy and serum creatinine of patients.

Table 5. Relation between contrast-induced nephropathy and the procedure specific parameters.

	CIN $n = 4$ (%)	No CIN $n = 396$ (%)	χ^2	P
Type of dye				
iohexol (Omnipaque)	0	212 (50.5 %)	Fisher	0.048*
Meglumine ioxithalamate (Telebrix)	4 (100 %)	184 (49.5 %)		
Procedure:				
Angio	0	234 (59.1 %)	Fisher	**0.029***
PCI	4 (100 %)	162 (40.9 %)		
Vessel:				
More than 2 vessels	0	238 (60.1 %)	MC	**0.025***
Simple	2 (50 %)	114 (28.8 %)		
Complex	2 (50 %)	44 (11.1 %)		
	Median (IQR)	**Median (IQR)**	**Z**	*p*
Amount of dye	3.5 (2.25–6.25)	1 (1–3)	−2.012	**0.044***
Time of procedure	16 (12–33.5)	6 (5–16.75)	−1.915	0.055

Z Mann Whitney test.

was significantly higher amounts of dye). There was statistically nonsubstantial correlation among development of CIN and time of procedure (Table 6).

Comorbid heart failure, higher baseline serum creatinine and nonuse of dapagliflozin significantly independently increase risk of CIN by 24.3 and 34.85

Table 6. Analysis of risk variables for contrast-induced nephropathy using the binary regression method.

	B	*P*	AOR	95 % C.I.	
				Lower	Upper
Age (y)	0.139	0.100	1.15	0.974	1.355
Heart failure	3.190	**0.047***	24.3	1.041	567.105
Serum creatinine	10.032	0.059	22733.97	0.696	742155139.278
Group I		0.113			
Group II	−19.289	0.993	0.000	0.000	.
Groups III	3.551	**0.037***	34.85	1.245	975.300

AOR, adjusted odds ratio; CI, Confidence interval.

folds, respectively. Older age and, higher baseline serum creatinine nonsignificantly independently increase risk of CIN by 1.15 and 22733.97 folds, respectively.

4. Discussion

Coronary artery disease (CAD) patients whose arteries were revascularized by PCI lived longer after the procedure.[7] In spite of this, some cases with CAD have experienced acute renal injury because of CM, with rates varying from 1.3 to 33.3 %.[8] This is known as contrast-induced acute kidney injury (CI-AKI), which can be described as the onset or worsening of renal dysfunction immediately following the consumption of CM, and excluding any other potential triggers.

The main results of this study were as follows:

To eliminate the consequence of any confounding factor that may affect the final outcome the current study enrolled two well-matched groups in baseline data, as There was not any variation that could be considered statistically significant among the examined groups concerning age, sex, comorbidities, procedure-related data (including vessels, procedure, amount, type of dye or time of procedure).

In the current study the Comparison amongst the examined groups concerning eGFR baseline and on follow up, showed that at baseline there is statistically nonsubstantial variance amongst the examined groups concerning estimated glomerular filtration.

There is statistically substantial distinction among the examined groups concerning follow-up estimated glomerular filtration. On doing post-hoc test, the variance is substantial among group I and each of groups II and III (highest level among group I).

Within group I, there is non-significant increase in eGFR, while within groups II and III, there is non-substantial decrease in eGFR.

This was agreed with the recent meta-analysis of 6 clinical trials by Ma and colleagues revealed that the SGLT2i considerably delayed the decline in eGFR [MD = 1.35 ml/min/1.73 m, 95 % CI 0.84, 1.86), *P* less than 0.0001].[9]

Also, consistent with the current study Clegg and colleagues indicated that eGFR slope was considerably better for SGLT2i users overall (+1.78 [95 % CI 0.87−2.69] ml/min/1.73 m^2/year) and for dapagliflozin users (+2.28 [1.01−3.54] ml/min/1.73 m^2/year). This was in comparison to people who did not use dapagliflozin.[10]

As well, in concordance with the current study Hua and colleagues indicated that the eGFR of dapagliflozin users was substantially greater than that of nonusers both at 48 and 72 h following PCI (93.14 26.51 vs. 87.33 32.12, $P = 0.031$; 91.26 21.38 vs. 84.39 42.76, $P = 0.026$).[11]

Comparison between the examined groups regarding serum creatinine baseline and on follow-up, revealed that There is some variation that is insignificant in terms of statistics amongst the examined groups concerning baseline serum creatinine.

There is statistically substantial variance amongst the examined groups concerning follow-up serum creatinine. On doing pairwise contrast, the variance is substantial amongst group I and each of groups II and III (lowest level among group I).

Within each group, there is a substantial rise in serum creatinine.

In concordance with the current study Özkan and Gürdoğan. 312 diabetic individuals were used in this study to investigate the efficiency of this medication group in avoiding the development of CIN. The examined group consisted of 104 diabetic individuals who were using SGLT2, whereas the control group did not take SGLT2. The study revealed that at baseline the creatinine level was similar in both groups, however, at 3- and 7-days post PCI the creatinine level was considerably elevated in both groups, and the increase was considerably greater in control group.[12]

Moreover, in accordance with the findings of the latest study in a research that involved many centers, Paolisso and colleagues investigated the relationship among chronic SGLT2-I therapy and the development of CI-AKI in 646 diabetic cases who had AMI and were treated with PCI. The results of this investigation showed that SGLT2 users

demonstrated substantially lower creatinine levels at 72 h following PCI.[13]

In the current study the comparison among the examined groups concerning CIN, showed that there is statistically substantial variance amongst the examined groups concerning incidence of CIN.

On comparing each two groups, distinction is substantial amongst control group and each other group (6 % within control group vs. 0.4 % within group I and 0 % within group II developed CIN).

In concordance with the current study Özkan and Gürdoğan found that the hazard of developing CIN was considerably lesser in the SGLT2 inhibitor group ($P = 0.03$). The incidence of new cases of CIN was 13.5 % in the group of diabetic cases utilizing an SGLT2 inhibitor, whereas it was 30.8 % in the group that did not.[12]

Also, in concordance with the current study Hua and colleagues revealed that in cases having PCI for CAD and T2D, the use of SGLT2 inhibitors did not correlate with a greater likelihood of Contrast-induced acute renal damage.[11]

Regarding the relation between CIN and the disease-specific parameters, it was revealed that there is statistically substantial correlation among development of CIN and all of procedure (all those with CIN underwent PCI), type of dye (all patients with CIN had sodium-meglumine-ioxithalamate), vessels affected and amount of dye (CIN is significantly higher amounts of dye). There is statistically non-substantial correlation amongst development of CIN and time of procedure.

Binary regression analysis of factors correlated with CIN revealed that Comorbid heart failure, higher baseline serum creatinine and nonuse of dapagliflozin significantly independently increase risk of CIN by 24.3 and 34.85 folds, respectively. Older age and, higher baseline serum creatinine nonsignificantly independently increase risk of CIN by 1.15 and 22 733.97 folds, respectively.

In concordance with the current study Paolisso and colleagues following controlling for potential confounders, multivariate analysis showed that the use of SGLT2i, along with the validated Mehran Score and discharge LVEF, was an independent predictor of decreased frequency of CI-AKI (OR 0.356; 95 % CI 0.134-0.943, $P = 0.038$).[13]

In addition, as Hossain and colleagues summed up, contrast material is still a frequent source of AKI. CI-AKI is more common in those with preexisting kidney disease, diabetes, advanced age, and intravascular volume depletion.[14]

The meta-analysis by He and colleagues revealed that the general frequency of CIN was not low in cases with STEMI undergoing PCI, and that it was strongly correlated with hypertension, myocardial infarction, prior age, diabetes, damaged left anterior descending artery, lower estimated GFR, Killip class greater than or equal to 2, reduced left ventricular ejection fraction, and left ventricular ejection fraction less than 40 %.[15]

4.1. Conclusion

The use of dapagliflozin was safe and effective in the treatment and avoidance of kidney damage caused by contrast material during cardiac catheterization and angioplasty. Our results suggested that SGLT2 inhibitors, particularly for cases with concomitant diseases like diabetes, may offer protection against the progression of CIN. Comorbid heart failure, higher baseline serum creatinine and non-use of dapagliflozin significantly independently increase risk of CIN.

Conflicts of interest

There is no conflict of interest.

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