Preventive and Therapeutic Effects of Mineralocorticoid Receptor Antagonists Pretreatment on Contrast-induced Acute Kidney Injury in Patients Undergoing Coronary Angioplasty

Abstract

Background: Contrast-induced nephropathy (CIN) is a serious complication of angiographic procedures and results from administration of iodinated contrast media (CM). **Aim:** To study the preventive and therapeutic effects of Mineralocorticoid receptor antagonist's pretreatment on contrast-induced acute kidney injury in patients undergoing coronary angioplasty. **Methods**: This case control study was carried out on patients admitted for coronary angioplasty in Benha University Hospitals (cardiology department), in which 100 patients were selected and divided in two groups "active & control". Group (A)(control): received placebo. Group (B) (Active): received Spironolactone 50 mg. **Results**: Blood Urea in Group (A) showed a significant increase during follow up when it was compared to baseline values while Group (B) showed an increase during follow up but without any statistically significant difference. Serum Creatinine in Group (A) showed a significant increase after 2 days of follow up with a mean value of 1.30±0.248 when it was compared to baseline values. While Group (B) showed a significant increase after 2 days of follow up with a mean value of 1.15±0.406 when it was compared to baseline values and also when compared to values after 7 days of follow up with a mean value of 1.19±0.384. **Conclusion:** The administering of Mineralocorticoid therapy prior to coronary angioplasty obtains additional benefit in terms of decrease incidence of CI-AKI in CAD patients.

Keywords: Mineralocorticoid; Contrast; Kidney; Injury; Coronary angioplasty

Introduction

Contrast-induced nephropathy (CIN) is a serious complication of angiographic procedures and results from administration of iodinated contrast media (CM) (1).

CIN is defined as an elevation of serum creatinine (Scr) of more than 25% or ≥0.5 mg/dl (44 μmol/ l) from baseline within 48 h 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).

CIN is the third most common cause of hospital acquired acute renal injury representing about 12% of the cases. The incidence of CIN varies between 0 and 24% depending on patient's risk factors. It is generally a transient and reversible form of acute renal failure. However, the development of CIN is associated with a longer hospital stay, an increased morbidity and mortality, in addition to a higher financial cost (3**).**

Treatment of CIN is mainly supportive, consisting of careful fluid and electrolyte management, although dialysis may be required in some cases. The limitation in the available treatment options makes prevention the cornerstone of management (4).

Patients who opt for percutaneous coronary intervention (PCI) to help them with their ischemic heart disease (IHD) problems are at high risk of developing contrast-induced nephropathy (CIN) (5).

Several interventions have been done to limit this negative effect on such patients, but the evidence is still lacking on the best method, and the maximum benefit that can be achieved to prevent CIN. Several approaches may include aggressive hydration prior to the procedure, but results are still pending. Furthermore, it has been reported that another innovative approach was based on blocking the neurohormonal activation known to cause or aggravate acute kidney injury (AKI). One such approach is the use of spironolactone, where animal studies highlighted the damaging effect of aldosterone on causing and aggravating AKI and specifically CIN (6).

Aldosterone plays a central role in renal injury induced by ischemia reperfusion (I/R) and emphasizes that spironolactone administration for 24–96 h before induction of renal I/R injury prevents the renal dysfunction and structural damage observed in this model. Aldosterone mediates a dose- dependent contraction in clonal adult human vascular smooth muscle cells, which spironolactone and eplerenone inhibits, suggesting that the vasoconstrictor effect was due to the MR blockade. Aldosterone participates in promoting renal vasoconstriction during renal I/R, an effect that was prevented by spironolactone, implying that aldosterone induces renal vasoconstriction by a mechanism that requires the coupling of aldosterone to its receptor. In support of this possibility, a recent study shows that aldosterone induced vasoconstriction by decreasing the endothelial expression of glucose-6-phosphate dehydrogenase, which, in turn, decreases the NO availability, and these effects were reversed by spironolactone administration, implying that the MR is involved **(7).**

Given all the previous information, we designed this study to measure the effect of aldosterone blockage promoted by the utilization of spironolactone prior to coronary angiography on CIN incidence measured by different biochemical approaches and definitions

Patients and methods

This case-control study was carried out on patients admitted for coronary angioplasty in the cardiology department in Benha University Hospitals. It was conducted on 100 patients. The duration of the study was done from January 2021 to July 2021.

Inclusion criteria:

Indication of invasive coronary angiography by ACS with or without percutaneous coronary intervention

Exclusion criteria:

- Patients <18 years.
- Previous renal replacement therapy.
- Women with possibilities of being pregnant.
- Allergy to iodinated contrast previously known, that cannot receive premedication.
- Exposure to iodinated contrast in the previous 10 days.
- Previous myocardial revascularization surgery.
- AMI with ST-segment elevation of <12h of evolution.

- Cardiogenic shock.
- Inability to understand the nature of the study or medical or social disability that may interfere with the collection of data or appropriate follow up.
- Inclusion in other clinical trials or registries.

From each patient the following data were collected upon admission;

1. Complete full history taking,
2. Clinical examination
3. Laboratory investigations as Complete blood picture (CBC), Renal function test, Liver Test Profile, Random Blood glucose level, Lipid profile, Uric acid (mg/dL), Hemoglobin A1c, Serum sodium (mmol/L), Serum potassium (mEq/L)
4. Echocardiography:

   ✓ Examination involves using an echo probe at various windows to obtain views of the heart and capturing images/videos for later playback while formally "reading" the study to come up with findings of the study.

   ✓ Examination is usually done while laying flat and tilted onto the left side to bring the heart into better view. Ultrasound gel is used to improve the acoustic windows and increase quality of the captured images.

5. Urine output mL/kg/h:

   ✓ Collect patient's weight, age, urine output, and the period over which the urine was collected.
   The following equation was used to compute how much urine is output per hour: Urine output (ml/kg/hr) = Collected urine / (Weight * Time) where, creatinine and urine output measurement every 2 days for one week. Weight is given in kilograms (kg); collected urine is given in milliliters (mL); and time is given in hours

   ✓ Use the patient's age to determine if the urine output is within the normal range.

An Official permission was obtained from Faculty of Medicine, Benha University. An official permission was obtained from cardiology department in Benha university, Approval from ethical committee in the faculty of medicine (Institutional Research Board IRB).

Procedures: All patients had received the standard and recommended general medical care for prevention of CIN

- **Group (A)**: 50 patients received placebo serving as a control group.
- **Group (B)**: 50 patients received Spironolactone 50 mg once daily for 7 days before coronary angiography.

  ➢ Serum creatinine and urine output were measured 3 days before and in the 2nd and 7th day after contrast.

  ➢ Spironolactone 12.5 -25 mg for patients with contrast-induced acute kidney injury in placebo group, followed by serum creatinine and urine output measurement every 2 days for one week.

Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean and standard deviation. Significance of the obtained results was judged at the 5% level. Statistical analysis of the data; Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) [(2)] Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean and standard deviation. Significance of the obtained results was judged at the 5% level. The used tests were; Chi-square test For categorical variables, to compare between different groups, Student t-test; For normally quantitative variables, to compare between two studied groups . Mann Whitney test; For abnormally quantitative variables, to compare between two studied groups

Results

Blood Urea in Group (A) showed a significant increase during follow up with highly statistically significant differences when it was compared to baseline values and after 7 days of follow up of the same group with a mean value of 34.06±16.929. While in Group (B) it showed an increase during follow up but without any statistically significant difference when it was compared to baseline values and after 7 days of follow up with a mean value of 33.34±15.799 (Table 1).

Serum Creatinine in Group (A) showed a significant increase after 2 days of follow up with a mean value of 1.30±0.248 when it was compared to baseline values and 7 days of follow up with a mean value of 1.48±0.453. While in Group (B) it showed a significant increase after 2 days of follow up with a mean value of 1.15±0.406 when it was compared to baseline values and to values after 7 days of follow up with a mean value of 1.19±0.384 (Table 1).

Urine pH in Group (A) showed a highly significant increase after 2 days of follow up when it was compared to baseline values with a mean value of 7.15±1.245 ,also when compared to follow up values after 7 days with a mean value of 7.96±1.124. While in Group (B) it showed an increase at follow with highly significant differences when it compared to baseline values and to values after 7 days of follow up with a mean value of 7.27±0.286. (Table 1).

Serum sodium in Group (A) showed a highly significant increase after 2 days of follow up when it compared to baseline values with a mean value of 142.42±10.635 and when compared to values after 7 days of follow up with a mean value of 147.00±14.588. While in Group (B) it showed an increase at follow with highly significant differences when compared between baseline values and after 7 days of follow up, with a mean value of 146.59±14.566 . (Table 2).

Serum potassium in Group (A) showed a highly significant increase after 2 days of follow up when compared to baseline values with a mean value of 4.98±0.815 and also when compared to values after 7 days of follow up with a mean value of 5.68±0.996. While in Group (B) it showed an increase at follow with highly significant differences when it compared to baseline values and after 7 days of

follow up values ,with a mean value of 5.08±1.037. (Table 2)

When comparing the percentage of increase of different parameters of follow up between group (A) and group (B) across the follow up period we found that :

Serum creatinine had increased in group (A) by 52.0% with a mean value of 1.60±0.377 and in group (B) by 26.0% with a mean value of 1.22±0.258and so there was a statistically significant difference (P=0.003) between both groups (Table 3).

Blood urea nitrogen had increased in group (A) by 28.0% with a mean value of 45.64±15.315 and in group (B) by 52.0% with a mean value of 40.35±13.520 but there was no statistically significant difference (p=0.210) between both groups (Table 3).

Urine PH had increased in group (A) by 20.0% with a mean value of 6.80±1.619 and in group (B) by 32.0 %with a mean value of 6.50±1.265 but there was no statistically significant difference (p=0.737) between both groups (Table 3).

Serum sodium had increased in group (A) by 62.0% with a mean value of 154.03±13.544 and in group (B) by 56.0% with a mean value of 153.86±12.607 but there was no statistically significant difference (p=0.959) between both groups. (Table 3).

Serum potassium had increased in group (A) by 52.0% with a mean value of 4.60±0.937and in group (B) by 36.0% with a mean value of 5.39±0.813 and so there was a statistically significant difference between both groups (P= 0.009) (Table 3).

When comparing the percentage of decrease of different parameters of follow up between group (A) and group (B) across the follow up period we found that: Serum creatinine had decreased in group (A) by 44.0% with a mean value of 0.94±0.238 and in group (B) by 52.0% with a mean value of 1.13±0.200 and so there was a statistically significant difference (p=0.012) between both group (Table 3).

Blood urea nitrogen had decreased in group (A) by 70.0% with a mean value of 26.57±14.128 and in group (B) by 46.0% with a mean value of 24.78±14.280 but there was no statistically significant difference (P=0.616) between both groups. and and this could be explained by the mechanism of action of aldosterone (Table 3).

Urine PH had decreased in group (A) by 32.0% with a mean value of 5.00±1.155 and in group (B) by 26.0% with a mean value of 4.77±0.832 but there was no statistically significant difference (p>0.05) between both groups (Table 3).

Serum sodium had decreased in group (A) by 34.0% with a mean value of 136.12±7.201and in group (B) by 38.0% with a mean value of 136.53±11.330 but there was no statistically significant difference (p>0.05) (Table 3).

Serum potassium had decreased in group (A) by 44.0% with a mean value of 3.53±0.710 and in group (B) by 42.0% with a mean value of 3.97±0.788 and so there was a statistically significant difference (p<0.05) between both groups (Table 3).

Contrast-induced nephropathy outcome in group (A) showed that more than one quarter of the studied patients had contrast-induced nephropathy (26%) which

occurred in 13 patients out of 50 patients while in group (B) only 7 patients out of 50 patients with a percentage of 14.0% had contrast-induced nephropathy. Although this was clinically significant there was no statistically significant differences ($p>0.05$) between groups **Table (4) and Figure (1).**

On evaluation of effect of Spironolactone on Contrast-induced nephropathy as a therapeutic option after occurrence of injury in group (A) we found that 4 patients out of 13 patients had improved with a percentage of 30.8 while no improvement was observed in 9 patients with a percentage of (69.2%) **Table (5) and Figure (2).**

When comparing between group (A) and group (B) regarding risk factors we found that Diabetes mellitus was present in 23 patients in group (A) which present 46% from total while in group (B) it was present in 28 patients which presented 56% from total. Regarding hypertension it was present in 21 (42%) patients in group (A) which while in group (B) it was present in 26 (52%) patients **(Table 6).** As regard hyperlipidemia it was present in 29 patients (58%) in group (A) while in group (B) it was present in 22 patients (44%) while, smoking was present in 15 patients (30%) in group (A) and in 8 patients (16%) in group (B) **(Table 6).**

Discussion

Contrast-induced nephropathy (CIN), occurs in 1–33% of patients undergoing invasive coronary angiography procedures. It is one of the most common causes of acute renal failure in cardiac patients, especially in cases of acute coronary syndrome (ACS). The development of CIN after an invasive coronary procedure is associated with prolonged hospitalization, marked increase in morbidity and mortality, and an increase in health costs (8).

Many studies in humans and experimental models have shown that aldosterone plays a pivotal role in the pathophysiology of cardiovascular and renal injury. In this regard, clinical trials have evidenced that mineralocorticoid receptor (MR) blockade improves the survival of patients with chronic heart disease and chronic renal failure. The protective effect of MR blockade is associated with decreased fibrosis and vascular inflammation, suggesting that aldosterone is a profibrotic hormone. In addition, the effectiveness of MR antagonism in ameliorating glomerular and/or tubulointerstitial injury has also been documented in several models of nephropathy, including spontaneously hypertensive stroke-prone rats, angiotensin II- and nitric oxide synthase inhibitor- treated rats, aldosterone-treated rats, diabetic nephropathy type 1 and 2 and in a model of unilateral ureteral obstruction (9).

The main aim of this study was to study the preventive and the therapeutic effects of Mineralocorticoid receptor antagonist's pretreatment on contrast-induced acute kidney injury in patients undergoing coronary angioplasty.

In our study, we found that Serum creatinine had increased significantly between both studied groups. P value 0.003* and Serum creatinine had decreased in group (A) by 44.0% with a mean value of 0.94±0.238and in group (B) by 52.0% with a mean value of 1.13±0.200 and so there was a statistically significant difference between both group. P value 0.012*, so the percentage of improvement was higher in group (B). (Table 3)

The explanation for this is that the most accepted mechanism of c i-AKI was vasoconstriction of the vessels in the renal medulla leading to reduced oxygen delivery and enhanced production of oxygen-free radicals like hydrogen peroxide and superoxide leading to increased damage and as the outer medulla is more vulnerable to hypoxia and ischemia all of these pathophysiological derangement can be reversed by the protective mechanism of aldosterone antagonist administration in AKI and this was concordant with another study(10) who reported that aldosterone suppresses nitric oxide (NO) synthesis and triggers an

inflammatory cascade, leading to vascular smooth muscle contraction and tissue fibrosis and its blockade will prevent renal ischemia. Also, this was concordant with a previous study (11) who stated that spironolactone administration resulted in the prevention of tubular injury and reduction of oxidative stress, inflammation, and intrarenal apoptosis. Also, this agreed with other researchers (6) who hypothesized that perioperative spironolactone administration to patients undergoing cardiac surgery would protect against postoperative AKI. Also, this was in line with another study (13)**,** who reported that recovery of ischemic renal injury with the administration of spironolactone

Blood urea nitrogen had increased in group (A) by 28.0% and in group (B) by 52.0% but there was no statistically significant difference between both group. P value 0.210 and this could be explained by the mechanism of action of aldosterone antagonism. and Blood urea nitrogen had decreased in group (A) by 70.0% and in group (B) by 46.0% but there was no statistically significant difference between both groups. P value 0.616 and and this could be explained by the mechanism of action of aldosterone antagonism which had made the blood urea nitrogen level values was increased more in group (B) during follow up more than in group (A).
As vasoconstriction and renal ischemia was most evident with contrast media administration and blood urea depends on glomerular filtration so if blood urea level is increased and this could be reversed by the protective mechanism of aldosterone antagonist administration and this was in agreement with (10) & (11) , who reported reduction of renal ischemia with spironolactone administration also this was concordant with the experimental studies (12) , which reported that mineralocorticoid receptor blockade confers protection against ischemic injury. In their study, rats pretreated with spironolactone before undergoing ischemia-reperfusion injury did not develop AKI. The mechanism was related to increase NO synthase expression and decreased oxidative stress. These researchers next established that adrenalectomy prior to ischemia-reperfusion injury prevents decreased kidney function and tubular injury, which was also associated with reestablishment of NO metabolites. Also, this agreed with other researchers(6)**,** who hypothesized that perioperative spironolactone administration to patients undergoing cardiac surgery would protect against postoperative AKI. Also, this was in line with another study(13)**,** who reported that recovery of ischemic renal injury with the administration of spironolactone.

Urine PH had increased in group (A) by 20.0% and in group (B) by 32.0 % but there was no statistically significant difference between both groups. P value 0.737 and this could be explained by the mechanism of action of aldosterone antagonism. Urine PH had decreased in group (A) by 32.0% and in group (B) by 26.0% but there was no statistically significant difference between both groups. P value 0.714 and this could be explained by the mechanism of action of aldosterone antagonism which had made that urine PH values was increased more in group (B) during follow up more than in group (A).

Serum sodium had increased in group (A) by 62.0% and in group (B) by 56.0% but there was no statistically significant difference between both groups. P value 0.959 and this could be explained by the mechanism of action of aldosterone antagonism. and Serum sodium had decreased in group (A) by 34.0% and in group (B) by 38.0% but there was no statistically significant difference between both groups. P value 0.899 and this could be explained by the mechanism of action of aldosterone antagonism which had made that serum sodium level values was increased more in group (B) during follow up more than in group (A).
This was concordant with other researchers (14)**,** who reported in his study that there was no statistically significant difference between groups of his study regarding serum sodium with administration of spironolactone

Serum potassium had increased in group (A) by 52.0% and in group (B) by 36.0% and so there was a statistically significant difference between both groups. P value 0.009* and this could be explained that the baseline values of potassium in group (B) was lower than baseline values in group (A) and also it may be explained by the small dose used in the study. and Serum potassium had decreased in group (A) by 44.0% and in group (B) by 42.0% and so there was a statistically significant difference between both groups. P value 0.035*and this could be explained that the baseline values of potassium in group (B) was lower than baseline values in group (A) so the percentage of decrease was more in group (A).

This was concordant with other researchers (14)**,** who reported that serum potassium had increased in the spironolactone group more than the other group and only one patient had discontinued treatment due to significant hyperkalemia.

When comparing between group (A) and group (B) regarding risk factors we found that Diabetes mellitus was present in 23 patients in group (A) which present 46% from total while in group (B) it was present in 28 patients which presented 56% from total. Regarding hypertension it was present in 21 (42%) patients in group (A) which while in group (B) it was present in 26 (52%) patients**.** As regard hyperlipidemia it was present in 29 patients (58%) in group (A) while in group (B) it was present in 22 patients (44%) while, smoking was present in 15 patients (30%) in group (A) and in 8 patients (16%) in group (B

Conclusion

Spironolactone can be used as an additional preventive measure for CI-AKI together with conventional measures and also as a therapeutic option after occurrence of CI-AKI without significant side effects especially hyperkalemia

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

References

1. Dangas G, Iakovou I, Nikolsky E, Aymong ED, Mintz GS, Kipshidze NN, et al. Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol. 2005;95(1):13–9.
2. Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. Cmaj. 2005;172(11):1461–71.
3. Perrin T, Descombes E, Cook S. Contrast-induced nephropathy in invasive cardiology: Incidence, pathophysiology, diagnosis, prevention and prognosis. Swiss Med Wkly. 2012;142:w13608.
4. Chui WCM. Contrast-induced nephropathy. Hong Kong Med Diary. 2010;15:18–9.

5. Tehrani S, Laing C, Yellon DM, Hausenloy DJ. Contrast- induced acute kidney injury following PCI. Eur J Clin Invest. 2013;43(5):483–90.

6. Barba-Navarro R, Tapia-Silva M, Garza-Garcia C, López-Giacoman S, Melgoza-Toral I, Vázquez-Rangel A, et al. The effect of spironolactone on acute kidney injury after cardiac surgery: a randomized, placebo-controlled trial. Am J Kidney Dis. 2017;69(2):192–9.

7. Gros, R., Ding, Q., Armstrong, S., O'Neil, C., Pickering, J. G., & Feldman, R. D. Rapid effects of aldosterone on clonal human vascular smooth muscle cells. American Journal of Physiology-Cell Physiology, 2007;292(2), C788-C794.

8. Roffi, C. Patrono, J.P. Collet, C. Mueller, M. Valgimigli, F. Andreotti, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST- Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J, 37, 2016, pp. 267-315.

9. Bar-Nur, D., & Jaber, B. L. Mineralocorticoid receptor blockade for prevention of acute kidney injury: an elusive target. American Journal of Kidney Diseases, 2007; 69(2), 166-168.

10. Jaisser F, Farman N. Emerging roles of the mineralocorticoid receptor in pathology: toward new paradigms in clinical pharmacology. Pharmacol Rev. 2016;68(1):49–75.

11. Moguel-González B, Wasung-de-Lay M, Tella-Vega P, Riquelme-Mc-Loughlin C, Villa AR, et al. Acute kidney injury in cardiac surgery. Rev Investig Clin. 2013;65(6):467–75.

12. Mejía-Vilet JM, Ramírez V, Cruz C, Uribe N, Gamba G, Bobadilla NA. Renal ischemia-reperfusion injury is prevented by the mineralocorticoid receptor blocker spironolactone. Am J Physiol Physiol. 2007;293(1):F78–86.

13. Sánchez-Pozos K, Barrera-Chimal J, Garzón-Muvdi J, Pérez-Villalva R, Rodríguez-Romo R, Cruz C, et al. Recovery from ischemic acute kidney injury by spironolactone administration. Nephrol Dial Transplant. 2012;27(8):3160–9.

14. Pretorius, M., Murray, K. T., Yu, C., Byrne, J. G., Billings IV, Petracek, M. R., et al. Angiotensin– Converting Enzyme Inhibition or Mineralocorticoid ReceptorBlockade Do Not Affect Incidence of Atrial Fibrillation in Patients Undergoing Cardiac Surgery. Critical care medicine, 2012;40(10), 2805.

15. Fernández-Rodríguez, D., Grillo-Pérez, J. J., Pérez-Hernández, H., Rodríguez-Esteban, M., Pimienta, R., Acosta-Materán, C., et al. Prospective evaluation of the development of contrast-induced nephropathy in patients with acute coronary syndrome undergoing rotational coronary angiography vs. conventional coronary angiography: CINERAMA study. Nefrología (English Edition), 2018;38(2), 169-178.

Table (1): Comparison between the two studied groups according to kidney functions

		Baseline	Follow-up	
			After 2 days	After 7 days
blood Urea (mg/dL)				
Group (A)	Mean±S.D.	27.70±9.916	40.82±20.576	34.06±16.929
	Increasing %		74.0%	28.0%
	Decreasing %		26.0%	72.0%
	P value		0.001*	0.014*
Group (B)	Mean±S.D.	32.54±14.158	30.20±16.205	33.34±15.799
	Increasing %		48.0%	52.0%
	Decreasing %		52.0%	48.0%
	P value		0.496	0.562
Serum Creatinine (mg/dL)				
Group (A)	Mean±S.D.	1.02±0.116	1.30±0.248	1.48±0.453
	Increasing %		86.0%	52.0%
	Decreasing %		10.0%	44.0%
	P value		<0.001*	<0.001*
Group (B)	Mean±S.D.	1.02±0.135	1.15±0.406	1.19±0.384
	Increasing %		68.0%	26.0%
	Decreasing %		26.0%	52.0%
	P value		<0.001*	<0.001*
Urine pH				
Group (A)	Mean±S.D.	6.16±0.842	7.15±1.245	7.96±1.124
	Increasing %		75.0%	57.0%
	Decreasing %		13.0%	31.0%
	P value		0.013*	0.043*
Group (B)	Mean±S.D.	5.98±0.820	6.76±0.409	7.27±0.286
	Increasing %		56.0%	23.0%
	Decreasing %		17.0%	48.0%
	P value		<0.001*	0.001*

U: Mann-Whitney test; *: Statistically significant at P <0.05

Table (2): Comparison between the two studied groups according to serum electrolytes and urine output.

		Baseline	Follow-up	
			After 2 days	After 7 days
Serum sodium (mEq/L)				
Group (A)	Mean±S.D.	137.62±4.928	142.42±10.635	147.00±14.588
	Increasing %		64.0%	62.0%
	Decreasing %		14.0%	34.0%
	P value		0.001*	0.011*
Group (B)	Mean±S.D.	139.30±6.031	142.28±10.316	146.59±14.566
	Increasing %		58.0%	56.0%
	Decreasing %		37.0%	38.0%
	P value		0.006*	0.013*
Serum potassium (mEq/L)				
Group (A)	Mean±S.D.	4.48±0.412	4.98±0.815	5.68±0.996
	Increasing %		86.0%	52.0%
	Decreasing %		10.0%	44.0%
	P value		0.248	<0.001*
Group (B)	Mean±S.D.	4.03±0.596	4.60±0.701	5.08±1.037
	Increasing %		66.0%	36.0%
	Decreasing %		14.0%	42.0%
	P value		0.347	0.038*
Urine out put (L/24h)				
Group (A)	Mean±S.D.	1.70±0.50	1.754±0.821	1.454±0.521
	P value		0.56	0.72
Group (B)	Mean±S.D.	1.65±0.56	1.66±0.78	1.46±0.58
	P value		0.64	0.67

U: Mann-Whitney test; *: Statistically significant at P <0.05

Table (3): Comparison between the two studied groups according to different parameters

		Group (A)		Group (B)		P value
		Mean±S.D.	**increase%**	**Mean±S.D.**	**Increase %**	
Increasing	Serum Creatinine (mg/dL)	1.60±0.377	52.0%	1.22±0.258	26.0%	0.003*
	Urea nitrogen (mg/dL)	45.64±15.315	28.0%	40.35±13.520	52.0%	0.210
	Urine pH	6.80±1.619	20.0%	6.50±1.265	32.0%	0.737
	Serum sodium (mEq/L)	154.03±13.544	62.0%	153.86±12.607	56.0%	0.959
	Serum potassium (mEq/L)	4.60±0.937	52.0%	5.39±0.813	36.0%	0.009*
Decreasing	Serum Creatinine (mg/dL)	0.94±0.238	44.0%	1.13±0.200	52.0%	0.012*
	Urea nitrogen (mg/dL)	26.57±14.128	70.0%	24.78±14.280	46.0%	0.616
	Urine pH	5.00±1.155	32.0%	4.77±0.832	26.0%	0.714
	Serum sodium (mEq/L)	136.12±7.201	34.0%	136.53±11.330	38.0%	0.899
	Serum potassium (mEq/L)	3.53±0.710	44.0%	3.97±0.788	42.0%	0.035*

Mann Whitney test*: Statistically significant at P <0.05

*increasing means increasing from base line while decreasing means decreasing after administration of spironolactone or placebo

* All patients in group (A)and (B) received general medical care for prevention of CIN

Table (4): Comparison between two groups as regard to patient's Contrast-induced nephropathy outcome

Contrast-induced nephropathy outcome	Group (A) (n=50)		Group (B) (n=50)		P Value
	No.	%	No.	%	
No	37	74.0	43	86.0	0.211
Yes	13	26.0	7	14.0	
Total	50	100	50	100	

p: p value for comparing between the two studied groups
*: Statistically significant at P <0.05

Table (5): Distribution of CIN patient in group (A) after treated Spironolactone

Contrast-induced nephropathy outcome	Group (A) (n=13)	
	No.	%
No	4	30.8
Yes	9	69.2
Total	13	100

Table (6): Comparison between two groups as regard to patient's risk factors

Risk Factors	Group (A) (n=50)		Group (B) (n=50)		*P Value
	No.	%	No.	%	
Diabetes Mellitus	23	46.0	28	56.0	0.424
Hypertension	21	42.0	26	52.0	0.423
Hyperlipidemia	29	58.0	22	44.0	0.230
Smoking	15	30.0	8	16.0	0.153

 Chi square test

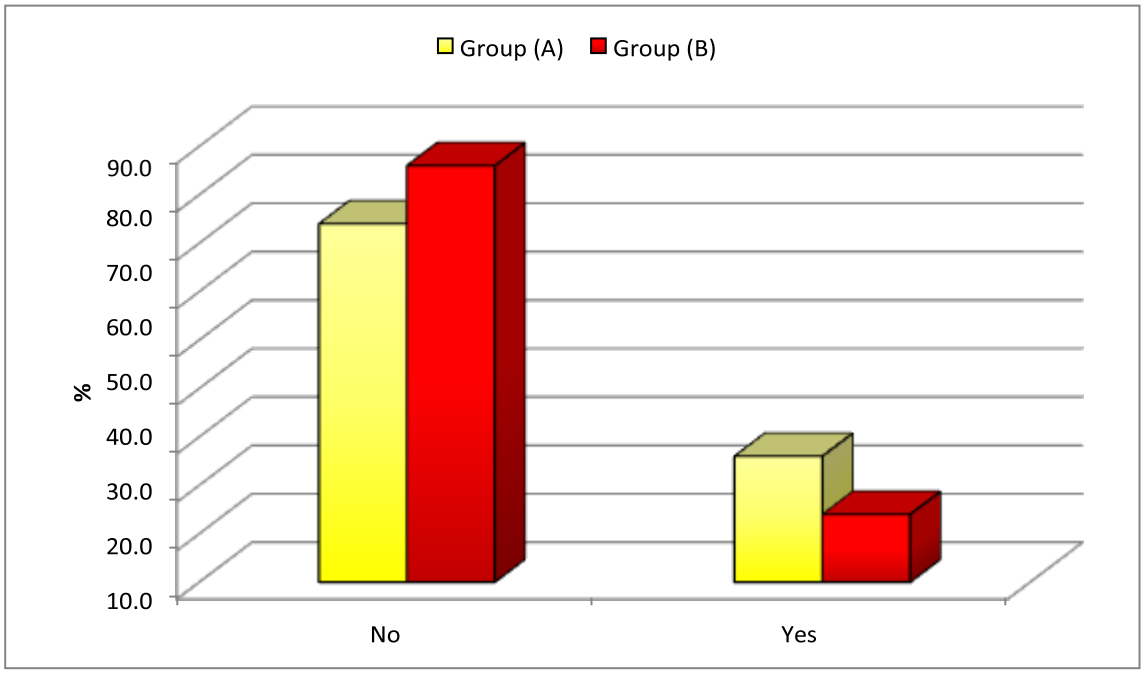

Figure (1): Comparison between two groups as regard to patient's Contrast-induced nephropathy outcome

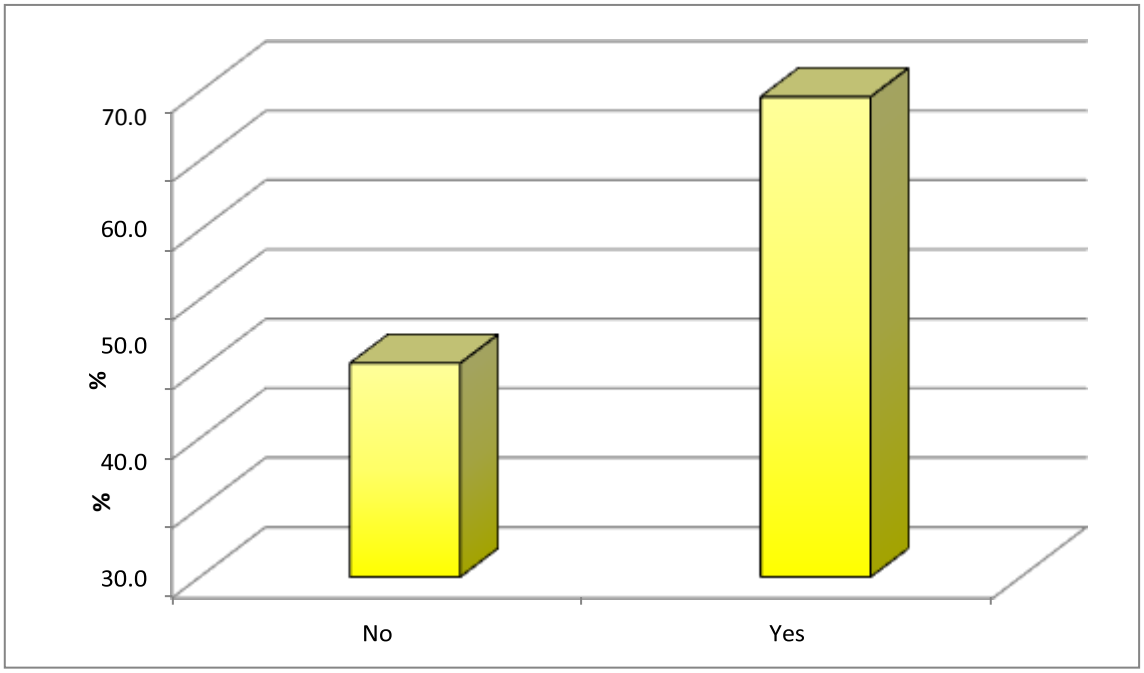

Figure (2): Distribution of CIN patient in group (B) after treated Spironolactone