Original Article

DOI: 10.17354/ijss/2016/228

Usefulness of Bolus Intravenous Sodium Bicarbonate in Prevention of Contrast-Induced Nephropathy in Patients Undergoing Percutaneous Cardiac Interventions

G Varghese[1], Sethu Babu[2], V Kiron[3], S S Iyengar[4]

[1]Assistant Professor, Department of Cardiology, Pushpagiri Medical College, Thiruvalla, Kerala, India, [2]Associate Professor, Department of Critical Care, Pushpagiri Medical College, Thiruvalla, Kerala, India, [3]Professor and Head, Department of Cardiology, St. Johns Medical College, Bengaluru, Karnataka, India, [4]Senior Consultant, Department of Cardiology, Manipal Hospitals, Bengaluru, Karnataka, India

Abstract

Introduction: Contrast-induced nephropathy (CIN) is the third most common cause for acute kidney injury and occurs in 13-2s0% of patients undergoing catheter procedures.

Materials and Methods: A study was conducted to assess the effectiveness of an additional intravenous bolus soda bicarbonate to the standard regimen which was followed in our institution (i.e., 12 h hydration and 3 days of N-acetyl cysteine).

Results: In this study of 185 patients, the incidence of CIN was not statistically different, but there was a trend toward lower serum creatinine levels and higher estimated glomerular filtration rate (eGFR) in the test group which could suggest a lower incidence of CIN if the sample size was larger.

Conclusion: Significant improvement in eGFR was seen in patients who received sodium bicarbonate in addition to the standard treatment.

Key words: Contrast induced nephropathy, Estimated glomerular filtration rate, Intravenous sodium bicarbonate, N acetyl cysteine

INTRODUCTION

Contrast-induced nephropathy (CIN) is estimated to occur in up to 13-20% of patients with chronic renal impairment undergoing cardiac catheterization. 0.5-12% of these patients require hemodialysis and longer hospitalization. Therapeutic measures available for decreasing CIN includes (1) Hydration with saline, (2) N-acetyl cysteine (NAC), and (3) intravenous (IV) sodium bicarbonate. Recent studies have suggested that a single bolus IV administration of sodium bicarbonate is more protective than plain hydration alone in the prevention of CIN. This finding has to be validated in the South Indian population and compared with the previous data from studies done in other populations.

Access this article online

www.ijss-sn.com

Month of Submission : 03-2016
Month of Peer Review : 03-2016
Month of Acceptance : 04-2016
Month of Publishing : 04-2016

Aim and Objectives

1. To estimate the burden of CIN in South Indian population undergoing cardiac interventions
2. To compare the efficacy of IV sodium bicarbonate with isotonic saline and NAC versus isotonic saline and NAC to prevent CIN in patients with renal dysfunction undergoing cardiac interventions.

MATERIALS AND METHODS

Patients with mild to moderate renal dysfunction undergoing cath procedures were randomised to test and control groups according to randomisation table. 105

Corresponding Author: Dr Varghese George, Assistant Professor, Department of Cardiology, Pushpagiri Heart Institute, Thiruvalla - 689101, Kerala, India. Email: drvgcardio@outlook.com

patients were randomised to test group (Group A) and 80 patients to control group (Group B).

Group A (sodium bicarbonate + hydration + NAC)

Or

Group B (hydration + NAC)

Patients in the Group A received single bolus IV administration of sodium bicarbonate (25 ml of 7.5% $NaHCO_3$ = 22.5 meq) 5 min before the contrast exposure in addition to standard hydration and NAC.

Standard hydration consisted of 0.9% NaCl at 1 ml/kg/h (0.5 ml/kg/h for patients with left ventricular ejection fraction [LVEF] <40%) for 12 h. Diuretics were withheld for the day of the procedure. NAC was given at 1200 mg twice daily 1 day before the procedure and 2 days after the procedure.

Non-ionic contrast agent was used for all patients. Elective procedures were done using the radial/femoral approach. Serum creatinine and S.K+ levels were measured at baseline and on day three after the procedure.

The primary endpoint was the development of CIN defined as an increase in the creatinine of >25% or >0.5 mg/dl within the first 3 days after the procedure compared to baseline.

Inclusion Criteria

1. Age >18 years
2. eGFR between 30 and 90 ml/m
3. Elective coronary angiograms/percutaneous coronary interventions/cardiac catheterizations/peripheral angiograms.

Exclusion Criteria

1. Allergy to contrast medium
2. Pregnancy
3. Dialysis dependency
4. Exposure to contrast agent within the preceding 48 h of the study
5. Class 4 NYHA heart failure
6. LVEF <20%
7. Single functioning kidney
8. Use of concomitant nephrotoxic agents.

RESULTS

The baseline characteristics were similar in the test group and control group. The mean amount of contrast used was also similar (Table 1).

The majority of procedures done in the test group were coronary angiograms (Group A) (Graph 1).

The majority of procedures done in the test group were also coronary angiograms (Group B) (Graph 2).

Table 2 shows that there was a statistically significant improvement in eGFR in the test group. There was an improvement in creatinine values also which did not reach statistical significance (Table 2).

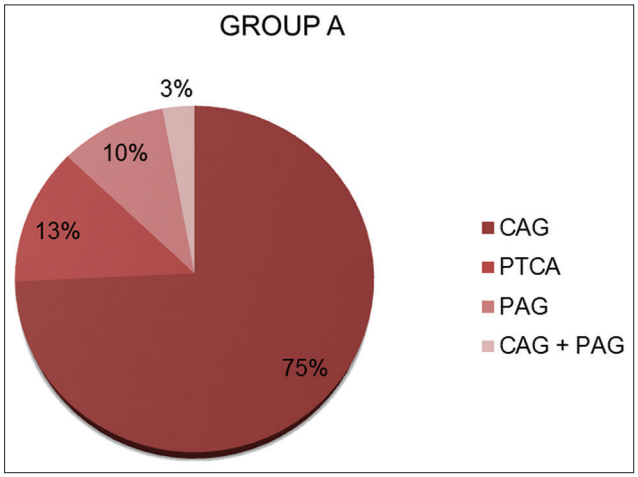
Table 3 shows that there was no statistically significant difference of baseline creatinine or day 3 creatinine between the test and control groups.

Graph 3 depicts in a bar diagram format the baseline and day 3 creatinine of Group A (test group) and baseline and day 3 creatinine of Group B (control group). There is a decrease in the serum creatinine on day 3 in the test group but it was not statistically significant (Graph 3).

Table 4 compares the baseline eGFR of test versus control groups and day 3 eGFR of test versus control groups. A statistically significant improvement in eGFR was observed in the test group on day 3 with $P = 0.01$ (Table 4).

Table 1: Baseline characteristics of the test group (Group A) versus the control group (Group B)

Characteristics	Group A -105 (test)	Group B - 80 (control)	*P* value
Mean age	57.60 years	59.60 years	-
Males (%)	45 (71.4)	48 (76.2)	0.69
Diabetes (%)	37 (58.73)	35 (55.55)	0.86
Hypertension (%)	46 (73)	43 (68.25)	0.70
Dyslipidemia (%)	34 (53.97)	40 (63.49)	0.37
Smoking (%)	33 (52.38)	36 (57.14)	0.72
Contrast volume	58 ml	61 ml	0.69



Graph 1: The cath procedures done in Group A

Table 2: A comparison of baseline creatinine versus day 3 creatinine and baseline eGFR versus day 3 eGFR in Group A and B

Groups	*P* value
Group A	
Creat baseline versus creat D3 (1.26 vs. 1.21)	0.11
eGFR baseline versus eGFR D3 (58.19 vs. 62.49)	0.02
Group B	
Creat baseline versus creat D3 (1.26 vs. 1.29)	0.17
eGFR baseline versus eGFR D3 (56.37 vs. 54.86)	0.19
Group A versus Group B	
Creat baseline Group A versus Group B (1.257 vs. 1.263)	0.87
Creat D3 Group A versus Group B (1.211 vs. 1.294)	0.12

eGFR: Estimated glomerular filtration rate

Table 3: A comparison of baseline creatinine values of test and control group and day 3 creatinine values of test and control group

Group A versus Group B	*P* value
Creat baseline Group A versus Group B (1.257 vs. 1.263)	0.87
Creat D3 Group A versus Group B (1.211 vs. 1.294)	0.12

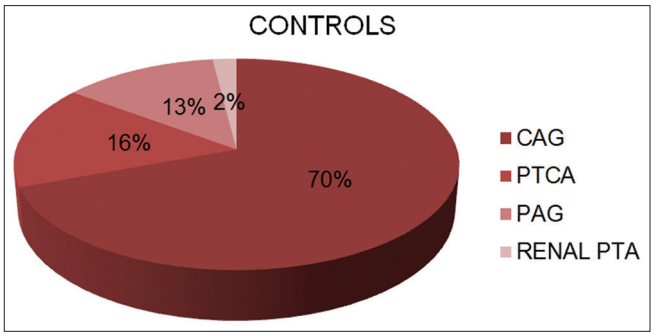
Table 4: A comparison of baseline eGFR values of test versus control group and day 3 eGFR values of test versus control group

Group A versus Group B	*P* value
eGFR baseline Group A versus Group B	0.40
eGFR D3 Group A versus Group B	0.01

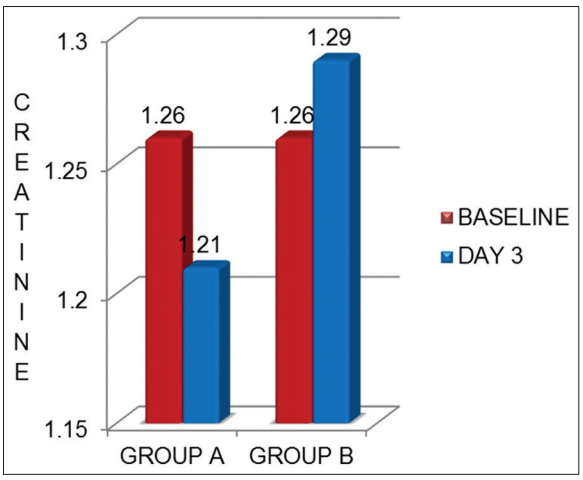
eGFR: Estimated glomerular filtration rate

Graph 4 depicts in a bar diagram format the baseline and day 3 eGFR of Group A (test group) and baseline and day 3 eGFR of Group B (control group). There is an increase in the eGFR on day 3 in the test group, whereas in the control group there was a decrease of eGFR (Graph 4).

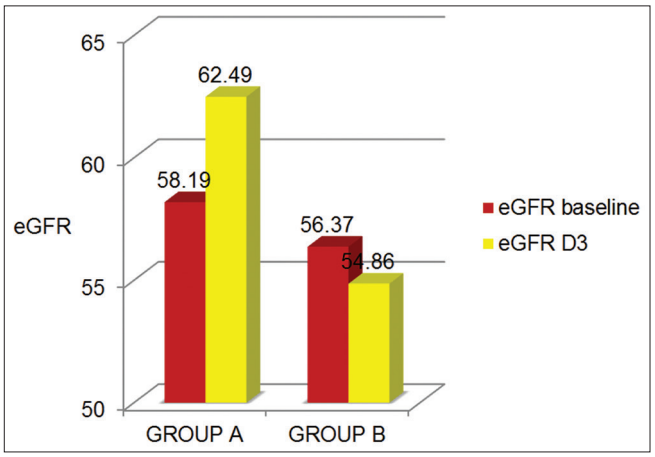
The incidence of primary endpoint – CIN was 3.78% (7 patients) in the study 3.81% (4 patients) in the Group A and 4.76% (3 patients) in the Group B (*P* – 0.65). There was no statistically significant difference in the primary endpoint CIN between the test and control groups. The majority of patients who developed CIN had a percutaneous transluminal coronary angioplasty as the cath procedure, which may be due to the higher amount of contrast used (Graph 5).



Graph 2: The cath procedures done in Group B



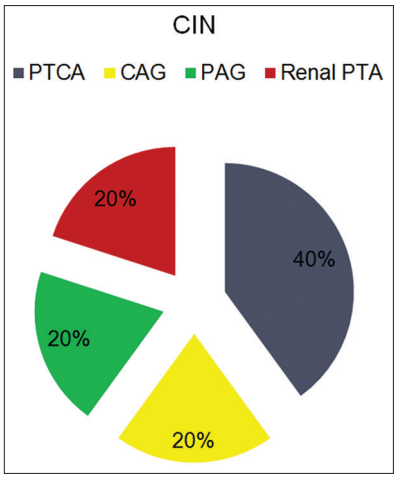
Graph 3: A graph comparing baseline creatinine values of test and control group and day 3 creatinine values of test and control group



Graph 4: A graph comparing baseline estimated glomerular filtration rate (eGFR) values of test and control group and day 3 eGFR values of test and control group

DISCUSSION

CIN occurs in 13-20% patients following IV contact administration. It is defined as an increase in serum creatinine by 25% from baseline or an increase in absolute value by 0.5 mg/dl within 48-72 h of exposure to contrast material. The incidence is more in patients with prior kidney disease, diabetes mellitus, dehydration, congestive heart failure, larger volumes of contrast used, and in patients with recent exposure to contrast material (<48 h).[1]



Graph 5: The procedures done for 7 patients who developed contrast induced nephropathy expressed in percentage

There are various mechanisms by which contrast agents cause kidney damage. They are:

1. Direct cytotoxic effect on the renal proximal tubular cells
2. Increased cellular damage by reactive O_2 species
3. Increased resistance to blood flow
4. Renal vasoconstriction particularly in deeper portions of outer medulla:
   a. By direct action on V.S.M.C
   b. From metabolites such as adenosine and endothelian
   c. Osmotic contrast agents decrease water reabsorption leading to increased interstitial pressures:
      - Decreases GFR and causes local compression of vasa recta.
5. Contrast agents increase resistance to blood flow by increasing blood viscosity and increasing red cell deformability:
   - This sludging generates local ischemia
   - Activate reactive oxygen species that result in tubular damage at a cellular level.[2,3]

The cornerstone for prevention of CIN is hydration. The renal blood flow is compromised for about 20 h following a contrast administration. Intravascular volume expansion maintains renal blood flow, preserves NO production, prevents hypoxemia, and increases contrast elimination.[4-7]

A number of other strategies are also investigated including statins, IV soda bicarbonate, NAC, vitamin C, theophylline, aminophylline, and even hemodialysis.

IV sodium bicarbonate has many proposed mechanisms of action.[8,9] $NaHCO_3$ makes urine more alkaline and thus increases free radical and peroxide-mediated injury as they are generated more in an acidic environment.[10]

Most of the previous systematic reviews and relevant meta-analyses demonstrated that IV $NaHCO_3$ could decrease the incidence of CIN.[11-21] However, secondary endpoints like RRT and mortality were not improved with soda bicarbonate therapy. The result of this study did not show any significant differences in the incidence of CIN among patients who received IV saline plus NAC versus those who received additional $NaHCO_3$ as a single IV bolus. The overall incidence of CIN was very low which was probably due to the aggressive hydration protocol. There was even one study from Mayo clinic wherein they found that $NaHCO_3$ was associated with an increase in incidence of CIN.[22]

Although it was not statistically significant, there was a trend which could suggest an added benefit of $NaHCO_3$ and NAC, when the changes in creatinine values were analyzed. The reason for not reaching a statistically meaning conclusion may be the smaller size of the study group. With more patients trend might have reached statistical significance. The patients needed for a statistically significant study was much higher than our initial calculation. The remedial trial, with a much larger sample size, was an adequately powered study and it demonstrated a significant benefit from addition of IV $NaHCO_3$ to the existing therapies.[23]

A number of trials and meta-analyses have found that a combination of NAC and $NaHCO_3$ is superior to either agent used alone in the prevention of CIN. Three studies on patients who got NAC in both groups and additional $NaHCO_3$ for the test group favored the $NaHCO_3$ group.[23-25]

In a study hydration with $NaHCO_3$ in addition to NAC high dose was associated with lesser incidence of CIN in the setting of urgent percutaneous coronary intervention for ST-elevation myocardial infarction.[26] However, in studies done by Yang *et al.* and Thayssen *et al.*, they could not derive any additional benefit by addition of IV $NaHCO_3$.[27,28] Our study was in mild to moderate renal dysfunction patients and probably the incidence of CIN was too low in this group of patients with intense hydration. Hence, a large-scale well designed randomized controlled trials is required to determine whether $NaHCO_3$ in addition to hydration and NAC is more useful.

CONCLUSIONS

1. Intensive hydration is the cornerstone for prevention of CIN and it can reduce the incidence of CIN to very low levels
2. Addition of sodium bicarbonate was not more effective to reduce the incidence of CIN in our patients with mild to moderate renal dysfunction

3. Significant improvement in eGFR was seen in patients who received sodium bicarbonate in addition to the standard treatment.

LIMITATIONS

The incidence of primary endpoint was very low in the study. Studies in larger subset of patients will be required to derive a conclusion.

REFERENCES

1. Caixeta A, Nikolsky E, Mehran R. Prevention and treatment of contrast-associated nephropathy in interventional cardiology. Curr Cardiol Rep 2009;11:377-83.
2. Lameire NH. Contrast-induced nephropathy – Prevention and risk reduction. Nephrol Dial Transplant 2006;21:i11-23.
3. (Guideline) Department of Veteran Affairs Department of Defense. VA/DOD Clinical Practice Guideline for Management of Chronic Kidney Disease in Primary Care December 2014. Available from: http://www.guideline.gov/content.aspx?Id=48951. [Last accessed on 2016 Apr 5].
4. Solomon R. Radiocontrast-induced nephropathy. Semin Nephrol 1998;18:551-7.
5. Mueller C. Prevention of contrast-induced nephropathy with volume supplementation. Kidney Int Suppl 2006:S16-9.
6. Pannu N, Wiebe N, Tonelli M; Alberta Kidney Disease Network. Prophylaxis strategies for contrast-induced nephropathy. JAMA 2006;295:2765-79.
7. Friedewald VE, Goldfarb S, Laskey WK, McCullough PA, Roberts WC. The editor's roundtable: Contrast-induced nephropathy. Am J Cardiol 2007;100:544-51.
8. Atkins JL. Effect of sodium bicarbonate preloading on ischemic renal failure. Nephron 1986;44:70-4.
9. McCullough PA, Adam A, Becker CR, Davidson C, Lameire N, Stacul F, *et al.* Risk prediction of contrast-induced nephropathy. Am J Cardiol 2006 18;98:27K-36.
10. Burgess WP, Walker PJ. Mechanisms of contrast-induced nephropathy reduction for saline (NaCl) and sodium bicarbonate (NaHCO3). Biomed Res Int 2014;2014:510385.
11. Meier P, Ko DT, Tamura A, Tamhane U, Gurm HS. Sodium bicarbonate-based hydration prevents contrast-induced nephropathy: A meta-analysis. BMC Med 2009;7:23.
12. Trivedi H, Nadella R, Szabo A. Hydration with sodium bicarbonate for the prevention of contrast-induced nephropathy: A meta-analysis of randomized controlled trials. Clin Nephrol 2010;74:288-96.
13. Hogan SE, L'Allier P, Chetcuti S, Grossman PM, Nallamothu BK, Duvernoy C, *et al.* Current role of sodium bicarbonate-based preprocedural hydration for the prevention of contrast-induced acute kidney injury: A meta-analysis. Am Heart J 2008;156:414-21.
14. Joannidis M, Schmid M, Wiedermann CJ. Prevention of contrast media-induced nephropathy by isotonic sodium bicarbonate: A meta-analysis. Wien Klin Wochenschr 2008;120:742-8.
15. Ho KM, Morgan DJ. Use of isotonic sodium bicarbonate to prevent radiocontrast nephropathy in patients with mild pre-existing renal impairment: A meta-analysis. Anaesth Intensive Care 2008;36:646-53.
16. Navaneethan SD, Singh S, Appasamy S, Wing RE, Sehgal AR. Sodium bicarbonate therapy for prevention of contrast-induced nephropathy: A systematic review and meta-analysis. Am J Kidney Dis 2009;53:617-27.
17. Brar SS, Hiremath S, Dangas G, Mehran R, Brar SK, Leon MB. Sodium bicarbonate for the prevention of contrast induced-acute kidney injury: A systematic review and meta-analysis. Clin J Am Soc Nephrol 2009;4:1584-92.
18. Kanbay M, Covic A, Coca SG, Turgut F, Akcay A, Parikh CR. Sodium bicarbonate for the prevention of contrast-induced nephropathy: A meta-analysis of 17 randomized trials. Int Urol Nephrol 2009;41:617-27.
19. Hoste EA, De Waele JJ, Gevaert SA, Uchino S, Kellum JA. Sodium bicarbonate for prevention of contrast-induced acute kidney injury: A systematic review and meta-analysis. Nephrol Dial Transplant 2010;25:747-58.
20. Kunadian V, Zaman A, Spyridopoulos I, Qiu W. Sodium bicarbonate for the prevention of contrast induced nephropathy: A meta-analysis of published clinical trials. Eur J Radiol 2011;79:48-55.
21. Jang JS, Jin HY, Seo JS, Yang TH, Kim DK, Kim TH, *et al.* Sodium bicarbonate therapy for the prevention of contrast-induced acute kidney injury – A systematic review and meta-analysis. Circ J 2012;76:2255-65.
22. From AM, Bartholmai BJ, Williams AW, Cha SS, Pflueger A, McDonald FS. Sodium bicarbonate is associated with an increased incidence of contrast nephropathy: A retrospective cohort study of 7977 patients at mayo clinic. Clin J Am Soc Nephrol 2008;3:10-8.
23. Briguori C, Airoldi F, D' Andrea D, Bonizzoni E, Morici N, Focaccio A, *et al.* Renal insufficiency following contract media administration trial (REMEDIAL): A randomized comparison of 3 preventive strategies. Circulation 2007;115:1211-7.
24. Recio-Mayoral A, Chaparro M, Prado B, Cózar R, Méndez I, Banerjee D, *et al.* The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcystine in patients undergoing emergency percutanous coronary intervention: The Reno study. J Am Coll Cardiol 2007;49:1283-8.
25. Mahmoodi K, Sohrabi B, Ilkhchooyi F, Malaki M, Khaniani ME, Hemmati M, *et al.* The efficacy of hydration with normal saline versus hydration with sodium bicarbonate in the prevention of contrast-induced nephropathy. Heart Views 2014;15:33.
26. Leone AM, De Caterina AR, Sciahbasi A, Aurelio A, Basile E, Porto I, *et al.* Sodium bicarbonate plus N-acetylcysteine to prevent contrast-induced nephropathy in primary and rescue percutaneous coronary interventions: The BINARIO (BIcarbonato e N-Acetil-cisteina nell'infaRto mIocardico acutO) study. EuroIntervention 2012;8:839-47.
27. Yang K, Liu W, Ren W, Lv S. Different interventions in preventing contrast-induced nephropathy after percutaneous coronary intervention. Int Urol Nephrol 2014;46:1801-7.
28. Thayssen P, Lassen JF, Jensen SE, Hansen KN, Hansen HS, Christiansen EH, *et al.* Prevention of contrast-induced nephropathy with N-acetylcysteine or sodium bicarbonate in patients with ST-segment-myocardial infarction: A prospective, randomized, open-labeled trial. Circ Cardiovasc Interv 2014;7:216-24.

How to cite this article: Varghese G, Babu S, Kiron V, Iyengar SS. Usefulness of Bolus Intravenous Sodium Bicarbonate in Prevention of Contrast Induced Nephropathy in Patients Undergoing Percutaneous Cardiac Interventions. Int J Sci Stud 2016;4(1):258-262.

Source of Support: Nil, **Conflict of Interest:** None declared.