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Original Research Article

Prevention of Acute Renal Failure Post Cardiac Surgery under Cardiopulmonary Bypass Using Preoperative Infusion of Sodium Bicarbonate: A Prospective Randomized Controlled Trial

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ABSTRACT

Introduction: Acute renal dysfunction is a common and serious postoperative complication of cardiopulmonary bypass. Theoretically alkalinisation can protect acute kidney injury post cardiopulmonary bypass.
Methods: In a prospective randomized controlled trial we enrolled 200 adult patients undergoing open heart surgery with the use of cardiopulmonary bypass (CPB). 100 patients received 150ml of 7.5% sodium bicarbonate (SBIC) mixed to 750 ml of 5% dextrose, infused at 1 ml/kg/hour through a dedicated intravenous line for 6 hours prior to the initiation of CPB and 100 patients (control group) received 0.9% sodium chloride given at same rate and volume. Post-operative serum creatinine, urine output, increase in serum creatinine value and several other parameters were evaluated. The primary endpoint was the proportion of patients developing acute kidney injury.
Results: Renal replacement therapy (RRT) was initiated in 8.2% of patients in the Control group and 7.2%ofpatients in the SBIC group. Time to initiateRRTwas29.0 (19.0to39.0) hrs in the Control group and 35.5(24.5to49.0) hrs in the SBIC group (P value not significant).
Conclusion: In our study urinary alkalinisation using sodium bicarbonate infusion was not found to reduce the incidence of acute kidney injury following open heart surgery; however less number (7.2%) of the patients in SBIC group required RRT than 8.2% patients of the control group. There were no differences indirect or indirect measures of morbidity and mortality in both groups. However a larger sample and a multi-centre trial may yield different outcome.

Key words: Acute kidney injury; cardiopulmonary bypass; sodium bicarbonate.

INTRODUCTION

With over one million operations a year, cardiac surgery with cardiopulmonary bypass is one of the most common major surgical procedures worldwide. [1] Acute renal dysfunction is a common and serious postoperative complication of cardiopulmonary bypass and may affect 25% to 50% of patients.[2-4] Acute renal dysfunction carries significant costs, [4] and is independently associated with increased morbidity and mortality. Urinary acidity may enhance the generation and toxicity of reactive oxygen species induced by cardiopulmonary bypass. [8] Urinary alkalinisation may protect from renal injury. To date, no simple, safe, and effective intervention to

prevent cardiopulmonary bypass associated acute renal dysfunction in a broad patient population has been found. [11-14]

The use of sodium bicarbonate has shown efficacy in reducing the incidence of ARF due to contrast-induced nephropathy in those patients with moderate, [6] stable renal dysfunction. The postulated mechanism of renal protection has been described through the prevention of free radical generation and damage. [7] If it is presumed that initiation and extension of ischemic renal injury occurs during cardiac surgery via oxidant injury, [5] the use of sodium bicarbonate to disrupt this process could possibly be an effective therapeutic option to prevent ARF.

The generation of a higher renal proximal tubule pH with bicarbonate therapy may slow down the superoxide-generating Haber-Weiss reaction, limiting the formation of free radical oxidants. In addition, sodium bicarbonate may be directly scavenging reactive oxygen species generated from nitric oxide, at a physiologic PH. [15]

The objective of this study is to evaluate the renal protective effect of near-isotonic sodium bicarbonate as compared to sodium chloride when given as prophylaxis to patients with chronic kidney disease prior to non-emergent surgery involving the use of cardiopulmonary bypass.

My hypothesis is that bicarbonate therapy may disrupt ischemia-induced, oxidant-mediated injury and this may prevent the propagation of renal damage. These events may be demonstrated clinically by a reduced incidence of ARF following surgery, decreased requirements for renal replacement therapy after surgery, and improved survival both in perioperative and in a longer-term follow up.

Aims & Objectives: To evaluate whether sodium bicarbonate (SBIC) is effective in reducing kidney injury that may occur following cardiac surgery using cardiopulmonary bypass.

MATERIALS & METHODS

The study was conducted at a tertiary care hospital with a huge load for open heart surgery. This is a prospective randomized controlled trial. Total 200 adult patients undergoing open heart surgery with the use of cardiopulmonary bypass (CPB) were enrolled and were randomly divided into two groups as test and control. Postoperatively serum creatinine value is checked for 1st 7 days (1st, 3rd and 7th postoperative days), and 25% increase in serum creatinine from preoperative baseline value was considered as positive one. Other co-morbidities and risk factors associated with acute kidney injury will also be studied.

Randomization: Randomization done by peaking a paper in which case or control was written.

Consent:

All patients gave written consent for undergoing the procedure.

Ethical committee clearance was taken and the study was approved by our ethical committee board.

Inclusion Criteria: (a)Age 18-65 years of both sex,(b)Elective or urgent CABG +/- valve surgery, or elective or urgent isolated valve surgery, (c)Exposure to cardio-pulmonary bypass time within one and half hour. (d)Pre-operative GFR within 60ml per minute (stable creatinine for last 1 month), (e)Non-diabetic patients

Exclusion Criteria: (a)Emergency CABG, cardiac transplantation or insertion of VAD, (b)Planned off-pump surgery (c)N-acetyle cysteine given 72 hours prior to operation, (d)Radio contrast given 48 hours prior to operation (e)Acute renal failure (greater than 25% increase of serum creatinine from pre-admission baseline) (f)Prior renal transplant operation. (g)LVEF less than or equals to 20% (h)Diabetic patients. The Study span

was 2 years from1st February, 2012 to 31st January 2015.

Parameter studied: Demographic and clinical characteristics, Pre-operative renal function status, Serum creatinine level in last 1months (Table 1), Identification of risk factors like increased age, valvular surgery (Graph 1), duration of cardiopulmonary bypass etc, Postoperative serum urea, creatinine value and urine output. Increase in serum creatinine value by 44micromole per litre or by 25% within first 7 days of surgery (serum creatinine will be measured on 1st,3rd,and 7th postoperative day) (Table 2), ICU stay, Hospital stay, Other co-morbidities related to acute renal failure, Mean Arterial Pressure, serum creatinine, urine output 1st,3rd,7th postoperative day, Drugs used, Sepsis present or not, requirement of mechanical ventilation, incidence of renal replacement therapy, side effects of Bicarbonate therapy such as - hypernatremia, metabolic alkalosis etc.

Study technique: Under eligibility criteria at CTVS department, SSKM, who are planned for cardiac surgery under cardiopulmonary bypass were given three ampoules of 7.5% sodium bicarbonate (89.3 mOsm/ampoule; total 150 ml for three ampoules) added to 750 ml of 5% dextrose in water, given at 1 ml/kg/hour through a dedicated intravenous line for 6 hours, and completed prior to the initiation of cardiopulmonary bypass and Control group given 0.9% sodium chloride at 1 ml/kg/hour through a dedicated intravenous line for 6 hours, and completed prior to the initiation of cardiopulmonary bypass.

Statistical analysis: For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS 10.0.1 and Graph Pad Prism version 5. Data have been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. The median and the inter quartile range have been stated for numerical variables that are not normally distributed. viz. Student's independent sample's t-test was applied to compare normally distributed numerical variables between groups, Mann Whitney U-test was employed for intergroup comparison of non-parametric numerical variables. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

RESULTS

Renal Outcome: Patients in the SBIC group had a higher diuresis within the first 24 hours after surgery. No differences were observed in the use of diuretics. Renal replacement therapy (RRT) was initiated in 8.2% of patients in the Control group and 7.2%ofpatients in the SBIC group. Time to initiation of RRT was 29.0 (19.0to39.0) hrs in the Control group and 35.5 (24.5to49.0) hrs in the BIC group (P value not significant). The specific changes in plasma creatinine, eGF Rand the grading according to the Acute Kidney Injury Network criteria are depicted in Table 2 & 3.

Table 1: Comparison of demographic characteristics of patients

	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
Age (yrs)	Case	43.6100	7.5784	32.0000	58.0000	43.5000	0.0202
	Control	44.1600	7.8209	32.0000	58.0000	46.0000	
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
Weight (Kg)	Case	50.7100	4.0609	44.0000	56.0000	49.0000	0.8894
	Control	50.7900	4.0634	44.0000	56.0000	51.0000	
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
Height (Cm)	Case	158.3400	3.8012	152.0000	164.0000	159.0000	0.7640
	Control	158.1800	3.7237	152.0000	164.0000	158.5000	

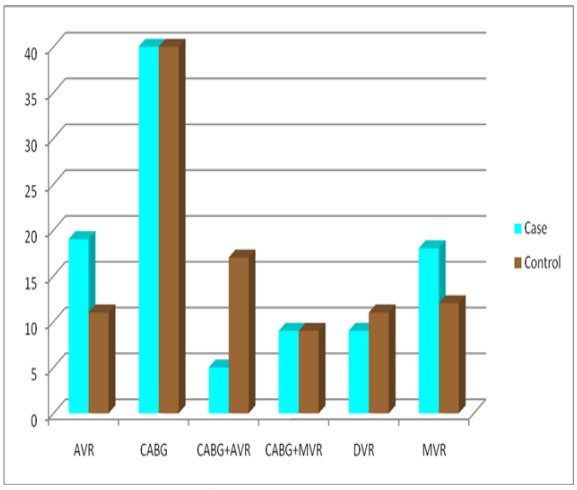
P- Value for all the variables were comparable preoperatively

Table: 2 Distribution of Pre-op and Post-op Serum Creatinine (mg/dl) in cases and control

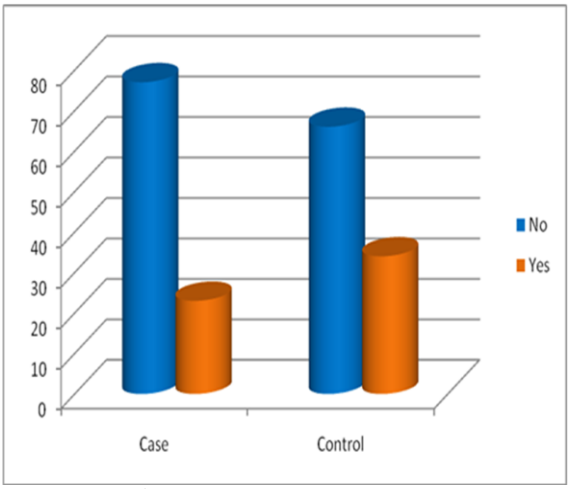
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
Pre-op Serum Creatinine (mg/dl)	Case	1.4573	.0255	1.4200	1.4900	1.4600	
	Control	1.4588	.0253	1.4200	1.4900	1.4600	0.6768
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
1st Post-op Serum Creatinine (mg/dl)	Case	2.3067	1.5441	1.6000	8.5300	1.7300	
	Control	2.6006	1.7814	1.5600	8.5300	1.7100	0.2140
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
3rd Post-op Serum Creatinine (mg/dl)	Case	2.2267	1.6416	1.5800	8.3100	1.6900	
	Control	2.5406	2.0998	1.5800	8.4500	1.6900	0.2403
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
7th Post-op Serum Creatinine (mg/dl)	Case	1.8928	1.1585	1.4400	5.9000	1.5100	
	Control	2.0788	1.3885	1.4400	6.1000	1.5300	0.3049

Table: 3 Distribution of 1st Post-op UO (ml/24hrs) in cases and controls

	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
1st Post-op UO (ml/24hrs)	Case	2565.7400	838.1720	64.0000	2996.0000	2828.0000	
	Control	2448.8000	966.0079	56.0000	2998.0000	2818.0000	0.3616
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
3rd Post-op UO (ml/24hrs)	Case	2526.8600	829.8889	69.0000	3010.0000	2754.0000	
	Control	2433.3100	962.9510	56.0000	3048.0000	2755.0000	0.4627
	Group	Mean	Std Dev	Minimum	Maximum	Median	p-value
7th Post-op UO (ml/24hrs)	Case	2658.1600	478.3063	1043.0000	3083.0000	2775.0000	
	Control	2620.9500	554.8594	1002.0000	3048.0000	2814.5000	0.5079



Graph-1: Type of procedure done in both groups



Distribution of Acute Kidney Injury in cases (SBIC group) and controls

General clinical outcome: Despite comparable postoperative ventilation times, duration of treatment in the ICU and in the high dependency unit (HDU) was significantly prolonged in the BIC group. No differences indirect or indirect measures of morbidity and mortality were observed in both groups.

DISCUSSION

Acute kidney injury (AKI) is not only a frequent complicationincardiac surgical patient, [1] but has also been shown to be independently associated with morbidity and mortality. [2] Unfortunately, little progress has been made within the last years in the development of strategies to reduce the incidence and improve the prognosis of this complication.

Recently, Haase and coworkers have elegantly delineated a pathophysiological line of evidence that the severity of the renal insult induced byon-pumpcardiac surgery may, at least in part, be related to the degree of haemoglobinuria: the histological features of CSA-AKI resemble the pigment nephropathy typically observed during rhabdomyolysis. [9,10] Since alkalization of the urine is among the established measures to treat rhabdomyolysis, [11,12] they used this

concept successfully as a strategy for the prevention of CSA-AKI in a small pilot trial, [7] into our clinical study. It is of note that anointer disciplinary working group on this topical so gave a positive recommendation to use hydration and bicarbonate to reduce the nephrotoxic effects of myoglobinuria and haemoglobinuria. [14]

In contrast to these promising findings, the results of the present prospective observational cohort study show that, in heterogeneous patient population and under the real life conditions Govt. hospital, perioperative treatment with BIC does not reduce the incidence of CSA-AKI as measured by postoperative changes in creatinine, and the need for dialysis.

CONCLUSION

In our study urinary alkalinisation using sodium bicarbonate infusion was not found to reduce the incidence of acute kidney injury following open heart surgery, however less number (7.2%) of the patients in SBIC group required RRT than 8.2% patients of the control group. There were no differences indirect or indirect measures of morbidity and mortality in both groups. However a larger sample and a multi-centre trial may yield different outcome.

REFERENCES

1. Albert MA, Antman EM: Preoperative evaluation for cardiac surgery. *In:* Cardiac Surgery in the Adult. Cohn LH, Edmunds LH Jr (Eds). New York, McGraw-Hill, 2003, pp 235–248
2. Chertow GM: Independent associations between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104:343–348
3. Stafford-Smith M, Podgoreanu M, Swaminathan M, et al: Association of genetic polymorphisms with risk of renal injury after coronary bypass graft surgery. *Am J Kidney Dis* 2005; 45:519–530
4. Ghotkar SV, Grayson AD, Fabri BM, et al: Preoperative calculation of risk for prolonged intensive care unit stay following coronary artery bypass grafting. *J Cardiothorac Surg*,2006; 1:14
5. Lassnigg A, Schmidlin D, Mouhieddine M, et al: Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: A prospective cohort study. *J Am Soc Nephrol* 2004; 15:1597–1605
6. Zanardo G, Michielon P, Paccagnella A, et al: Acute renal failure in the patient undergoing cardiac operation. Prevalence, mortality rate, and main risk factors. *J Thorac Cardiovasc Surg* 1994; 107:1489–1495
7. Doi K, Suzuki Y, Nakao A, et al: Radical scavenger edaravone developed for clinical use ameliorates ischemia/reperfusion injury in rat kidney. *Kidney Int* 2004; 65: 1714–1723
8. McCord JM: Oxygen-derived free radicals in postischemic tissue injury. *N Engl J Med* 1985; 312:159–163
9. Zager RA, Gamelin LM: Pathogenetic mechanisms in experimental hemoglobinuric acute renal failure. *Am J Physiol* 1989; 256: F446–F455
10. Paller MS: Hemoglobin- and myoglobin induced acute renal failure in rats: Role of iron in nephrotoxicity. *Am J Physiol* 1988; 255: F539–F544
11. Bove T, Landoni G, Calabro MG, et al: Renoprotective action of fenoldopam in high-risk patients undergoing cardiac surgery: A prospective, double-blind, randomized clinical trial. *Circulation* 2005; 111: 3230 –3235.
12. Burns KE, Chu MW, Novick RJ, et al: Perioperative *N*-acetylcysteine to prevent renal injury in high-risk patients undergoing CABG surgery: A randomized controlled trial. *JAMA* 2005; 294:342–350
13. Haase M, Haase-Fielitz A, Bagshaw SM, et al: A phase II randomized controlled trial of high-dose *N*-acetylcysteine in high-risk cardiac

surgery patients. *Crit Care Med* 2007;35:1324–1331
14. Mentzer RM Jr, Oz MC, Sladen RN, et al: Effects of perioperative nesiritide in patients with left ventricular injury undergoing cardiac surgery. *J Am Coll Cardiol* 2007; 49: 716–726
15. Halliwell B, Gutteridge JM: Role of free radicals and catalytic metal ions in human disease: An overview. *Methods Enzymol* 1990; 186:1–85.

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