PERIOPERATIVE INTRAVENOUS SODIUM BICARBONATE TO PREVENT RENAL DYSFUNCTION AFTER OPEN HEART SURGERY

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ABSTRACT

Background: Renal dysfunction is acommon complication of cardiac surgery after cardiopulmonary bypass. Many interventions try to solve this problem.

Objective: to determine whether perioperative intravenous sodium bicarbonate can preserve renal function or not after cardiopulmonary bypass in cardiac surgery.

Patients and methods: Double blind controlled study was done in the period from March to September 2011 in cardiothoracic operating rooms then completed in surgical intensive care unit. Fifty patients were scheduled for elective valvular heart surgery and randomized into two groups, group A (25 patients) received IV sodium bicarbonate and group B (25 patients) received sodium chloride as control group.

Intervention:The patientsreceived IV sodium bicarbonate or sodium chloride after induction of anaesthesia.Sodium bicarbonate bolus dose 0.5 mmoL/kg diluted in 250 ml glucose 5% was given followed by 0.1 mmol/kg/h diluted in 1000 ml glucose postoperative in the first 24 hour maintenance infusion dose. Similar volumes of sodium chloride were given.

Results: There was no significant difference between two groups as regard personal data, type of valve surgery, cardio pulmonary bypass time,and aortic cross clamp time. There was significant decrease ($P < 0.05$)in total number of cases in which serum creatinine increased and acute kidney injury occured(in group A 14/25 and in group B 24/25). There was a significant difference between both groups regardingserumcreatinine and urinaryneutrophil gelatinase-associated lipocalin(NGAL)($P < 0.001$). There was significant increase in acid base parameters (plasma PH, plasma bicarbonate, urinary PH) in group Acompared to group B.there was significant increase in serum sodium mean values in group A in comparison to group B at 6, 24, 48 and 72 h . **Conclusion:** Intravenous sodium bicarbonate can be used to attenuate serumcreatinineelevation andoccurrence of AKI after cardiopulmonary bypass in cardiac surgery without potential hazard on the patients

Key Words: Sodium bicarbonate, acute kidney injury,cardiopulmonary bypass.

INTRODUCTION

Acute kidney injury (AKI) is a common postoperative complication after cardiopulmonary bypass (CPB)[1].

The term AKI represents the entire spectrum of acute renal failure. Diagnostic criteria for AKI based on acute changes in plasma creatinine level or urine output [2].

The mortality rate after cardiac surgery ranges from 2-8% and increases in patients who develop postoperative acute kidney injury to mortality rate over 60%[3. 4].

Acidity of urine increases generation and toxicity of reactive oxygen species induced by cardiopulmonary bypass which enhance complement activation, all of them sharing in acute kidney injury and tubular haemoglobin cast formation[5,6].Alkalinisation of urine may protect from occurrence of AKI induced by these substances [7].

There is evidence thatSodium bicarbonate may attenuate CPB-associated AKI, potentially directly affecting iron-related toxicity, as indicated by a smaller increase in urinaryneutrophil gelatinase-associated lipocalin (NGAL)[6]

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UrinaryNGAL is an early predicator marker of AKI, morbidity and mortality after CPB [8].

The detrimental effect of CPB on red cell destruction is increased by prolongation of CPB time. Thus, the longer the duration of CPB, the more hemolysis should occur and the more free hemoglobinand free toxic iron secondary to mechanical trauma of red cells within CPB system[9,10].Pigment nephropathy is known to result from hemoglobinuriaand myoglobinuria. During CPB, increasedplasma-free hemoglobin was correlated with early post-operative tubular injury andwas associated with the development of subsequent deterioration of renal function [11].

Aim of this study was to determine whether perioperative intravenous sodium administration bicarbonate can preserve renal function or not after cardiopulmonary bypass in cardiac surgery

PATIENTS AND METHODS

This study was done in cardiothoracic surgical rooms and then was completed in surgical ICU in Zagazig University Hospitals during the period from march to September 2011.After approval of medical ethics committee and taking written consent from the patients, fifty patients with normal serum creatinine levels were scheduled for valvular heart surgery and were randomizedblindly into two groups. Group A in which the patients received sodium bicarbonate 0.5 mmoL/kg 8.4%

diluted in 250 ml glucose 5% (bolus dose) after induction of anaesthesia then followed by 0.1 mmol/kg/h (maintenance infusion dose) diluted in 1000 ml glucose 5% over 24 hours,(total dose of 2 mmol/kg). Group B(control group) received sodium chloride 0.9% with the same amount as group A.

Data collected preoperatively :-

- Personal data as age,weight,gender
- Haemodynamic data (heart rate, blood pressure, C.V.P).
- Blood and urine samples were taken for :
- Serum creatinine.
- Serum urea..
- Urinary NGAL (neutrophil gelatinase-associated lipocalin).
- Arterial blood samples were taken forArterial blood gases and electrolytes (Na^+-K^+).

Intraoperative data collection:

- Type of valvular surgery.
- Haemodynamic data (heart rate, blood pressure, C.V.P).
- Cardiopulmonary bypass time.
- Aortic cross-clamp time
- Mean arterial blood pressure.
- Urine output during 24h after starting CPB.

Postoperative data collected for 3 days in intensive care unit (after 6h, 24h, 48h, 72h).

- Urinary NGAL at 6 h after starting CPB.
- Serum creatinine.
- Urinary PH.
- Arterial blood gases for plasma PH and bicarbonate.
- Serum Na^+, K^+

Diagnostic criteria for acute kidney injury

- An increase in serum creatinine of more than or equal 0.3 mg/dl (≥ 26.4 μmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5 fold from baseline) or reduction in urine output (oliguria of less than 0.5 ml/kg/h for more than 6 hours)[(2)].
- Staging of acute kidney injury (AKI) to stage 1,2,3 was done according to the acute kidney injury network (AKIN)[(2)].

STATISTICAL ANALYSIS

Data collected were analysed between groups with the use of the student t test and for categorical data with the use of fisher's exact test or chi-square test. We considered P valve <0.05 to indicate statistical significance. We record values as means with standard deviation .Odds ratio with 95% confidence interval was used. SPSS version 15.0 (SPSS INC. Chicago, II) was used to perform the statistical analysis .

RESULTS

Patientsdata (table1) showed that there were no significant differences between the two groups regarding age, weight and sex. Also there were no significant differences in the baselinemean values of serum creatinine, serum urea, urinary NGAL.

Intraoperatively there were no significant differences between two groups in type of valvularsurgery, time of cardio pulmonary bypass and aortic cross clamp time also there were no significant differences between two groups in mean arterial pressure and urine output during first 24h after starting CPB (table 2).

There were nostatistical significant difference between two groups in the number of patients with elevation in serum creatinine (25%-50%-100%) from baseline values and in acute kidney injury staging .However ,there was significant decreasein the total number of cases who reported elevation in serum creatinine and AKI (14/25 patients in group A versus 24/25 patients in group B) Odds ratio 0.05, 95% CI (0.0 -0.48),P=0.04 (table 3).

As regard changes inserum creatinine within 72 h after starting CPB,and urinary NGAL at 6 h after starting CPB.There was significant difference between the two groups in serum creatinine change (1.5±0.5 in group A versus 2.5±0.6 mg/dl in group B, p<0.001) similarly, there was significant difference between both groups in the urinary NGAL change (50±1.5 in group A versus 156.4±12.5ng/l in group B, p<0.001) (table 4).

Regarding acid base changes,there were significant differences between two groups at 6, 24, 48 and 72 h, in plasma bicarbonate, arterial PH and urinary PH mean values (P<0.001).However, the alkalosis in group A was not dangerous for the patients(table 5).Also there were significant increase in serum sodium mean values in group A in comparison to group B at 6, 24, 48 and 72 h (P<0.001). however, no patient reported hypernatremia (Na > 150 meq/L) in both groups. In addition there was statistically significant differences between two groups in serum potassium mean values (P<0.05) (table 6).However, two patients reported hypokalemia (K<3.5 meq/L) in group A. finally there were no significant differences between two groups in length of ICU stay (P=0.93) or in hospital mortality (P=1.0) (table 7).

Table (1): preoperative characteristics

	Group A (sodium bicarbonate)	**Group B (sodium chloride)**	**P**
	N=25	**N=25**	
Age (years) X ± SD	42.5±7.1	43.1±6.9	0.76
Gender			
Male	15 60%	17 68%	0.55
Female	10 40%	8 32%	
Weight (kg) X ± SD	76.5±10	77.3±9.1	0.75
SerumCreatinine mg/dL	0.6± 0.17	0.7 ± 0.12	0.17
Serum urea mg/dL	13±3.6	15±2.2	0.11
Urinary NGAL ng/ml	4.8 ± 2.2	4.4 ± 3	0.4

Table (2): intraoperative data

	Group A N=25	**Group B N=25**	**P**
Valve surgery			
-Aortic valve replacement.	10 40.0%	11 44.0%	0.77
-Mitral valve replacement.	6 24.0%	6 24.0%	1.0
-Double valve surgery	9 36.0%	8 32.0%	0.76
Cardiopulmonary bypass time/min	145.1±60	148.6±70	0.85
Aortic cross-clamp time/min	107.3±40	115.7±50	0.51
Mean arterial pressure	74.3±6.0	76.5±5.1	0.16
Urine output (ml)*	2750±500	2800±300	0.9

***Urine outputduring 24 hour after starting CPB**

Table (3): acute kidney injury

	Group A N=25		**Group B N=25**		**Odds ratio (95%)**	**P**
Serum creatinine	N	%	N	%		
>25%	8	32.0	13	52.0	0.43 (0.12-1.58)	0.15
>50%	4	16.0	7	28.0	0.49 (0.1-2.31)	0.3
>100%	2	8.0	4	16.0	0.46 (0.05-3.39)	0.66
Total number of patients with Serum creatinine changes	14	56.0	24	59.0	0.05 (0.0-0.48)	0.04*
Total number of AKI patients	**8**	**44.0**	**14**	**64.0**	**0.44 (0.12-1.59)**	**0.15**
AKI stage 1	**5**	**20.0**	**8**	**32.0**	**0.53 (0.12-2.28)**	**0.33**
AKI stage 2	**2**	**8.0**	**4**	**16.0**	**0.46 (0.05-3.39)**	**0.3**
AKI stage 3	**1**	**4.0**	**2**	**8.0**	**0.48 (0.02-7.51)**	**1.0**

*significant difference **P** <0.05

Table (4): change in serum creatinine andUrinary NGAL

	Group A	**Group B**	**P**
Serum Creatinine mg/dL[#]	1.5±0.5	2.5±0.6	<0.001
Urinary NGAL ng/ml[*]	50±1.5	156.4±12.5	<0.001

P <0.001 high significant difference

 # Mean values within 72 hrs.

*** Mean values at 6 hrs after starting CPB.**

Table (5): Acid base changes

	Group A N=25	**Group B N=25**	**P**
Plasma bicarbonate			
Baseline	25.9±1.5	25.6±1.4	0.46
6 hours	26.7±2.0	24.1±2.0	<0.001
24 hours	29.9±3.0	23.9±1.5	<0.001
48 hours	29.6±3	24±2	<0.001
72 hour	29.9±3	23.89±2.5	<0.001
Plasma PH			
Base line	7.43±0.06	7.42±0.05	0.52
6 hours	7.44±0.05	7.38±0.06	<0.001
24 hours	7.47±0.06	7.37±0.04	<0.001
48 hours	7.46±0.05	7.36±0.06	<0.001
72 hours	7.47±0.05	7.37±0.04	<0.001
Urinary PH			
Base line	5.8±0.1	5.76±0.1	0.16
6	6.7±0.2	5.5±0.11	<0.001
24	6.7±0.2	5.3±0.12	<0.001
48	6.6±0.14	5.2±0.1	<0.001
72	6.5±0.1	5.25±0.11	<0.001

Table (6): changes in serum sodiumand Potasium

	Group A	**Group B**	**P**
Base line serum sodium	135±1.9	135±2.2	0.17
6 hours	140.0±1.9	137±2.8	<0.001
24 hours	141±1.89	138±3.0	<0.001
48 hours	140±2.0	137±2	<0.001
72 hours	141±2.0	138±4	<0.001
Base line serum potasium	3.5±1.2	3.7±0.7	<0.05
6 hours	3.5±0.3	3.8±0.5	<0.05
24 hours	3.3±0.3	3.6±0.2	<0.05
48 hours	3.7±0.2	3.9±0.7	<0.05
72 hours	3.6±0.4	3.9±0.6	<0.05

Table (7):hospital out comes

	Group A	Group B	P
Length of stay in ICU (hours)	75.0±40	73.9±50	0.93
Mortality rate	1	2	1.0

DISCUSSION

AKI after cardiac surgery is associated with many adverse effects as prolonged ICU stay and increased short-term mortality even when there is only increase 0.36 mg/dl in serum creatinine above baseline value. [12].

Urinary alkalinisation carries the beneficial effect of higher PH which might protect from pathophysiological mechanisms due to cardiopulmonary bypass associated AKI. Alkaline PH reduces the generation of injurious hydroxyl radicals and lipid peroxidation [13,14].

Several mechanisms had been studied to overcome the occurrence of AKI after CPB. Benedetto et al used miniaturized cardiopulmonary bypass (mini-CPB) in comparison with conventional CPB and conclude that mini-CPB was associated with lower incidence of AKI [15] .

Haase et al suggested that hemoglobinuria is the main cause of AKI and used sodium bicarbonate to protect against tubular cast formation from met-haemoglobin proximal tubular cell necrosis by reduced endocytotic haemoglobin uptake and free iron-mediated radical oxygen species production and related injury [16].

Burns et al tried to use N-acetylcystine to prevent renal impairment after cardiopulmonary bypass in CABG surgery and concluded that this drug cannot prevent renal dysfunction, complications in high risk patients undergoing CABG surgery but Recio-Mayoral et al when adding sodium bicarbonate to N-acetyl cystine in their study, the results were different and they conclude that intravenous administration of sodium bicarbonate plus N-acetylcystine is effective and safe which agree with our results[17,18].

Meta analysis was done by Meier et al who tried to assess the effectiveness of normal saline versus sodium bicarbonate for prevention of contrast induced nephropathy and found that sodium bicarbonate was superior than normal saline in the prevention of contrast induced nephropathywhich concedes with the results of this study[19].

OZCan et al trial compared sodium bicarbonate, N-acetylcystine and saline for prevention of radio-contrast induced nephropathy in patients undergoing coronary procedures and concluded that hydration with sodium bicarbonate provide better protection than sodium chloride infusion alone and in combination with N-acetylcystine which is in agreement with our results [20].

The results of this study were in agreement with the results of Merten et al who found that hydration with sodium bicarbonate before contrast exposure is more effective than with sodium chloride for prophylaxis of contrast induced renal failure[21].

The results of Masouda et al were in agreement with the results of this study but they compare sodium bicarbonate versus sodium chloride in chronic kidney diseased patients and follow up till ≥1 year and conclude that sodium bicarbonate reduce incidence of renal replacement therapy and death[22].

From et al study results were against the results of this study and they conclude that the clinical use of sodium bicarbonate for renal protection should be reconsidered until further investigation can elucidate its proper use. This difference was due to co morbidities in study patients groups[23].

Vasheghani-Farahaniet al found that sodium bicarbonate does not offer additional benefits over saline in the prevention of contrast induced nephropathy which is not in agreement with our results but this contrast may be explained by the inclusion of patients with uncontrolled hypertension, compensated severe heart failure or history of pulmonary oedema in the study patients group[24].

Elevated serum creatinine level is a late indicator of renal injury and indicating that damage has occurred and patient has lost the renal reserve. Serum creatinine and urine output have limited sensitivity and specificity, also serumcreatinine level has slow rate of change, thus limiting their usefulness in the early detection of AKI [25].

Plasma and urinary neutrophil gelatinase-associated lipocalin (NGAL) is massively synthetized and released from distal nephron as a rapid response to AKI. So, NGAL is considered as an early predicator marker of AKI, morbidity and mortality after CPB[8] so we use it with biomarkers in this study .

Haaseet al in a recent pilot study concluded that sodium bicarbonate might attenuate CPB-associated AKI, directly affecting iron-related toxicity as indicated by smaller increase in urinary NGAL. However, their study was conducted on old aged patients (>70 y) who had already

preexisting renal impairment (preoperative serum creatinine>120 ug/l)[5]which in agreement with the results of this study.

Conclusion: Perioperative intravenous sodium bicarbonate can be used to attenuate occurrence of elevation of serum creatinine and AKI after cardiopulmonary bypass in cardiac surgery without potential hazard on the patients.

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الحقن الوريدي لعقار بيكربونات الصوديوم ما حول عمليات القلب المفتوح لمنع الخلل في وظائف الكلى الذي يحدث بعدها

المشتركون في البحث
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إن الخلل في وظائف الكلى إحدى مضاعفات جراحة القلب المفتوح وهناك الكثير من التداخلات لحل هذه المشكلة.

الهدف من البحث:

دراسة مدى تأثير استخدام الحقن الوريدي لعقار بيكربونات الصوديوم عن طريق الحقن الوريدىما حول عمليات القلب المفتوح للمحافظة على وظائف الكلى.

طريقة البحث:

اجرى البحث في عمليات جراحة القلب والصدر ثم استكمل في وحدة العناية المركزة الجراحية. اجرى البحث على خمسين مريض يعانون من خلل في وظائف صمامات القلب وتم تقسيم المرضى بطريقه عشوائيه الى مجموعتين . مجموعة " أ " اعطيت عقار بيكربونات الصوديوم عن طريق الحقن الوريدى ومجموعة " ب " اعطيت عقار كلوريد الصوديوم عن طريق الحقن الوريدى.

نتائج البحث:

وجد ان هناك فروق احصائية ذات دلالة بين المجموعتين من حيث عدد الحالات التي حدث فيها زيادة في معدل نسبة الكرياتينين في المصل حيث أصيب في المجموعة الاولى ١٤ مريض من ٢٥ مريض وفي المجموعة الثانية اصيب ٢٤ مريض من ٢٥ مريض. كما وجد أن هناك فروق احصائية ذات دلالة في نسبة جيلاتينيز خلايا الدم المتعادلة المرتبط بالليبوكالينفي البو ل وهو احدى الطرق المعملية لاكتشاف الخلل في وظائف الكلى مبكرا. كما وجد فروق احصائية ذات دلالة في غازات الدم.

الخلاصة:

خلص البحث الى ان استخدام الحقن الوريدي لعقار بيكربونات الصوديوم حول عمليات القلب المفتوح يمكن ان يمنع التغيرات في وظائف الكلى التي تحدث بعدها.