Original Article

Indian Journal of Anesthesia and Analgesia
Volume 9 Number 2 March-April 2022
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.9222.11

The Use of Intravenous Sodium Bicarbonate in the Treatment of Metabolic Acidosis with Septic Shock

Vijaya Kumar HN[1], Satish Kumar Madabhavi[2]

Author's Affiliation:

[1]Associate Professor, [2]Junior Resident, Department of Anesthesiology, Bangalore Medical College and Research Institute, Bangalore, Karnataka 560002, India.

Abstract

Background: Acute metabolic acidemia, defined as a decrease in blood pH originating from a primary reduction in bicarbonate concentration that is accompanied by an appropriate secondary reduction in PaCO2 and is present for up to a few days, can impair hemodynamics and increase mortality, particularly when severe (arterial blood pH<7.20). Septic shock constitutes an important cause of morbidity and mortality in the critically ill patient. The Surviving Sepsis Campaign recommends against treatment with bicarbonate in patients with lactic acidosis due to hypo perfusion when pH is >7.15 but does not explicate what should be done in cases with lower pH.

Methodology: Prospective randomized, Double-blind controlled study was conducted in ICU of Bangalore Medical College and Research Institute, Bangalore for a period of 4 months (November 2020 to February 2021). Sample size calculation was based on previous prospective, randomized double bind, controlled study by Jung B et al, calculated to be 27 in each group.

Results: Mean age of subjects in Study group was 43.7 ± 14.0 years and in control group was 43.3 ± 17.1 years. A statistically significant difference was found in mean final pH and HCO3 levels and with respect to need for ventilation and Multi Organ Dysfunction Syndrome among the groups.

Conclusion: Metabolic acidosis is a common acid-base disorder and its management should be directed by the current guidelines of therapy. Rational treatment of metabolic acidosis in sepsis is directed towards addressing the underlying causes of acidosis and optimizing tissue oxygen delivery through optimization of cardiopulmonary parameters. Limitations of the previous studies prevent reaching definite conclusions and further investigations are required in order to ensure the validity of this therapeutic approach.

Keywords: Metabolic acidemia; Septic shock; Sodium Bicarbonate; Multi Organ Dysfunction Syndrome.

How to cite this article:

Vijaya Kumar HN, Satish Kumar Madabhavi/The Use of Intravenous Sodium Bicarbonate in the Treatment of Metabolic Acidosis with Septic Shock/Indian J Anesth Analg. 2022; 9(2): 81-86.

Corresponding Author: Satish Kumar Madabhavi, Junior Resident, Department of Anesthesiology, Bangalore Medical College and Research Institute, Bangalore, Karnataka 560002, India.

Email: drsatishkumarjm@gmail.com, **Received on:** 23.11.2021, **Accepted on:** 30.11.2021

Introduction

Acute metabolic acidemia, defined as a decrease in blood pH originating from a primary reduction in bicarbonate concentration that is accompanied by an appropriate secondary reduction in $PaCO_2$ and is present for up to a few days, can impair hemodynamics and increase mortality, particularly when severe (arterial blood pH < 7.20).[1]

Septic shock constitutes an important cause of morbidity and mortality in the critically ill patient. Metabolic acidosis, including lactic acidosis, is part of the underlying pathophysiology in sepsis and is related to poor prognosis. Septic shock is life threatening condition caused by a severe localized or system-wide infection causing organ failure and dangerously low blood pressure that requires immediate medical attention.[2]

The treatment of metabolic acidosis is based on control of the underlying pathophysiologic process and reversal of organ dysfunction. Etiologic treatment is essential in metabolic acidosis, but optimization of oxygen delivery to tissues and reduction of tissue oxygen demand through sedation and mechanical ventilation are parts of the therapeutic strategy. Severe acidemia in sepsis contributes to hemodynamic instability, which is the result of reduced myocardial contractility, arterial vasodilation, and impaired responsiveness to catecholamine. the effect of alkaline therapy on vasopressor requirements and hemodynamic profile in severe acidosis (pH ≤ 7.15) is unknown.[3]

Despite lack of data on the effect of bicarbonate therapy, many intensivists attempt to alkalinize blood with intravenous administration of sodium bicarbonate as part of the treatment of sepsis. However, the benefit of bicarbonate administration in metabolic acidosis in sepsis is controversial and remains a matter of debate in clinical practice.[4]

The Surviving Sepsis Campaign recommends against treatment with bicarbonate in patients with lactic acidosis due to hypo perfusion when pH is >7.15 but does not explicate what should be done in cases with lower pH (9). In daily practice sodium bicarbonate is frequently prescribed in patients with severe acidemia (pH <7.15).[6]

Replacement of sodium bicarbonate to patients with sodium bicarbonate loss due to diarrhea or renal proximal tubular acidosis is useful, but there is no definite evidence that sodium bicarbonate administration to patients with acute metabolic acidosis with septic shock.[7] Hence this study was undertaken to evaluate the use of intravenous sodium bicarbonate in the treatment of metabolic acidosis with septic shock in terms of changes in Arterial blood pH, Need for vasopressor agents, Frequency of multiple organ dysfunction, Duration of mechanical ventilation, Duration of ICU and hospital stay and Reduction in mortality.

Material and Methods

Prospective randomized, Double-blind controlled study was conducted in ICU of hospitals attached to Bangalore Medical College and Research Institute, Bangalore for a period of 4 months (November 2020 to February 2021).

Patients in the age 18-60 yrs, presenting with metabolic acidosis and septic shock. (Arterial blood pH < 7.201 and Systolic blood pressure i.e SBP < 80 mm of Hg2), admitted to ICU or emergency ward and Patients with intra-abdominal sepsis and who need explorative laparotomy were included.

Patients with confirmed diagnosis of Multi Organ Dysfunction, Diabetic Keto-Acidosis and Chronic Kidney Disease. Post cardiac arrest, Bleeding and coagulation disorders, Neurological and Epileptic disorders were excluded from the study.

Sample size calculation was based on previous prospective, randomized double bind, controlled study by Jung B et al[4], assuming equal variance and minimum expected difference will be 10 in two groups.

Sample size is calculated using the formula, n = n = 2 $(Z_\alpha + Z_{1-\beta})^2 \sigma^2/d^2$

Where Zα = Standard table value for 95% confidence interval =1.96

$Z_{1-\beta}$ = Standard table value for 80% power = 0.84, σ = standard deviation = 13

d = expected difference between the two mean heart rates = 10

$n = 2(1.96+ 0.84)^2 (13)^2/(10)^2 = 26.4992$

n-27 in each group

Methodology

Written informed consent was obtained from relatives of all patients. Patients were divided into 2 groups, study and control group consisting of 27 patients in each group. Randomization was done using numbers generated from www.randomization.org. The study drug syringes were prepared by a physician not involved in the patient care. Patient, treating physician and nurses will not be aware of study drug. Study group (S)-received

intravenous Injection Sodium bicarbonate 75meql in 0.45% Normal saline bolus and maintenance fluid for 24hrs till target pH of >7.3 and bicarbonate of > 18mmol. Control group(C)- received placebo 0.9% normal saline.

In study, each patient received sodium bicarbonate (1 mmol/kg infused over 15 minutes) and equimolar sodium chloride sequentially in random order. After sodium bicarbonate administration, arterial pH, serum bicarbonate, and arterial blood partial CO_2 pressure ($PaCO_2$) increases, while plasma ionized calcium decreases.

Both sodium bicarbonate and sodium chloride transiently increases pulmonary capillary wedge pressure and cardiac output, mean arterial pressure and hemodynamic responses to sodium bicarbonate increases and sodium chloride remains the same. While control group will receive 0.9% normal saline along with vasopressor agents to maintain mean blood pressure.

Efficacy Parameters measured

- Hemodynamic parameters- HR, SBP, DBP, SP02, ETCO2 every 60 minutes.
- Arterial blood gas analysis every day
- Time since admission to develop metabolic acidosis and septic shock
- Number of days on mechanical ventilator / ICU stay
- Requirement of sodium bicarbonate.

Statistical analysis

Software: SPSS version 20 (IBM SPSS Statistics) was used to analyze data. Representation of data: Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and SD. *Tests of Significance:* Chi-square test was used as test of significance for categorical data.

Independent Student t test was used as test of significance to identify the mean difference between two quantitative variables. Paired t test was used as the test of significance for paired data such as before and after treatment for quantitative data. p value (Probability that the result is true) <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results

Table 1: Profile of subjects.

	Group					P value
	Study Group		Control Group			
	Count	%	Count	%		
Age	Mean ± SD	43.7	14.0	43.3	17.1	0.924
Sex	Female	4	14.8%	5	18.5%	0.715
	Male	23	85.2%	22	81.5%	

Mean age of subjects in Study group was 43.7 ± 14.0 years and in control group was 43.3 ± 17.1 years. There was no significant difference in age and gender distribution between two groups.

Table 2: Vital signs between two groups.

	Group				P value
	Study Group		Control Group		
	Mean	SD	Mean	SD	
HR	111.0	9.1	112.4	10.9	0.590
SBP	98.9	6.1	98.3	8.0	0.776
DBP	53.8	5.6	53.0	5.7	0.616
SPO_2	100.0	0.2	99.8	0.5	0.082

In the study there was no significant difference in mean HR, SBP, DBP and SPO_2 between two groups.

In the study there was no significant difference in mean pH between two groups at admission. However, there was significant difference in mean final pH between two groups. Mean pH was high in Study group compared to control group.

Table 3: PH and HCO_3 comparison between two groups at Admission and after treatment.

		Group						P value
		Study Group			Control Group			
		Mean	SD	P value with in group	Mean	SD	P value with in group	
PH	Initial	7.2	0.0		7.2	0.1		0.939
	Final	7.4	0.0	<0.001*	7.3	0.1	<0.001*	0.007*
HCO3	Initial	13.8	1.8		13.7	2.2		0.945
	Final	18.9	1.1	<0.001*	17.3	1.8	<0.001*	<0.001*

In the study there was no significant difference in mean HCO_3 between two groups at admission. However, there was significant difference in mean final HCO_3 between two groups. Mean HCO_3 was high in Study group compared to control group.

Table 4: Mean Number of Days on Ventilation between Cases and Controls.

Parameters	Cases		Controls		p value
	Mean	SD	Mean	SD	
No. of days on ventilation	2.6	0.3	3.1	1.1	0.041*

Note:* significant at 5% level of significance (p<0.05)

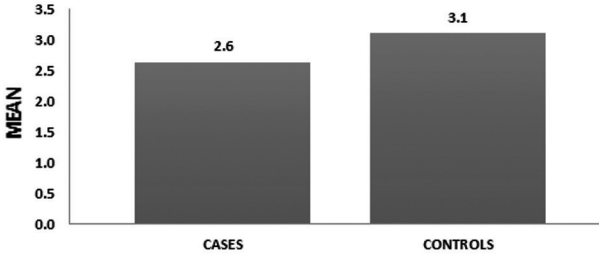

Fig. 1: Mean Number of Days on Ventilation between Cases and Controls.

Table 5: Distribution of IV Drugs between Cases and Controls.

IV Drugs	Cases		Controls		P Value
	N	%	N	%	
Noradrenaline	5	18.5%	6	22.2%	
Noradrenaline+ Vasopressin	1	3.7%	3	11.1%	0.576
Noradrenaline+ Vasopressin+ Adrenaline	0	0.0%	2	7.4%	

Note:*significant at 5% level of significance (p<0.05).

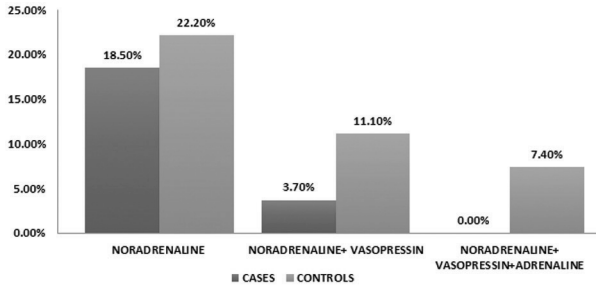

Fig. 2: Distribution of IV Drugs between Cases and Controls.

Table 6: Incidence of Mods Between Cases and Controls.

Parameters	Cases		Controls		p value
	N	%	N	%	
MODS	3	11.1%	12	44.4%	0.021*

Note:* significant at 5% level of significance (p<0.05).

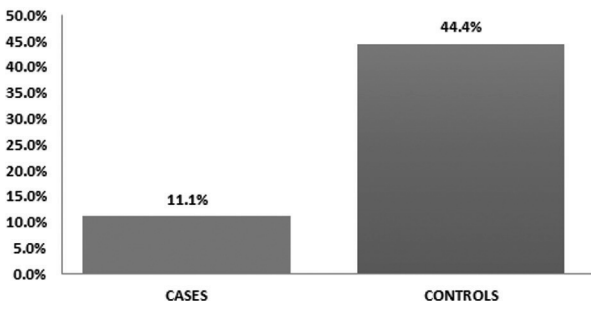

Fig. 3: Incidence of Mods Between Cases and Controls.

Table 7: Outcome distribution between two groups.

		Group			
		Study Group		Control Group	
		Count	%	Count	%
Outcome	Alive	25	92.6%	21	77.8%
	Death	2	7.4%	6	22.2%

χ 2 =2.348, df =1, p =0.125

In Study group mortality rate was 7.4% and in Control group mortality rate was 22.2%. However, there was no statistically significant difference in outcome between two groups.

Discussion

The present study was conducted at BMCRI Bengaluru including 27 study subjects in study group and control group respectively. Sepsis is considered to be one of most serious and very fatal disease seen among the patients who are admitted in ICU . The presence of metabolic Acidosis reflects the severity of the underlying disease and the progression of the patient condition towards worse. The treatment of the metabolic acidosis will help in the recovery of the patients . Causes of metabolic acidosis include sepsis, cardiogenic shock, severe hypoxemia, hepatic failure, and intoxication. Most of these conditions share similar pathogenic mechanisms, including reduced oxygen delivery to cells and impaired oxygen consumption in cell mitochondria, yet some conditions are due to more complex derangements.

In the present study nearly 85.2% of the subjects in study group were male and 81.5% subjects in control group were also male with mean age of 43.7+ 14 years in study group and 43.3+ 17.1 years in control group. In the study done by Samir Jaber et al[11] the median age among study subjects was 65 years in control and 66 years in study group with majority of the subjects being male (59% in study group and 63% in control group). The vital parameters in both the groups were found to

be comparable between both the study subjects and the p value was also found to be statistically insignificant.

The Ph of the study subjects was found to be 7.2 in the initial set up in both the groups and it was increased to 7.4 in study group and 7.3 in the control group. There was statistical significant improvement in Ph between study and control group on bicarbonate supplementation. The Bicarbonate level also found to be increased from 13.8 to 18.9 in study group and 13.7 to 17.3 in control group with significant statistical association between both the groups.

In the study done by Cooper et al[12] in the study group increased arterial pH from 7.22 to 7.36 with $p < 0.001$ and serum bicarbonate increased from 12 to 18 mmol/L, $P < 0.001$. In Another study done by Ahn et al[13] in the Sodium bicarbonate group had significant effect on pH (6.99 vs.6.90, $P = 0.038$) and bicarbonate levels (21.0 vs. 8.0 mEq/L, $P = 0.007$) when compared with placebo group. In the study done by Mintzer et al[14] sodium bicarbonate corrections lowered base deficit from 7.6 ± 1.8 to 3.4 ± 2.1 mmol l(-1) ($P < 0.05$), and increased median (±SD) pH from 7.23 ± 0.06 to 7.31 ± 0.05 ($P< 0.05$) . All these studies were found to be comparable to the present study findings and showed that sodium bicarbonate supplementation had better and significant impact on Ph and HCO_3 level among the subjects with metabolic acidosis.

The number of days on ventillations was also found to be more in control group 3.1+1.1 in control group and 2.6+0.3 days in study group with significant p value of 0.04 in the present study which is comparable to the findings of study done by El Solh et al[8] where among bicarbonate group the median time to liberation of mechanical ventilation was reduced (10 days [95% CI, 5.0 to 13.0] vs. 14 days [95% CI, 9.0 to 19.0], $p = 0.02$) and the length of intensive care unit stay was shorter (11.5 days (95% CI, 6.0 to 16.0) vs. 16.0 days (95% CI, 13.5 to 19.0), $p = 0.01$). In the study done by Jung Et al 4 there was found to be no difference in length of ICU stay or mortality in pts receiving sodium bicarbonate compared with those who received routine solutions.

Among the subjects in the present study acute Kidney injury was seen in 11.1% of the subjects and 44.4 % of the control groups. Chen et al[10] also opined that dysfunctional organs was less in bicarbonate group when compared to normal group. Zhang et al[15] studied 1718 septic patients (1218 controls and 500 patients who received sodium bicarbonate) and reported no significant mortality change in the overall population (hazard ratio [HR], 1.04; 95% CI, 0.86 to 1.26; $p = 0.67$], but bicarbonate proved to be beneficial in patients with acute kidney injury (HR, 0.74; 95% CI, 0.51 to 0.86; $p = 0.021$). In Kim H J et al[16] study suggest that unlike the overall population of patients with metabolic acidosis, those suffering from concomitant acute kidney injury may experience improved outcomes and a reduced rate of mortality from enrolment to day 28 with sodium bicarbonate infusion therapy.

Conclusion

Metabolic acidosis is a common acid-base disorder and its management should be directed by the current guidelines of therapy

Rational treatment of metabolic acidosis in sepsis is directed towards addressing the underlying causes of acidosis and optimizing tissue oxygen delivery through optimization of cardiopulmonary parameters.

Available evidence suggests that the severity of metabolic acidosis in these conditions reflects the gravity of the underlying illness rather than being itself a contributor to mortality.

Recent studies have suggested that metabolic acidosis might contribute to worsening kidney disease and sodium bicarbonate supplementation has been proposed as a renoprotective strategy. However, limitations of these studies prevent reaching definite conclusions and further investigations are required in order to ensure the validity of this therapeutic approach.

References

1. Kraut JA, Madias NE. Intravenous Sodium Bicarbonate in Treating Patients With Severe Metabolic Acidemia. Am J Kidney Dis. 2019 Apr;73(4):572-575.
2. Velissaris D, Karamouzos V, Ktenopoulos N, Pierrakos C, Karanikolas M. The Use of Sodium Bicarbonate in the Treatment of Acidosis in Sepsis: A Literature Update on a Long Term Debate. Critical Care Research and Practice. 2015;2015:1–7.
3. Ghauri SK, Javaeed A, Mustafa KJ, Podlasek A, Khan AS. Bicarbonate Therapy for Critically Ill Patients with Metabolic Acidosis: A Systematic Review. Cureus. 2019;11(3):e4297.
4. Jung B, Rimmele T, Le Goff C, Chanques G, Corne P, Jonquet O, et al. Severe metabolic or mixed acidemia on intensive care unit admission: incidence, prognosis and administration of buffer therapy. a prospective, multiple-center study. Crit Care. 2011;15(5):R238.

5. Halperin ML, Kamel KS. Some Observations on the Clinical Approach to Metabolic Acidosis. J Am Soc Nephrol. 2010 Jun 1;21(6):894-897.
6. Kooter AJ, Nanayakkara PW. Sodium bicarbonate for critically ill patients with metabolic acidaemia, treatment or window dressing? J Emerg Crit Care Med 2018;2:74.
7. Adeva-Andany MM, Fernández-Fernández C, Mouriño-Bayolo D, Castro-Quintela E, Domínguez-Montero A. Sodium Bicarbonate Therapy in Patients with Metabolic Acidosis. Di Iorio BR, editor. The Scientific World Journal. 2014 Oct 21;2014:627673.
8. El-Solh AA, Abou Jaoude P, Porhomayon J. Bicarbonate therapy in the treatment of septic shock: a second look. Internal and Emergency Medicine. 2010 Aug 1;5(4):341–7.
9. Kim HJ, Son YK, An WS. Effect of sodium bicarbonate administration on mortality in patients with lactic acidosis: a retrospective analysis. PLoS One. 2013;8(6):e65283.
10. Chen X, Ye J, Zhu Z. [The use of sodium bicarbonate in stages in treating hypoperfusion induced lactic acidemia in septic shock]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2013 Jan;25(1):24–7.
11. Samir Jaber, Catherine Paugam, Emmanuel Futier, Jean-Yves Lefrant, Sigismond Lasocki, Thomas Lesco et al . Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial.The Lancet .2018 ;6736(18):31080-8.
12. Cooper DJ, Walley KR, Wiggs BR, Russell JA. Bicarbonate does not improve hemodynamics in critically ill patients who have lactic acidosis. A prospective, controlled clinical study. Ann Intern Med 1990; 112: 492–98.
13. Ahn S, Kim Y-J, Sohn CH, Seo DW, Lim KS, Donnino MW, Kim WY: Sodium bicarbonate on severe metabolic acidosis during prolonged cardiopulmonary resuscitation: a double-blind, randomized, placebo-controlled pilot study. J Thorac Dis. 2018, 10:2295-2302.
14. Mintzer JP, Parvez B, Alpan G, LaGamma EF: Effects of sodium bicarbonate correction of metabolic acidosis on regional tissue oxygenation in very low birth weight neonates. J Perinatol. 2015, 35:601-6.
15. Zhang Z, Zhu C, Mo L, Hong Y: Effectiveness of sodium bicarbonate infusion on mortality in septic patients with metabolic acidosis. Intensive Care Med. 2018, 44:1888-1895.
16. Kim HJ, Son YK, An WS: Effect of sodium bicarbonate administration on mortality in patients with lactic acidosis: a retrospective analysis. PLoS One. 2013, 8:65283.

References for Statistical Methods

1. Dakhale GN, Hiware SK, Shinde AT, Mahatme MS. Basic biostatistics for post-graduate students. Indian J Pharmacol. 2012;44(4):435-442.
2. Sunder Rao P S S, Richard J: An Introduction to Biostatistics, A manual for students in health sciences, New Delhi: Prentice hall of India. 4th edition. 2006; 86-160.
3. Elenbaas, RM, Elenbaas, JK, Cuddy, PG. Evaluating the medical literature, part II: Statistical analysis. AnnEmerg Med. 1983; 12:610–620.