Original Research Article

A study on mean anion gap over six hours after admission as a predictor of pediatric mortality in pediatric intensive care unit

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ABSTRACT

Background: The aims of the study was to correlate change in anion gap at 0 and 6 hours of admission with mortality in pediatric intensive care unit (PICU).
Methods: Fifty children up to 12 years of age, admitted in PICU were included in the study. Blood gas anion gap levels were taken at 0 and 6 hours of admission and change in anion gap was calculated. Final outcome was recorded.
Results: Out of 50 patients enrolled in the study, 18 (36%) patients died and 32 (64%) survived. Mortality was higher in group with increased anion gap after 6 hours of admission as compared to survived. Change in anion gap was higher in expired patient as compared to survivors.
Conclusions: Mortality was higher in group with increased anion gap after 6 hours of admission.

Keywords: Anion gap, Lactates, Mortality, PICU, Blood gas

INTRODUCTION

Children admitted in pediatric intensive care unit (PICU) are seriously sick and at risk of death. Many of these patients have multiple organ dysfunction and shock of different etiology which causes tissue hypoperfusion and tissue hypoxia leading to accumulation of lactic acid and various other metabolites.[1]

Lactic acid is a product of anaerobic glycolysis and accumulates if it cannot be converted to pyruvate. Hyperlactatemia and lactic acidosis are common findings in critically ill patients and have significant prognostic implications.[2]

Clearance of the accumulated lactates after initial management has been used to predict outcome in critically ill patients. Study done previously showed that lactate clearance after initiating treatment was an indicator of responsiveness to treatment and of overall prognosis.[3] Lactates are only one of the metabolites that accumulate in shock.

Anion gap is the difference between primary measured cations and primary measured anions in blood gases. All the metabolites including lactates are part of the unmeasured ions of the anion gap.[4] We postulate that fall in the anion gap (anion gap clearance) with initial management may be a better predictor of survival then lactate clearance alone.

To the best of our knowledge no study has been conducted so far, which correlate change in anion gap after 6 hours with outcome of critically ill patients admitted in PICU. We studied the anion gap clearance as a marker of severity of illness.

METHODS

A prospective, observational study was conducted on 50 patients (age group >1 month and <12 years) admitted

between September 2016 to May 2017 in pediatric intensive care unit, St. Stephens Hospital, Delhi. Children with inborn error of metabolism and trauma were excluded. The study was approved by the hospital ethics committee. As a pilot study, a convenience sample of 50 patients admitted consecutively was enrolled. Heparinized syringe was used to collect venous blood. Anion gap estimation was done by radiometer Copenhagen ABL 555 blood gas analyzer. All pediatric patients in PICU had blood gas measured. Patients whose parents consent to participate in the study were included for analysis. The values at admission and 6 hours from the blood gas report were used for anion gap

Inclusion criteria

Inclusion criteria were children admitted to PICU between the age of 1 month and 12 years.

Exclusion criteria

Exclusion criteria were children with surgical condition needing surgery or admitted to PICU in the immediate post-surgical period.

Statistical analysis

The data was entered in MS excel spreadsheet and analysis was done using statistical package for social sciences (SPSS) version 21.0. Categorical variables are presented as totals and percentages (%) and continuous variables were presented as mean±SD and median. Normality of data was tested by Kolmogorov-Smirnov test. Parametric data was analyzed using unpaired t-test. If the normality was rejected then non parametric data was analyzed using Mann-Whitney test.

RESULTS

A total of fifty children fulfilling inclusion criteria, admitted to PICU during the study period were included in this study. Out of these eighteen patients expired (36.0%) and thirty-two patients survived (64.0%) (Table 1).

Table 1: Age distribution and mortality.

Variables	E	S	P value
Sample size	18	32	
Mean±SD	36.56±49.05	23.12±38.21	
Median	8.5	6	0.611
Min-max	1-144	1-132	
Inter quartile range	1-48	2-18	

Mean age of expired patients was 36.56±49.05 months and that of survived patients was 23.12±38.21 months (Table 1). Cases were divided into four age groups. Majority of cases (58.0%) belonged to ≤1 year group (Table 2).

Table 2: Age distribution.

Age (year)	Frequency	Percentage (%)
<1	29	58.00
1-5	13	26.00
6-10	4	8.00
>10	4	8.00
Total	50	100.00

Table 3: Anion gap at 0 hour of admission.

Anion gap (at the time of admission)	E	S	P value
Sample size	18	32	
Mean±SD	12.88±5.44	11.8±4.41	
Median	12.95	12	0.451
Min-Max	4-22.4	4.1-25	
Inter quartile range	7.900-16.200	9-15.050	

Table 4: Anion gap at 6 hours of admission.

Anion gap (6 hours after admission)	E	S	P value
Sample size	18	32	
Mean±SD	15.07±7.48	10.92±3.14	
Median	15.15	11.9	0.024
Min-Max	3-31.9	5-16.7	
Inter quartile range	8.600-20.500	8.150-13.400	

Table 5: Change in anion gap at 0 and 6 hours of admission.

Change in anion gap	E	S	P value
Sample size	18	32	
Mean±SD	2.19±4.44	-0.88±5.14	
Median	1.35	-1.4	0.017
Min-Max	-3.5-16.6	-19.7-9.6	
Inter quartile range	-0.700-4.100	-2.750-1.450	

The mean anion gap at 0 and 6 hours was measured separately. Also calculated was change in anion gap between 0 and 6 hours in both improved and expired patients. The mean anion gap in expired and improved patients at the time of admission was 12.88±5.44 and 11.8±4.41 respectively (p=0.451) (Table 3). The mean anion gap in expired and improved patients after 6 hours of admission was 15.07±7.48 and 10.92±3.14 respectively (p=0.024) (Table 4).

The mean change in anion gap in expired and improved patients was 2.19±4.44 and -0.88±5.14 respectively (p=0.017) (Table 5).

DISCUSSION

In our study anion gap levels were same in both the groups initially. However, those who survived had greater improvement in 6 hours. It may be presumed that those who had increased change in anion gap were those who had short duration of illness at presentation. Those with longer duration of illness improved more slowly and had greater risk of death. This was not studied in our project but is merely a speculation.

We found the anion gap of 12.88±5.44 among those who died and anion gap of 11.8±4.41 among those who survived at the time of admission (p value 0.451) while that after 6 hours it came out to be 15.07±7.48 and 10.92±3.14 respectively (p value 0.024). We found the change in anion gap (anion gap clearance) in expired in dead patients 2.19±4.44 and survived patients -0.88±5.14 (p value 0.017).

A study done by Fernandez et al found that in a total of 201 patients, median age was 7.5 years (~6.1), mechanical ventilation days were 12 days (~17) and the overall mortality was 9% (18 patients). Patients with elevated AG had more mechanical ventilation days, 7 (4-8) (p=0.035). Also, patients with elevated AG had increased mortality, 15% (10/65) (p=0.027) and concluded that elevated AG in critically ill children can be used as a predictor of mortality.[5]

Kim et al studied a data of 461 pediatric patients on PICU admission to test whether anion gap at admission can predict mortality or morbidity in PICU patients which was significantly lower in survivors compared with non-survivors (p<0.001). In terms of the multivariable logistic regression analysis for mortality prediction, anion gap at admission was identified as the strongest independent factor associated with in-hospital death.[6]

Kaplan et al studied that the initial acid-base variables of pH, base deficit, lactate, anion gap, apparent strong ion difference, and strong ion gap discriminate survivors from non survivors of major vascular injury and concluded that anion gap can predict mortality following major vascular trauma.[7]

Anion gap is made of unmeasured ions like lactates etc. Previous studies have found increase in lactates as a predictor of death.[8] Other studies have found, positive lactate clearance is a good predictor, as it signifies the recovery process. Munde et al studied the correlation of lactate clearance with that of pediatric intensive care unit (PICU) mortality and found that lactate clearance <30% at 6 hours and PRISM score >30 have high predicted mortality with sensitivity of 75%, specificity of 97%, positive predictive value of 90%, and negative predictive value of 91.42%.[3]

But besides lactates many other anions accumulate due to tissue hypoxia, therefore like lactate clearance we calculated anion gap clearance which predicted significant association with that of survival (p value 0.017).

CONCLUSION

Total 50 patients were enrolled, who were admitted in PICU from September 2016 to May 2017 in the study. Mean age of expired patients was 36.56±49.05 months and that of survived patients was 23.12±38.21 months. Among 50 children, 64% were male and 36% female. Out of 50 patients enrolled in the study, 18 (36%) patients died and 32 (64%) survived. Mortality was higher in group with increased anion gap at admission with mean 12.88 as compared to 11.8 in survived. Mortality was higher in group with increased anion gap after 6 hours of admission with 15.07 mean as compared to 10.92 in survived. Change in anion gap was higher in expired patient with a mean of 2.19 as compared to -0.88 in survivors. Further research in multi-centre context is needed to validate our finding.

Limitations

This study was done in a private charitable hospital. The patients that come to private hospital have different character compared to patient in a public hospital. This is a single center study. More studies in a multicenter context will add to the extended validity of the finding. We did not look at this indicator of mortality against other standard predictors of mortality like PRISM 3 (pediatric risk of mortality), PIM 2 (pediatric index of mortality).

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