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SHORT COMMUNICATION

Discrepancy in Chloride Measurement with Decreasing Bicarbonate Concentrations

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SUMMARY

Background: **Accurate chloride measurement is important in critically ill patients.**
Methods: **Chloride concentration measured simultaneously between the central laboratory (indirect ion-selective electrode) and blood gas analysis (direct ion-selective electrode) were compared.**
Results: **We report a discrepancy with chloride measurement between the central laboratory and blood gas analysis at low bicarbonate levels.**
Conclusions: **Caution should be applied while interpreting the chloride concentration when indirect ion-selective electrode methodology is used, especially in the setting of low serum bicarbonate levels.**
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KEY WORDS

chloride, bicarbonate, ion-selective electrode

INTRODUCTION

Accurate measurement of chloride concentration is of paramount importance in critically ill patients. Not only it is used to calculate the anion gap to delineate causes of metabolic acidosis, but increased plasma chloride per se may be associated with renal dysfunction. Conventionally, chloride is measured either by a central laboratory utilizing auto-analyzers (AA) (indirect ion-selective electrode (ISE)) or with blood gas analysis (BGA) (direct ISE).

Previously, there have been concerns raised about the validity of chloride measurement with indirect ISE, with results potentially affected by metabolic acidosis (specifically, low bicarbonate concentrations), and possibly renal failure [1,2]. In the past, discordance in chloride measurement between measures from BGA and AA has been reported [3,4]. We have previously shown concordance correlation coefficient values of 0.89 (95% CI 0.89 - 0.90) between these chloride measures [3]. We hypothesize that the difference between measures from BGA and AA will be exaggerated with a decrease in bi-

Table 1. The effect of bicarbonate concentration on chloride measurement with blood gas analysis (BGA) and central laboratory based automated analyzer (AA).

Bicarbonate range (mmol/L)	Number of samples	Chloride BGA (mmol/L)	Chloride AA (mmol/L)	p-value *	Chloride gap (BGA-AA)	Bicarbonate (mmol/L)	Pearson's r	p-value #
All ranges	9370	105.1 (5.7)	103.7 (5.6)	< 0.001	1.4 (2.4)	24.5 (5.1)	-0.39	< 0.001
< 10	51	109.9 (6.8)	104.9 (7.6)	< 0.001	5.1 (5.0)	6.8 (2.0)	-0.49	0.005
10 ≥ to < 20	1242	107.6 (2.6)	104.9 (6.3)	< 0.001	2.7 (2.6)	16.8 (2.2)	-0.33	< 0.001
20 ≥ to < 30	6666	105.4 (5.3)	104.1 (5.4)	< 0.001	1.3 (2.2)	24.2 (2.5)	-0.14	< 0.001
30 ≥ to < 40	1372	101.3 (4.8)	101.1 (4.7)	0.287	0.2 (2.2)	32.5 (2.6)	-0.19	< 0.001
≥ 40	39	95.1 (3.8)	96.4 (4.3)	0.148	-1.4 (2.6)	41.7 (1.5)	-0.13	0.444

There was an increase in discrepancy in chloride concentration with a decrease in bicarbonate concentration when measured as chloride gap and its correlation with low bicarbonate concentration.
Data presented as mean (SD). BGA - Blood gas analysis, AA - Automated analyzer (Laboratory based), * - Analyzed with independent sample *t*-test, # - Pearson's Correlation between chloride gap (BGA - AA) and bicarbonate concentration.

carbonate concentrations. We examined data from a tertiary level mixed medical and surgical Intensive Care Unit in the year 2015. The study was approved by Southern Adelaide Clinical Human Research Ethics Committee.

MATERIALS AND METHODS

Simultaneously measured concentration pairs of chloride, bicarbonate, sodium, and potassium from the two methods (BGA and AA) were extracted. Concentrations were measured by BGAe (ABL Flex 800, Radiometer Medical A/S, Bronshoj, Denmark) and AA (Roche/Hitachi Modular Analyzer; Hitachi High-Technologies, Tokyo, Japan) in the central biochemistry laboratory. Results from the two measures were compared with independent sample *t*-test. Pearson's correlation was used to examine the relationship between chloride gap (BGA - AA values) and plasma bicarbonate concentrations. Furthermore, we also examined this relationship at various bicarbonate thresholds (< 10, 10 - 20, 20 - 30, 30 - 40 and > 40 mmol/L). The median (IQR) time interval between sampling for BGA and AA was 5 (3 - 10) minutes.

RESULTS

We found a negative correlation between the chloride gap and bicarbonate concentration ($r = -0.39$, $p < 0.001$). The chloride gap was maximal at lower bicarbonate concentration; in the group with bicarbonate less than 10 mmol/L, the maximum chloride difference (mean +/- SD) was 5.1 +/- 5.0 mmol/L (Table). No such discrepancy was present with sodium or potassium measurement.

DISCUSSION

Addition of bicarbonate under experimental conditions can decrease this discrepancy [1], indicating possible bicarbonate-mediated interference with AA chloride measurement. However, the coupling of bicarbonate to pH and $PaCO_2$ values makes it difficult to determine the specific attribution to bicarbonate. We also cannot determine from this dataset the possibility of interference due to renal failure [1]. Other factors such as hypertriglyceridemia, dysproteinemia or other interfering ions are less plausible explanations, as the effects only apply to chloride, and no other electrolytes. Finally, this difference could also be due to the bicarbonate interference with ion selective electrodes containing a quaternary nitrogen compound [5].

CONCLUSION

Our results have implications for bedside clinicians, clinical laboratories, and researchers. Caution should be applied when interpreting the anion gap when indirect ISE methodology is used, especially in the setting of low serum bicarbonate concentrations.

Declaration of Interest:
None to report.

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