A COMPARISON OF TWO APPROACHES IN ACID-BASE ANALYSIS IN THE CRITICALLY ILL

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A. Introduction

Identification of acid base disturbances in the critically ill patients is of central importance, as it may lend valuable insight into the status of a patient or provide information about the underlying pathophysiology of a patient's disease process. To this end, mathematical models aid the clinician in conceptualizing acid-base alterations involved in order to better treat and diagnose the patients. Several models and algorithms exist to evaluate this. The traditional approach to evaluating these perturbations has been using pCO2, HCO3, pH, and the anion gap. The criticism of this approach is its use of these variables as independent variables when in fact they are very closely interrelated (1). Also, the anion gap, as used without an adjustment for albumin, is a poor indicator of unmeasured anions (5). A very commonly missed entity in critically ill patients is hypoalbuminemic alkalosis (3). Another entity noted in the ICU that is commonly missed is dilution acidosis. Given the degree of fluid resuscitation often seen in the ICUs, this is a commonly encountered process. It is the fact that disturbances in acid-base physiology, such as the two just mentioned, are in fact frequently overlooked by the traditional model that necessitates a possibly more comprehensive approach.

In the 1980s, Peter Stewart, a Canadian physiologist, used physical chemical principles to develop an alternative approach to acid-base disorder determination (4). His model was based on the principle that the standard Henderson-Hasselbach approach failed to incorporate non-bicarbonate buffers into its calculations and along these lines his theory rests on the notion that the acid-base state of the body is physically determined by several independent variables. These independent variables are pCO2, the strong ion difference (SID), and the concentrations of the nonvolatile weak acids. The principle non-bicarbonate-based organic nonvolatile weak acid buffers that are physiologically significant at body pH values are albumin, as the principal protein component, and phosphorus. Stewart's approach has been used increasingly worldwide in human and animal studies.

The clinical utility of this physicochemical approach to acid-base (AB) analysis remains unclear in critically ill patients. There have been some earlier studies evaluating the efficacy of the SF approach in certain circumstances, or its utility when compared to the traditional approach for isolated AB disturbances. No study, however, to date has evaluated its impact on ICU length of stay.

B. Hypothesis

Our hypothesis is that AB disturbances overlooked by the traditional method and identified by the SF approach will impact length of stay of critically ill patients in the ICU. We hypothesize that patients with "residual" AB processes will have a longer length of stay in the ICU. We also expect to see that these same overlooked processes will be prevalent in the patients included in the study. There is also expected to be a positive correlation between length of time that an AB disturbance is overlooked and its impact on lenth of stay. There may also be a mortality difference noted in the two groups based on the underlying missed AB process.

C. Methods

This is a non-randomized prospective non-blinded study comparing critically ill patients in the CPMC MICU. It is being done to evaluate the efficacy and potential consequences of recognition of an alternate approach to assessing acid-base disturbances.

The primary outcome will be length of stay in the ICU. This will be defined by the number of days spent in the ICU after the traditional method has evaluated the patient as being without any acid-base abnormality (per the traditional approach) and that day will be day zero. Days with abnormal SF measurements after this time will also be recorded. Prevalence of patients with abnormal SF measurements in the setting of normal traditional measurements will also be measured. Evaluation of when the patients have achieved acid-base homeostasis by the traditional method will be done by acid base physiology assessment software. All SF calculations will then be recorded from day zero onwards until either the patient leaves the MICU, the traditional approach detects an abnormality, the patient expires, incomplete data is present for the evaluation of both approaches, or the SF value changes.

Data will be collected from the Columbia Presbyterian Medical Center Medical Intensive Care Unit over the course of one year. All samples collected will be part of the routine ICU monitoring of patients and will include basic metabolic panels, phosphorus, hepatic function panels, and arterial blood gases. Analysis of the blood collected will be done in the hospital laboratory as part of its routine care of patients.

Traditional approach acid base analysis will be done by the acid-base physiology software to assess for acid base abnormalities. When the patients acid base status as assessed solely by the traditional approach becomes "normal" ie. no acid base disturbance can be isolated by the traditional approach, assessment of the strong ion difference will be made using the SF approach. Continuation of measurements of both the traditional approach and the SF approach will be done on the patient until either the patient is discharged from the MICU, the patient expires, data becomes incomplete, or the traditional approach again shows an alteration in acid base equilibrium. The number of days that the patient retained a normal acid-base status per the traditional approach will be recorded and the patient will be categorized into either SID normal or SID abnormal based on that calculation also done by the investigating physician.

Acid base physiology software will be used to assess the anion gap, pCO2, HCO3, and the pH. These variables will be used to determine the traditional approach readings. SID calculations will be made by the application of standard equations used by Stewart et al (4) and also by Fencl et al (3). These equations will produce a value for the SID. When this calculation deviates from its normal range, it will be recognized by simple database logic statements and will be recorded.

A simple comparison of the length of stay of the two groups will be done using the student t-test. This will compare the number of days in the ICU that each group spent based on their categorization on day zero into either SF normal or SF abnormal. Correlation between number of days with altered SID values and length of stay in the ICU will also be done using Pearson correlation coefficient analysis. Simple calculations of the prevalence of overlooked AB abnormalities will also be recorded. A chi square analysis will be done comparing mortality in the two groups.

Sample size was calculated using the unpaired t-test. This was done using the following assumptions: mean length of stay, the primary outcome, was 5 days in the SF normal group, and 6 days in the SF abnormal group; standard deviation of 3 days was used for both groups. Also, it was assumed that 33% of patients admitted to the ICU will have incomplete data. Given these calculations, and using an assumption of an average of 2 ICU admissions per day, approximately one year will be needed to conduct the study with a total number needed of 430 patients.

D. Subjects

All patients admitted to the Medical Intensive Care Unit at Columbia Presbyterian Medical Center during the year following IRB approval will be included in the study. Patients admitted without

the aforementioned data as part of their laboratory workup will be excluded. If at points during the ICU stay of a patient, the above data is no longer available, the data acquisition for that patient will be regarded as incomplete and that patients data file will be closed as "incomplete data." Because acid base physiology cannot be assessed without the availability of certain pieces of information, patients without those data points must be excluded. However, as is the case many times, patients clinically improve and no longer require ABGs or daily chemistry profiles and are very frequently then transferred out of the ICU anyway. The cessation of data collection secondary to incomplete data in a patient record will not alter the end calculations. This would be similar to a patient being transferred out of the ICU.

These inclusion criteria ensure a general sampling of the community given the tertiary nature of the medical center and its ICU. There will be no exclusion of minorities or underrepresented groups. There will be no gender consideration in the enrollment of the patients. The exclusion criteria are also general in nature and will not effect the external validity of the study nor will it cause the study groups to become disproportionately homogeneous.

Given the study design, we feel that this study warrants expedited review and approval. The nature of the study presents no additional risk to the patients involved. The information gathered is the same gathered in routine care administration in the ICU. Therefore, we feel that informed consent for enrollment in the study can be bypassed.

An interim safety board will assess at 3 month intervals whether the length of stay is impacted by the alternate approach. ICU physicians at the medical center will be notified of the difference, should it be detected, and the method of its calculation will be explained. Also, efforts to incorporate its calculations into standard data presentation models will be made to ensure further use of the approach as part of routine ICU care. Efforts to teach nursing and institute recordings of SID on nursing flowsheets in the ICU will also be made.

E. Confidentiality and Informed Consent

All patient's data will remain confidential by following a strict protocol. This protocol will attain this by the following method. All subjects names and medical record numbers will be assigned an identifier number. This identifier number will be used to record all physicochemical data. The file matching names to identifier numbers will be kept safe at the primary investigators office and not accessible to those during the data analysis phase of the study.

The data obtained from patient's medical records will be the same data that is gathered during routine ICU care of the patients. There will be no intervention made nor will any additional tests be conducted on the patients involved in the study.

F. Potential Risks and Benefits

Because the data gathered is from routine bloodwork done in the ICU setting, the patients will incur no additional potential risks. The benefits from the data gathered will help in evaluating whether future use of this approach will aid in better assessing acid/base disturbances in critically patients, thus helping this same group of patients in the long run. Although the information gathered will not immediately benefit the patients from whom it is gathered from.

G. Compensation/Cost

There will be no monetary compensation given to the patients involved in the study. There will be no cost to the patients involved.

H. Bibliography

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