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Metabolic alkalosis is related to delayed response to treatment of hypokalemia in non-surgical critically ill patients

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ABSTRACT

Background: Potassium (K+) homeostasis is closely related to acid – base disorders. The aim of this study is to analyze the possible causes of hypokalemia non-surgical critically ill patients including acid – base disorders and its relationship with response to K+ supplementation.
Methods: We performed a retrospective cohort study of 122 consecutive non-surgical patients admitted to the Intensive Care Unit during July 2016 Patients were classified according to the presence of hypokalemia or not. Demographic data, morbidities associated with hypokalemia, with emphasis in acid-base disorders and response to treatment were described and analyzed.
Results: Hypokalemia was observed in 32,7% (n = 40) of the patients included. Hypokalemic group had a higher value of base excess (median of −0.65 [IQR −3.3–5.2] Vs −3.2 [IQR −5.1–−1.4]; p < 0.001). The patients with hypokalemia that achieved normal serum K+ in more than 25 h had a higher value of excess base than those who did so in less than 24 h (median of 4.3 [IQR −2.1–5.5] vs −1.9 [IQR −4.8–3]; p < 0.05). Neither the degree of hypokalemia, the time to development, route of administration or solution concentration, speed of infusion, the amount of K+ administered per day per kg of weight were related with the response of treatment.
Conclusions: Hypokalemia is a common disorder in non-surgical critically ill patients. Hypokalemic patients had a higher incidence of metabolic alkalosis. Patients with hypokalemia and metabolic alkalosis needed a higher amount of potassium administration and higher time to achieve correction.

Hypokalemia, defined as a serum concentration of potassium (K+) below 3.5 meq/L, is a frequent electrolyte disorder encountered in hospitalized patients, with a reported prevalence between 14% and 37% [1]. It has been associated with an increased risk of death mostly seen in the first 7 days of admission to the hospital [2].

Many mechanisms of hypokalemia have been described and some of them are related to metabolic alkalosis [3]. However, the relationship between hypokalemia and it causes with the response to treatment is unknown. The aim of this study is to analyze the possible causes of hypokalemia non-surgical critically ill patients including acid – base disorders and its relationship with response to K+ supplementation.

We develop a retrospective cohort study of 122 consecutive non-surgical patients admitted to the Intensive Care Unit (ICU) during July 2016. Patients with hypokalemia at admission or stayed less than 48 h in the ICU were excluded. Patients who had hypokalemia were compared with patients with normal serum potassium levels. Demographic data, causes of hypokalemia, acid-base disorders and

response to treatment (achieve a serum potassium ≥3.5 meq/dl) were described and analyzed. Response to treatment was defined as more than 25 h (delayed response) or less than 24 h (early response).

Hypokalemia was observed in 32,7% (n = 40) of the patients included, 82% (n = 33) had a serum K+ concentration that ranged from 3.1 to 3.5 meq/L.

Low ingestion prevalence (fasting, lack of nutritional support or intravenous fluids without potassium) was not statistically significant differences between groups (33% vs. 22%, p = 0.5). We considered renal loss whenever there was a serum bicarbonate >26 meq/L, hypovolemia, furosemide usage (any dose), hypomagnesemia (<1.6 meq/L), aminoglycosides usage, amphotericin B usage, polyuria (>3 L/day), vomit (only the mention on the records was considered positive) or the presence nasogastric tube. There was a significantly higher proportion of patients who had two or more conditions related with renal losses in the hypokalemia group, than the control group (68% vs. 17%; p < 0.001). Hypomagnesemia was also more common in the hypokalemic group (17% vs 2%; p < 0.03). More patients in the hypokalemia group had higher levels of bicarbonate

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(>26 meq/L) than the control group (43% vs 10%, p < 0.001). This was reflected in a statistically significant higher value of base excess (−0.65 [IQR −3.3–5.2] Vs −3.2 [IQR −5.1 − −1.4]; p < 0.001). There were no differences between groups for pH value.

Neither the degree of hypokalemia, the time to development, route of administration or solution concentration, the speed of infusion, usage of Mg^+ supplementation nor the amount of K^+ administered per day were related to the time of response to treatment (Table 1). The group that responded in more than 25 h did so at a median of 62 h (IQR 48–93). The group that responded ≤24 hours required less total K^+ administration in comparison to the >25 h group, with a median of 76 meq (IQR 48–96) vs 204 meq (IQR 119.7–320; p < 0.01). Remarkably, the patients that responded >25 h had a higher and more positive value of excess base than the ≤24 h group, 4.3 (IQR −2.1–5.5) vs. −1.9 (IQR −4.8–3; p < 0.05).

Acid–based disturbances have a close relationship with K^+ levels due to redistribution or renal loss [3]. In our study, metabolic alkalosis was related strongly to the development of hypokalemia and delay in response to treatment. Metabolic alkalosis can be a potential cause of hypokalemia, by redistribution into intracellular space or induction of renal losses [3].

On the other hand, K^+ depletion causes a metabolic alkalosis because hydrogen ions are exchanged for K^+ [4]. Several conditions may cause both hypokalemia and metabolic alkalosis such as vomiting or nasogastric suctioning, diuretics, volume contraction, hyperaldosteronism (appropriate and inappropriate), Mg^+ depletion, among others. In this series, patients with metabolic alkalosis required more K^+ to resolve the imbalance, reflecting indirectly a true K^+ deficiency.

K+ deficit estimation has been described, primary based on formulas or the serum K+ level [5–7]. Nevertheless, there is not a firm relationship between serum potassium and total body potassium, and this formulas are usually not recommended [8]. In fact, some hospitalized patients might return to normal K+ levels without K+ supplementation, suggesting a cellular shift as the main cause [9]. Actually, five patients (12%) in our cohort improved in less than 25 h without supplementation.

One limitation in our study is that we did not perform urine potassium studies of the renal response in hypokalemia [7]. We only do it in selected scenarios such as acute and severe cases (serum K+ <2.5 meq/Lt), clinical and paraclinical data suggestive of tubulopathies or endocrinological disorders, frequent recurrences or unclear mechanism. In the studied cohort, there were no such cases. Although urine studies are used in algorithms of the diagnostic approach to a patient with hypokalemia [4,10,11], they are not intended to quantify the K+ deficit. Also, urine tests suggest a single mechanism and in critically care scenarios multiple mechanisms may overlap such as fasting, usage of diuretics, volume contraction and hyperadrenergic state, as seen in our cohort.

In daily practice, it is common to treat, either orally or intravenously, and perform frequent serum K+ measurements [6]. Our observation suggests that

Table 1. Conditions related with response to treatment.

Variable	Correction time to achieve normal serum K^+		
	≤ 24 hours (n = 24)*	>24 hours (n = 11)	p value
Time from admission to development of hypokalemia (hours)	62 (48–96)	57 (51–76)	0,55
Time needed for correction of hypokalemia (hours)	24 (19–24)	62 (48–93)	
Average serum potassium (meq/L)	3.26 (3.07–3.41)	3.32 (3.26–3.38)	0,82
Arterial blood gases and electrolytes			
PCO2 (mmHg)	36 (32–42)	39 (35–42)	0,24
Bicarbonate levels (meq/L)	22.9 (19.2–27.9)	27.9 (22.3–29.1)	0,07
Base excess	−1.9 (−4.8–3)	4.3 (−2.1–5.5)	**0,03**
Sodium (meq/L)	140 (137–143)	145 (139–148)	**0,04**
Magnesium (Mg++) **	20 (83%)	8 (73%)	
Magnesium (meq/L)	1.85 (159 − 1.98)	2.02 (1.43–2.3)	0,51
Magnesium <1.6 meq/L	4 (20)	2 (25)	1
Treatment			
Weight (kg)	64 (54–72)	70 (64–80)	**0,049**
Only oral	2 (8.7)	1 (10)	1
Only Intravenous¶	18 (78.3)	5 (50)	0,22
Oral and Intravenous	3 (13)	4 (40)	0,16
Magnesium supplementation¶¶	4 (17.4)	3 (30)	0,63
mEq/day	76 (48–96)	82.16 (59.8–120)	0,64
% of dairy requirement ¶¶¶	115 (77–178)	113.5 (63–160)	0,61
mEq/total	76 (48–96)	203.8 (119.7–320)	**0,0035**

Results are expressed as n (%) or median (IQR).
*Five Patients were excluded from analysis as they did not receive any treatment for hypokalemia and had a normal serum K+ in less than 24 h.
**Number of patients tested.
¶Included concentrations of 40 meq/L (periphery venous access) and 200 meq/L (central venous access).
¶¶regardless if they were hypomagnesemic or not.
¶¶¶defined as 1 meq/kg/day = 100 %.

patients with metabolic alkalosis will probably need a higher amount of K+ supplementation and will take longer to correct. In the other way, patients without metabolic alkalosis might correct alone or rapidly and overcome in a subsequent hyperkalemia [12]. Metabolic alkalosis and severe forms of hypokalemia were been described in hospitalized patients [13].

Despite that hypokalemia is a frequent clinical condition, there are surprisingly few data on hypokalemia, treatment and outcomes such as mortality in critically ill patients. This lack of information has been observed by others [14]. In one study, the implementation of a computer-assisted potassium regulation protocol reduced overall mortality [14]. In this study, the presence of metabolic alkalosis was not taken into account.

In conclusion, the present study shows that hypokalemia is a common disorder in critical non-surgical patients, and it is related to metabolic alkalosis. Higher bicarbonate and base excess values were the most significant characteristic of patients with delayed response to treatment. Further prospective studies are needed to validate this observation and its impact in treatment protocols and outcomes.

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