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Original Contribution

Diseases associated with electrolyte imbalance in the ED: age-related differences

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ABSTRACT

Objective: The objective of the study is to investigate the prevalence of electrolyte imbalance (EI) in the emergency department (ED) with systemic diseases in different decades of life.
Methods: We enrolled patients admitted to the ED. The population study included 7941 patients, subdivided in 3 groups: young group (Y), middle-aged group (MA), and elderly group (E).
Results: We observed EI in 13.7% of the whole population. Hyponatremia (hNa^+) is the most frequent EI (44%) followed by hypokalemia (hK^+) (39%), hyperkalemia (HK^+) (13%), and hypernatremia (HNa^+) (4.4%). In the Y group, the EI occurred in 7.1% of all patients ($P< .05$ vs MA and E), whereas in the MA group, they were shown in 11.5% of patients and in the E group in 22% of all patients group ($P< .05$ vs MA and Y). In the Y group, gastrointestinal diseases are the most frequently associated disease (24.6%; $P< .05$ vs MA and E). In the MA group, the most frequently associated disease was a current cardiovascular disease (29.7%; $P< .05$ vs Y and E). In the E group, the frequently associated diseases are cardiovascular (22.8%; $P< .05$ vs Y) and lung diseases (16.7%; $P< .05$ vs MA and Y).
Conclusions: In our study, 13.7% of all patients showed an EI, and only 2% of cases were alone without any associated systemic disease. Most EIs are associated to other systemic diseases. The present data also depict different age-related and disease-associated prevalence patterns of EI, thus highlighting a complex clinical scenario.

1. Introduction

Electrolyte imbalance (EI) is an independent predictor of mortality, and the prevalence and incidence of EI in the emergency department (ED) are of great clinical importance because these disorders have been associated with an increased risk of mortality [1–3]. Thus, prompt diagnosis and treatment are crucial in the management of patients admitted to the ED [4]. Although dysnatremias and dyskalemias are commonly shown in hospitalized patients [5], little is so far known data on the prevalence in the ED [6]. Recently, age-related differences in EI have been reported in the ED [5]. In addition, EI in the ED is often associated with systemic diseases [7–8].

To our knowledge, the association between EI with systemic disease in the ED has yet to be reported. Thus, we aimed to investigate the prevalence of dysnatremias and dyskalemias in ED patients and their association to major systemic diseases in different age groups.

2. Methods

We carried out an observational study by recruiting all patients admitted to the ED of the Marcianise Hospital, at the Second University of Naples, between January 1, 2014, and December 31, 2014, with assessment of EI upon admission. The study design is a cross-sectional retrospective chart review. Investigators trained in the systematic chart review manually reviewed all charts meeting inclusion criteria. Patients with incomplete charts were excluded. The abstracted data were stored using an electronic spreadsheet on password-protected computers. The study population included 7941 patients. It was subdivided into 3 groups: the young group (Y), consisting of 2358 patients aged between 18 and 40 years; the middle-aged group (MA) consisting of 2975 patients aged between 41 and 65 years; and the elderly group (E),

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including 2608 patients older than 65 years. Demographic data were obtained from all patients, and final diagnosis was derived from the *International Classification of Diseases, 10th Revision*. Blood samples were collected within 5 minutes after patient's arrival in the ED. We used baseline characteristics and serum creatinine to calculate the estimated glomerular filtration rate in accordance with the Chronic Kidney Disease Epidemiology formula [9]. The blood sample from each patient was divided into several tubes or syringes for immediate analysis. The blood samples in BD Vacutainer Blood Collection Tubes (Becton, Dickinson and Company, Franklin Lakes, NJ) containing lithium heparin were cooled in ice-cold water before analysis for their ammonia levels. The blood samples in BD Vacutainer Blood Collection Tubes containing plasma separating tube gels and lithium heparin were sent to the clinical laboratory for other biochemistry analyses. Biochemical data were measured using a Vitros Fusion 5,1 FS Automated Chemistry Analyzer (Ortho Clinical Diagnostics, Johnson & Johnson Co, New Brunswick, NJ). The analyses included serum creatinine, glucose, aspartate aminotransferase, alanine aminotransferase, creatine kinase (CK), CK-MB, troponin T, potassium, sodium, calcium, magnesium, chloride, lactate, and ammonia. The blood samples in BD Vacutainer Blood Collection Tubes containing potassium EDTA were immediately sent to the clinical laboratory. Complete blood counts were determined using a COULTER LH 750 Hematology Analyzer (Beckman Coulter Co, Brea, CA) for white blood cells, hemoglobin, and platelets. The blood gas samples in Luer Slip syringes containing heparin were analyzed to obtain pH values. The blood gas analyses were determined using a Gem Premier 4000 Analyzer (Instrumentation Laboratory Company, Inc, Bedford, MA). Using these data, we calculated the prevalence rates for dyskalemias and dysnatremias defined according to the reference range of our central laboratory. *Hypokalemia* was defined as a serum potassium level less than 3.5 mmol/mol; and *hyperkalemia*, as a serum potassium level exceeding 5.5 mmol/L. *Hyponatremia* was defined as a serum sodium level less than 135 mmol/L; and *hypernatremia*, as a serum sodium exceeding 145 mmol/L. In addition, we gathered laboratory data on serum electrolytes, creatinine, and venous blood gas analyses of all patients presenting with EI. Patients with a known pregnancy and severe hypothermia (defined as a body temperature body 30°C) as well as patients who were younger than 18 years and, finally, surgical patients were excluded from the study. The experimental protocol was reviewed and approved by the Ethics Committee of the Second University of Naples. Voluntary written consent was obtained before their participation. The study was carried out according to the Helsinki declaration.

3. Results

During the study period (from January 1 to December 31, 2014), a total of 7941 patients presented to the Department of Emergency Medicine, and all received a general evaluation and assessment of blood serum samples.

The mean age of patients was 52.3 ± 3 years, and 52% of patients were male. Patients were divided in 3 age groups: patients aged from 18 to 40, Y group; patients aged from 41 to 65 years, MA group; and patients aged older than 65 years, E group.

The Y group was characterized by 2358 patients with the mean age of 30.3 ± 2 years. The MA group was characterized by 2975 patients with the mean age of 52.0 ± 3 years. The E group was characterized by 2608 patients with the mean age of 74.8 ± 2 years. The characteristics of all patients subdivided for age are reported in Table 1.

Electrolyte imbalance was present in 1087 (13.7%) of the cohort. In particular, hyponatremia (hNa^+) resulted the most frequent EI in 468 patients (44%) followed by hypokalemia (hK^+) in 431 patients (39%), hyperkalemia (HK^+) in 141 patients (13%), and hypernatremia (HNa^+) in 47 patients (4.4%).

According to age, the prevalence of EI in the Y group occurred in 167 patients (7.1%) (P< .05 vs MA and E) but increased in the MA group as showed in 342 patients (11.5%) and in the E group as occurred in 578 patients (22.2%) (P< .05 vs MA and Y).

Table 1
Clinical characteristics of study population divided in 3 groups: Y (18-40 years old), MA (41-65 years old), and E (>65 years old)

	All patients	Y	MA	E
n (M)	7941	2358 (1174)	2975 (1480)	2608 (1300)
Age (y)	52.3 ± 3	30.3 ± 2	52.0 ± 3	74.8 ± 2
CrCl (mL/min/1.73 m^2)	88 ± 2.0	116 ± 5.0	89 ± 3.9	59 ± 2.7[a,b]
Cr (mg/dL)	1.01 ± 0.2	0.87 ± 0.3	0.97 ± 0.2	1.21 ± 0.2[a,b]
All EI (%)	13.7	7.1	11.5	22.0[a,b]
hNa^+ (%)	44.0	33.4	39.8	47.7[a,b]
hNa^+ (mean)	116.5 ± 0.6	120.1 ± 0.5	117.3 ± 0.4	112.2 ± 0.6[a,b]
HNa^+ (%)	4.4	5.6	4.7	3.7
HNa^+ (mean)	147.6 ± 0.9	149.3 ± 0.6	147.3 ± 0.6	146.3 ± 0.6
hK^+ (%)	39.0	58.7[b,c]	48.0[b]	29.1
hK^+ (mean)	3.1 ± 0.1	2.9 ± 0.6[b,c]	3.1 ± 0.4	3.2 ± 0.5
HK^+ (%)	13	2.4	7.4	19.5[a,b]
HK^+ (mean)	5.7 ± 0.8	5.5 ± 0.6	5.9 ± 0.6	6.2 ± 0.6[a,b]

Abbreviations: CrCl, creatinine clearance; Cr, serum creatinine.
[a] P< .05 vs Y group.
[b] P< .05 vs MA group.
[c] P< .05 vs E group.

In particular, in the Y group (2358 patients), the hK^+ was the most frequent EI as it was present in 58.7% (99/167 patients) (P< .05 vs MA and E), followed by the hNa^+ showed in 33.4% (56/167 patients); the HNa^+ occurred in 5.6% (9/167 patients), and the HK^+ was reported in 2.4% (4/167 patients). In the MA group (2975 patients), the most frequent EI was hK^+ and occurred in 48% (164/342 patients) (P< .05 vs E), followed by the hNa^+ that occurred in 39.8% (136/342 patients); the HK^+ was reported in 7.4% (25/342 patients), and the HNa^+ was observed in 4.7% (16/342 patients). In the E group (2608 patients), the most frequent EI was hNa^+ and occurred in 47.7% (276/578 patients) (P< .05 vs MA and Y), followed by the hK^+ that occurred in 29.1% (168/578 patients), the HK^+ that occurred in 19.5% (112/578 patients), and HNa^+ that occurred in 3.7% (21/578 patients) (Fig. 1; Table 1).

The most frequent diseases associated with EI are cardiovascular in 1802 patients (22.7%), followed by lung in 984 patients (12.4%) and gastrointestinal (GI) diseases in 1151 patients (14.5%) (Table 2). We also reported the most frequently associated disease in 3 groups (Table 2). In the Y group, GI disease is the most frequent pathology that occurred in 580 patients (24.6%) (P< .05 vs MA and E). In the MA group, the most frequently associated disease represented is cardiovascular disease that occurred in 883 patients (29.7%) (P< .05 vs Y and E). In the E group, the most frequent pathologies were cardiovascular in 594 of the patients (22.8%) (P< .05 vs Y) and lung diseases in 435 of the patients (16.7%) (P< .05 vs MA and Y) (Fig. 2).

Hospitalization rate in EI patients greatly varied in the 3 age groups. In fact, in the Y group, it occurred in only 3.6% (6 of the 167 patients); in the MA group, it increased to 16% (55 of the 342 patients) (P< 0.01 vs Y);

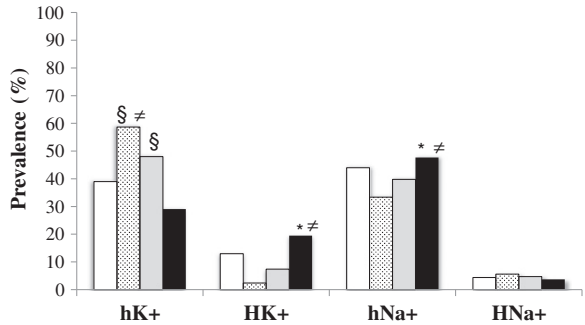

Fig. 1. Hypernatremia (HNa), hyponatremia (hNa), hyperkalemia (HKa), and hypokaliemia (hK) in all patients group (white column), Y group (dotted column), MA group (gray column), and E group (black column). Values are expressed as percentages. *P< .05 vs Y group; ≠P< .05 vs MA group; §P< .05 vs E group.

Table 2
Diseases associated with EI on admission to the ED in study population divided in 3 groups: Y (18-40 years old), MA (41-65 years old), and E (>65 years old)

Associated disease	All	Y	MA	E
Cardiovascular (%)	22.7	8.7	29.7[a,b]	22.8[a]
Lung (%)	12.4	4.0	9.4[a]	16.7[a,c]
Neurologic (%)	9.2	13.0	9.0	8.1
Hepatological (%)	5.7	0.1	5.5	7.5[a,c]
GI (%)	14.5	24.6[b,c]	11.3	7.7
Pain (%)	8.1	15.9[b,c]	6.6	1.9
Psychiatric (%)	11.4	17.6	16.3	18.3
Kidney (%)	1.0	0.1	0.8	1.6[a,c]
EI (%)	1.6	0.8	2.0	2.3[a]
Immunological (%)	0.6	0.8	0.4	0.5
Endocrine (%)	3.6	2.4	3.5	4.0[a]
Hematological (%)	1.5	0.8	2.0[a]	1.4
Infectious (%)	5.1	6.3[c]	3.5	5.6
Other (%)	3.3	5.6	2.0	2.3

Values are reported as percentages.
[a] $P< .05$ vs Y group.
[b] $P< .05$ vs E group.
[c] $P< .05$ vs MA group.

and in the E group, it markedly increased to 39% (225 of the 578 patients) ($P< .01$ vs Y and MA).

4. Statistical analyses

Data analyses were performed using SPSS, version 19.0 (IBM Corp, Armonk, NY). Statistical significance was set at $P< .05$ for all procedures. Analyses of variance or *t* tests as well as statistical differences for trend were used to compare means for continuously measured variables. χ^2 Tests for independence were used to test statistical differences for categorical variables. Data are presented as percentage and mean ± SE.

5. Discussion

In the present study, we found a high prevalence of EI (13.7%) in patients admitted to the ED. These relevant data are in agreement with a previous observation demonstrating a prevalence of more than 10% as far as dysnatremia and dyskalemia are concerned [5]. In addition, we also observed crucial difference in EI as related to life decades. In fact, in the E group, we found that EI had the highest prevalence, 22%, whereas it was 11.5% in the MA group and only 7.1% in the Y group.

These important data suggest an involvement of aging in determining the different pattern of EI across different decades of life. In this regard, it has been recently reported that the prevalence of hyponatremia and hypokalemia varies with the age [5]. These authors reported that although serum sodium concentration inversely correlated with age, serum potassium, by contrast, did the opposite [5].

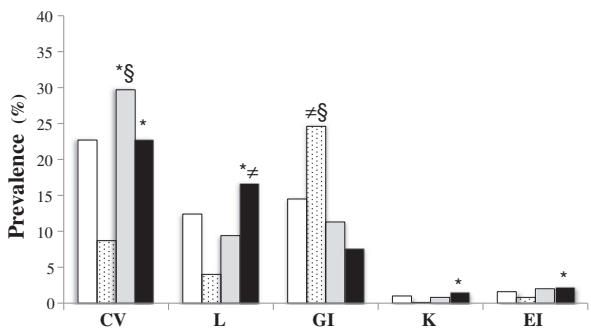

Fig. 2. Diseases associated with EI: cardiovascular disease, lung disease, GI disease, kidney diseases, and EI alone in all patients group (white column), Y group (dotted column), MA group (gray column), and E group (black column). Values are expressed as percentages. *$P< .05$ vs Y group; ≠$P< .05$ vs MA group; §$P< 0.05$ vs E group.

Moreover, Tareen et al [10] have reported that the prevalence of hyponatremia ranges from 2.5% in younger patients to 50% in the elderly population. In our study, in particular, hyponatremia occurred in 47.7% of the E group, in 39.8% in the MA group, and only in 33.4% of the Y group (Fig. 1). Similarly, Lindner et al [5] recently showed that the prevalence of hyponatremia in the ED was increased with age up to 15.2% and 16.9% in patients older than 71 and 80 years, respectively.

Of interest, we also found that hyponatremia was the most frequent EI in the ED only in the E group, whereas hypokalemia appeared to be the most frequent EI in the MA and Y groups (48% and 58.7%, respectively). This age-related trend of hypokalemia is in agreement with data reported by Lindner et al [5], who previously showed that the prevalence of hypokalemia was 12.8% in patients between 21 and 30 years old, 11.4% in patients between 51 and 60 years old, and 10.9% in patients between 71 and 80 years old.

The reason for such differences remains circumstantial. However, it has been postulated that a loss in kidney function in parallel with aging may plays a crucial role in the age-related derangement of electrolyte metabolism shown in patients admitted to ED [5]. In this regard, we observed, as expected, a significant age-related decline in renal function in parallel with aging (Table 1). As a matter of fact, the physiological age-related decline in renal function, as demonstrated by Lindeman et al [11], would be expected to be approximately 0.75 mL/min per year. Thus, it cannot be excluded that the physiological age-related decline in renal function could affect at least in part sodium balance through either volume expansion or distal tubule dysfunction, thus inducing hyponatremia. Similarly, an age-related decline in renal function may cause hyperkalemia through tubule dysfunction; we also observed a rising prevalence of hyperkalemia with age in the ED. In fact, we found that the prevalence of hyperkalemia was 2.4% and 7.4% in the Y and MA groups, respectively, whereas it rose up to 19.5% in the E group. This pattern goes in parallel with the decline of renal function.

As to EI without associated diseases, we found a negligible prevalence of EI (1.6%). By contrast, we observed that EI was more frequently associated in the Y group with GI diseases (24.6% of all EI); in the MA group, with cardiovascular diseases (29.7% of all EI); and in the E group, with both cardiovascular and lung diseases (22.8% and 16.7%, respectively) (Fig. 2).

These data could also explain the high prevalence of hypokalemia observed in the Y group because GI diseases are often associated with hypokalemia. In fact, the prevalence of hypokalemia was reduced in the MA and E groups, who were characterized by only 11.3% and 7.7% of GI diseases, respectively (Fig. 2). The reason for such differences could be that young patients may be mainly affect by vomiting and diarrhea that could account for the higher prevalence of hypokalemia. In this regard, we also find a significant inverse correlation in all patients between potassium levels and a prevalence of GI diseases ($r= -0.66$).

It is not surprising to find that MA and E groups were mainly characterized by EI associated with cardiovascular diseases. In fact, these patients are more frequently treated with drugs somehow affecting electrolyte metabolism (diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, etc). Our data also demonstrated that, in the E group, at variance with the MA group, EI was mainly associated with both cardiovascular and lung diseases. These associations may underline the importance of lung diseases in addition to the cardiovascular diseases in the prevalence of EI in the elderly.

In conclusion, we reported that the prevalence of EI was 13.7% of all patients admitted to ED and increased to 22% in the elderly. In addition, the prevalence of EI alone at the ED was only in 1.6% of cases. So, most patients showing EI are affected by other systemic diseases. As to age influence, EI was more frequently associated in the Y group with GI disease (24.6%); in the MA group, with cardiovascular disease (29.7%); and in the E group, with both cardiovascular and lung diseases (22.8% and 16.7%, respectively). Therefore, the burden of comorbidity as well as aging seems to influence the complex scenario of electrolyte metabolism derangement in ED. Thus, present data suggest that ED physicians

need to be aware of the potential electrolyte abnormalities that can arise on patient age and its pathologic conditions associated to prevent adverse outcomes.

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