View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Bern Open Repository and Information System (BORIS)

OPEN ACCESS Freely available online

PLOS ONE

Electrolyte Disorders and In-Hospital Mortality during Prolonged Heat Periods: A Cross-Sectional Analysis

Carmen A. Pfortmueller[1,2], Georg-Christian Funk[3], Alexander B. Leichtle[4], Georg M. Fiedler[4], Christoph Schwarz[5], Aristomenis K. Exadaktylos[1], Gregor Lindner[1]*

1 Department of Emergency Medicine, Inselspital, University Hospital Bern, Bern, Switzerland, **2** Department of General Internal Medicine, Inselspital, University Hospital Bern, Bern, Switzerland, **3** Department of Respiratory and Critical Care Medicine, Otto Wagner Spital Vienna and Ludwig-Boltzmann Institute for COPD and Respiratory Epidemiology, Vienna, Austria, **4** Center for Laboratory Medicine, Inselspital, University Hospital Bern, Bern, Switzerland, **5** Department of Nephrology, Landeskrankenhaus Steyr, Steyr, Austria

Abstract

Background: Heat periods during recent years were associated with excess hospitalization and mortality rates, especially in the elderly. We intended to study whether prolonged warmth/heat periods are associated with an increased prevalence of disorders of serum sodium and potassium and an increased hospital mortality.

Methods: In this cross-sectional analysis all patients admitted to the Department of Emergency Medicine of a large tertiary care facility between January 2009 and December 2010 with measurements of serum sodium were included. Demographic data along with detailed data on diuretic medication, length of hospital stay and hospital mortality were obtained for all patients. Data on daily temperatures (maximum, mean, minimum) and humidity were retrieved by *Meteo Swiss*.

Results: A total of 22.239 patients were included in the study. 5 periods with a temperature exceeding 25°C for 3 to 5 days were noticed and 2 periods with temperatures exceeding 25°C for more than 5 days were noted. Additionally, 2 periods with 3 to 5 days with daily temperatures exceeding 30°C were noted during the study period. We found a significantly increased prevalence of hyponatremia during heat periods. However, in the Cox regression analysis, prolonged heat was not associated with the prevalence of disorders of serum sodium or potassium. Admission during a heat period was an independent predictor for hospital mortality.

Conclusions: Although we found an increased prevalence of hyponatremia during heat periods, no convincing connection could be found for hypernatremia or disorders of serum potassium.

Citation: Pfortmueller CA, Funk G-C, Leichtle AB, Fiedler GM, Schwarz C, et al. (2014) Electrolyte Disorders and In-Hospital Mortality during Prolonged Heat Periods: A Cross-Sectional Analysis. PLoS ONE 9(3): e92150. doi:10.1371/journal.pone.0092150

Editor: Antonio Carlos Seguro, University of São Paulo School of Medicine, Brazil

Received December 30, 2013; **Accepted** February 17, 2014; **Published** March 20, 2014

Copyright: © 2014 Pfortmueller et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The authors have no support or funding to report.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: lindner.gregor@gmail.com

Introduction

Disorders of serum sodium and potassium are common in hospitalized as well as outpatients with a prevalence of about 15% in emergency patients [1]. Both, hypo- as well as hypernatremia and dyskalemias have been reported to be independent predictors of mortality [1,2]. In the outpatient setting the etiology of disorders of serum sodium and potassium has been mostly linked to diuretic use [1]. Ambulatory acquired hypernatremia was found to be common in elderly patients and residents of nursing homes and it was concluded that it might be due to insufficient accessibility of free water due to immobility and or a decreased sensation of thirst in these patients [3–5].

The impact of temperature extremes on the health of vulnerable patient collectives such as the poor, children or especially the elderly is discussed in the medical literature [6,7]. Even a relationship between heat periods and mortality in the overall population has been shown previously and the high number of deaths during the heat period in Europe in 2003 especially among the elderly found attention by the popular media [8,9]. Given the pathophysiology of disorders of serum sodium, but also of serum potassium it is well imaginable that during prolonged periods of extreme temperatures with increased sweating an increase in the prevalence of electrolyte disorders due to dehydration or excess intake of free water, as described in endurance runners can be observed [10,11]. However, so far no study has investigated the impact of temperature extremes on the prevalence of electrolyte disorders. We wanted to investigate whether periods of temperature extremes are associated with an increased prevalence of electrolyte disorders in patients presenting to the emergency department of a large tertiary care facility and whether there is an association between temperature extremes and in-hospital mortality in patients hospitalized during heat periods.

source: http://boris.unibe.ch/64173/ | downloaded: 6.3.2015

Table 1. Overview on the diuretic medications and median doses (quartile 1 and quartile 3).

Diuretic	Number of patients (%)	Median dose
Torasemide	1.196 (48)	10 (5 to 20)
Furosemide	231 (9)	40 (40 to 80)
Hydrochlorothiazide	975 (39)	12.5 (12.5 to 12.5)
Chlorthalidone	102 (4)	12.5 (12.5 to 25)
Butizide	16 (1)	2.5 (2.5 to 5)
Amiloride	97 (4)	5 (2.5 to 5)
Spironolactone	403 (16)	25 (25 to 50)
Eplerenone	15 (1)	25 (25 to 50)
Indapamide	58 (2)	1.5 (1.5 to 1.5)
Metolazone	121 (5)	5 (2.5 to 5)
Acetazolamide	20 (1)	250 (250 to 500)

doi:10.1371/journal.pone.0092150.t001

Materials and Methods

The study was approved and the need for written informed consent was waived by the local institutional review board, the Ethics Commission of the Canton of Bern, Switzerland.

In this cross-sectional analysis, we included all patients presenting to the Department of Emergency Medicine of the Inselspital, University Hospital Bern between 01 January 2009 and 31 December 2010 with measurement of serum sodium, as ordered by the emergency physician in charge. The decision whether to order serum sodium measurement was at the discretion of the emergency physician. Exclusion criteria was age <16 years.

Serum sodium and potassium were determined by the Center for Laboratory Medicine using the Roche Modular ISE 900, Roche Diagnostics, Basel, Switzerland. Creatinine was determined enzimatically using the Roche Modular P800, Roche Diagnostics, Basel, Switzerland. Hyponatremia was defined as a serum sodium <135 mmol/L and hypernatremia as a serum sodium > 145 mmol/L. Stratification of serum sodium disorders into borderline, moderate and severe was performed as published earlier [2]. Hypokalemia was defined as a serum potassium < 3.5 mmol/L and hyperkalemia as >4.7 mmol/L according to the reference ranges of the Center for Laboratory Medicine.

Of all administered patients we gathered the following data: age, gender, data on hospitalization including length of hospital stay and in-hospital mortality. Additionally, data regarding current diuretic medication including type of diuretic medication and current daily dose was obtained.

Data on daily temperatures including maximum and mean temperatures from the official weather station in the area of Bern was obtained from Meteo Suisse, the official weather service of the Swiss Confederation. Definition of temperature extremes was performed in accordance with Meteo Suisse due to a lack of an internationally accepted definition: period of warmth: 3–5 days with maximum daily temperatures ≥25°C; prolonged period of warmth: ≥5 days with maximum daily temperatures ≥25°C; heat period: 3–5 days with maximum daily temperatures ≥30°C; heat wave: ≥5 days with maximum daily temperatures ≥30°C. We used baseline characteristics and serum creatinine to calculate the estimated glomerular filtration rate in accordance with the Modified Diet in Renal Disease (MDRD) formula.

Statistical Analysis

Data are presented as means ± standard deviations, medians with 1st to 3rd quartiles or proportions, as appropriate. Between-group comparisons of categorical variables were performed using χ^2 test.

In order to describe an association between electrolyte disorders and mortality we used a Cox regression model. Predefined covariates were included in the model. The proportionality assumption was tested using log-log plots or Schoenfeld residuals. A two-sided p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS (SPSS for Windows release 15.0, Chicago, IL) and STATA (STATA/MP 10.0, College Station, TX).

Results

During the study period a total of 22,239 patients received measurement of serum sodium at the Department of Emergency Medicine. Median age was 53 years (35 to 67) and 57% of patients were male. 2.229 patients (10%) were 80 years of age or older. 12.864 (42%) were admitted for medical and 9.375 for a surgical reason. Mean serum creatinine was 82 μmol/L (SD 64) and serum urea was 6.4 mmol/L (SD 5.1). 1.626 patients (7.3%) had a MDRD eGFR between 30 and 60 ml/min and 516 patients (2.3%) had a MDRD eGFR below 30 ml/min. Mean serum osmolality, present for 3.524 patients was 304 mosm/kg (SD 23). 2,514 patients (11%) currently took a diuretic medication on presentation with loop diuretics (torasemide and furosemide) being the most common with 1,427 patients (6.4%) taking them. 1,884 (8.5%) had one, 547 (2.5%) had two, and 83 (0.4%) had three or four different diuretic substances as medication. Table 1 gives an overview on the diuretic substances and dosages taken by patients.

During the study period a total of 88 days were noted with a daily maximum temperature exceeding 25°C in the area of Bern, while on 16 days the temperature exceeded 30°C. All of these days occurred in the time period from May to September. 5 periods of a temperature exceeding 25°C for 3 to 5 days were noticed and 2 periods with temperatures exceeding 25°C for more than 5 days were noted. Additionally, 2 periods with 3 to 5 days with daily temperatures exceeding 30°C were noted during the study period. An overview on the mean monthly temperatures and humidity during the study period is given in Tables 2 and 3.

Of the 22.239 patients (58%) included in the analysis, a total of 2.459 (11.1%) presented with hypokalemia and 974 (4%) with

Table 2. Overview on monthly mean and mean daily maximum temperatures and humidity as well as prevalence rates of electrolyte disorders according to month of admission.

	January 2009	February 2009	March 2009	April 2009	May 2009	June 2009	July 2009	August 2009	September 2009	October 2009	November 2009	December 2009
Tmean	–2.9±3.3	–0.4±2.6	4.1±2.2	10.7±2.2	15.2±3.5	16.5±2.6	18.6±2.7	19.6±2.6	15.2±2	9.2±4.5	6.7±2.4	0.7±3.9
Tmax	–0.3±3.6	3.1±3.4	8.4±3.5	16.8±3.8	21.2±4.5	22.2±3.6	24.6±3.6	25.9±4.9	20.5±2.9	13.8±4.9	10.3±2.8	3.1±4.1
Humidity	87.8±4.8	82.9±6.4	74.8±11.6	69.8±9.4	71±9.8	71.4±8.7	72.7±6.3	72.4±8.2	79.4±5.2	80.9±6.6	84.8±5.3	85.2±5.6
Hyponatremia cases	107	85	98	90	87	87	96	87	93	76	72	85
Hyponatremia %	10,2	8,7	9,6	9,2	8,8	9,3	9,6	8,7	10,1	8,2	8,3	9,4
Hypernatremia cases	20	2	13	11	12	12	10	14	10	12	15	13
Hypernatremia %	2	0,2	1,3	1,1	1,2	1,3	1	1,4	1,1	1,3	1,7	1,4
Hypokalemia cases	130	90	104	108	88	84	115	106	120	97	90	106
Hypokalemia %	12,4	9,2	10,2	11,1	8,9	8,9	11,5	10,6	13,1	10,4	10,4	11,8
Hyperkalemia cases	58	35	64	45	52	34	43	40	34	43	38	35
Hyperkalemia %	5,6	3,5	6,3	4,6	5,3	3,6	4,3	4	3,7	4,6	4,4	3,9

While Tmean is mean monthly temperature, Tmax is mean maximum daily temperature and Humidity is mean monthly humidity. Temperatures given in °Celsius and humidity in percent.
doi:10.1371/journal.pone.0092150.t002

Table 3. Overview on monthly mean and mean daily maximum temperatures and humidity as well as prevalence rates of electrolyte disorders according to month of admission.

	January 2010	February 2010	March 2010	April 2010	May 2010	June 2010	July2010	August 2010	September 2010	October 2010	November 2010	December 2010
Tmean	–2.0±2.5	0.1±4.3	4.1±5.3	9.7±3.8	11.8±3.3	16.6±3.5	20.3±3.1	17.4±2.9	13.3±2.3	8.6±3.7	4.8±5.2	–1.5±4.0
Tmax	0.1±2.8	3.5±4.9	8.9±6.6	15.6±4.8	15.9±4.8	21.8±4.7	26.3±4.4	22.1±4.2	18.7±3.3	12.6±4.4	7.9±6.2	1.6±4.1
Humidity	84.9±5.8	78.9±8.7	70.7±9.8	66.2±6.6	76.2±9.4	74.9±8.3	68.8±7.5	75.4±5.9	76.8±4.5	82.8±4.2	83.9±5.3	84.5±6.5
Hyponatremia cases	75	67	75	76	88	62	99	76	91	89	60	65
Hyponatremia %	8,3	7,8	8,5	8,9	9,9	6,7	10,2	8,3	10,4	9,8	7,2	7,2
Hypernatremia cases	22	17	22	15	18	17	9	9	13	18	12	19
Hypernatremia %	2,4	2	2,5	1,8	2	1,8	0,9	0,9	1,5	2	1,4	2,1
Hypokalemia cases	86	91	88	107	90	122	130	104	117	109	86	91
Hypokalemia %	9,5	10,7	10	12,6	10,1	13,3	13,4	11,4	13,4	12	10,3	10,1
Hyperkalemia cases	42	33	36	42	40	31	42	38	42	35	32	40
Hyperkalemia %	4,6	3,9	4,1	4,9	4,5	3,4	4,3	4,2	4,8	3,9	3,9	4,4

While Tmean is mean monthly temperature, Tmax is mean maximum daily temperature and Humidity is mean monthly humidity. Temperatures given in °Celsius and humidity in percent.
doi:10.1371/journal.pone.0092150.t003

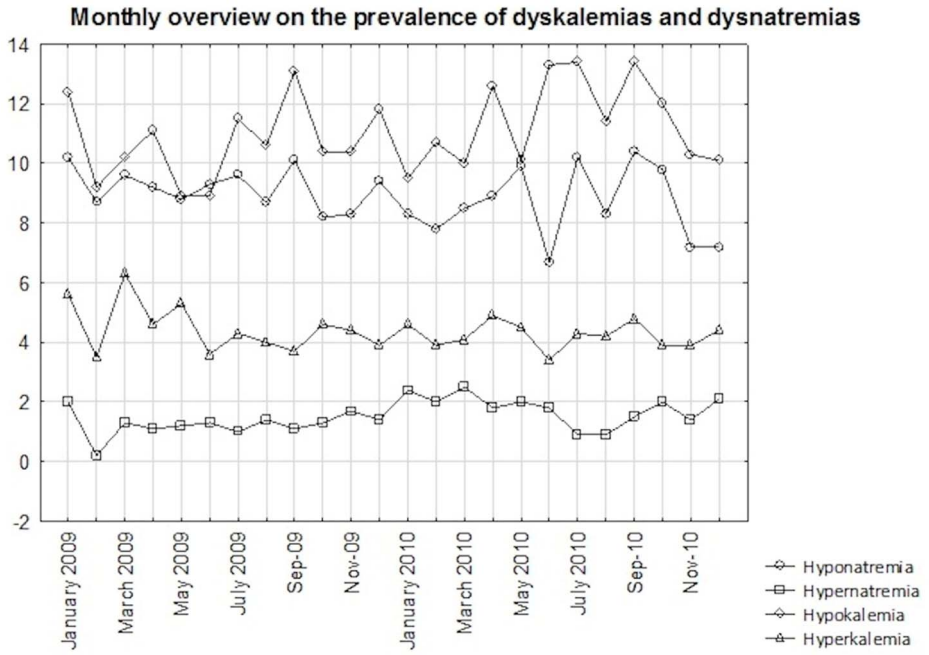

Figure 1. Monthly prevalence of electrolyte disorders. Numbers are given in percent.
doi:10.1371/journal.pone.0092150.g001

hyperkalemia. 1.986 (8.9%) patients had hyponatremia defined as a serum sodium <135 mmol/L. 1.337 patients (67% of patients with hyponatremia) had borderline hyponatremia (>130 and < 135 mmol/L), 459 (23%) had moderate (>125 and ≤130 mmol/L) and 190 (10%) had severe (≤125 mmol/L) hyponatremia. 335 patients (1.5%) had hypernatremia with a serum sodium exceeding 145 mmol/L. 306 patients had borderline hypernatremia (>145 and ≤150 mmol/L), 21 had moderate (>150 and ≤155 mmol/L) and 8 patients had severe (>155 mmol/L) hypernatremia. The median monthly prevalence of hyponatremia was 8.85% (8.3–9.65), of hypernatremia 1.4% (1.18–2), of hypokalemia 10.65% (10.1–12.1) and of hyperkalemia 4.3% (3.9–4.6). An overview of the monthly prevalences of electrolyte disorders is given in Figure 1. Tables 2 and 3 give the prevalence rates of electrolyte disorders according to the admission month.

There were weak inverse correlations between the daily maximum temperatures and serum sodium ($R = -0.04$, $p<0.05$) and serum potassium ($R = -0.03$, $p<0.05$) and a positive correlation with serum creatinine ($R = 0.01$, $p<0.05$). Also, we saw an inverse correlation with daily sunshine duration with serum sodium ($R = -0.02$, $p<0.05$) and serum potassium ($R = -0.02$, $p<0.05$). A significant correlation between humidity levels and serum sodium was found ($R = 0.02$, $p<0.05$).

Comparing the prevalences of electrolyte disorders of patients admitted during days with a daily maximum temperatures above or equaling 30°C, significantly more patients presented with hyponatremia during hot days (11 versus 9%, $p = 0.04$. No difference was found for hypernatremia (2.1 versus 1.5%, $p = 0.28$), hypokalemia (9.8 versus 11%, $p = 0.34$) and hyperkalemia (4.6 versus 4%, $p = 0.76$). During heat periods (3 to 5 days with daily maximum temperatures ≥30°C) no difference was found for hyponatremia (8.5 versus 9%, $p = 0.54$), hypernatremia (1.3 versus 1.5%, $p = 0.46$), hypokalemia (11.9 versus 11%, $p = 0.34$) and hyperkalemia (3.7 versus 4%, $p = 0.23$).

In the group of the elderly patients with an age ≥80 years also no difference between patients admitted during heat periods and those admitted during a time without heat periods was found for hyponatremia (18.3 versus 16.9%, $p = 0.66$), hypernatremia (0 versus 1.9%, $p = 0.09$), hypokalemia (10.1 versus 10%, $p = 0.83$) and hyperkalemia (10.6 versus 10.1%, $p = 0.95$).

Overall, 588 patients (2.6%) died during hospitalization. Detailed mortality rates for subgroups are given in Table 4.

Table 4. Mortality rates overall and in patient subgroups.

Patient group	Died	Survived	Mortality
Overall	588	21.651	2.6%
Age ≥80 years	141	2.088	6.3%
Hyponatremia	130	1.856	6.5%
Hypernatremia	26	309	7.8%
Hypokalemia	112	2347	4.6%
Hyperkalemia	102	862	10.5%

doi:10.1371/journal.pone.0092150.t004

Table 5. Factors associated with mortality in the multivariate Cox regression model.

Factor	Odds ratio	95% confidence interval	Significance
Serum sodium			
Normal serum sodium (reference)			
Hyponatremia	1.72	1.36–2.18	p<0.0001
Hypernatremia	3.62	2.34–5.59	p<0.0001
Age ≥80 years	1.51	1.04–2.19	p<0.0001
Admission during heat period	1.58	1.24–2.0	P = 0.03
Serum creatinine	1.002	1.001–1.002	p<0.0001

doi:10.1371/journal.pone.0092150.t005

In the multivariate Cox regression model the presence of hyponatremia, hypernatremia, elderly age (≥80 years) as well as admission to the hospital during a heat period were independent predictors of mortality. Details on the results of the Cox regression are given in Table 5.

Discussion

In the present study we investigated the impact on temperature extremes on the prevalence of electrolyte disorders in patients presenting to the emergency department of a large tertiary care hospital. Although we found weak inverse correlations between daily maximum temperatures and serum sodium and potassium and a significantly higher prevalence of hyponatremia during extremely hot days, a clear link between temperature extremes and the prevalence of dysnatremias and dyskalemias could not be shown. Even in the group of suspectedly most vulnerable patients above age 80 years we could not find a connection between hot periods and an increased prevalence of disorders of serum sodium and potassium in patients presenting to our emergency department. However interestingly we found admission to the hospital during periods of (for the region) extraordinary warmth to be independently associated with mortality.

So far, this is the first study investigating the effect of temperature extremes on the prevalence of dysnatremias and dyskalemias in a large set of outpatients presenting to the emergency department of a large university hospital. The theoretic link between hot temperatures and the development of dysnatremias is obvious: Hot temperatures usually result in increased sweating and loss of hypotonic fluids [12]. In patients with either a disturbed sense of thirst or an impaired access to free water, as for example some patients in nursing homes, this can result in development of dehydration and development of hypernatremia [3,5,13]. On the other hand, increased sweating and excess substitution of fluid losses by ingestion of hypotonic fluids has been described in the setting of endurance exercisers [11,14,15]. Both mechanisms may also play a role in the development of dyskalemias. However, although we found an increased prevalence of hyponatremia in patients admitted during periods of heat, no such connection could be shown for hypernatremia, hypokalemia or hyperkalemia. Surprisingly, also in elderly patients we did not find a convincing connection between temperature extremes and the prevalence of electrolyte disorders.

On the other hand, our study showed that patients admitted to the hospital during periods of heat had an independently increased mortality compared to those hospitalized during cooler periods. A recent study found that patients with bradyarrythmias with need for transient pacing were significantly more often presenting during the hottest months of the year and many of them showing signs of dehydration [16]. It was found in sports medicine studies that dehydration leads to decreased strength and power [17]. Also, decrements in physical, visuomotor, psychomotor, and cognitive performance were noted in previous studies [18]. Taken together it appears that there are enough reasons to explain an increased mortality in patients exposed to excess temperatures during heat periods. However, although often suspected, based on our current data, electrolyte disorders seem not to play a part.

Our study is limited by some factors: we do not have data on how many of our patients were nursing home residents or had an impaired excess to free water for other reasons. Naturally, we do not have information on the exact temperatures the patients were exposed to before admission due to variances in living conditions (air condition, homes situated at higher sea level, etc.).

Conclusions

We present the first study investigating the effect of heat periods on the prevalence of dysnatremias and dyskalemias. Although we found an increased prevalence of hyponatremia during heat periods, no convincing connection could be found for hypernatremia or disorders of serum potassium.

Author Contributions

Conceived and designed the experiments: GL CAP GCF AKE. Performed the experiments: CS ABL GMF. Analyzed the data: GL CAP GCF. Contributed reagents/materials/analysis tools: ABL GMF. Wrote the paper: GL CAP.

References

1. Arampatzis S, Funk GC, Leichtle AB, Fiedler GM, Schwarz C, et al. (2013) Impact of diuretic therapy-associated electrolyte disorders present on admission to the emergency department: a cross-sectional analysis. BMC Med 11: 83.
2. Funk GC, Lindner G, Druml W, Metnitz B, Schwarz C, et al. (2010) Incidence and prognosis of dysnatremias present on ICU admission. Intensive Care Med 36: 304–311.
3. Himmelstein DU, Jones AA, Woolhandler S (1983) Hypernatremic dehydration in nursing home patients: an indicator of neglect. J Am Geriatr Soc 31: 466–471.
4. Hawkins RC (2003) Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta 337: 169–172.
5. Lindner G, Funk GC (2013) Hypernatremia in critically ill patients. J Crit Care 28: 216 e211–220.
6. O'Neill MS, Ebi KL (2009) Temperature extremes and health: impacts of climate variability and change in the United States. J Occup Environ Med 51: 13–25.
7. Rikkert MG, Melis RJ, Claassen JA (2009) Heat waves and dehydration in the elderly. BMJ 339: b2663.

8. Nayha S (2007) Heat mortality in Finland in the 2000s. Int J Circumpolar Health 66: 418–424.
9. Robine J, Cheung S, Le Roy S, Van Oyen H, Herrmann F (2003) Report on excess mortality in Europe in Summer 2003. EU Community Action Programme for Public Health, Grant Agreement 2005114.
10. Knechtle B, Gnadinger M, Knechtle P, Imoberdorf R, Kohler G, et al. (2011) Prevalence of exercise-associated hyponatremia in male ultraendurance athletes. Clin J Sport Med 21: 226–232.
11. Almond CS, Shin AY, Fortescue EB, Mannix RC, Wypij D, et al. (2005) Hyponatremia among runners in the Boston Marathon. N Engl J Med 352: 1550–1556.
12. Rose DB, Post TW (2001) Clinical physiology of acid-base and electrolyte disorders. New York: McGraw-Hill.
13. Adrogue HJ, Madias NE (2000) Hypernatremia. N Engl J Med 342: 1493–1499.
14. Flinn SD, Sherer RJ (2000) Seizure after exercise in the heat: recognizing life-threatening hyponatremia. Phys Sportsmed 28: 61–67.
15. Armstrong LE, Curtis WC, Hubbard RW, Francesconi RP, Moore R, et al. (1993) Symptomatic hyponatremia during prolonged exercise in heat. Med Sci Sports Exerc 25: 543–549.
16. Palmisano P, Accogli M, Zaccaria M, Vergari A, De Luca De Masi G, et al. (2013) Relationship between seasonal weather changes, risk of dehydration, and incidence of severe bradyarrhythmias requiring urgent temporary transvenous cardiac pacing in an elderly population. Int J Biometeorol.
17. Hayes LD, Morse CI (2010) The effects of progressive dehydration on strength and power: is there a dose response? Eur J Appl Physiol 108: 701–707.
18. Grandjean AC, Grandjean NR (2007) Dehydration and cognitive performance. J Am Coll Nutr 26: 549S–554S.