Sodium Supplementation and Exercise-Associated Hyponatremia during Prolonged Exercise

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ABSTRACT

HOFFMAN, M. D., and K. J. STUEMPFLE. Sodium Supplementation and Exercise-Associated Hyponatremia during Prolonged Exercise. *Med. Sci. Sports Exerc.*, Vol. 47, No. 9, pp. 1781–1787, 2015. **Purpose**: This work examines whether sodium supplementation is important in prevention of hyponatremia during continuous exercise up to 30 h and whether any distinguishing characteristics of those developing hyponatremia could be identified. **Methods**: Participants of the 161-km Western States Endurance Run underwent body weight measurements before, during, and after the race, completed a postrace questionnaire about drinking strategies and use of sodium supplementation during four race segments, and underwent analysis of postrace serum sodium concentration. **Results**: The postrace questionnaire was completed by 74.5% of the 376 starters, a postrace blood sample was provided by 61.1% of the 296 finishers, and 53.0% of finishers completed the postrace survey and also provided a postrace blood sample. Among this population, the incidence of hyponatremia among finishers was 6.6% and sodium supplements were used by 93.9% of the runners. Postrace serum sodium concentration was found to be directly related to the rate of sodium intake in supplements ($r = 0.24$, $P = 0.0027$) and indirectly related to the percentage change in body weight from immediately before the race start ($r = -0.19$, $P = 0.010$). There was no difference in rate of sodium intake in supplements between the hyponatremic and normonatremic finishers, and none of the hyponatremic finishers lost >4.3% body weight. Hyponatremic finishers were not distinguished from normonatremic or hypernatremic finishers by other runner characteristics considered, drinking strategies, or gastrointestinal symptoms of nausea and vomiting. **Conclusions**: We conclude that a low sodium intake in supplements has minimal responsibility for development of hyponatremia during continuous exercise up to 30 h, whereas overhydration is the primary characteristic of those developing hyponatremia. Therefore, avoiding overhydration seems to be the most important means for preventing hyponatremia under these conditions. **Key Words:** DEHYDRATION, ENDURANCE EXERCISE, EXERCISE, NAUSEA, SODIUM, WATER–ELECTROLYTE IMBALANCE

Sodium supplementation during ultramarathon running has become common practice. Our work at the 161.3-km Western States Endurance Run (WSER) demonstrated that 90%–96% of runners used sodium supplements during the event in 2011 and 2013 (17,38). Such extensive use of sodium supplementation is due to a common believe that it can prevent muscle cramping, dehydration, and hyponatremia and that it may even reduce nausea. Such claims are widespread in the marketing material of sodium supplement manufacturers. Some of these touted benefits are also found in the medical literature (2–4,22).

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Despite the claims, sodium supplementation during exercise has not been shown to prevent the development of exercise-associated hyponatremia (EAH) during activities lasting <18 h (5,12,33,35). In cases where an athlete drinks beyond thirst or fully replaces body weight losses during exercise of this duration, supplemental sodium may attenuate the decline in blood sodium concentration (5,36) but it will not prevent hyponatremia when overdrinking persists (12). Whether supplemental sodium during exercise lasting beyond 18 h has greater importance has not been systematically examined.

The primary purpose of this study was to investigate whether sodium supplementation is important for preventing EAH in a 161-km ultramarathon. Secondarily, we explored whether any distinguishing characteristics of runners developing EAH could be identified.

METHODS

Subjects and setting. This study was performed at the 2014 161.3-km WSER. The course runs through the Sierra Nevada of northern California, with 5500 m of cumulative

climb and 7000 m of cumulative descent. Other race details have been provided elsewhere (13,16,18,20,25,26). Nearby weather station ambient temperatures during the race ranged from a low of 0°C just after the start to a high of 31.7°C, which was similar to the historical median high temperature for this event, although on-course measurements (Vantage Vue Wireless Weather Station, Davis Instruments, Vernon Hills, IL) revealed a maximum air temperature of 39°C at which time the relative humidity was 13%. Our institutional review boards provided approval for the research, with electronic consent obtained from those participating in the questionnaire.

Measurements. All race participants underwent body weight measurements during registration the day before the race, within 1.5 h before the start of the race, when reaching 47.8, 89.6, and 125.5 km during the race, as well as immediately again after finishing the race. All weight measurements were made with calibrated scales (Sunbeam Products, Inc., Health O Meter, model 349KLX; Boca Raton, FL) placed on firm, level surfaces. During each measurement, the runner wore running clothes and shoes, but other items such as jackets, waist packs, and hydration vests were removed and nothing was permitted in the runner's hands. Before the event, the scales were examined for consistency. Although the maximum variation between scales was less than 0.5% across the weight range of our subjects, correction equations were developed to standardize all weight measurements to a single scale.

Runners who were willing to provide blood samples at the finish had samples drawn within a few minutes after completing the race. The runner was seated while blood was drawn into heparinized tubes via an antecubital vein. Samples were stored in a cooler until analyzed by a clinical laboratory for serum sodium as well as blood urea nitrogen and creatine kinase (CK) concentrations (Dimension EXL; Siemens Aktiengesellschaft, Munich, Germany).

Race participants were alerted in prerace correspondence that they would be requested to complete a postrace Web-based questionnaire. An electronic invitation to complete the questionnaire was sent to all race starters during the event. Reminder e-mails were sent to those who had not completed the survey 7 and 12 d later, and the survey was closed 15 d after the race. The questionnaire requested information on running background and training during the 3 months before the race, information about the main factors that were used to determine fluid intake (thirst, predetermined drinking schedule, maximum tolerated, change in body weight, urine color, other), and presence or absence of nausea and vomiting during each of the four race segments defined by the location of body weight measurements.

The questionnaire also requested information about the fluid type consumed (only water, mostly water, and some electrolyte drink, about equal water and electrolyte drink, mostly electrolyte drink, and only electrolyte drink) and the number and brand of sodium supplements used, if any, during each of the four race segments. The questionnaire listed the most commonly used commercially available products from which the runner could select, and the runner also had the opportunity to specify other forms of sodium supplementation that might have been used. Rate of sodium intake in supplements was then determined using the known sodium content of each brand of sodium supplement and official split times.

Analysis of data. To allow for comparison with previous publications, we used the same definitions for serum sodium and hydration status, as used previously (15,24). Serum sodium concentrations >145 $mmol \cdot L^{-1}$ were defined as hypernatremia, 135 to ≤145 $mmol \cdot L^{-1}$, as normonatremia, 129 to <135 $mmol \cdot L^{-1}$, as biochemical hyponatremia, and <129 $mmol \cdot L^{-1}$, as clinically significant hyponatremia. We used body weight change from that at registration of ≥0 as overhydration, <0 to −3% as euhydration, and less than −3% as dehydration. For analyses of body weight change that did not involve classifying a runner by hydration status, the weight immediately before the start was also considered.

Between-group comparisons of categorical data were made with the Fisher exact test or chi-square test. Continuous data underwent normality testing with the D'Agostino–Pearson test. Group comparisons of continuous data were made with one-way ANOVA and Tukey posttest or the Kruskal–Wallis test and Dunn multiple comparison test, depending on whether the data passed normality testing. Correlations between two variables were determined with Pearson correlation analyses. Because percentage weight change and supplemental sodium intake are pertinent variables under control by the runner, multiple regression analysis was performed with these as independent variables and serum sodium concentration as the dependent variable. Statistical significance was set at $P < 0.05$.

RESULTS

Characteristics of participants. The race had 376 starters and 296 (78.7%) finishers. There were 280 (74.5%) starters completing the postrace questionnaire, and completion rate was similar ($P = 0.46$) between men and women but higher ($P = 0.0005$) among finishers (78.7%) than that among nonfinishers (58.8%). Of those completing the survey, it was done so within 7 d after the race by 55.7% and within 10 d by 88.9%. A postrace blood sample was provided by 181 (61.1%) finishers, and there were 155 (53.0%) finishers who completed the postrace questionnaire and also provided a postrace blood sample.

Among the finishers providing a postrace blood sample, 6.6% were hyponatremic (biochemical or clinically significant), 86.2% were normonatremic, and 7.2% were hypernatremic. The distribution into the four groups based on serum sodium concentration and three groups based on hydration status is shown in Table 1. The incidence of hyponatremia was comparable ($P = 0.72$) between men (6.3%) and women (7.9%).

Comparison of hyponatremic, normonatremic, and hypernatremic runners. Finishers with hyponatremia,

TABLE 1. Number (%) of 181 finishers who underwent postrace blood analysis classified into different groups by postrace hydration and serum sodium status.

Category	Overhydration	Euhydration	Dehydration	Total
Clinically significant hyponatremia	1 (0.6)	0 (0)	0 (0)	1 (0.6)
Biochemical hyponatremia	3 (1.7)	7 (3.9)	1 (0.6)	11 (6.1)
Normonatremia	31 (17.1)	94 (51.9)	31 (17.1)	156 (86.2)
Hypernatremia	3 (1.7)	6 (3.3)	4 (2.2)	13 (7.2)
Total	38 (21.0)	107 (59.1)	36 (19.9)	181 (100.0)

For comparison with previous work, these data are based on change in finish weight from weight measured during registration. See text for criteria used for each group.

normonatremia, and hypernatremia were compared across a number of variables. As expected, postrace serum sodium concentration was different ($P < 0.0001$) among groups, but there were no other runner characteristic or postrace blood values that were different among the groups (Table 2).

Factors determining the fluid volume and fluid type consumed also did not differ among groups. This was true when considering an affirmative response for at least one of the four segments of the race, as displayed in Table 3, and when considering just the last race segment.

Comparison of changes in body weight and hydration behaviors also revealed no group differences except with regard to the intake rate of sodium in supplements during the last race segment (Table 4). Hypernatremic finishers had a higher ($P < 0.05$) rate of sodium consumption in supplements during the last race segment than hyponatremic finishers, but there was no difference in rate of sodium intake in supplements between the hyponatremic and normonatremic finishers.

The presence of nausea did not differ among groups whether considering the presence of the symptom during at least one segment of the race (50.0% for hyponatremics, 54.8% for normonatremics, and 75.0% for hypernatremics; $P = 0.50$) or during the last race segment (50.0% for hyponatremics, 37.8% for normonatremics, and 50.0% for hypernatremics; $P = 0.60$). The presence of vomiting also did not differ among groups.

Associations with postrace serum sodium concentration. There was direct relation between postrace serum sodium concentration and rate of sodium consumption in supplements, whether considering rate of sodium supplementation intake across the entire race or the last segment (Fig. 1).

Other significant relations were found for postrace serum sodium concentration with blood CK concentration ($r = -0.19$, $P = 0.012$), finish time ($r = -0.21$, $P = 0.004$), and percentage weight change whether the weight change was based on the weight at registration ($r = -0.16$, $P = 0.031$) or immediately before the start ($r = -0.19$, $P = 0.010$), as displayed in Figure 2.

Multiple regression analysis with percentage weight change and supplemental sodium intake rate as independent variables and serum sodium concentration as the dependent variable revealed r^2 values of 0.10–0.11, depending on whether the data over the entire race or the last segment were analyzed.

DISCUSSION

A key finding of this study is that the rate of sodium intake in supplements was found to have a weak positive relation with postrace serum sodium concentration (Fig. 1). Inspection of Figure 1 shows the hyponatremic finishers clustered at the lower sodium supplement intake rate of <300 mg·h^{-1} considering the entire race and <150 mg·h^{-1} considering the final segment. Yet the rate of sodium intake in supplements accounted for only 6%–8% of the variability in postrace serum sodium concentration whether considering the entire race or the last segment. Furthermore, the majority of runners with these rates of sodium intake in supplements were normonatremic, thus accounting for the lack of statistical difference in rate of sodium intake in supplements

TABLE 2. Comparison of selected runner characteristics and results of postrace blood analyses among hyponatremic ($n = 12$), normonatremic ($n = 135$), and hypernatremic ($n = 8$) finishers.

Variable	Hyponatremic	Normonatremic	Hypernatremic	*P* Value
Runner characteristics				
Age (yr)	36 ± 11	42 ± 8	44 ± 11	0.053
Sex (% men)	75.0	77.0	87.5	0.52
Ultramarathon running experience (yr)	4 (2–7)	5 (3–8)	6 (5–12)	0.18
Previous 161-km ultramarathon finishes (*n*)	2 (0–4)	2 (1–5)	6 (1–8)	0.27
Previous 161-km ultramarathon drops (*n*)	0 (0–2)	0 (0–1)	0 (0–6)	0.66
Average running distance (km·wk^{-1})[a]	99 (74–127)	97 (80–113)	109 (61–129)	0.78
Highest running distance in 1 wk (km)[a]	166 (114–193)	145 (122–169)	160 (132–176)	0.40
Longest single run (km)[a]	97 (68–100)	80 (64–100)	80 (80–100)	0.56
Finish time (h)	26.70 (23.00–29.20)	26.69 (23.19–28.73)	22.95 (18.74–26.12)	0.21
Postrace blood analyses				
Serum sodium (mmol·L^{-1})	133 (131–134)*	140 (138–142)*	146 (146–147)*	<0.0001
Blood CK (IU·L^{-1})	29,248 (11,056–44,585)	14,275 (6829–30,924)	9409 (5321–14,043)	0.21
Blood urea nitrogen (mg·dL^{-1})	34 (25–40)	26 (20–34)	30 (25–33)	0.060
Blood creatinine (mg·dL^{-1})	1.35 (1.08–1.50)	1.20 (1.05–1.41)	1.36 (1.22–1.52)	0.29

Data are for those who completed the postrace questionnaire and obtained postrace blood studies. Values are reported as mean ± SD if normally distributed for all groups, median and interquartile range if not normally distributed, or percentage.

[a]During the 3 months before the event.

*$P < 0.05$ on posttest for each pairwise comparison between conditions where symbol is present.

TABLE 3. Percentage of hyponatremic (n = 12), normonatremic (n = 135), and hypernatremic (n = 8) finishers reporting different factors determining how much fluid was consumed and the type of fluid consumed during at least one of the four segments of the race.

Fluid Consumption Approach	Hyponatremic	Normonatremic	Hypernatremic	*P* Value
Main determinants of fluid volume				
Thirst	66.7	83.0	87.5	0.34
Predetermined schedule	41.7	31.9	25.0	0.71
Change in body weight	50.0	29.6	12.5	0.18
Maximum tolerated	25.0	26.7	37.5	0.79
Urine color	41.7	25.2	25.0	0.46
Other[a]	16.7	9.6	0	0.33
Fluid type consumed				
Only water	16.7	37.0	62.5	0.11
Mostly water and some electrolyte drink	66.7	40.0	62.5	0.11
Approximately equal water and electrolyte drink	58.3	40.7	12.5	0.12
Mostly electrolyte drink	8.3	34.8	50.0	0.11
Only electrolyte drink[a]	0	7.4	25.0	0.60

Data are for those who completed the postrace questionnaire and obtained postrace blood studies.
[a]Because of small values, the normonatremic and hypernatremic groups were combined for analysis.

between the hyponatremic and normonatremic groups. Therefore, it is evident that a low sodium intake in supplements is not a prime factor responsible for EAH during continuous exercise in moderately hot conditions for up to 30 h.

A weak negative relation was also found between postrace serum sodium concentration and percentage change in body weight (Fig. 2), with the latter accounting for only 3%–4% of the variability in serum sodium concentration. In fact, neither percentage change in body weight nor rate of sodium intake in supplements contributed much to determining serum sodium concentration even when considered together in multiple regression analysis. Nonetheless, it is noteworthy that only one of 12 of those with hyponatremia at the finish had lost more than 4% body weight from immediately before the start and that this particular individual had only lost 4.3%. A weight loss of around 4% relative to the weight immediately before the start should be anticipated to maintain euhydration in an event of this duration (15). From previous work, it is now recognized that those who become symptomatic with EAH have gained weight or lost less than 3%–4% body weight (19,24) and that EAH can be associated with considerable sodium intake (19). Given this, our interpretation of the present findings is that overhydration rather than inadequate supplemental sodium intake is a greater contributor to the development of EAH, particularly symptomatic EAH.

The incidence of EAH in the present study was 6.6%, and as far as we are aware, none of the cases were symptomatic. Fortunately, symptomatic cases of EAH have been quite rare at the WSER (19), but in an analysis of data from 2008 through 2012, the overall EAH incidence ranged from 4.6% to 51.0% (15). In that analysis, a relation was observed between EAH incidence and ambient temperature. On the basis of those findings, we might have anticipated a somewhat higher EAH incidence of approximately 15%–30% under the ambient temperature conditions of the present study rather than the 6.6% that was observed.

Interestingly, the incidence of overhydration in the present study was 21.0% compared with an average of 36.5% in our analysis of data from 2008 through 2012 (15). In addition, of note is the present finding of the weak negative relation between postrace serum sodium concentration and percentage change in body weight discussed previously. We had previously found these variables to be directly related in our combined analysis across 5 yr and 669 observations (15), which had been in contrast with the inverse relations found by others (1,7,9,10,12,21,24,27,30–32,37). It is now

TABLE 4. Comparison of body weight change and hydration behaviors across entire course and last segment (36 km) among hyponatremic (n = 12), normonatremic (n = 135), and hypernatremic (n = 8) finishers.

Variable	Hyponatremic	Normonatremic	Hypernatremic	*P* Value
Body weight change				
Weight change from across course relative to start (%)	−1.7 ± 1.7	−2.2 ± 1.8	−2.8 ± 1.5	0.43
Minimum weight across course relative to start (%)	−2.7 ± 1.3	−3.1 ± 1.4	−3.5 ± 1.0	0.39
Maximum weight across course relative to start (%)	−1.0 ± 1.6	−1.5 ± 1.6	−2.2 ± 0.9	0.22
Weight change across last segment (%)	0.1 (−0.6 to 0.5)	0.0 (−0.5 to 0.5)	0.4 (−0.1 to 0.6)	0.66
Hydration behaviors across entire course				
Sodium supplementation all segments (%)	41.7	55.6	62.5	0.59
No sodium supplementation any segment (%)[a]	0	8.9	0	0.60
Drink to thirst all segments (%)	33.3	50.4	75.0	0.19
No sodium supplementation + drink to thirst all segments (%)[a]	0	6.7	0	1.0
Sodium supplement intake rate ($mg \cdot h^{-1}$)	85 (34–181)	128 (50–254)	233 (182–349)	0.10
Hydration behaviors across last segment				
Sodium supplementation (%)	58.3	68.9	100.0	0.12
Drink to thirst (%)	41.7	66.7	75.0	0.18
No sodium supplementation + drink to thirst (%)	8.3	23.0	0	0.16
Sodium supplement intake rate ($mg \cdot h^{-1}$)	84 (0–120)*	90 (0–229)	218 (195–332)*	0.007

Data are for those who completed the postrace questionnaire and obtained postrace blood studies. Values are reported as mean ± SD if normally distributed for all groups, median and interquartile range if not normally distributed, or percentage.
[a]Because of small values, the normonatremic and hypernatremic groups were combined for analysis.
*$P < 0.05$ on posttest for each pairwise comparison between conditions where symbol is present.

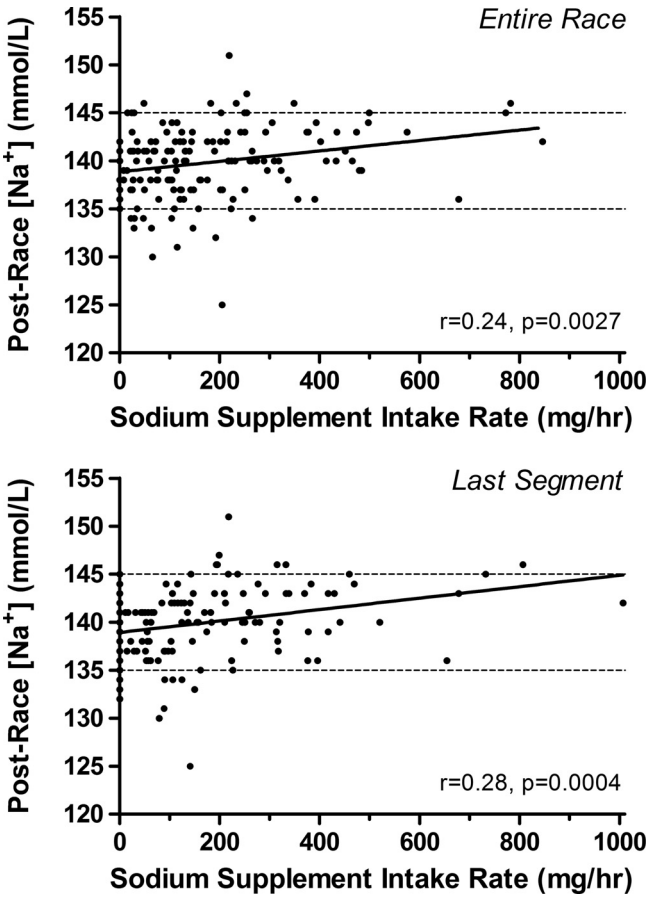

FIGURE 1—Relation of postrace serum sodium concentration ([Na^+]) with rate of sodium intake in supplements averaged across the entire course (top) and over the last 36 km (bottom) for the 155 finishers completing the postrace questionnaire and providing postrace blood samples. *Dashed lines* show the upper and lower limits of normal serum sodium concentration.

evident that the explanation for our unique finding of a direct relation between postrace serum sodium concentration and percentage change in body weight was related to a high frequency of overhydration combined with excessive sodium supplementation. Educational efforts at this event about proper hydration may account for what seems to be a lower incidence of EAH and overhydration in 2014 as well as the reversal of the relation between postrace serum sodium concentration and percentage change in body weight.

This study found that those who were hyponatremic at the finish were not distinguished from those who were normonatremic or hypernatremic by any runner characteristic examined, drinking strategies, or by the presence of gastrointestinal symptoms of nausea and vomiting. These findings are similar to those of our previous work (14), except that we had previously found that those who were hyponatremic had completed fewer 161-km ultramarathons than those who were not hyponatremic. This effect seems to have been lost as a result of participants of the WSER on the whole having less ultramarathon running experience than in the past.

Findings of the previous study (14) also differed from those of the present in that those with and without hyponatremia had statistically different postrace blood CK concentrations. Because of wide variability in CK concentrations, a statistical difference was not evident in the present study. However, a significant relation between postrace serum sodium and CK concentration was evident. This finding offers further support to the suggested link between rhabdomyolysis and EAH (6,8,16,28,29,34). It has been proposed that rhabdomyolysis is a stimulus for EAH on the basis of a strong relation between postexercise blood interleukin-6 and CK concentrations (29) and the recognition that interleukin-6 is a nonosmotic stimulus for arginine vasopressin secretion (29,34). Yet it should be noted that no statistical relation was found between postrace interleukin-6 and arginine vasopressin concentrations at a 56-km ultramarathon (11). The reverse causal relation has also been proposed in that EAH could augment rhabdomyolysis through changes in intracellular potassium and/or calcium concentrations or through hypotonic cell swelling, both of which destabilize the muscle cell membrane and facilitate lysis (8). Unfortunately, the present work does not clarify the mechanism that might be involved.

Hyponatremic finishers did not seem to consume a higher proportion of their fluid in the form of water (as opposed to electrolyte containing beverages) than normonatremics, nor were the hyponatremics more likely to have not used sodium supplements or less likely to drink to thirst. Overall, 79.6% of runners reported that drinking to thirst was a main determinant for the amount of fluid consumed during at least one race segment and 41.1% reported this strategy for all segments. This indicates that drinking to thirst as a hydration strategy has increased at this event from 2011 in which only 17% reported they planned to use drinking to thirst (38). It is this change in behavior that likely accounts for the apparent decrease in overhydration.

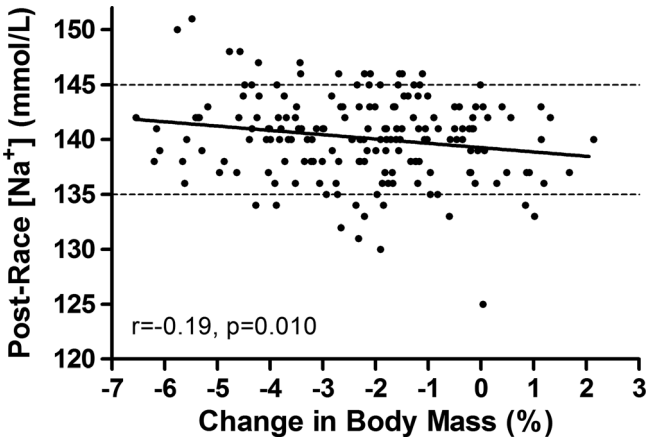

FIGURE 2—Relation of postrace serum sodium concentration ([Na^+]) with percentage change in body weight at the finish from immediately before the start for 181 finishers who underwent postrace blood testing. *Dashed lines* show the upper and lower limits of normal serum sodium concentration.

Sodium supplementation was practiced by over 90% of runners in this study, which is consistent with our previous findings of 90%–96% (17,38). Presumably, this high use of sodium supplements is due to widespread belief that it is valuable for preventing muscle cramping, dehydration, hyponatremia, and nausea. The present work demonstrates that sodium supplementation is not necessary for prevention of EAH during prolonged exercise. This is important information because sodium supplementation has potential adverse effects associated with water retention from excessive sodium intake (19,23).

We acknowledge that this study has some limitations largely because of the restraints of performing research at a competitive event, which generally requires an observational design. As a result, we had to accept that most participants in the present event would be using sodium supplements. We were also limited by an inability to quantify total sodium intake, which requires a full dietary analysis and would not be feasible to accomplish on a large scale. Of course, the postrace questionnaire depended on subject recall, which offered an opportunity for bias, although runners were alerted in advance that they would be asked to provide the information we requested, most completed the survey within a few days of the race, and significant memory distortion relative to sodium supplementation and hydration strategies was not likely because most runners avoid adopting new hydration approaches for an event of this nature. Finally, the blood work was only performed at the finish and it would have been ideal to have also known intermediate serum sodium concentrations but obtaining blood during a race of this nature on a large scale is not feasible.

From this work, we conclude that use of sodium supplements is not necessary to avoid hyponatremia during continuous exercise in moderately hot conditions for up to 30 h. Avoiding overhydration seems to be the most important means for preventing hyponatremia under these conditions.

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The authors declare no conflicts of interest.

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