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Sweat Potassium Decreases with Increased Sweating in Perimenopausal Women

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Authors' contributions

This work was carried out in collaboration between all authors. Authors EA, SIO, JOO and ACU designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors EA and SIO managed the literature searches, managed the experimental process and performed the statistical analyses. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objective: To investigate the relationship between rate of sweat production and sweat potassium concentration in premenopausal (PreM), perimenopausal (PeriM) and postmenopausal (PostM) women after a moderate exercise.

Study Design: This is a cross-sectional study conducted in May 2012 at the Department of Physiology, University of Benin, Nigeria.

Methods: Thirty healthy female volunteers comprising of PreM (aged: 22.5 ± 0.8 yrs, n = 10), PeriM (aged: 46.5 ± 1.1 yrs, n = 10), and PostM (aged: 52.2 ± 0.9 yrs, n=10) participated in the study. Sweat was obtained with a sweat suction apparatus from a 120 cm² circular area marked on the skin of the face and neck after a 15 min walk on a calibrated treadmill at a speed of 4.2 km/h at 27°C and a relative humidity of 85-95%, followed by measurement of sweat volume (SV) and [K⁺]. Sweat rate (SR) was determined by dividing the volume of sweat produced by the duration of exercise. Thirst perception (TP) was self-rated using the Visual Analogue Scale (VAS).

*Corresponding author: E-mail: emmanuelamabebe@yahco.com; *Joint first author **Results:** The PeriM women demonstrated higher SR (ml/min) (P = .01) and SV (ml) (P = .0006) compared to women in the other groups: SR (PeriM = 0.12±0.01; PreM = 0.07±0.02; PostM = 0.06±0.01), and SV (PeriM = 1.7±0.2; PostM = 0.9±0.1). However, they had lower sweat [K⁺] (mmol/l) (P = .04), compared to their PostM counterparts (PeriM = 19.98±1.5; PostM = 24.90±1.8). Furthermore, sweat [K⁺] was inversely associated with SR (r = -0.4, P = .02). Also, change in TP (cm) was highest (P = .001) in the PeriM women (PeriM = 2.5±0.2; PreM = 2.1±0.3; PostM = 0.99±0.2). **Conclusion:** Although excessive sweating can lead to depletion of the body's potassium concentration, the sweat potassium concentration decreases with increased sweating especially in perimenopausal women. This requires further investigation, as it could be an adaptive mechanism inhibiting excessive potassium loss.

Keywords: Sweat rate; sweat volume; sweat potassium; menopause; exercise.

1. INTRODUCTION

Perimenopause also known as menopausal transition is the period of a woman's life preceding the occurrence of the menopause. It includes the period shortly before menopause and the first year after menopause, signalling the onset of the biological, hormonal and clinical symptoms characteristic of menopause [1,2]. During perimenopause, there is frequent amenorrhea and/or increased menstrual irregularities resulting from fluctuations in levels of hypothalamic, pituitary and ovarian hormones [3,4]. Though it can occur earlier, it usually begins in a woman's 40s (mean age 47.5 years), and continues until the cessation of ovulation and menses [3,5-6]. It can last from only a few months to 10 years (average of 4-5 years), terminating at the absence of menstrual flow for more than 12 months (menopause) [2,6-8].

During the menopausal transition stage, increased hot flushes and night sweats are the most frequently reported symptoms [6,9-12]. About 78-85% of perimenopausal women experience hot flushes [13-15]. This is attributed to the decline in ovarian oestrogen levels and thermoregulatory vasodilatory effect of Gonadotrophin releasing hormone (GnRH) and elevated Follicle-stimulating hormone (FSH) [16-18]. Excessive sweating from hot flushes and night sweats can deplete the body's potassium concentration [19].

Sweat rate is higher in perimenopausal women than in premenopausal and postmenopausal women [11], and excessive sweating during menopause depletes some of the body's essential nutrients, especially potassium [19].

In premenopausal women, cyclic changes in plasma and sweat Na^+ concentrations (but not K^+) corresponding with hormonal fluctuations

during menstrual cycle have been documented [20]. Antidiuretic hormone levels undergo fluctuations parallel to that of oestrogen during the menstrual cycle and are increased in postmenopausal women after oestrogen administration indicative of a resultant increase in fluid retention [20,21]. This is due to the osmotic effect of oestrogen leading to increased salt and water retention in reproductive-age women, compared to postmenopausal women [22,23], which appears to be unaffected by changes in potassium excretion [23]. However, progesterone can increase sodium and water excretion through its antagonistic effect on mineralocorticoid receptors [23]. Oestrogen also reduces hot flushes by elevating the core body temperature sweating threshold [24].

Though the sweat patterns and hot flushes of women in menopausal transition stage has been studied extensively [15,25], there is a dearth of information on the variations in sweat electrolytes especially potassium in these women. Since the sweat rate is greater in the perimenopausal stage of a woman's life and excessive sweating can lead to depletion of the body's electrolytes including potassium, this study sought to determine the association between rate of sweat production and sweat potassium excretion in premenopausal (PreM), perimenopausal (PeriM) and postmenopausal (PostM) women. We hypothesise that women in the perimenopausal stage will have higher sweat potassium levels compared to their pre- and postmenopausal counterparts.

2. MATERIALS AND METHODS

2.1 Participants and Experimental Procedure

This is a cross-sectional study conducted in May 2012 at the Department of Physiology, University

of Benin, Nigeria. Eligible participants were randomly selected, healthy active women who consented to being part of the study following adequate information of the experimental procedures. Thirty minutes after presentation at the laboratory, participants were allowed to acclimatise and baseline anthropometric parameters, medical and menstrual histories were obtained. From information obtained via questionnaires completed by participants, trained athletes, smokers, diabetics, pregnant women patients with musculoskeletal and/or and cardiopulmonary diseases were prohibited from this study. Also none of the participants had any clinically proven thyroid dysfunction, depression, sleep disturbances nor was involved in regular physical exercise within the last six months before recruitment. Following recruitment, the women who satisfied the inclusion criteria (N = 30), were classified into PreM (n = 10), PeriM (n= 10), and PostM (n = 10), based on their ages and menstrual cycle history.

Participants' body mass index (BMI), was estimated by dividing their weight by the square of their height (m), i.e. BMI = weight (kg)/height (m²) [26]. The baseline skin temperature, systolic (SBP) and diastolic (DBP) blood pressures were also measured and the mean arterial pressure (MAP) estimated [i.e. MAP = DBP + 1/3 (SBP-DBP)], while the arterial pulse was measured from the right radial artery during exercise.

2.1.1Sweat collection, handling and analysis

Sweat samples were obtained with the aid of a sweat suction apparatus from a 120 cm² circular area marked on the skin of the face and neck regions, after a 15 min walk on a calibrated treadmill, at a speed of 4.2 km per hour at an ambient temperature of ~27°C and a relative humidity of 85-95% [26]. After sweat collection, Sweat volume (SV) was measured and samples were preserved at -4°C until required for further analysis. Sweat rate (SR) was determined by dividing the volume of sweat produced by the duration of exercise.

From the collected sweat sample, sweat potassium concentration $[K^+]$ was determined by photoelectric flame photometry using the improved FP-640 (Ningbo Hinotek Technology Co., Ltd, CN).

2.1.2 Thirst perception rating

Thirst perception (TP) was self-rated before and after the exercise protocol by a mark across a 10

cm scale (Visual analogue scale), with its top and bottom labelled "very thirsty" and "not thirsty" respectively [27-28]. This was performed in response to the question "How thirsty do you feel now?" in each instance i.e. before and after exercise. The change in TP was subsequently estimated. This method of thirst rating is highly reliable and reproducible within individuals [23,29], and correlates with amount of water ingested [30].

2.1.3 Data analyses

All statistical analyses were performed on GraphPad Prism 6.0c (GraphPad Software, Inc. CA). Both Student's t-test and one-way Analysis of variance (ANOVA), were performed to compare differences in SR, SV, S[K⁺], and TP changes between the groups. The Student's tperformed when test was comparing observations between 2 groups (e.g. PreM vs. PeriM or PeriM vs. PostM), while ANOVA was used when comparison was made between the 3 groups (i.e. PreM vs. PeriM vs. PostM). Values are quoted as mean ± SEM, and relationships between the variables were determined by Pearson's correlation coefficient (r). Probability (P) values < 0.05 were considered statistically significant. In addition, using the MetaboAnalyst 3.0 software (TMIC, CA), Partial Least Squares -Discriminant Analysis (PLS-DA) was performed in order to enhance the separation between the groups, and to determine which variable(s) possess the highest discriminative information.

3. RESULTS

As expected the older women in the PeriM and PostM groups had significantly higher BMI and systolic blood pressure compared to the PreM women. However, the baseline skin temperature, diastolic blood pressure, mean arterial pressure, and pulse rate (during exercise) were similar between the groups (Table 1).

Our data showed the PeriM women demonstrated a significantly higher SR compared to the PreM and PostM women (P = .01), whilst their SV was significantly higher than that of the PostM women only (P = .0006) (Fig. 1A-B). However, the sweat [K⁺] was significantly lower in the PeriM women compared with their PostM counterparts (P = .04) (Fig. 1C). Also, the PeriM women indicated the most significant change in TP, whilst their PostM counterparts recorded the least change (P = .001) (Fig. 1D).

	Premenopausal women (n = 10)	Perimenopausal women (n = 10)	Postmenopausal women (n = 10)	P value
Age (years)	22.5±0.8	46.5±1.1	52.2±0.9	< .0001
BMI (kgm⁻²)	23.7±1.3	28.0±1.2	28.4±0.7	.009
Skin temperature (℃)	36.9±0.2	36.2±0.1	36.2±0.2	.052
SBP (mmHg)	113.4±2.7	123.0±2.1	120.2±2.8	.04
DBP (mmHg)	73.7±2.3	80.0±2.6	82.0±2.9	.08
MAP (mmHg)	86.9±2.3	94.3±2.1	94.7±2.8	.051
Pulse rate/min	110.8±4.7	113.1±1.9	114.6±2.2	.7
(during exercise)				

Table 1. Baseline characteristics	of study participants ((Mean±SEM)
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BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure





Fig. 1. Comparison of (A) Sweat rate, (B) Sweat volume, (C) Sweat [K⁺], and (D) change in thirst perception between pre-, peri- and postmenopausal women Bars represent Mean ± SEM, *P < 0.05, **P < 0.001

3.1 Relationship between Sweat Secretion, Thirst Perception and Sweat Potassium Concentration

While we observed an inverse relationship between rate of sweat production (i.e. SR and SV), and sweat [K⁺], this correlation was only statistically significant between SR and sweat [K⁺] (P = .02) (Fig. 2A-B). In other words there was a significant decrease in sweat potassium excretion with increase in SR. Although not statistically significant, there was also a positive correlation between change in TP and sweat [K⁺].

3.2 Discriminative Ability of Measured Variables

Analysis of the median variable importance in projection (VIP) scores showed sweat $[K^+]$ with a VIP score > 1 in all groups had the highest discriminative capacity (Fig. 3). The PeriM women had lower sweat $[K^+]$, but higher SR, SV and TP compared to the PreM and PostM women (Fig. 3A and B), whilst the PostM women showed higher sweat $[K^+]$ and SR, but lower SV and TP compared to the PreM women (Fig. 3C).

Β.









C.

Fig. 2. Association between Sweat [K⁺] and (A) Sweat rate, (B) Sweat volume, and (C) change in thirst perception in pre-, peri- and postmenopausal women. The data show a decrease in Sweat [K⁺] as sweat rate increases



Impact of rate of sweat secretion, sweat potassium concentration and change in thirst perception pre-, peri and postmenopausal women

Fig. 3. PLS-DA model of participants' sweat and thirst data

Sweat [K⁺] had the highest median variable importance in projection (VIP) scores in all three groups. The coloured boxes on the right indicate the relative amount of the corresponding variable in each group. TP, change in thirst perception; SV, sweat volume; SR, sweat rate

4. DISCUSSION

The aim of the current study was to examine the association between rate of sweat production and sweat potassium excretion in middle-age women in different stages of their reproductive life (pre-, peri- and postmenopause). In contrast to our initial conjecture, we observed an inverse association between rate of sweat production and sweat potassium excretion. Moreover, compared to the postmenopausal women, the perimenopausal women excreted significantly greater volume of sweat at a higher rate but with lesser amounts of potassium. A similar trend was also observed in relation to the premenopausal women, albeit it was not statistically significant.

Previously, we demonstrated a significantly higher sweat rate in perimenopausal women compared to their pre- and postmenopausal counterparts, and an association between rate of sweat production, sweat sodium concentration and degree of thirst perception [26]. In line with this, our current data indicate a decrease in sweat potassium with an increase in sweat rate. and a decrease in sweat potassium in the perimenopausal women compared to the other groups despite their higher rate of sweat production. The perimenopausal women excreted higher amounts of hypotonic sweat in relation to their pre- and postmenopausal counterparts. It is not surprising that the premenopausal women exhibited decreased sweat rate and volume compared to the perimenopausal women. This is in agreement with established evidences that oestrogen stimulates increased body water retention via arginine vasopressin (AVP) [22-23], and mitigates hot flushes by elevating the core body temperature sweating threshold [24]. But unexpectedly, the postmenopausal women also excreted lesser volumes of sweat compared to the perimenopausal women despite the knowledge of higher oestrogen levels in perimenopausal transition than in postmenopausal stage [6,25].

Although the perimenopausal women excreted the least amounts of sweat potassium, they also exhibited the highest degree of change in thirst perception after a moderate physical exercise compared to women in the other groups. Change in thirst perception was also directly related to potassium though not statistically sweat significant. This is similar to our previous observation with sweat sodium level [26], and can be attributed to the increased desire to drink induced by excess fluid and electrolytes loss [31]. The high degree of thirst sensation in this group of women could be due to the higher amount of fluid lost in form of sweat and the attendant increase in plasma osmolality as a consequence of increased electrolyte (K^{+}) retention [32-33].

Sweat sodium loss is reduced by aldosterone at the expense of potassium. Aldosterone secretion is mainly regulated by the renin-angiotensin system and serum potassium ion concentration. Aldosterone secretion by the adrenal cortex is directly stimulated by potassium levels while aldosterone in turn decreases serum potassium by stimulating its excretion by the sweat glands, kidney, salivary glands and distal intestinal tract [34]. In contrast to this established viewpoint, our current data show a reduction in sweat potassium excretion with increased sweat production. The reason for as well as the mechanism of this observation is unclear. However, it is suggestive of an adaptive mechanism inhibiting depletion of the body's potassium level especially in the perimenopausal women who also indicated the least sweat potassium levels.

We have also previously reported a nonsignificant reduction in sweat sodium level in perimenopausal women despite higher sweat rate [26]. Similarly, the current study shows significantly lower sweat potassium in the same group of women at least in relation to the postmenopausal women. In addition to the wellestablished role of aldosterone on sodium and potassium regulation, cortisol is also known to exert some level of mineralocorticoid activity comparable to that of aldosterone. Interestingly, alteration in the circadian rhythm of cortisol in women with greater frequency of hot flushes has been reported [35], and sex hormones (i.e. oestrogen and progesterone) have been shown to increase sodium and water retention via AVP and renin-angiotensin-aldosterone stimulation in young and postmenopausal women [22-23]. Taken together, our data could be indicative of a reduced or altered physiological role of the sex hormones and/or mineralocorticoids in the perimenopausal women. Further investigation of the role of these hormones on sweat sodium:potassium ratio in a larger cohort of women across various stages of menopause is necessary.

5. LIMITATIONS

Though our current findings are thoughtprovoking, to substantiate these claims, there is the need for a more robust investigation of the possible factors and mechanisms responsible for these observations particularly in the perimenopausal women. The relatively small sample population (due to our strict exclusion criteria) and the absence data on the stage of menstrual cycle and hormonal levels, as well as thyroid function test at the time of recruitment are identifiable limitations to this study. Also, we obtained sweat samples from the face because

menopausal sweating is reported most frequently around the face, head, neck and chest [15,25]. However, the site or region of sweat sample collection could be a source of variation in sweat production and tonicity. Furthermore, though anticipated, the significantly higher BMI of the perimenopausal older the in and postmenopausal groups compared to the premenopausal women may have impacted our findings. This is because women with high BMI are known to experience more severe and longer durations of hot flushes [25,36-37]. Lastly, being a cross-sectional study conducted at a specific time point [38], the progression of events especially during the menopausal transition stage was not monitored; hence we do not infer a causal relationship between rate of sweat production and sweat potassium loss in menopausal women. Despite these limitations, our findings have rekindled more interest in the endocrinology, metabolism and fluid homeostasis of women in the menopausal transition stage. which has hitherto suffered considerable neglect. Going forward, longitudinal investigations in larger cohorts with defined stages of menstrual cycle, sex hormone levels, thyroid function status etc. are recommended.

6. CONCLUSION

Our data indicate that sweat potassium concentration decreases with increased sweating in middle-age women, and perimenopausal women excrete higher volumes of hypotonic sweat in relation to pre- and postmenopausal women. Although excessive sweating can lead to depletion of the body's electrolytes including potassium, the sweat potassium decreases with increased sweating especially in perimenopausal women. This warrants further investigation, as it could be an adaptive mechanism inhibiting excessive potassium loss.

ETHICAL APPROVAL

This study was reviewed and approved by University of Benin Ethical Committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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