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Underhydration – Another Piece of the Thrombotic Risk Puzzle?

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ABSTRACT

Mitigating thrombosis risk could improve numerous ischemia concerns, including venous thromboembolism and thrombotic stroke. Whereas dehydration has been a scientifically informed proposed risk factor for thrombus formation, routine underhydration (non-clinical, insufficient daily water balance) remains unexamined in this regard. **PURPOSE:** Explore blood concentrations of select coagulation factors in consistently well- (WH) vs. underhydrated (UH) adults. **METHODS:** EDTA plasma was collected from WH and UH healthy, young (21±1y) women (WH n=16; UH n=4) and men (WH n=6; UH n=14). Hydration status was assigned by the collective of morning plasma osmolality (pOsm: WH=286±3; UH=297±4 mOsm·kg^{-1}), morning plasma copeptin (pCop: WH=4.2±1.0; UH=11.4±5.9 pmol·L^{-1}), first morning urine osmolality (fmuOsm: WH=627±234; UH=894±171 mOsm·kg^{-1}), prior 24h uOsm (24uOsm: WH=513±266; UH=781±235 mOsm·kg^{-1}), and prior 5d average uOsm (5duOsm: WH=474±209; UH=714±198 mOsm·kg^{-1}). Plasma was assayed for fibrinogen (pro-coagulant) and tissue plasminogen activator (tPA; anti-coagulant) via ELISA. Unpaired t-tests determined significance between WH and UH, and linear regression was used to reveal the strength of these hydration indicators in predicting coagulation markers. **RESULTS:** All hydration indices were significantly different between WH and UH (<0.05; as defined) with no differences in coagulation markers when measured. However, immediate prior 24h TWI (WH=49.6±21.5; UH=20.9±7.3 ml·kg·d^{-1}) alone may indicate a behavioral response to a differentiation of coagulation states characterized by pOsm and fibrinogen ($p < 0.001$; WH=1236±259; UH=928±260) during temporal conditions of WH and UH and a concomitant tPA response. Accordingly, pOsm significantly and positively contributed to determining tPA ($p=0.04$, $R^2 = 0.13$). **CONCLUSION:** In alignment with clinical (e.g., post-acute stroke) and at large middle- to older-aged populations, we exhibit preliminary data suggesting that elevated pOsm (consequent to underhydration) can contribute to a pro-coagulation state and anti-coagulation response (tPA) in a healthy, young population. Optimizing routine water balance could be a valuable strategy in reducing widespread thrombotic risk.

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INTRODUCTION

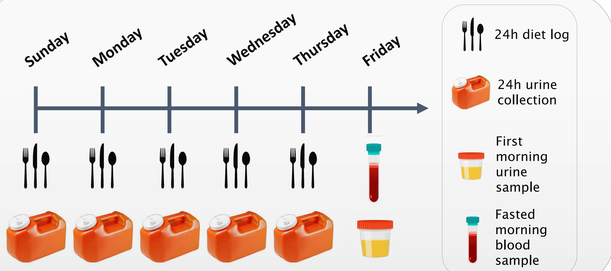
Mitigating thrombosis risk could improve numerous ischemia concerns, including venous thromboembolism (VTE), pulmonary embolism, and thrombotic stroke. Traditional risk factors for VTEs include inactivity/bedrest, recent surgeries, significant injuries, cancer, increased estrogen (including some contraception), and familial predispositions. Whereas dehydration has been a scientifically informed proposed risk factor for thrombus formation, routine underhydration (non-clinical, insufficient daily water balance) remains unexamined in this regard.

PURPOSE

Explore blood concentrations of select coagulation factors in consistently well- (WH) vs. underhydrated (UH) adults.

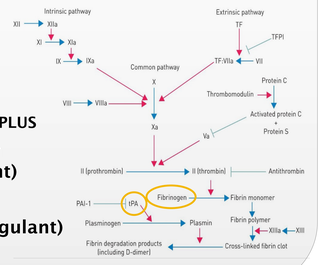
METHODS

Healthy, non-smoking, young (age 20±1y) women (WH n=16; UH n=4) and men (WH n=6; UH n=14) from a variety of racial and ethnic backgrounds were observed for five consecutive mornings for observation.



Data derived:

- **Total water intake (TWI; ml·kg·d^{-1}; self-reported from all beverages and foods)**
- **Urine Osmolality (uOsm)**
- **Plasma Osmolality (pOsm)**
- **Plasma Copeptin (pCop)**
  - **BRAHMS KRYPTOR Compact PLUS**
- **Plasma tissue plasminogen activator (tPA; anticoagulant)**
  - **ELISA (Abcam AB241383)**
- **Plasma fibrinogen (pro-coagulant)**
  - **ELISA (Abcam AB270210)**

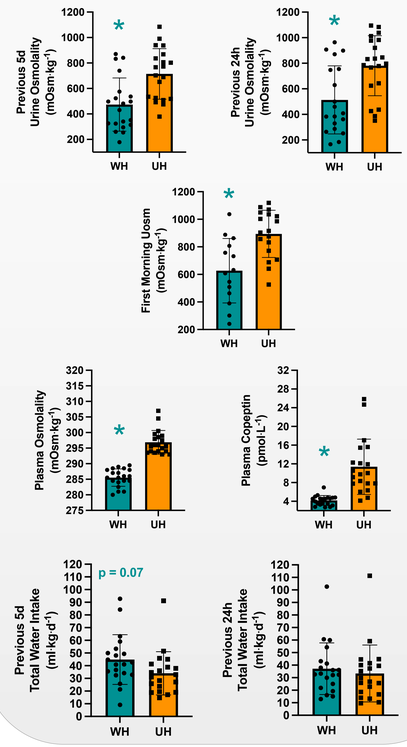


Statistics:

- **Unpaired t-tests determined mean differences between WH and UH participants. (α = 0.05)**
- **Simple linear regression was used to reveal the strength of these hydration indicators in predicting coagulation markers. (α = 0.05)**

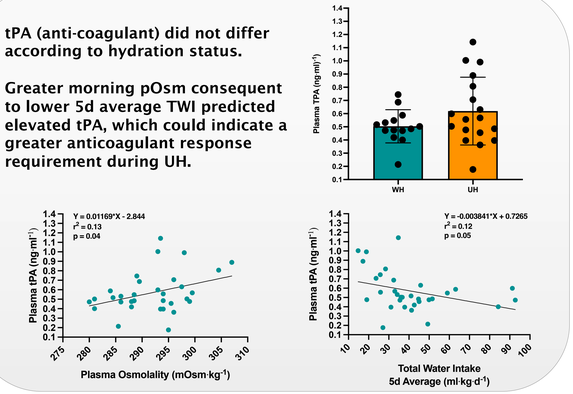
RESULTS

Well-Hydrated (WH) and Under-Hydrated (UH) groups differed by hydration status but not dietary water intake.

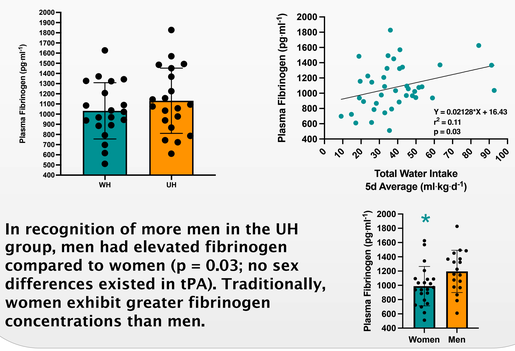


tPA (anti-coagulant) did not differ according to hydration status.

Greater morning pOsm consequent to lower 5d average TWI predicted elevated tPA, which could indicate a greater anticoagulant response requirement during UH.



Fibrinogen (pro-coagulant) did not differ according to hydration status but TWI positively predicted fibrinogen. Elevated tPA likely contributes to greater fibrinogen degradation.



In recognition of more men in the UH group, men had elevated fibrinogen compared to women (p = 0.03; no sex differences existed in tPA). Traditionally, women exhibit greater fibrinogen concentrations than men.

CONCLUSION

In alignment with clinical (i.e., post-acute stroke) and in large middle- to older-aged populations, we exhibit preliminary data suggesting that elevated plasma osmolality consequent to underhydration might contribute to a greater procoagulant state and anticoagulant response in a healthy, young population. Optimizing routine hydration status could be a valuable (simple and cost effective) strategy in maintaining optimal coagulation factor balance. Subsequent research should include evaluation of additional coagulation markers (e.g., PAI-1, D-Dimer, etc.) and a water intervention to determine practical impact of water intake on coagulation balance and VTE risk.