Hepatic Stress: Implications of Underhydration on Hepatorenal Function

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INTRODUCTION

The liver and kidneys function as an integrated system to regulate nutrient metabolism and waste elimination. Adequate water intake supports these systems by conserving plasma volume, hepatic and renal blood flow, and urine output. Whereas the effects of dehydration on renal function are well established, its impact on hepatic physiology remains less understood. Further, short-term underhydration (low water intake, elevated urine osmolality, elevated AVP/copeptin, with no change in total body water, thirst, or plasma osmolality) may disrupt hepatorenal homeostasis, placing undue strain on key metabolic and clearance pathways. Several successive days of underhydration may, in turn, stress liver and renal waste processing, challenging primary aspects of overall health.

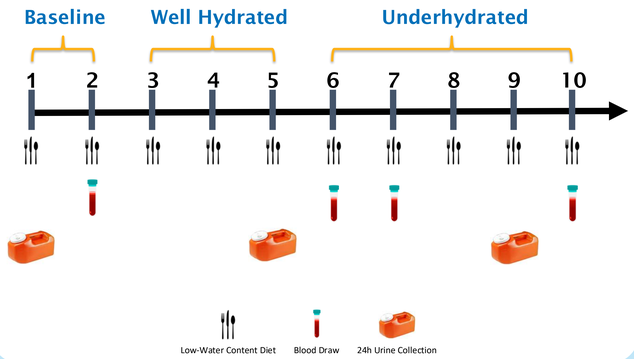
PURPOSE

This study was designed to examine the effects of controlled variations in daily water intake on biomarkers of liver and kidney function in healthy young adults. Specifically, we aimed to determine how short-term underhydration alters hepatic and renal health indicators and to evaluate the relationship between hydration status, as measured by urine and plasma osmolality, and markers of hepatorenal function.

METHODS

Forty-one healthy young adults (27 female, 14 male), 21.5 (4.4) years old, underwent 3 phases of water intake observation or intervention over 10 consecutive days as indicated below. 24h urine samples were analyzed for urine osmolality (uOsm) and fasted morning blood from D2, D6, D7, and D10 were analyzed for hepatic and renal health indicators (Comprehensive Metabolic Panel) and plasma osmolality (pOsm).

METHODS



Intervention Protocol:

- Participants replicated a low-water content diet throughout the study
- Participants followed a hydration intervention as follows:
  - **Phase 1: (Days 1&2) Baseline, Habitual hydration**
  - **Phase 2: (Days 3-5) Well hydrated (35ml·kg^{-1}·d^{-1})**
  - **Phase 3: (Days 6-10) Underhydrated (20ml·kg^{-1}·d^{-1})**

Statistics:

- Data were dichotomized by distinct baseline hydration status using reported 24h uOsm thresholds
  - <500mOsm·kg^{-1}=well hydrated
  - >800mOsm·kg^{-1}=underhydrated
- Change from baseline measures across groupings were determined by mixed effects analyses with Tukey post hoc tests (alpha = 0.05)
- Correlation analyses were conducted between liver and kidney markers and uOsm and pOsm. Spearman or Pearson correlation was performed depending on the normality of the data in each measure (alpha = 0.05)

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RESULTS

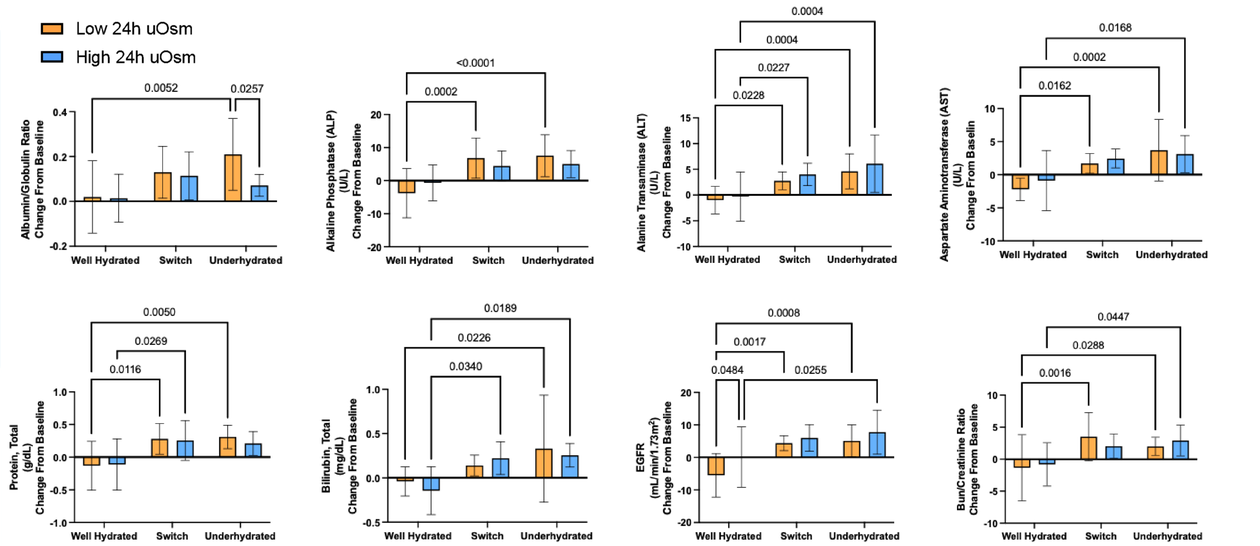


Figure 1. Altered hepatorenal blood biomarkers across hydration phases. Intervention phases are identified on the x-axis. Blood collection on D6 represents the well hydrated phase, D7 represents the one-day transition ("switch") from the well hydrated to underhydrated phase, and D10 represents the underhydrated phase. Participants were dichotomized by baseline 24h urine osmolality (uOsm) as described. Change from baseline was calculated for each biomarker as the difference between the value at each phase and the individual's D2 (baseline) value.

Table 1a. Correlations between baseline 24-hour uOsm and hydration phase

	Baseline	Well-hydrated	Switch	Under-hydrated
Measure	D2	D6	D7	D10
Albumin/Globulin	Rho= .30; p= .060; n= 39	Rho= .13; p= .452; n= 37	Rho= .07; p= .675; n= 34	Rho= .18; p= .277; n= 40
ALT	Rho= .09; p= .592; n= 39	Rho= .29; p= .082; n= 37	Rho= .36; p= .031; n= 35	Rho= .02; p= .883; n= 38
Bilirubin, Total	Rho= .19; p= .254; n= 39	Rho= .11; p= .509; n= 37	Rho= .13; p= .453; n= 35	Rho= .26; p= .117; n= 38
Bun	Rho= .38; p= .017; n= 39	Rho= .35; p= .036; n= 37	Rho= .36; p= .033; n= 35	Rho= .33; p= .040; n= 39
Creatinine	Rho= .33; p= .041; n= 39	Rho= .16; p= .335; n= 37	Rho= .35; p= .037; n= 35	Rho= .45; p= .004; n= 39
EGFR	Rho= -.24; p= .142; n= 39	Rho= -.09; p= .591; n= 37	Rho= -.21; p= .234; n= 35	Rho= -.43; p= .006; n= 39
Glucose	Rho= .36; p= .023; n= 39	Rho= .26; p= .123; n= 37	Rho= .29; p= .087; n= 35	Rho= .13; p= .409; n= 39

Table 1b. Correlations between baseline 24-hour pOsm and hydration phase

	Baseline	Well-hydrated	Switch	Under-hydrated
Measure	D2	D6	D7	D10
Albumin	R= .14; p= .401; n= 39	R= .27; p= .107; n= 36	R= .40; p= .018; n= 34	R= .20; p= .228; n= 37
Globulin	R= .03; p= .852; n= 39	R= .13; p= .441; n= 36	R= .34; p= .046; n= 34	R= .20; p= .236.; n= 37
Alk Phos	Rho= -.37; p= .019; n= 39	Rho= -.26; p= .123; n= 36	Rho= -.22; p= .219; n= 34	Rho= -.27; p= .108; n= 37
Bun/Creatinine	Rho= .31; p= .052; n= 39	Rho= .27; p= .109; n= 36	Rho= .28; p= .109; n= 34	Rho= .08; p= .645; n= 37
Protein, Total	R= .13; p= .435; n= 39	R= .35; p= .037; n= 36	R= .55; p= .000; n= 34	R= .31; p= .059; n= 37
Calcium	R= .24; p= .146; n= 39	R= .34; p= .041; n= 36	R= .38; p= .026; n= 34	R= .19; p= .265; n= 37

Table 1. Correlations between hydration markers and hepatorenal biomarkers. Baseline 24-hour first-morning urine osmolality (uOsm) **(a)** and plasma osmolality (pOsm) **(b)** were used to assess relationships with comprehensive metabolic panel markers.

CONCLUSIONS

Transient reductions in daily water intake were associated with measurable changes in both hepatic and renal biomarkers, suggesting that even short periods of underhydration may stress and place undue strain on integrated metabolic and waste-processing systems. These findings extend beyond the traditional focus on renal outcomes by highlighting the liver's sensitivity to hydration status. Considering the interconnected nature of hepatorenal function, evaluating hydration through a systems-level lens may provide a more comprehensive understanding of its role in maintaining metabolic health.