Short-term vasomotor adjustments to post immersion dehydration are hindered by natriuretic peptides.

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Mourot L, Wolf JP, Galland F, Robinet C, Courtiere A, Bouhaddi M, Meliet JL, Regnard J. Short-term vasomotor adjustments to post immersion dehydration are hindered by natriuretic peptides. Undersea Hyperb Med 2004, 31(2):203-210. Many studies have described the physiology of water immersion (WI), whereas few have focused on post WI physiology, which faces the global water loss of the large WI diuresis. Therefore, we compared hemodynamics and vasomotor tone in 10 trained supine divers before and after two 6h sessions in dry (DY) and head out WI environments. During each exposure (DY and WI) two exercise periods (each one hour 75W ergometer cycling) started after the 3⁰ and 5⁰ hours. Weight losses were significant (-2.24 ± 0.13 kg and -2.38 ± 0.19 kg, after DY and WI, respectively), but not different between the two conditions. Plasma volume was reduced at the end of the two conditions (-9.7 ± 1.6 % and -14.7 ± 1.6 %, respectively; p<0.05). This post-WI decrease was deeper than post DY (p<0.05). Cardiac output (CO) and mean arterial blood pressure were maintained after the two exposures. Plasma levels of noradrenaline, antidiuretic hormone and ANP were twofold higher after WI than after DY (p<0.05). After DY total peripheral resistances (TPR) were increased (p<0.05) and heart rate (HR) was reduced (p<0.05). After WI there was a trend for a decrease in stroke volume (p=0.07) with unchanged TPR and HR, despite more sizeable increases in plasma noradrenaline and vasopressin than after DY. We hypothesized that the higher levels of plasma natriuretic peptides after WI were likely counteracting the dehydration-required vasomotor adjustments.

INTRODUCTION

The physiological effects of thermoneutral (34.5°C) head-out water immersion (WI) are well understood (1, 2, 3). The hydrostatic pressure gradient applied on the body causes an immediate shift of peripheral venous blood towards the thorax (4). Also, a pressure gradient is developed between the interstitial and intravascular compartments, resulting in capillary transmural fluid shifts (5, 6, 7), dilution of the blood (8) and increased in plasma volume (9) as assessed by a transient decrease in plasma protein concentration, colloid osmotic pressure (5), blood hemoglobin (Hb) and hematocrit (Hct) (5, 10, 11). The major central blood volume expansion is paralleled by an increase in central venous pressure (12), an increase or a preservation of diastolic (DAP) and systolic (SAP) arterial pressures (11, 13, 14) with an increased arterial pulse pressure (PP; 13, 15). The increase in pressures, heart volume, and left atrial diameter (13, 14) lead to the release of atrial natriuretic peptide (ANP; 1) and to stimulation of low-and high-pressure baroreceptors (14), triggering in turn important changes in autonomic balance (16, 17). Adrenaline, noradrenaline (Nor), arginine vasopressin (AVP), aldosterone (Aldo), and plasma renin activity or active renin (RA) are lowered (3, 13, 18, 19, 20). Thus, facing an acute relative hypervolemia, the physiological responses tend to restore an
adequate volume through a high diuresis (up to 10-11 mL/min; 21). This high diuresis rate lasts as long as a several hours WI (e.g., during 6h; 11) leading to global water loss. With cessation of immersion, the disappearance of hydrostatic pressure releases important vascular beds resulting in acute hypovolemia (decrease in PV at the end of WI; 11), which might require rapid neuro-endocrine and systemic vasomotor adjustments (9, 22), as in evidence after dehydration on land (23, 24). However, while many studies describe physiological status during immersion, very few focus on post-immersion physiology.

The aim of the present study was to compare the hemodynamic status of healthy subjects before and after dehydration linked or not to a 6 hour immersion. Specific attention was paid to the changes in vasomotor tone in both dehydration conditions.

METHODS

Subjects

10 trained military divers (males, aged: 31 ± 3 years [mean ± SEM], and height 181 ± 3 cm) took part in the experiment. All subjects had a negative history of hypertension and cardiovascular or kidney diseases, and none was taking any medication at the time of the study. The experiment protocol was approved by the local Ethics Committee, and written informed consent was obtained after careful oral and written explanation of the experiment.

Study protocol

Each subject underwent two similar 6-h exposures performing a dry session (DY), and, after 4 weeks, a wet session with immersion up to the neck (sternoclavicular notch) in 15°C water (WI) while wearing wet suits. During the sessions, the subjects sat in a tank containing a submersible mechanical cycle ergometer designed for the study. Each experimental exposure comprised the same pattern of alternating periods of rest and exercise (two periods of 1h cycling at 75 W starting respectively after 3 and 5h of exposure to simulate fin swimming during a field operation). During the DY and WI exposures, subjects could neither eat nor drink. Before each exposure, venous blood samples from an antecubital vein, electrocardiographic (ECG) data, thoracic impedance measurements of stroke volume (SV) and cardiac output (CO), and measurements of SAP and DAP were taken while the subject was resting in a supine position for 20 min. The subject was weighed on a precision scale (± 0.5 g, Ohaus, Pine Brook, NJ, USA), and then voided before donning the immersion suit and entering the immersion tank. After the exposure, the subject unclothed, voided, was weighed and the same measurements repeated after 20 min of rest in a supine position. All the measurements pre- and post-exposure were performed in a quiet room at 23-24 °C.

Measurements

From venous blood samples, Hct, Hb were measured as well as the plasma concentrations of adrenaline, noradrenaline, AVP, AR, aldosterone (Aldo), ANP, brain natriuretic peptide (BNP), and cyclic guanosine monophosphate (cGMP). Percent changes in plasma volume (PV) were calculated from concomitant Hct and Hb concentrations, using the formula of Dill and Costill (25). Adrenaline, noradrenaline were determined by a sensitive and specific radio-enzymatic method (26). Radioimmunological methods were used for measurements of Aldo (AldoCTK, DiaSorin S.A., France), AVP (Nichols Institute Diagnostics, CA, USA), ANP (RPA512, Amersham Pharmacia Biotech, United Kingdom), BNP (Shionaria BNP, CisBio
International, France), cGMP (RIAKit, Immunotech, Beckman Coulter Company, France), and AR (Renin III Generation, Bio-Rad, France).

Stroke volume (SV), heart rate (HR) and CO were assessed non-invasively with a thoracic impedance device (PhysioFlow®, Manatec, Paris, France), which has been validated versus the direct Fick and the CO2 rebreathing methods (27, 28, 29). The recorded values of HR, SV, and CO were averaged for periods of 10 consecutive minutes. SAP and DAP were measured with a mercury sphygmomanometer and a stethoscope. Arterial pulse pressure (PP) was calculated from SAP minus DAP, and mean arterial pressure (MAP) was calculated as DAP plus one third of PP. Total peripheral resistance (TPR) was calculated as the ratio of MAP/CO.

Statistics

Data are presented as means ± SEM. Analysis of variance (ANOVA; Statview, SAS 5.0) for repeated measures with the variable dry or wet dive as the main variable and subjects as factor was used to assess the significance level of changes in a variable over different conditions. Differences between mean values were evaluated by a post hoc Fischer test and, when the values were skewed, a Wilcoxon’s paired test was used. Differences were considered significant when p<0.05.

RESULTS

There was no significant difference between the baseline values on the two days. The major findings are presented in Table 1.

| Table 1. Values of plasma concentrations of vasomotor mediators and hemodynamic variables before and after dry exposure (DY) and water immersion (WI). |
|-----------------|-----------------|-----------------|-----------------|
| Weight (kg)     | Before          | DY             | After           |
| ANP (pg/mL)     | 11.8 ± 2.0      | 17.2 ± 1.7     | 16.0 ± 2.7      |
| BNP (pg/mL)     | 3.1 ± 1.0       | 3.0 ± 0.6      | 4.9 ± 1.5       |
| cGMP (pmol/mL)  | 2.47 ± 0.59     | 3.46 ± 0.50    | 3.23 ± 0.26     |
| Adrenaline (pg/mL) | 71.4 ± 14.5     | 65.1 ± 3.9     | 55.0 ± 5.9      |
| Noradrenalin (pg/mL) | 608 ± 84       | 935 ± 141     | 733 ± 94        |
| AVP (pg/mL)     | 2.15 ± 0.45     | 2.88 ± 0.39    | 2.49 ± 0.56     |
| AR (pg/mL)      | 11.1 ± 2.3      | 13.2 ± 1.9     | 13.5 ± 1.5      |
| Aldosterone (pg/mL) | 139.2 ± 14.0    | 110.0 ± 9.6    | 134.8 ± 9.9     |
| Hb (g/dL)       | 14.8 ± 0.3      | 15.5 ± 0.2     | 14.8 ± 0.3      |
| Hct (%)         | 43.8 ± 0.9      | 47.0 ± 0.7     | 43.3 ± 0.9      |
| HR (bpm)        | 64.8 ± 3.1      | 58.1 ± 2.5     | 59.7 ± 3.6      |
| SV (mL)         | 82.4 ± 3.9      | 87.9 ± 5.1     | 91.8 ± 4.7      |
| CO (L/min)      | 5.9 ± 0.3       | 5.1 ± 0.3      | 5.3 ± 0.3       |
| SAP (mmHg)      | 127.9 ± 6.8     | 125.4 ± 6.8    | 118.5 ± 4.2     |
| DAP (mmHg)      | 70.0 ± 5.0      | 76.3 ± 3.8     | 75.3 ± 2.6      |
| PP (mmHg)       | 57.9 ± 10.6     | 49.1 ± 7.8     | 43.3 ± 5.2      |
| MAP (mmHg)      | 89.3 ± 2.6      | 92.6 ± 3.5     | 89.7 ± 2.2      |
| TPR (mmHg/L/min)| 15.8 ± 1.0      | 19.7 ± 2.1     | 17.5 ± 1.0      |

ANP = atrial natriuretic peptide, BNP = brain natriuretic peptide, cGMP = guanosine monophosphate cyclic, Nor = noradrenalin, AVP = arginine vasopressin, AR = active renin, Hb = haemoglobin, Hct = hematocrit, HR = heart rate.
rate, SV = stroke volume, CO = cardiac output, SAP = systolic arterial pressure, DAP = diastolic arterial pressure, 
PP = pulse pressure, MAP = mean arterial pressure, TPR = total peripheral resistances *: significantly different from
before exposure at the 0.05 level. §: significantly different from DY at the 0.05 level.

Similar decreases in body weight (p<0.05) were induced by six hours exposures to dry
(DY) and immersed (WI) environments (-2.2 ± 0.1 kg and -2.4 ± 0.2 kg, respectively; Figure 1). Hb and Hct increased after DY (changes by 4.4 ± 1.0 % and 6.8 ± 1.0 %, respectively; p<0.05) and WI (7.0 ± 1.0 % and 10.0 ± 1.1 %, respectively; p<0.05) leading to a PV decrease that was less after DY than after WI (-9.7 ± 1.6 % and -14.7 ± 1.6 %, respectively; p<0.05; Figure 1).

Fig.1. Changes in body weight (white bars) and plasma volume (PV, hatched bars) after dry exposure (DY) and after water immersion (WI).
* = significantly different at p< 0.05.

While SV was unchanged after DY, there was a marked trend for a decrease after WI (-14.4 ± 6.6 %, p = 0.07; Table 1). HR was decreased after DY (-12.2 ± 4.9 %, p<0.05; Table 1) but unchanged after WI. There were no significant changes in CO post DY and post WI. No significant changes were observed in MAP, SAP and DAP, despite a slight increase in DAP after DY (Figure 2). TPR was increased after DY (17.6 ± 5.8 %; p<0.05), but unchanged after WI (Figure 2). The plasma concentrations of Nor, AVP, and ANP were increased (p<0.05) after both DY and WI (Figure 3). However, the increases in Nor, AVP, and ANP were about twofold greater after WI (58.0 ± 4.6 %, 52.4 ± 4.8 %, and 45.2 ± 13.3 %, respectively) than after DY (26.8 ± 11.9 %, 25.5 ± 8.3 %, and 29.2 ± 7.3 %, respectively).
DISCUSSION

The physiological changes of immersion have been studied for many years: changes in neuro-endocrine (3, 13, 18, 19, 20) and autonomic (16, 17) activities likely reflect physiological responses to the relative hypervolemia. These changes are also instrumental in fitting plasma volume to the reduced circulatory capacity after an immersion diuresis (21). An often forgotten sequel of immersion is the state of dehydration following its termination. In this study, we assessed hemodynamic conditions during the water loss state following WI. We found that DY and WI exposures led to similar acute body weight loss, although different fluid losses may have contributed to the global dehydration (30, 31).

During DY the average urine output was 1.2 L and thus the average sweat loss accounted for about 0.9 L. Since exercising in cool water leads to a lower sweating rate (32), it can be hypothesized that sweating accounted for a smaller part of fluid loss during WI at 15°C than during DY whereas urine output likely reached higher rates during cool WI than during comfortable DY (3). Unfortunately urine volume could not be assessed during the WI session. Moreover, fluid shifts from the interstitial to the intravascular space occurring during WI (8) lead to hemodilution (15, 33). A reverse fluid shift may occur after termination of WI, which in turn reinforces the decrease in plasma volume. A markedly greater decrease in PV, as estimated from Hb and Hct, occurred after WI than after DY. A dye measurement might have provided an even larger figure for the PV decrease than the computation from changes in Hb and Hct (34, 35).

After DY, the hemodynamic responses indicated a consistent pattern of coping with the decreased PV through increased levels of noradrenaline and antidiuretic hormone, i.e. involvement of vasoconstrictor agents (24). In rats these neuro-hormonal mediators also have been found to increase during dehydration (23). Greater stimulation of vasomotor tone increased TPR and maintained blood pressure and SV. Finally, the increased vasomotor tone and TPR might have led to a lower HR through baroreflex stimulation. The moderately increased plasma ANP at the end of DY likely resulted from the exercise period in the last hour of the session (36).

The changes in the variables describing the short-term post-WI state at first seemed inconsistent. With a larger decrease in PV than post-DY, the plasma levels of noradrenaline, dopamine, AR, and AVP were much higher than post-DY, as if greater physiological counter-
regulation was required. However, despite high concentrations of vasoconstrictor agents, TPR was not significantly different from baseline and the trend for a decrease in SV was nearly significant (p = 0.07). Together with the trend for a decrease in SV, HR remained unchanged. Thus, within the first hour post-WI, a large loss of PV and quite high plasma levels of vasoconstrictive mediators were concordant with an unchanged vasomotor tone as indicated by TPR. Since the vasoconstrictive adjustment was efficient at maintaining SV after DY, its non-operating effects after WI seem paradoxical. In this circumstance, the persistent effects of high levels of plasma ANP, BNP, and their second messenger cGMP, were likely opposing the action of vasoconstrictive mediators (37, 38, 39) and favoring the uncompensated hemodynamic state. Indeed, ANP has been found to potently reverse the $\alpha_1$-adrenoreceptors-mediated constriction of large arterioles and venules (39). ANP also opposes the sympathetic activity (40) and its vasoconstrictor effects (22).

A prompt return of ANP towards baseline levels has been documented during recovery from several hours of WI (1). However, our finding of elevated ANP levels 20 min after the end of WI was consistent with the observations of Stadeager et al. who described significantly higher than baseline ANP 30 min and even 60 min after 12h of resting immersion (9). The persistence of high plasma ANP has also been reported 30 min after the termination of a 30 min immersion with sustained exercise (41). To our knowledge, the precise kinetics of ANP decrease towards baseline has not been described after WI. By causing marked stretching of the walls of the cardiac chambers, immersion provides a specific stimulus for release of ANP (atrial walls; 42) and BNP (ventricular myocytes; 43). In this way, water immersion constitutes a unique model to investigate the physiological importance of ANP in humans (1).

CONCLUSION

When dehydration follows a dry session, the increase in plasma vasoconstrictive mediators likely supports the increased venous and arterial vasomotor tone required to preserve cardiac output and mean arterial pressure. Heart rate is lowered in turn, most likely through baroreflex activation. In contrast, dehydration observed within one hour after immersion shows an unchanged vasomotor tone that parallels high levels of noradrenaline and arginine-vasopressin, which 1) is consistent with a decreased stroke volume and unchanged heart rate and 2) could be explained by the persistence of high level of natriuretic peptides. The physiological hemodynamic conditions following water immersion, its complex fluid balance effects, and its pathophysiological consequences are still incompletely understood.

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