

Endocrinology of the Heart

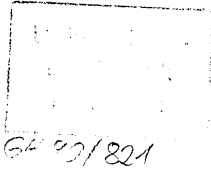
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Prof. Dr. W. Kaufmann
Prof. Dr. G. Wambach
Medizinische Klinik II und Poliklinik der Universität
Ostmerheimer Straße 200
D-5000 Köln 91



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Renal and Hormonal Reactions During Water Immersion in Healthy Pregnant Women and Patients with EPH-Gestosis

W. Schnizer¹, M. Mesroglı², A. L. Gerbes³, R. M. Arendt⁴, H. Knorr¹, P. Schöps¹, M. Waßmann², and J. Schneider²

¹ Institute of Medical Balneology and Climatology, University of Munich, FRG

² Department of OB/GYN, University of Hannover, FRG

³ Department of Medicine II, Klinikum Großhadern, University of Munich, FRG

⁴ Department of Medicine I, Klinikum Großhadern, University of Munich, FRG

Key words: Atrial natriuretic factor – Water immersion – EPH-gestosis – Renal excretion – Renin – Aldosterone

garding renal functions, plasma volume, renin, aldosterone and especially the atrial natriuretic factor.

Introduction

Head-out water immersion (WI) increases central venous and atrial volume by shifting blood from peripheral vessels to the intrathoracic venous bed. Because of stimulation of central low pressure and volume receptors there is an influence in hemodynamic and renal regulations. Thus thermoneutral WI results in a progressive diuresis, natriuresis and kaliuresis; concerning hormonal reactions WI leads to a decrease of antidiuretic hormone (ADH), renin and aldosterone in the blood (for Rev. see [4]). Furthermore it could be demonstrated in a previous study, that WI stimulates atrial natriuretic factor (ANF) in man [5] and thus seems to be a useful mean to study the physiological role of ANF in acute volume regulation.

In pregnancy there are changes in the control of extracellular water and electrolyte homeostasis and therefore it may be of interest to look at the responses of healthy pregnant women and patients with EPH-gestosis in a standardized water bath, re-

Methods

Experiments were done with 27 women (group I [n = 13]: no pathological symptoms; group II [n = 14]: EPH-gestosis) after obtaining their informed consent. At the time of the studies the women were pregnant between the 28th and the 38th week. Furthermore a group (n = 9) of healthy non-pregnant women were investigated concerning ANF. The subjects were on an ordinary diet; alcohol, tobacco, tea and coffee were forbidden at the day of the experiment. The procedure consisted of a 40 min control period, followed by a 40 min bath (35°C) and a 40 min recovery period. Blood samples drawn from a brachial vein by means of a butterfly needle were analysed for ANF (radio-immuno-assay with XAD-extracted plasma [1]), plasma renin activity (PRA) and aldosterone (commercial kits). Urine samples were collected after every period for determinations of urine output, sodium and potassium (flame photometry), creatinine (Jaffe reaction) and osmolality (freezing point depression). Changes of the hematocrit allowed the calculation of changes in the plasma volume. If necessary

patients received medication. Data are given as means and standard errors of the mean.

Results

As can be seen in Fig. 1, WI significantly increased ANF plasma levels in all three groups. After 40 minutes there was an increase of about 50–70%. In the recovery period the hormone decreased with tendency to baseline levels. Neither basal nor stimulated values showed statistical differences between the groups. Only three pregnant women didn't respond.

WI was followed by a significant decrease in PRA and aldosterone. The drop in plasma levels was similar in the groups. No relationship between these hormonal changes and ANF could be found.

There were distinct effects of WI concerning renal excretion. Urinary flow rate was enhanced to 3 or 4 times of controls. Mean values of sodium and potassium excretion were increased, too. The gestosis-group showed lower basal values for sodium and significantly higher excretion rates after WI compared to the healthy pregnant women. Correspondingly there was an increase in fractionated excretions. In all groups WI resulted in increased osmotic and free water clearance. Creatinine clearance reached significantly higher values

only in the gestosis group. During WI rises of plasma volume of about 8 or 9% could be demonstrated.

Discussion

A striking change in hemodynamics occurs in women during pregnancy and some 900 mmol sodium progressively accumulates and total body water increases by 6 to 8 liters, distributed amongst the fetus, the placenta and enlarged maternal blood and interstitial fluid volumes. Abnormalities of sodium and water balance are thought to be connected with diseases such as pre-eclampsia. On the other side pregnancies complicated by pre-eclampsia are associated with a reduction of plasma volume and central venous pressure. Furthermore the renin-aldosterone axis is involved in circulatory regulation and water and electrolyte balance.

Some authors demonstrated an elevation of plasma ANF levels during normal pregnancy and much higher levels in patients suffering from EPH-gestosis [2, 7, 8, 10]. Higher ANF levels in normal pregnancy were thought to be a consequence of the increased blood volume. Other results suggest that plasma ANF levels are normal in women during uncomplicated pregnancy [6, 3]. In our studies the basal values didn't show any significant differences between the groups.

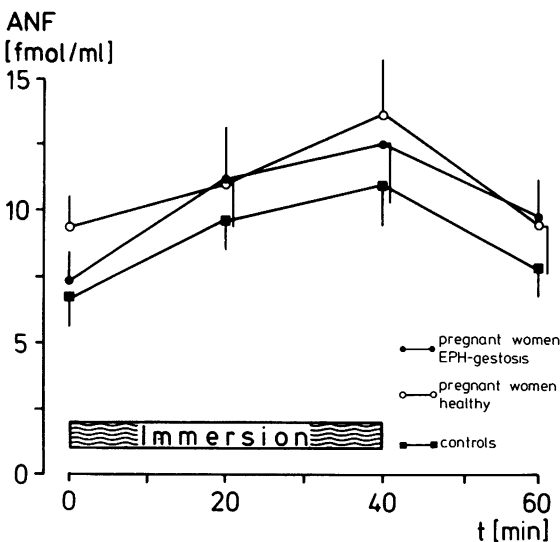


Fig. 1. Behaviour of plasma ANF during and after thermoneutral water immersion in healthy pregnant women, patients with EPH-gestosis and non-pregnant controls

There is the question if the trigger mechanisms of ANF secretion are less sensitive to central blood volume changes in pregnancy and uncomplicated pregnancy. Results from investigations with the WI model published Doniec-Ulman et al. [3] are consistent with this hypothesis. They documented a less stimulation rate for ANF in healthy pregnant women and women with moderate EPH-gestosis as compared to non-pregnant controls. Contrary to this we found comparable values of stimulated ANF during WI in all groups. We didn't observe any changes in the slope of the ANF-increases. That might not indicate a desensitisation of ANF secretion. Also an intact ANF-system seems to be necessary to normalize the water and electrolyte balance in the postnatal period [9]. However, statements about the WI-induced maximum concentrations of ANF cannot be given by our studies. Renin and aldosterone showed the decrease which is known in immersion physiology.

References

1. Arendt RM, Gerbes AL, Ritter D, Stangl E (1986) Molecular weight heterogeneity of plasma-ANF in cardiovascular disease. *Klin Wochenschr* 6 [Suppl VI]:97–102
2. Cusson JR, Gutkowska J, Rey E, Michon N, Boucher M, Larochelle P (1985) Plasma concentration of atrial natriuretic factor in normal pregnancy. *N Engl J Med* 313: 1230–1231
3. Doniec-Ulman I, Kokot F, Wambach G, Drab M (1987) Water immersion-induced endocrine alterations in women with EPH gestosis. *Clin Nephrol* 28:51–55
4. Epstein M (1978) Renal effects of head-out water immersion in man: implications for an understanding of volume homeostasis. *Physiol Rev* 58:529–581
5. Gerbes AL, Arendt RM, Schnizer W, Silz S, Jüngst D, Zähringer J, Paumgartner G (1986) Regulation of atrial natriuretic factor release in man: effect of water immersion. *Klin Wochenschr* 64:666–667
6. Hirai N, Yanaihara T, Nakayama T, Ishibashi M, Yamaji T (1988) Plasma levels of atrial natriuretic peptide during normal pregnancy and in pregnancy complicated by hypertension. *Am J Obstet Gynecol* 159: 27–31
7. Miyamoto S, Shimokawa H, Sumioki H, Tuono A, Nakano H (1988) Circadian rhythm of plasma atrial natriuretic peptide, aldosterone and blood pressure during the third trimester in normal and preeclamptic pregnancies. *Am J Obstet Gynecol* 158: 393–399
8. Otsuki Y, Okamoto E, Iwata I, Nishino E, Mitsuda N, Mori M, Takagi T, Sugita N, Tanizawa O (1987) Changes of concentration of human atrial natriuretic peptide in normal pregnancy and toxemia. *J Endocrin* 114: 325–328
9. Rutherford AJ, Anderson JV, Elder MG, Bloom SR (1987) Release of atrial natriuretic peptide during pregnancy and immediate puerperium. *Lancet* I:928–929
10. Thomsen JK, Storm TL, Thamsborg G, de Nully M, Bodker B, Skouby S (1987) Atrial natriuretic peptide concentrations in preeclampsia. *Br Med J* 294:1508–1510