

Plasma level of atrial natriuretic peptide during normal pregnancy and preeclampsia

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ABSTRACT

Objective: To assess plasma atrial natriuretic peptide (ANP) level in pregnant and preeclamptic women, and to evaluate the role of this hormone in the defense mechanism against body fluids and electrolytes disorders encountered under such physiological and pathophysiological conditions.

Design: A case- series study.

Setting: Al - Batool Teaching Hospital for Gynecology and Obstetrics, Mosul, during the period from December 2003 to September 2004.

Participants: Twenty five women with normal pregnancy (group I), 25 pregnant women with preeclampsia (group II) and 25 healthy non pregnant women (control group) were included in this study.

Methods: Plasma ANP, serum creatinine, urea, sodium and potassium were measured in all groups. unpaired -t-test was used to examine the difference in the mean of the studied parameters between different groups. Pearson correlation was used to assess the relation between different parameters within each group.

Results: The mean of plasma ANP level was significantly higher in group I ($p < 0.05$) and group II ($p < 0.0001$) than that in the control group. Furthermore, the plasma ANP level was significantly higher in group II ($p < 0.0001$) than that in group I. The mean of serum creatinine and serum urea were significantly higher in group II than that in group I ($p < 0.005$ and $p < 0.0001$) and control group ($p < 0.0001$ and $p < 0.0001$).

Conclusion: The results of this study indicate that plasma ANP level significantly increases during pregnancy especially among those who develop preeclampsia. Since ANP plays an important role in the maintenance of body fluids and electrolytes homeostasis and blood pressure regulation, estimation of plasma ANP level may be of value in better understanding and management of pathophysiological conditions that challenge the body homeostatic mechanisms during pregnancy.

Key words: Atrial natriuretic peptide, preeclampsia.

الخلاصة

الهدف: دراسة مستوى هورمون البيبتيد الاذيني المدر للصوديوم في البلازما لدى النساء الحوامل الطبيعيين والنساء اللواتي لديهن تسمم الحمل. وللتعرف على دور هذا الهورمون في مواجهة الخلل في توازن الماء والشوارد أثناء تلك الحالات.

التصميم: دراسة حالات متسلسلة.

المكان: مستشفى البتول التعليمي للنسائية والتوليد - الموصل.

الزمان: كانون الأول ٢٠٠٣ إلى أيلول ٢٠٠٤.

المشاركون: أجريت الدراسة على ٢٥ امرأة ممن لديهن حمل طبيعي كمجموعة أولى و ٢٥ امرأة ممن لديهن تسمم الحمل كمجموعة ثانية وعينة ضابطة مكونة من ٢٥ امرأة من النساء الأصحاء اللواتي ليست لديهن حمل.

الطريقة: تم قياس مستوى هورمون البيبتيد الاذيني المدر للصوديوم في البلازما والمستوى المصلى للكرياتينين- اليوريا (جوهر البول)، الصوديوم والبوتاسيوم للنساء الحوامل والعينة الضابطة. تمت مقارنة التغيرات الخاصة

في المستوى المصلى للقياسات المذكورة أعلاه باستعمال اختبار -ت-. كما تمت دراسة العلاقة بين هذه المتغيرات باستخدام معامل ارتباط بيرسون.

النتائج: أظهرت الدراسة وجود زيادة إحصائية معنوية في قيم مستوى هرمون البيبتيد الاذيني المدر للصوديوم في البلازما لدى أفراد المجموعة الأولى ($P < 0.05$) و المجموعة الثانية ($P < 0.0001$) بالمقارنة مع العينة الضابطة. إضافة على ذلك لوحظ ان مستوى هذا الهرمون لدى أفراد المجموعة الثانية اعلى مما هو عليه لدى أفراد المجموعة الأولى وبقيمة احصائية مقدارها ($P < 0.0001$). كما تبين من نتائج الدراسة وجود زيادة إحصائية معنوية في تركيز الكرياتينين واليوريا لدى أفراد المجموعة الثانية بالمقارنة مع أفراد المجموعة الأولى ($P < 0.0001, P < 0.005$) والعينة الضابطة ($P < 0.001, P < 0.001$) على التوالي.

الاستنتاج: يستدل من نتائج الدراسة أن ارتفاع مستوى هرمون البيبتيد الاذيني المدر للصوديوم في البلازما حالة مألوفة لدى النساء الحوامل وخاصة اللواتي لديهن تسمم الحمل وبما ان لهذا الهرمون دور كبير في عملية المحافظة على توازن الماء والشوارد وتنظيم ضغط الدم خاصة في الحالات الطارئة التي تواجه الجسم، وبناء على ذلك فان قياس مستوى هذا الهرمون في البلازما خلال فترة الحمل قد يكون ذو فائدة في فهم ومعالجة الخلل الحاصل في توازن الماء والشوارد في الجسم أثناء تلك الفترة.

SUBJECTS, MATERIALS AND METHODS

The study included 25 women with normal pregnancy (group I), their age ranged from 18 - 40 years with a mean \pm SD of (26.72 \pm 8.15) and 25 preeclamptic pregnant women (group II), their age ranged from 17-39 years (25.60 \pm 7.95) in their third trimesters. All were selected from those who attend outpatient clinics of Al - Batool Teaching Hospital for Gynecology and Obstetrics, Mosul, for their periodic pregnancy examinations, during the period from December 2003 to September 2004. All women included in the study had no evidence of renal and /or cardiovascular disorders. Since hypertension in the third trimester is defined as a blood pressure of 140/85 mmHg or greater that is sustained during repeated measurements for 6 hours⁽⁶⁾, all selected preeclamptic women had blood pressures \geq 140/85 mmHg, associated with proteinuria and edema. The study also included 25 apparently healthy non pregnant women as control group. Their age ranged from 15 - 38 years, with a mean \pm SD of (24.5 \pm 6.11).

Ten ml of venous blood was obtained from a suitable forearm vein. Five ml of the sample was collected in a heparinized tube and immediately placed in ice for the measurement of the plasma ANP level. The other 5 ml was placed in plain tube for the measurement of serum creatinine, urea, sodium and potassium levels. Both tubes were centrifuged within 30 minutes, the plasma and serum then separated and kept frozen in capped plastic tubes at (-20C) until analysis. Plasma ANP concentration was determined by Enzyme Linked ImmunoSorbent Assay (ELISA)⁽⁷⁾ utilising kit provided by DRG International Inc., USA. (Cat. No. : Eia-1524). Serum creatinine was measured manually by Jaffe end point method⁽⁸⁾ using

The major hemodynamic changes induced by pregnancy include reduction in systemic vascular resistance and systemic blood pressure leading to sodium and water retention and blood volume expansion⁽¹⁾ with subsequent increase in cardiac output. Plasma volume increases by 10 to 15 percent at 6 to 12 weeks of gestation and expands rapidly until 30 to 34 weeks, after which there is only a modest rise. The total gain at term averages 1100 to 1600 ml and results in a plasma volume which is, 30 to 50 percent above that found in nonpregnant women⁽²⁾. The gradual development of hypertension, proteinuria, and edema in pregnancy is most often due to preeclampsia, particularly in a primigravida. Preeclampsia occurs in approximately 6 to 8 percent of all pregnancies worldwide, and characterized by generalized vasospasm, activation of the coagulation system, and changes in several humoral and autoregulatory systems related to body fluid volume and blood pressure control⁽³⁾. Atrial natriuretic peptide is known to have natriuretic, diuretic, vasorelaxant properties and may have antagonistic effects on the renin-angiotensin -aldosterone system. Thus, it is thought to participate in the normal homeostatic mechanisms that maintain the composition and volume of the body fluids^(4,5).

The aim of this study was to determine the rate of increment in the plasma level of ANP in normal pregnancy and in preeclampsia, and to evaluate the role of this hormone in the defense mechanism against body fluids and electrolytes disorders encountered under such physiological and pathophysiological conditions.

kit from Randox colorimetric (with deproteinization). Serum urea concentration was determined enzymatically. In an alkaline medium, the ammonium ions react with the phenol and hypochlorite to form a green colored indophenol⁽⁹⁾. Serum sodium and potassium levels were measured by flame photometer (Corning 400 England)⁽¹⁰⁾. Statistical analysis was performed using unpaired-t-test to assess the differences in the mean of plasma ANP, serum creatinine, urea, sodium and potassium level between different groups. Pearson correlation coefficient test was used to study the relation between the different studied parameters within each patient group. All values were expressed as mean \pm SD.

RESULTS

The mean \pm SD of plasma ANP, serum creatinine, urea, sodium and potassium of group I, group II and control group are shown in Table 1. The mean of plasma ANP level was significantly higher in group I ($p < 0.05$) and group II ($p < 0.0001$) than that in control group. Furthermore, the plasma ANP level was significantly higher in group II ($p < 0.0001$) than that in group I, (Fig 1). The means of serum creatinine and serum urea were significantly higher in group II than those in group I ($p < 0.005$ and $p < 0.0001$) and control group ($p < 0.0001$ and $p < 0.0001$) respectively. There was no correlation between plasma ANP level and serum creatinine nor between plasma ANP level and serum urea both in group I and group II. There were no significant differences in serum sodium and potassium concentration between group I and group II themselves nor between these groups and the control group.

Table (1): The mean \pm SD of plasma ANP, serum creatinine, urea, sodium and potassium of group I, group II and control group.

Parameters	Mean \pm S.D.		
	Control group, N = 25	Group I, N= 25	Group II, N=25
Plasma ANP pg/ml	34.84 \pm 5.52	39.08 \pm 4.98	49.96 \pm 10.09
	A,B	P<0.0001	
Serum creatinine μ mol/l	84.48 \pm 8.94	88.96 \pm 7.28	99.80 \pm 15.22
	B	p<0.005	
Serum urea mmol/l	4.44 \pm 0.62	4.64 \pm 0.73	6.14 \pm 0.96
	B	P<0.0001	
Serum sodium mmol/l	138.16 \pm 2.15	137.28 \pm 2.38	136.88 \pm 2.18
	NS	NS	
Serum potassium mmol/l	3.82 \pm 0.16	3.78 \pm 0.21	3.72 \pm 0.23
	NS	NS	

A : significantly higher in group I from respective values in control group.

B : significantly higher in group II from respective values in control group.

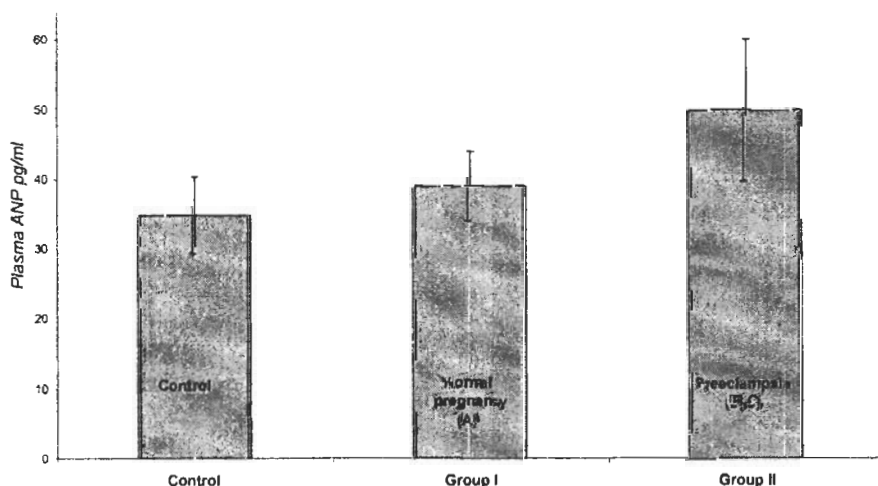


Figure (1): The mean \pm SD of plasma ANP in group I, group II and control group. (A: significantly higher in group I from respective values in control group, B: significantly higher in group II from respective values in control group, C: significantly higher in group II from respective values in group I).

DISCUSSION

Pregnancy is associated with a variety of maternal hemodynamic changes, which are compensatory in nature. The majority of these changes are triggered by systemic vasodilatation which results in reduction of plasma volume and stimulation of renin-angiotensin-aldosterone system activity with subsequent water and sodium retention⁽¹¹⁾. In normal pregnancy there is approximately 50% increase in the total extracellular fluid and blood volumes, which are the results of about (700-1000) mmol sodium retention⁽²⁾. Many studies have documented relative hypovolemia in preeclampsia in comparison with normal pregnancy⁽¹²⁾. Accordingly, preeclamptic pregnant have always had a sense of reduced plasma volume; this will initiate a number of compensatory mechanisms to counteract the intravascular volume contraction leading to extra sodium and water retention in preeclampsia⁽¹³⁾. The results of this study showed a significantly higher plasma ANP level in group I and group II in comparison with control group ($p < 0.05$ and $p < 0.0001$). Furthermore, the plasma ANP level in group II was significantly higher than that in group I ($p < 0.0001$). Increased blood volume during normal pregnancy as well as in preeclamptic women represents an ideal model for increase of intra-atrial pressure which leads to stretching of the atrial wall and subsequent release of ANP by atrial myocyte⁽¹⁴⁾. In addition to this mechanism a transplacental crossing of ANP secreted by fetal heart and placenta, might be, at least in part responsible for the high ANP level observed in preeclampsia⁽¹⁵⁾. Plasma creatinine and plasma urea levels in group II were significantly higher than those in group I ($p < 0.005$ and $p < 0.0001$) and control group ($p < 0.0001$ and $p < 0.001$) respectively. These changes are probably due to decreased glomerular filtration rate with subsequent creatinine and urea retention⁽¹⁶⁾. The results of this study indicate that an early detection of abnormally high levels of plasma ANP in pregnant women may be an indirect indicator of body fluids and electrolytes imbalance and a possible predictor of preeclampsia during pregnancy.

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