EVALUATION OF THE CHANGES IN SERUM IRON LEVELS IN PRE-ECLAMPSIA

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ABSTRACT

Serum iron levels were studied in 50 patients with pre-eclampsia and the results were compared with 50 control cases. Their serum iron levels were found to be higher than the controls. Increase in serum iron was directly proportional to the increased levels of uric acid, urea and creatinine. Mean reticulocyte counts, plasma free haemoglobin and unconjugated bilirubin levels were also higher in these patients. It is suggested that haemolysis may be a major contributory factor for the increased levels of serum iron in pre-eclampsia.

KEY WORDS: Serum iron, Pre-eclampsia.

INTRODUCTION

Pregnancy induced hypertension (PIH) is the development of high blood pressure during pregnancy in normotensive, nonproteinuric women and includes gestational hypertension, pre-eclampsia and eclampsia. Amongst these, pre-eclampsia is the most common and is characterized by the presence of proteinuria. In addition, higher levels of blood urea, serum creatinine and uric acid have been reported in such patients (1).

Recently, serum iron levels have also been shown to be increased in patients with pre-eclampsia (2). Increase in serum iron may be due to intracellular volume contraction, haemolysis or hepatocellular damage (3). The present study was designed to evaluate the changes in serum iron levels in pre-eclampsia. Further an attempt has also been made to know the mechanism responsible for the changes in serum iron concentrations, if any, in such patients.

MATERIALS AND METHODS

Fifty cases of pre-eclampsia (41 mild and 9

severe), in the age group of 17-30 years were selected for the study. A group of 50 control cases was also studied. Pre-eclampsia (PEC) was diagnosed on the basis of the following criteria, i.e. blood pressure of 140/90 mm Hg or more or an increase of 30 mm Hg systolic/15 mm Hg diastolic pressure over baseline values on at least 2 occasions 6 or more hours apart in the third trimester; normal blood pressure in the first or second trimester; presence of 300 mg or more protein in 24 hours urine or 1 g/L or more in at least 2 random specimens collected 6 hours or more apart; nullipara and no past history or laboratory evidence of hypertension, renal disease or collagen vascular disease.

Serum uric acid, creatinine and blood urea were estimated using phosphotungstic acid (4), alkaline picrate and diacetyl monoxime (5), respectively. Serum iron was estimated according to the principle of Higgins (6), using Autopak (Miles India Ltd, Baroda). The cause of the increase in serum iron was studied by evaluating the extent of (i) intracellular volume contraction (leading to haemoconcentration) by measuring haemoglobin concentration and by calculating blood urea nitrogen (BUN): creatinine ratio; (ii) hepatocellular damage (causing release of iron) by estimating serum alanine (ALT) as well as aspartate aminotransferases (AST) (7), γ glutamyltranspeptidase (γ -GT) (8) and conjugated bilirubin levels (5); and (iii) haemolysis by measuring plasma free haemoglobin

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Table 1: Blood urea, uric acid, creatinine and serum iron levels in patients with pre-eclampsia
[Values are mean $\pm$ SEM; No. of subjects given in parentheses]

Parameter	Controls (50)	Mild PEC (41)	Severe PEC (9)
Blood urea (mg/dl)	19.5 $\pm$ 0.54	23.8 $\pm$ 0.88*	33.0 $\pm$ 0.64*,**
Serum uric acid (mg/dl)	4.5 $\pm$ 0.07	5.9 $\pm$ 0.07*	6.8 $\pm$ 0.07*,**
Serum creatinine (mg/dl)	0.95 $\pm$ 0.04	1.07 $\pm$ 0.03	1.35 $\pm$ 0.02*,**
Serum iron (ug/dl)	65.4 $\pm$ 1.91	114.7 $\pm$ 2.29*	135.3 $\pm$ 1.30*,**

* Difference statistically significant when compared with the control group ($p < 0.05$).

** Difference statistically significant when compared with the patients with mild PEC ($p < 0.05$)

and reticulocyte counts (9) and unconjugated bilirubin (5). Results were statistically evaluated by Student's t-test or correlation coefficient (r).

RESULTS AND DISCUSSION

Mean serum uric acid, blood urea and creatinine levels were significantly higher in patients with pre-eclampsia than the controls ($p < 0.05$; Table 1). The correlation coefficient (r) between diastolic blood pressure and uric acid ($r = 0.86$; $p < 0.001$), urea ($r = 0.56$; $p < 0.001$) and creatinine ($r = 0.32$; $p < 0.01$), confirmed that the increase in uric acid, urea and creatinine was directly proportional to the severity of the disease. Glomerular pathology has been correlated with the degree of hyperuricemia which is a well known component of pre-eclampsia and results from a reduced renal clearance (1).

Some workers observed increased serum iron levels in such patients and reported that an elevation of serum iron in pre-eclampsia-eclampsia may be a better discriminator than the other forms of hypertension (2,10). Even in the present study, mean serum iron concentration was found to be significantly higher in patients with pre-eclampsia than that in the controls ($p < 0.05$). The increase in serum iron was found to be directly proportional to the severity of the disease (correlation coefficient between diastolic blood pressure and serum iron was positive i.e. $r = + 0.82$;

$p > 0.001$). Further the degree of hyperferrimia was directly related to hyperuricemia ($r = 0.78$; $p < 0.001$), uremia ($r = 0.44$; $p < 0.001$) and creatininemia ($r = 0.34$; $p < 0.05$).

Increased levels of serum iron in pre-eclampsia could be due to haemoconcentration, liver damage, cessation of erythropoiesis and/or haemolysis (2). As shown in table 2 haemoglobin as well as BUN: creatinine ratio was not significantly different in the two groups. Moreover, the relationships between serum iron and haemoglobin as well as between serum iron and BUN: creatinine ratio ($r = 0.03$ and $+ 0.08$, respectively; $p > 0.05$) were not statistically significant meaning thereby that the increase in serum iron in pre-eclampsia was not due to haemoconcentration (volume contraction).

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were found to be significantly increased in patients with pre-eclampsia ($p < 0.05$), however, γ -glutamyl transpeptidase activity remained unaltered. The increase in serum iron was directly proportional to the increased levels of ALT as well as AST ($r = 0.32$ and $+ 0.52$, respectively; $p < 0.001$). Liver damage is a well documented feature in pre-eclampsia and γ -GT levels are not significantly altered in such cases (11). However, Kaneshinge (12) reported that, since iron

Table 2: Changes in some of the biochemical parameters responsible for increase in serum iron in patients with PEC.
(Values are mean $\pm$ SEM; No. of subjects given in parentheses)

Parameter	Controls (50)	Mild PEC (41)	Severe PEC (9)
A. Intra Vascular Volume Contraction			
Haemoglobin (g/dl)	10.9 $\pm$ 0.10	10.8 $\pm$ 0.10	11.0 $\pm$ 0.09
BUN: Creatinine ratio	9.9 $\pm$ 0.28 9.9 $\pm$ 28	10.6 $\pm$ 0.39	11.4 $\pm$ 0.18*
B. Hepatocellular damage			
Aspartate aminotransferase (IU/L)	15.0 $\pm$ 0.87	22.2 $\pm$ 0.93*	29.7 $\pm$ 0.56*, *
Alanine aminotransferase (IU/L)	17.0 $\pm$ 1.24	24.2 $\pm$ 1.19*	26.0 $\pm$ 0.88*
Γ -Glutamyl transpeptidase (IU/L)	15.1 $\pm$ 0.93	14.2 $\pm$ 1.01	16.0 $\pm$ 1.20
Conjugated bilirubin (mg/dl)	0.18 $\pm$ 0.01	0.20 $\pm$ 0.01	0.27 $\pm$ 0.01*, **
C. Haemolysis			
Plasma free haemoglobin (mg/dl)	0.4 $\pm$ 0.02	2.5 $\pm$ 0.09*	4.0 $\pm$ 0.13*, **
Reticulocyte count (percentage)	1.3 $\pm$ 0.08	2.0 $\pm$ 0.09*	2.3 $\pm$ 0.10*
Unconjugated bilirubin (mg/dl)	0.4 $\pm$ 0.02	0.69 $\pm$ 0.02*	0.93 $\pm$ 0.02*, **

* Difference statistically significant when compared with the control group ($p < 0.05$)

** Difference statistically significant when compared with the patients with mild PEC ($p < 0.05$).

stores are already depleted, release of iron from ferritin as a result of liver damage may not contribute to the raised serum iron level in pre-eclampsia. Increase in serum iron cannot be due to the possibility of the cessation of erythropoiesis also since reticulocyte counts were found to be increased and not reduced.

Plasma free haemoglobin levels were found to be significantly higher in patients with pre-eclampsia.

There was also a rise in serum bilirubin which was mainly due to the rise in unconjugated bilirubin only. The rise in serum iron was found to be significantly correlated ($p < 0.001$) with the increase in reticulocyte counts, plasma free haemoglobin as well as conjugated bilirubin ($r = +0.42$; $+0.88$) and $+0.63$, respectively), thereby suggesting that the increase in serum iron during pre-eclampsia could possibly be due to increased haemolysis.

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