C4 and plasma protein in hypertension during pregnancy with and without proteinuria

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There is disagreement about whether an immune complex disorder contributes to the pathogenesis of pre-eclampsia.¹ Serum concentrations of C4 are increased during normal pregnancy^{2,3} and have been reported to be increased,⁴ unchanged,^{2,5} and decreased³ in pre-eclampsia. We studied circulating C4 concentrations in women with hypertension during pregnancy with and without proteinuria in relation to plasma protein concentrations and urinary excretion of C4.

Subjects, methods, and results

We studied 59 women attending our hospital. Venous blood was taken before and five days after delivery from 10 women with proteinuric pre-eclampsia (maximum antenatal blood pressure at least 170 mm Hg systolic or 110 mm Hg diastolic settling to normal after delivery and new proteinuria of at least 500 mg/24 h), 10 with non-proteinuric hypertension during pregnancy (at least 140 mm Hg systolic and 90 mm Hg diastolic), and only before delivery from 20 healthy controls matched for age, parity, and length of gestation. Serum C4 concentrations were measured by single radial immunodiffusion using Nor-partigen plates (Behring, Hounslow).

In the women with proteinuric hypertension antenatal C4, total protein, and albumin concentrations were significantly less than those of their matched controls (table). The concentrations in women with non-proteinuric hypertension were slightly lower than but not significantly different from those of the controls. At five days after delivery there were significant increases in C4 but not total protein or albumin concentrations in both hypertensive groups. The increase in C4 after delivery persisted after six weeks in a further group of 12 women with proteinuric pre-eclampsia (data not shown).

Median (range) values of serum C4, total protein, and albumin in proteinuric and non-proteinuric hypertensive women and controls before and five days after delivery. Comparisons are by Wilcoxon's matched pairs signed ranking test

	Women with proteinuria	Controls	Women without proteinuria	Controls	p Value for women with proteinuria v non-proteinuria
Before delivery					
No C4 (g/l)	10 0.27 (0.16-0.38)	10 0.39 (0.29-0.51)	10 0.35 (0.16-0.44)	10 0.41 (0.23-0.51)	
Total protein (g/l)	58 (50-68)	67 (58-74)	65 (61-81)	68 (65-74)	<0.002 NS <0.07
Albumin (g/l)	22 (16-26)	32 (20-40)	28 (25-34)	31 (26-39)	<0.02 NS <0.001
After delivery					
No C4 (g/l)*	10 0.43 (0.19-0.82)		9** 0.42 (0.19-0.56)		
Total protein (g/l)	61 (54-72)		69 (64-76)		
Albumin (g/l)	23 (19-30)		30 (23-32)		

*Proteinuric women: before v after delivery <0.01; non-proteinuric women before v after delivery <0.01.

**One sample lost.

To determine whether substantial amounts of C4 might be lost in the urine seven women with proteinuric pre-eclampsia were studied before birth and five days after birth. Urine samples collected into EDTA and frozen immediately were concentrated to 0.009-0.014 of the original volume using 10 000 daltons exclusion filters (Amicon, Stonehouse) and C4 measured with a nephelometer (Baker-Encore) in the department of immunology. Urinary C4 was detected at the lower limit of the assay (0.0005 g/l after correction for the concentration factor) in one postpartum sample, giving a urine to plasma ratio 0.04 times that of protein, and was undetectable in all other samples. In five samples the urine to plasma ratio of protein was sufficiently high for C4 to have been detectable if present in a urine to plasma ratio one tenth that of protein.

Comment

We have shown that reduced circulating C4 concentrations are a feature of proteinuric rather than non-proteinuric hypertension during pregnancy. Whether this represents a specific association of low C4 concentrations with proteinuria or merely reflects a more advanced pre-eclamptic process is not clear. There are several possible reasons for the reduced C4 concentrations in patients with proteinuric hypertension. There may be consumption of C4 as part of a specific immunological process, as in autoimmune disease (though the decreases are slight compared with those recorded in systemic lupus erythematosus); there may be a non-specific depression of protein synthesis or an increase in protein catabolism; or there may be increased urinary loss of C4. The last explanation is unlikely given our failure to detect appreciable amounts of C4 in the urine, though the possibility of breakdown of C4 in the urine cannot be excluded. The factors responsible are unlikely to be the same as those responsible for the low albumin concentrations as there was no correlation between C4 and albumin concentrations within the proteinuric hypertensive group ($r = -0.20$).

The decrease in circulating C4 concentrations may be relevant to the pathogenesis of pre-eclampsia and of diagnostic value, but at present the mechanisms for the change remain unclear.

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Correction

Effect of thiazide on rates of bone mineral loss: a longitudinal study

In the table of this article by Dr Richard Wasnich and colleagues (8 December 1990, p 1304) the p value for the distal radius should have read 0.3 rather than 0.03. This error does not affect the main conclusion that users of thiazide have significantly slower bone loss rates than controls.