study of past casualties. For example, our data indicate that a programme of preventing heroin use in the 1990s will be ineffective if it focuses on injecting: initiation into heroin use is now by chasing, and the progression (or non-progression) to injecting occurs at a later stage through influences of which we know little.

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Urinary 5-hydroxyindole acetate concentration in pregnancy induced hypertension

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The role of pressor agents, and particularly serotonin,[1] in the pathogenesis of pregnancy induced hypertension has been proposed. Abnormal circulating concentrations of serotonin have not been detected,[2] but serotonin concentrations in platelets of pre-eclamptic women are reduced.[3] A recent report of the successful treatment of an eclamptic patient with widespread cerebral ischaemia with nimodipine,[4] a potential inhibitor of serotonin, promised further study. Twenty four hour specimens of urine from patients with pregnancy induced hypertension and controls were analysed.

Patients, methods, and results

The study involved 13 women with pregnancy induced hypertension recruited from the antenatal ward over two weeks and 19 control patients of similar gestation. All but one patient had proteinuria as determined by an Albustix reagent strip. However, only five patients had proteinuria greater than 500 mg/24 h collection. In these five cases the proteinuria ranged from 0·65 to 3·64 g/24 h with a mean of 2·01 g/24 h. The clinical details are shown in the table. None of the patients with pregnancy induced hypertension were receiving treatment at the time of analysis.

Patients had a 24 hour specimen of urine collected into a bottle containing hydrochloric acid, which was frozen until analysed. The concentrations of 5-hydroxyindole acetate, a urinary metabolite of serotonin, was measured by gas chromatography and mass spectrometry without knowledge of subject group.

Clinical and laboratory details of subjects studied

	Normotensive group (n=19)		Hypertensive group (n=13)		(Mann-Whitney U test)
	Median	Range	Median	Range	
Total 24 hour urine volume (l)	1·43	0·56-2·9	1·06	0·62-1·56	NS
Gestational age at time of sampling (weeks)	33	29-39	37	30-39	NS
Maternal age (years)	26	18-31	28	19-36	NS
Systolic blood pressure (mm Hg)	120	100-130	150	140-177	
Diastolic blood pressure (mm Hg)	70	60-80	100	88-114	
5-Hydroxyindole acetate concentration (μmol/l)	18·0	8·5-51·1	30·6	17·9-44·6	<0·001
Total 24 hour excretion of 5-hydroxyindole acetate (μmol)	25·9	13·1-44·5	30·7	25·3-49·9	<0·005
5-Hydroxyindole acetate: creatinine (μmol/g)	21·8	14·1-32·5	23·6	20·0-45·4	<0·05
No of primiparous women	4		9		
No of multiparous women	15		4		

Results between the two groups were compared by the Mann-Whitney U test. Urinary excretion of 5-hydroxyindole acetate was significantly greater in the patients with pregnancy induced hypertension than in the controls (table). The difference was most marked for absolute concentrations, but was also apparent for excretion rate and concentration in relation to creatinine. There was no significant difference between the proteinuric hypertensive patients and the non-proteinuric hypertensive patients when comparing the 24 hour total urinary output of 5-hydroxyindole acetate or the μmol/g of creatinine ratio.

Comment

Serotonin is a neurotransmitter and is also found in platelets, being released into the circulation during the platelet release reaction. It is extensively metabolised, 5-hydroxyindole acetic acid being the major metabolite. We have found substantially more 5-hydroxyindole acetate in the urine of women with pregnancy induced hypertension than in normotensive controls of similar gestation. A possible contributory factor to this could be related to the significant increase in embolic trophoblastic fragments found in the venous circulation of women with pregnancy induced hypertension compared with non-hypertensive controls.[5] The trophoblastic fragments could attract platelets which in turn could release platelet serotonin. This trophoblastic factor is unique to pregnancy.

It is likely that the increased urinary excretion of 5-hydroxyindole acetate reflects increased circulating concentrations of serotonin, possibly related to trophoblastic fragmentation, which is significantly increased in women with pregnancy induced hypertension. Though this assumption contrasts with an earlier report,[2] it is doubtful if the methodologies used in previous studies were of sufficient sensitivity. We would also propose that the increased circulating serotonin is derived from platelets which have undergone aggregation as part of the pre-eclamptic process. Our observations were made when hypertension was already established and we cannot therefore draw inferences about the possible contribution of serotonin to the initiation of the pre-eclamptic process. However, we suggest that increased circulating concentrations of serotonin could contribute to at least some of the features of pre-eclampsia or eclampsia. In particular, serotonin alone or in combination with other vasoconstrictor agents could contribute to the cerebral vasospasm which seems to be a feature of eclampsia.[4]

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