Postprandial hypotension

Postural or orthostatic hypotension is well known, but severe symptomatic arterial hypotension provoked by eating has so far not been described.

Case report

A 65-year-old man was admitted because of Parkinsonism. He also complained that for about six months he had had attacks of severe dizziness and visual disturbances during almost every meal. In the ward he was observed several times during eating. Ten to 20 minutes after the start of a meal he regularly complained of blurred vision or diplopia, or both. The objects in the room usually appeared yellowish to him. At the same time there was a pronounced change in his voice, which became typically "bulbar."

Blood pressure and pulse rate were measured every 15 minutes throughout one day. The blood pressure was very unstable, reaching systolic values as high as 250 mm Hg at rest. The most remarkable feature, however, was a steep fall in blood pressure during meals. Systolic values were as low as 65 mm Hg, while the diastolic pressure was unmeasurable. The patient's subjective complaints were closely related to these hypotensive periods. The pulse rate was very stable despite the fluctuations in blood pressure.

The figure shows the results of an oral glucose tolerance test. Systolic blood pressure fell from 200 to 105 mm Hg within 10 minutes after the ingestion of 100 g glucose, but the pulse rate hardly rose. The patient's insulin response to oral glucose was very high, plasma insulin rising from 15 to 235 μ U/ml after 15 minutes. The rise in blood glucose concentration was very slow and sluggish, values never exceeding 7.2 mmol/l (130 mg/100 ml). There was no subjective discomfort.

Systolic blood pressure and pulse rate after oral ingestion of 100 g glucose and blood glucose and plasma insulin measured simultaneously during test.

Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Intravenous injection of two units of crystalline insulin every 10 minutes for 40 minutes resulted in a fall in systolic blood pressure from 170 to 100 mm Hg. The fall began about 10 minutes after the first insulin injection. There was no hypoglycaemia during this test, the lowest blood glucose value being 5.6 mmol/l (100 mg/100 ml). During this test the patient had slight diplopia and difficulties in speech.

Comment

Our patient obviously had severe Parkinsonism. But he also had attacks of basilar insufficiency with brain-stem and occipital symptoms, which were clearly precipitated by arterial hypotension.

The connection between meals and hypotension at first seems obscure. Recently, however, it has been shown repeatedly that insulin has cardiovascular effects, which are unrelated to hypoglycaemia. Intravenous insulin injections in patients with long-term

diabetes and autonomous neuropathy are followed by hypotension.¹ Gundersen and Christensen² have shown that intravenous insulin injections cause a considerable decrease in plasma volume. In people with a normally functioning sympathetic nervous system a fall in blood pressure is prevented by increased heart-rate and contraction of the vessels.

Our patient had a very high insulin response to glucose. At the same time he had a clear sympathetic dysfunction, as manifested by his fixed heart rate. When he was given insulin his blood pressure fell, even though no hypoglycaemia was seen. His symptoms were probably caused by a loss of plasma volume as an effect of high circulating concentrations of insulin after meals.

Such cardiovascular effects of insulin may operate in other conditions. When elderly diabetics are treated with insulin or oral hypoglycaemic agents it is often emphasised that hypoglycaemia is dangerous and may lead to myocardial infarction. Insulin-induced hypotension may be as harmful a factor as hypoglycaemia in these cases. After partial gastrectomy the insulin response to oral glucose is often increased. The decrease in plasma volume seen in the dumping syndrome³ may also be an effect of hyperinsulinaemia.

¹ Page, M M, and Watkins, P J, *Diabetes*, 1976, **25**, 90.

² Gundersen, H J G, and Christensen, N J, *Diabetes*, 1977, **26**, 551.

³ LeQuessne, L P, Hobsley, M, and Hand, B H, *British Medical Journal*, 1960, **1**, 141.

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Plasma renin activity and angiotensin II concentrations in sarcoidosis

Angiotensin I, a relatively inactive decapeptide, is converted to angiotensin II, a potent vasoconstrictor, by angiotensin-converting enzyme. Increased serum and tissue concentrations of converting enzyme have been found in patients with active, untreated sarcoidosis,¹⁻³ whereas patients receiving corticosteroids for sarcoidosis or with resolving or inactive disease have normal concentrations. Normal or reduced concentrations have been found in several other granulomatous lung diseases and various others, including cystic fibrosis, emphysema, asthma, lung cancer, tuberculosis, and fungal disease. In only one other condition—namely, Gaucher's disease—have the concentrations been found to be raised. No correlation has been found between concentrations of angiotensin-converting enzyme and systemic blood pressure.

Subjects, methods, and results

To investigate whether other components of the renin-angiotensin system are altered in active sarcoidosis we measured plasma angiotensin II concentrations and renin activity in 14 patients with sarcoidosis and 14 normal people. One patient with Gaucher's disease was also studied. The patients with sarcoidosis were examined within 12 months of presentation. Most had bilateral hilar lymphadenopathy and pulmonary infiltration, confirmed histologically. None were receiving steroids or antihypertensive or diuretic treatment. Plasma angiotensin II concentrations were measured by the radioimmunoassay method of Dusterdieck and McElwee.⁴ Plasma renin activity was estimated by radioimmunoassay of angiotensin I, which was generated by incubating plasma under the conditions defined by Haber *et al.*⁵

An analysis of covariance of the results showed no significant difference in the correlations between plasma renin activity and angiotensin II concentrations for the two groups (see fig). The results for the patient with Gaucher's disease were within normal limits.

Comment

Previous reports of high angiotensin-converting enzyme activity in sarcoidosis have not included measurement of plasma renin activity and angiotensin II concentrations. A difference in the correlations

Regressions of concentrations of angiotensin II on plasma renin activity in normal subjects and patients with sarcoidosis are also shown for one patient with Gaucher's disease.

between these two variables for the two groups might be expected if the conversion of angiotensin I to angiotensin II was a rate-limiting step. The absence of any difference in the correlations in patients with sarcoidosis and in normal subjects reported here suggests that converting enzyme does not have a regulatory role in the renin-angiotensin system. Increased concentrations of angiotensin-converting enzyme therefore have no apparent physiological consequences, although when the enzyme is inhibited a fall in blood pressure may occur.

¹ Lieberman, J Ann, *New York Academy of Sciences*, 1976, **278**, 488.

² Silverstein, E, *et al*, *New York Academy of Sciences*, 1976, **278**, 498.

³ Ashutosh, K, and Keighley, J F H, *Thorax*, 1976, **31**, 552.

⁴ Dusterdieck, G, and McElwee, G, *European Journal of Clinical Investigation*, 1971, **2**, 32.

⁵ Haber, E, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1969, **29**, 1349.

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Specific IgM responses after rubella vaccination; potential application following inadvertent vaccination during pregnancy

Despite recommendations from the DHSS that pregnancy should be excluded at the time of rubella vaccination and prevented for two months thereafter,¹ at least 120 terminations of pregnancy were reported in England and Wales between 1972 and 1975 after inadvertent vaccination during pregnancy or the eight weeks before estimated conception.² This figure almost certainly represents a considerable underestimate. Although the immune state of women of childbearing age should always be established before vaccination, a study in the USA reported that the immune state of 259 of 343 (70%) women inadvertently vaccinated during pregnancy was unknown³; probably a similar proportion of women whose pregnancies were terminated in England and Wales were not tested for rubella antibodies. Since roughly 80% of women of childbearing age are already immune, many pregnancies may have been terminated unnecessarily,

for the risk of giving rubella vaccine to a woman who is immune is negligible.

It may be difficult to determine whether a woman vaccinated without previous antibody screening was indeed susceptible unless she has virological investigation shortly after vaccination. Detection of rubella-specific IgM may be useful, for it is usually present for up to six weeks after naturally acquired primary infections, but in some cases it may persist much longer.⁴ In our experience, however, pregnant women who have been inadvertently vaccinated may not have virological investigations for some 8-12 weeks after vaccination. But less is known of the reliability of detecting rubella-specific IgM responses and their duration after rubella vaccination, since the number of specimens so far examined at varying intervals after vaccination with different vaccines is small.⁴ We have therefore tried to determine how consistently rubella-specific IgM may be detected in people given either of the two currently licensed vaccines in Britain, RA 27/3 or Cendehill. Results were compared with those obtained from patients who had acquired the disease naturally at similar times.

Materials and methods

Sera were collected from 40 susceptible nurses and female medical students who had been given RA 27/3 or Cendehill vaccines and 16 women who had acquired the infection naturally. Rubella-specific IgM was detected by serum fractionation on sucrose density gradients, the sensitivity of the haemagglutination-inhibition (HAI) test being enhanced by incubating serum fractions with rubella antigen overnight at 4°C, as described.⁴ Instead of using day-old chick erythrocytes, however, we used trypsinised, human O erythrocytes.⁵ Because it has been suggested that IgM titres may decline if sera are kept at ambient temperature during transport, two serum samples from vaccinated women which were known to contain high and low rubella-specific IgM titres were sent to the laboratory by second-class mail. Their virus-specific IgM titres were compared with aliquots of the same samples kept at -20°C.

Results and comment

Eight weeks after vaccination rubella-specific IgM was detected in the sera of all 16 patients with naturally acquired infection, all 20 women given RA 27/3, and 16 of the 20 given Cendehill vaccine (see table). Among women given Cendehill, three of the four in whom rubella-specific IgM was not detected had low total HAI antibody titres (<1/16). Among those given RA 27/3, however, rubella-specific IgM could be detected in the sera with low HAI titres (table).

Number of subjects found to be positive for rubella-specific IgM six weeks after naturally acquired infection and eight weeks* after vaccination with RA 27/3 and Cendehill vaccines. Results expressed as proportions of number tested

HAI titre 1 in:	8	16	32	≥64	Total (%)
Natural infection				16/16	16/16 (100)
RA 27/3	1/1	1/1	5/5	13/13	20/20 (100)
Cendehill	1/2	3/5	6/7	6/6	16/20 (80)
Total:	2/3	4/6	11/12	35/35	52/56 (92)

HAI = haemagglutination-inhibition.

*Six weeks after naturally acquired infection and eight weeks after vaccination represent comparable periods, as there is a delay of approximately two weeks before symptoms may occur and antibodies develop after vaccination.

By 12 weeks, rubella-specific IgM was detected less consistently: thus it was present in 10 of the 14 women given RA 27/3, four of the five given Cendehill, and three of the five who had had the natural disease. Since the results of testing at this time were apparently less reliable no further samples were tested. No difference in the IgM titres was observed in the two serum samples that had been posted, although they had been two days in the post, and had been held for five days at 4°C before being tested.

The risk of damaging the fetus when rubella vaccines are given in early pregnancy appears to be less than after naturally acquired disease, for no defects have so far been detected in 38 American babies born to rubella-susceptible mothers vaccinated in early pregnancy who chose to go to term.³ Nevertheless, it would be premature to conclude that rubella vaccination during pregnancy is without risk, since relatively few patients have been studied, and follow-up studies are too short to exclude the possibility that defects will subsequently be revealed. Furthermore, rubella virus has been recovered from the products of conception of susceptible women inadvertently vaccinated