SHORT REPORTS

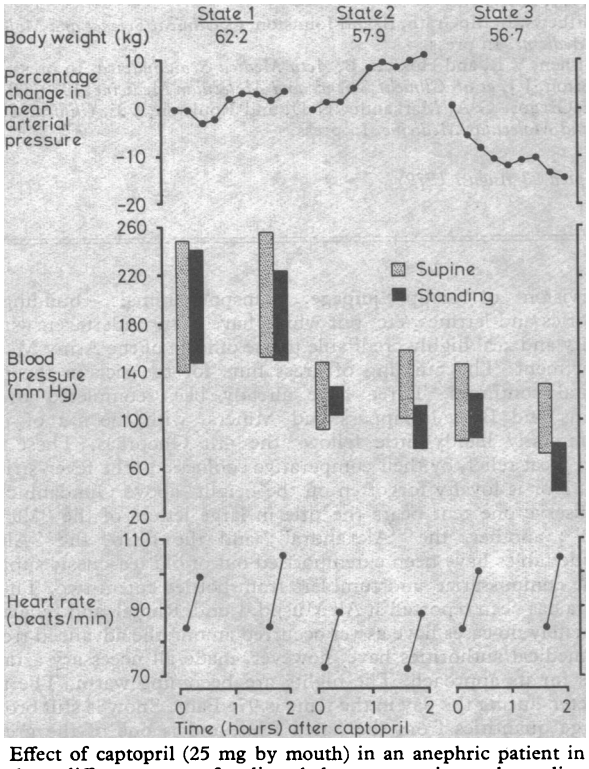
Does captopril lower blood pressure in anephric patients?

Captopril inhibits peptidyldipeptide hydrolase, the enzyme that converts angiotensin I to angiotensin II and degrades bradykinin. Captopril's antihypertensive action seems to depend on the activity of the renin-angiotensin system in relation to the state of sodium balance.[1-3] It is not clear, particularly in patients with normal or low plasma renin activity, whether captopril lowers blood pressure by eliminating the vasoconstrictor angiotensin II or by allowing the vasodilator bradykinin to accumulate. We have studied captopril's effect on supine and standing blood pressure in an anephric woman in three different states of sodium balance.

Patient, methods, and results

Captopril (25 mg by mouth) was given to a 36-year-old anephric woman on three occasions: one hour after haemodialysis when she was volume and sodium overloaded and weighed 62·2 kg; and then two and seven days after progressive ultrafiltration, when she weighed 57·9 kg and 56·7 kg respectively. Active plasma renin concentrations, measured by radioimmunoassay, ranged from 1·2 to 2·9 mU/l (normal 16-40 mU/l) in the three states and did not rise after captopril. Angiotensin-converting-enzyme activity was measured by spectrophotometric assay of the rate of production of hippuric acid from hippuryl—L—histidyl—L—leucine and expressed as a percentage of control values derived before captopril was given. Enzyme activity was inhibited by 56±6% (mean±SE of mean) 30 minutes after captopril was given and by 92±7% after 120 minutes. The blood pressure was measured with a random-zero sphygmomanometer (London School of Hygiene, mk 4, No 7125) to avoid digital preference and observer bias. Heart rate was determined from a continuous electrocardiograph.

The figure shows the effect of captopril on blood pressure and heart rate in the three different states. The patient was severely hypertensive when she weighed 62·2 kg, but captopril had no effect on standing or supine blood pressure. When the patient weighed 57·9 kg her supine blood pressure was 143/90 mm Hg. She did not have postural hypotension before captopril was given, but after captopril, although her supine blood pressure rose by 10%, her blood pressure dropped from 156/101 mm Hg to 98/61 mm Hg on standing and she complained of dizziness. When her weight had fallen to 56·7 kg, captopril caused a 15% drop in supine blood pressure (144/86 mm Hg to 128/71 mm Hg), and on standing her blood pressure fell further to 79/43 mm Hg and she felt that she was going to faint. Again before captopril was given there was no postural hypotension.



Effect of captopril (25 mg by mouth) in an anephric patient in three different states of sodium balance on supine and standing blood pressure, mean arterial pressure, and heart rate. (Mean arterial pressure was calculated from diastolic pressure and 1/3 of pulse pressure.)

Comments

Our findings show that captopril's effect on blood pressure in an anephric patient depends on the state of sodium balance. As little renin is available the effect cannot be through elimination of angiotensin II, but it may be through accumulation of bradykinin.[4] Others have not found any effect of captopril on blood pressure in anephric patients and rats,[3 4] but any hypotensive effect may have been masked by hypervolaemia. Also the blood pressure response to captopril may be partially independent of renin-sodium balance in subjects with a low plasma renin activity. If renin is inappropriately low in relation to total-body sodium then captopril may produce its effect by potentiating bradykinin action. Furthermore, our case illustrates that an extrarenal kallikrein-kinin system may be important. The postural hypotension that developed may support a suggestion[5] that vasoactive peptides may effect venous tone. The fact that heart rate increased considerably more when the patient stood in the sodium-depleted state suggests that the baroreceptor-induced changes in sympathetic tone were appropriate. The postural hypotension may have been caused by a fall in venous return and cardiac output caused by inhibition of the angiotensin-converting enzyme increasing the capacitance of the venous system.

1 Gavras, H, *et al*, *New England Journal of Medicine*, 1978, **298**, 991.
2 Case, D B, *et al*, *Progress in Cardiovascular Diseases*, 1978, **21**, 195.
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(*Accepted 7 August 1979*)

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"Pseudonormonatraemia"

In pseudohyponatraemia plasma concentrations of sodium are lowered owing to volume displacement by high concentrations of circulating lipids or paraprotein. We have recently investigated a patient in whom hyperlipidaemia masked the presence of hypernatraemia.

Case report

The patient, a 20-year-old woman, was thought to have the syndrome of essential hypernatraemia due to osmoreceptor dysfunction.[1] She was obese, had anterior pituitary hypofunction, episodes of acute encephalopathy, and a Fredericksen type V hyperlipoproteinaemia (fasting serum lipid concentrations: cholesterol 10·2 mmol/l (395 mg/100 ml), triglycerides 13·4 mmol/l (11·9 g/l), raised chylomicrons and prebeta-lipoproteins, and milky serum). Her plasma sodium concentrations, however, were only at the upper end of our laboratory reference range (134-147 mmol (mEq)/l) or slightly above it. We wondered if the severe lipaemia was artefactually lowering definitely raised sodium concentrations into the normal range. Plasma sodium concentrations were therefore measured before and after ultracentifugation. The concentrations measured by flame emission spectrometry on an Autoanalyser were 147 mmol (mEq)/l before ultracentrifugation and 153 mmol (mEq)/l afterwards. Interestingly, on the same day as this sample was taken a lumbar puncture was performed, and the cerebrospinal fluid sodium concentration was 155 mmol (mEq)/l.

Comment

This demonstration of "pseudonormonatraemia" may be relevant to the interpretation of electrolyte concentrations in patients with severe lipaemia or paraporteinaemia. Hypernatraemic states are associated with a high mortality,[2] and it is important that they should not be missed or underestimated.

[1] Halter, J B, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1977, **44**, 609.
[2] Daggett, P, *et al*, *British Medical Journal*, 1979, **1**, 1177.

(*Accepted 17 August 1979*)

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Waterhouse-Friderichsen syndrome caused by Haemophilus influenzae type b

The Waterhouse-Friderichsen syndrome describes a clinicopathological correlation between a catastrophic illness in childhood and bilateral adrenal haemorrhages found at necropsy. The clinical features include rapid onset and progression to shock and cyanosis with a petechial rash. Death follows rapidly, often within 24 hours of the first symptoms. The syndrome is often associated with meningococcal septicaemia, although it may occur with pneumococcal or staphylococcal sepsis. There are a few reports of an association with other septicaemic illnesses, some in immunologically compromised children. We report a case of the Waterhouse-Friderichsen syndrome associated with *Haemophilus influenzae* type b septicaemia.

Case report

A 9-month-old Caucasian girl presented with a four-hour history of listlessness, vomiting, and grunting respirations. The onset had been acute with a brief convulsion. She had been healthy until two weeks before admission, when she had received a seven-day course of penicillin for otitis media with complete recovery. She was pale and listless with grunting respiration and tachypnoea. The rectal temperature was 39°C and the heart rate 200 beats/min. There were no localising physical signs in any system. The white blood cell count was reduced at $4{\cdot}6 \times 10^9$/l (4600/mm^3), of which 28% were neutrophils. Plasma urea and electrolyte concentrations were normal. Lumbar puncture yielded clear CSF at normal pressure containing 3×10^6 white blood cells/l (3/mm^3) and 15×10^6 red blood cells/l (15/mm^3). The CSF protein and glucose were normal. A Gram-stained smear of a centrifuged deposit of the CSF showed no organisms. A septicaemic illness was suspected and treatment begun with intravenous penicillin and gentamicin. Five hours later the child collapsed with severe peripheral vasoconstriction and cyanosis. Despite vigorous resuscitation there was relentless clinical deterioration.

Ten hours after admission a few colonies of *H influenzae* were isolated from the CSF. Counter immunoelectrophoresis at this time showed *H influenzae* antigen in the blood culture, from which *H influenzae* was isolated the next day. Chloramphenicol was then added to the antibiotic regimen. Scattered petechiae appeared on the skin: coagulation studies suggested disseminated intravascular coagulation. The child died 15 hours after admission. CSF obtained immediately after death yielded a few colonies of *H influenzae* on culture after three days' incubation, but blood obtained simultaneously was sterile. *H influenzae* was not isolated from throat swabs from the child's family. Necropsy showed bilateral haemorrhagic adrenal infarction, but there was no focus of infection and no evidence of meningitis. Immunoglobulin concentrations assayed on a blood sample taken during resuscitation were all decreased: IgM 0·21 g/l, IgA 0·10 g/l, and IgG 2·50 g/l. There was, however, no confirmatory evidence of immune deficiency. Lymph node and thymus morphology was normal. The other members of the family had normal immunoglobulins and isohaemagglutinin titres.

Comment

H influenzae type b causes a septicaemic illness in young children, usually with a focus of infection in the meninges, epiglottis, or bones. Although the illness is often severe, with endotoxic shock, the Waterhouse-Friderichsen syndrome is rare. We have found only five reported cases where clinical details were given (table) and a further three probable cases in which clinical details were not reported.[1] In all cases where clinical details were available purulent meningitis was a presenting feature. Our case, however, shows that *H influenzae* type b may closely mimic the meningococcus in causing an overwhelming septicaemic illness with a normal cell count in the CSF.

We thank Dr Hugh Johnson for reporting on the necropsy.

[1] Harms, D, Pape, G R, and Bohle, A, *Deutsche medizinische Wochenschrift*, 1973, **98**, 542.
[2] Lindsay, J W, *et al*, *American Journal of the Medical Sciences*, 1941, **201**, 263.
[3] Ginandes, G T, and Howard, J E, *Journal of the Mount Sinai Hospital*, 1947, **14**, 778.
[4] Cavinato, G, and Rude, L, *Pediatria (Napoli)*, 1969, **77**, 452.
[5] Fox, B, *Archives of Disease in Childhood*, 1971, **46**, 680.

(*Accepted 3 August 1979*)

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Complication of mebendazole treatment for hydatid disease

Mebendazole may shrink or kill hydatid cysts, thus avoiding the need for operation.[1] Although the drug is used in high doses, few side effects or complications have been recorded. We describe two patients who became feverish during treatment, possibly as a response to drug-induced tissue necrosis.

Case reports

Case 1—A 11-year-old Libyan girl had progressive abdominal distension due to multiple hydatid cysts, which had been found at a laparotomy one year before. Her haemoglobin concentration was 10·1 g/dl and erythrocyte sedimentation rate over 100 mm in first hour. Blood urea, blood sugar, and plasma bilirubin concentrations were normal, as were serum alkaline phosphatase and serum aspartate aminotransferase activities. Serum albumin

Previously reported cases of H influenzae causing Waterhouse-Friderichsen syndrome

Author	Age (months)	Duration of illness (hours)	CSF white cell count ($\times 10^6$/l)	Cultures: Blood	Cultures: CSF	Necropsy
Lindsay *et al*[2]	36	48	1420	*H influenzae*	*H influenzae*	Purulent meningitis, bilateral adrenal haemorrhage
Lindsay *et al*[2]	6	13	986	*H influenzae*	*H influenzae*	Meningeal oedema and exudates, bilateral adrenal haemorrhage
Ginandes and Howard[3]	48	48	"Cloudy"	*H influenzae* type b	*H influenzae* type b	Focal adrenal haemorrhage. Brain not studied
Cavinato and Rude[4]	24	36	400	—	*H influenzae*	Purulent meningitis, bilateral adrenal haemorrhage
Fox[5]	7	33	"Purulent"	—	*H influenzae*	Purulent meningitis, bilateral adrenal haemorrhage