during the day (usually every one and a half hours) and must not do so earlier: she must either wait or be incontinent. We ignore the frequency of micturition at night. Once she has reached her target the interval is increased by half an hour daily until she is voiding four-hourly. (3) We encourage the patient to maintain her usual fluid intake and keep a fluid-balance chart. (4) We introduce the patient to someone successfully treated by the drill.

The table lists the symptoms of the 60 patients both before and six months after treatment. The groups were well matched for age, parity, duration of symptoms, and history of gynaecological and urological operations. Bladder capacity measured under general anaesthesia was 650 ml or more in all patients.

After treatment 27 of the 30 patients practising bladder drill were continent and 25 symptom free, whereas only seven of the 30 controls were both continent and symptom free. These results were significant for all symptoms ($p < 0.01$). The mean duration of stay in hospital after cytoscopy was 6·3 days (range 5-13). In no case did the symptoms subside without the cystogram reverting to normal, or vice versa, and only one patient relapsed after apparently successful bladder drill (at four months). The cystometrograms of patients who remained incontinent were closely similar before and after operation.

Comment

Treating detrusor instability with drugs is unsatisfactory, side effects being reported in up to 43% of cases and the cure rate being generally less than 60%.[1] Prolonged cystodistension cured 9% of cases in one series[2] yet 80% in another[3] and carries the risk of bladder rupture, while biofeedback, with a success rate of 81%,[4] is time consuming.

Bladder drill is a simple, effective treatment without side effects. For the best chance of success it should be conducted in hospital, away from the patient's home environment. The mode of action is presumably psychological, encouraging confidence, and its cure rate in an uncontrolled trial was 82·5%.[5] Our 23·3% cure rate after cystoscopy and urethral dilatation may represent a placebo effect. During this trial we omitted all drugs other than night sedation, but in clinical practice bladder drill could be augmented by drug treatment. We conclude that bladder drill is the treatment of choice for detrusor instability in women.

Requests for reprints should be sent to Dr G J Jarvis.

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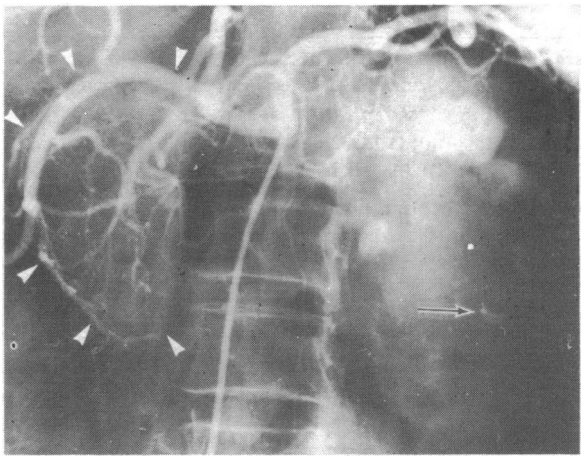
A renal vipoma

Renal tumours are not usually manifested by the watery diarrhoea-hypokalaemia-achlorhydria syndrome.[1 2] Only one renal tumour secreting gastrointestinal hormones has been reported.[3]

Case report

A 64-year-old woman with treated thyrotoxicosis and longstanding goitre presented in February 1979 with watery diarrhoea for three months. She had not lost weight and denied other symptoms. Findings on examination and sigmoidoscopy were otherwise normal, as were barium enema appearances, thyroid function values, full blood count, and renal and liver function values. Small-bowel barium meal showed an increase in jejunal diameter and thickness of mucosal folds, and xylose absorption was abnormal (14% excretion in five hours). In October she was admitted with an exacerbation of her diarrhoea, epigastric pain, and vomiting. She was dehydrated, hypotensive, and in fast atrial fibrillation. Serum potassium concentration was 2·1 mmol (mEq)/l. Despite intravenous fluids she deteriorated, passing 6 l watery diarrhoea daily and having 5·7 l alkaline fluid (pH 7·5-8·0) aspirated daily from her stomach. She became clinically acidotic (arterial pH 7·2), and serum potassium concentration fell to 1·9 mmol/l. Paralytic ileus developed.

In view of a clinical diagnosis of watery diarrhoea-hypokalaemia-achlorhydria syndrome treatment with steroids, intravenous fluids, and potassium supplements was instituted. Pancreatic angiography (figure) showed an expanded hypervascular pancreatic head with vessels of irregular calibre and a prominent venous blush. Calcification in the region of the left kidney was seen, and a left renal arteriogram confirmed a tumour at the lower pole. Radioimmunoassay disclosed grossly raised plasma concentrations of vasoactive intestinal polypeptide (over 400 pmol/l (13·2 pg/100 ml); normal below 30 pmol/l (1 pg/100 ml) and pancreatic polypeptide (over 1000 pmol/l (42 pg/100 ml); normal below 100 pmol/l (4·2 pg/100 ml)). At laparotomy an enlarged, firm pancreas was seen, with no tumour palpable. Multiple biopsy specimens from throughout the gland showed no evidence of adenoma or islet-cell hyperplasia at frozen section. The head and body were resected, leaving the tail in situ. The tail lifted easily off the left kidney, disclosing a large intracapsular tumour at the lower pole. Left nephrectomy was performed. Vasoactive intestinal polypeptide concentrations in portal and peripheral venous blood were similar, while there was a threefold increase in blood from the left renal vein.



Coeliac axis arteriogram showing expanded head of pancreas containing increased number of irregular calibre vessels (large arrows) and calcification in left kidney (small arrow).

Histologically the pancreas showed reduction in acinar and islet cells with increased fat and fibrosis (consistent with chronic pancreatitis), but no adenoma or islet-cell hyperplasia. The renal tumour was a typical malignant apudoma. The pancreas contained normal amounts of vasoactive intestinal and pancreatic polypeptides, somatostatin, and glucagon, whereas excessive quantities of immunoreactive vasoactive intestinal and pancreatic polypeptides were found in the renal tumour. Electron microscopy confirmed the presence of secreting granules 155-200 nm diameter, typical of vipoma.

The patient recovered well initially and her bowels returned to normal. Twelve days after operation, however, she developed septicaemia from a pancreatic abscess, from which she died. There was no residual tumour at necropsy, but the pancreatic tail had been destroyed by abscess.

Comment

Although this patient's symptoms were unequivocally the result of a functioning vipoma of the left kidney, we cannot exclude the possibility that this was a metastasis from an unrecognised primary lesion in the pancreatic tail. Such a tumour may metastasise while small enough to be overlooked at angiography and laparotomy. Nevertheless, the renal tumour was calcified, suggesting that it had been present for some time, and the patient's symptoms responded to its removal. A renal tumour producing enteroglucagon has been described,[3] and the presence of multiple pancreatic hormones in the tumour is not in itself evidence of a pancreatic origin.[4] The pancreas showed no evidence of the D-cell hyperplasia often seen in association with unrecognised adenoma.[5] A primary renal origin for this tumour therefore seems likely.

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Unpredictable response to nifedipine in severe cardiac failure

Nifedipine is a vasodilator with effects mainly on the arterioles and hence might have a place in the management of severe cardiac failure.[1 2] We set out to study the response to an oral dose of 30 mg but this was reduced to 20 mg after a patient developed severe hypotension. A similar reaction occurred in another patient on the smaller dose.

Patients, methods, and results

Six men with severe chronic cardiac failure were studied. Three had coronary artery disease and three had congestive cardiomyopathy. All were having treatment with diuretics and, when indicated, digoxin. Each gave his consent to the procedure, which was approved by the ethical committee. After diagnostic cardiac catheterisation a Swan-Ganz double lumen thermal dilution cardiac output catheter was positioned in the pulmonary artery and a fine polyethylene catheter in the brachial artery. On return to the ward control observations of systemic arterial pressure (SAP), pulmonary artery pressure (PAP), pulmonary artery "wedge" pressure (PAW), right atrial pressure (RAP), and cardiac output (in triplicate) were made at 15-minute intervals for one hour. Nifedipine 30 mg (cases 1 and 2) or 20 mg (cases 3-6) was given orally. Observations were then repeated at 15-minute intervals for the first hour and hourly for five hours.

Haemodynamic changes were detected within 15 minutes, peaked at 30 to 45 minutes, and persisted up to five hours (table). In all patients SAP fell by an average of 30%, PAP by 29%, and PAW by 25%. Systemic vascular resistance was reduced by an average of 47%. Cardiac output increased in three patients. In cases 2 and 6, the main subjects of this report, severe hypotension accompanied a fall in cardiac output. In case 2 the patient received 30 mg nifedipine. After 15 minutes he became cyanosed and confused, SAP fell progressively from 130/70 to 50/30 mm Hg, PAP from 80/30 to 50/24 mm Hg, and PAW from 34 to 25 mm Hg. Cardiac output declined from 4·8 to 2·4 l/min and stroke volume from 45 to 31 ml. In case 6 the patient received 20 mg nifedipine, and a similar reaction developed; SAP fell from 110/65 to 65/35, PAP from 70/35 to 40/22, and PAW from 35 to 22 mm Hg. Cardiac output decreased from 4·1 to 3·1 l/min and stroke volume from 57 to 52 ml.

Both patients responded to intravenous injection of 20 ml 10% calcium chloride followed by 10 ml 1:10 000 adrenaline. Cardiac output rose and systemic and pulmonary arterial pressures returned to their control levels. There were no further complications.

Comment

Vasodilators may cause hypotension by producing an excessive fall in peripheral resistance, and this leads to a reduced left ventricular filling pressure and volume. In case 2 peripheral resistance fell more than in any other patient and the resulting hypotension was aggravated by a concomitant reduction in cardiac output. In case 6 the decrease in peripheral resistance was modest and the fall in cardiac output was a major factor in the resulting circulatory collapse. In both the reduction in left ventricular filling pressure was substantial but no more than in case 4, where cardiac output was augmented. Furthermore, in previous studies in which filling pressure was reduced to a comparable extent cardiac output invariably rose.[1 2] This, and a recent report of a patient in whom pulmonary oedema was precipitated by nifedipine,[3] raises the possibility that in certain patients the drug can depress myocardial contraction. That this effect is not usually seen in man is ascribed to reflex beta-adrenergic stimulation from activation of the baroreceptor reflex. The fall in heart rate in our patients despite the extreme hypotension is therefore interesting.

Despite earlier promising reports nifedipine cannot be recommended unreservedly for the treatment of cardiac failure and it should be used cautiously in patients with poor left ventricular function.

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Haemodynamic observations before (control) and 45 minutes after nifedipine (cases 1, 3, 4, 5) or at peak effect before intervention (cases 2, 6)

Case No	Age (years)	Diagnosis	Concomitant treatment (mg/day)	Condition	Heart rate (min)	Pressures (mm Hg)				CO (l/min)	S Vol (ml)	SVR units	PVR units
						SAP	PAP	PAW	RA				
1	63	CAD	Frusemide 120 Amiloride 15	Control Nifedipine 30 mg	98 95	119 75	30 19	25 14	5 3	3·2 3·4	33 36	36 19	1·5 1·5
2	55	CCM	Frusemide 160 Amiloride 20	Control Nifedipine 30 mg	107 92	102 35	44 30	34 25	14 16	4·8 2·9	45 32	18 7	2·1 1·7
3	58	CCM	Frusemide 120 Amiloride 20 Digoxin 0·375	Control Nifedipine 20 mg	63* 65*	80 75	33 32	22 21	13 11	3·5 5·4	56 83	19 12	3·1 2·0
4	52	CCM	Frusemide 250 Spironolactone 100 Digoxin 0·25	Control Nifedipine 20 mg	120 115	100 82	46 33	37 25	14 11	4·3 5·1	36 44	20 14	2·1 1·6
5	61	CAD	Frusemide 120 Amiloride 10	Control Nifedipine 20 mg	83 80	140 127	50 40	40 35	4 4	5·0 6·8	60 85	27 18	2 0·7
6	59	CAD	Frusemide 120 Slow-K 3600	Control Nifedipine 20 mg	72 60	80 50	48 30	35 22	20 20	4·1 3·1	57 52	15 10	3·2 2·5

*Atrial fibrillation.
Abbreviations SAP = mean systemic arterial pressure. PAP = mean pulmonary artery pressure. PAW = mean pulmonary artery "wedge" pressure. RA = right atrial pressure. CO = cardiac output. S Vol = stroke volume. SVR = systemic vascular resistance. PVR = pulmonary vascular resistance. CAD = coronary artery disease. CCM = congestive cardiomyopathy.