SHORT REPORTS

Acute right heart failure complicated by hypovolaemia

The dangers of inducing diuresis in patients with pulmonary oedema and normal pulmonary wedge pressures have recently been described.¹ We report a complementary case of acute right heart failure due to right ventricular infarction complicated by hypovolaemia. In this, right ventricular output may provide an insufficient preload for the left ventricle, and there is the apparent paradox of an overloaded right ventricle and an inadequately primed "hypovolaemic" left ventricle. Failure to recognise this may lead to inappropriate diuretic or inotropic treatment and potentially irreversible hypovolaemic shock.

Case report

A 66-year-old tailor presented with inferior myocardial infarction. He was normotensive and well perfused, with raised jugular venous pressure. Auscultation of the heart was normal and he had no signs of left ventricular failure. Because of the raised jugular venous pressure he underwent diuresis. Over three days he became hypotensive and oliguric. Jugular venous pressure remained raised in the absence of pulmonary congestion, and he developed ankle oedema. Inotropic drugs and diuretics produced no improvement.

A Swan-Ganz catheter was inserted (figure). Right atrial pressure was

the risk of pulmonary oedema rises with uncontrolled administration of fluids. Similarly, diuresis reduces ventricular filling with little fall in performance. Should left ventricular function be normal, however, the Starling curve lies to the left, filling pressures are low, and further reduction in pulmonary capillary wedge pressure appreciably reduces stroke volume.

The concept of the heart as two separate pumps is established,^{3,4} but clinical teaching still equates raised jugular venous pressure with biventricular failure; pulmonary embolus, pericardial tamponade, and cor pulmonale are mentioned in parenthesis, and right ventricular infarction has not yet reached the general textbooks.⁵ Consequently the unwary tend to attribute falling cardiac output in the presence of raised jugular venous pressure to myocardial failure, and the patient receives inotropic drugs and diuretics. The need for adequate left ventricular filling is often forgotten in the anxiety to avoid pulmonary oedema. A competent but hypovolaemic ventricle is therefore deprived of fluid and driven with inotropic drugs. Cardiac and urine outputs remain low. The patient undergoes diuresis and is rendered more hypovolaemic. Death is inevitable.

We propose that patients with right ventricular failure, poor perfusion, and normal chest x-ray films may be hypovolaemic. A 200 ml bolus of colloid will improve hypovolaemia dramatically. This should be repeated until the patient is stable. Patients with biventricular failure will not respond. Deterioration in their condition may be reversed by diuresis or venesection. The Swan-Ganz catheter has made measurement of left-sided filling pressures accessible to most acute services, when fluid replacement may be tailored to provide a pulmonary capillary wedge pressure of 12-15 mm Hg.

We think that the life-saving potential of a fluid load in unsuspected hypovolaemia with right ventricular failure justifies fluid challenge when the diagnosis is in doubt.

¹ Timmis AD, Fowler MB, Burwood RJ, Gishen P, Vincent R, Chamberlain DA. Pulmonary oedema without critical increase in left atrial pressure in acute myocardial infarction. *Br Med J* 1981;283:636-8.

² McHugh TJ, Forrester JS, Adler L, Zion D, Swan HJC. Pulmonary vascular congestion in acute myocardial infarction, haemodynamic and radiological correlations. *Ann Intern Med* 1972;76:29-33.

³ Bradley R. *Studies in acute heart failure*. London: Edward Arnold, 1976:1-7.

⁴ Sarnoff SJ, Berglund E. Starling's law of the heart studied by means of simultaneous right and left ventricular function curves in the dog. *Circulation* 1954;9:706-18.

⁵ Rackley CE, Russell RO, Mantle JA, Rogers WJ, Papapietro SE, Schwarz KM. Right ventricular infarction and function. *Am J Cardiol* 1981;48:215-8.

(Accepted 8 January 1982)

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Effect of cimetidine on portal hypertension in cirrhotic patients

Cimetidine is claimed to reduce hepatic blood flow in normal subjects,¹ but its effect on portal pressure has not been reported. If cimetidine also reduces hepatic blood flow in patients with cirrhosis then it would be an alternative to propranolol, which reduces both hepatic blood flow and portal pressure and protects against recurrent variceal bleeding in these patients.² Cimetidine might have fewer side effects than propranolol, and long-term clinical trials of cimetidine prophylaxis for recurrent variceal haemorrhage in patients with cirrhosis have been advocated. We therefore studied the effect of intravenous cimetidine on the gradient between the wedged and free hepatic venous pressures, which is a reliable index of portal pressure, in patients with cirrhosis³ who had recently bled from oesophageal varices.

Left ventricular hypovolaemia due to right ventricular infarction. Top: Pressures on insertion of catheter. Bottom: Pressures after 250 ml colloid given immediately.

PAP=Pulmonary artery pressure. PCWP=Pulmonary capillary wedge pressure. Insp=Inspiration. Exp=Expiration.

raised with a mean systolic pressure of 12 mm Hg from the mid-axilla (normal range 12-20) and a mean pulmonary capillary wedge pressure of 1 mm Hg (normal range 8-12). These findings indicated isolated right ventricular failure with inadequate left ventricular filling. Fluid replacement restored the pulmonary wedge pressure, and his blood pressure and urine flow returned to normal. He recovered fully.

Comment

Clinical assessment of left ventricular filling is difficult. Radiologically the lung fields are clear when pulmonary capillary wedge pressure is below 18 mm Hg.² Normal left ventricular filling pressure (reflected by pulmonary capillary wedge pressure) is 8-12 mm Hg. When left ventricular function is mildly impaired, and particularly in biventricular failure, clear lung fields and a raised jugular venous pressure may co-exist. As the curves of ventricular function are flat

Patients, methods, and results

Twelve patients with cirrhosis (nine men, three women) aged 21-72 years, who were admitted consecutively with bleeding oesophageal varices, were studied three days after the bleeding had stopped. Three of these patients were studied again one month later. The study was approved by the hospital ethics committee. Wedged and free hepatic venous pressure were measured using a Cordis Cobra II torque-controlled balloon catheter, French gauge 7 (Cordis Corporation, Miami, USA), as described by Groszmann *et al.*³ Pressures were also recorded in the right atrium, and in the inferior vena cava within the liver and above and below it. Measurements were made with a Hewlett-Packard 1280 series physiologic pressure transducer linked to a Hewlett-Packard blood-pressure module 78205A. After the patient was settled three recordings of wedged and free hepatic venous pressures were taken over 10 minutes. Cimetidine 200 mg was then given intravenously, and after 10 minutes three more readings of wedged and free hepatic venous pressures were taken over the next 10 minutes.

The figure shows the gradients between wedged and free hepatic venous pressures in each patient before and 10 minutes after 200 mg cimetidine given intravenously. There was no significant difference between the means of the pressure gradients before ($16.8 \pm \text{SD } 4.2$ mm Hg) and after cimetidine (16.1 ± 3.1 mm Hg).

Effect of 200 mg cimetidine given intravenously on gradient between wedged and free hepatic venous pressures, using average of three readings. (*, Δ, □ = Patients studied twice one month apart.)

Comment

In this study of patients with cirrhosis 200 mg cimetidine given intravenously did not reduce portal hypertension as measured by the gradient between wedged and free hepatic venous pressures. The dose of cimetidine used is unlikely to have been insufficient to produce a reduction in portal pressure, since the same dose saturates H_2 -receptors in the systemic circulation within minutes.⁴ This largely removes the proposed rationale for long-term use of cimetidine to prevent recurrent variceal haemorrhage. Prospective trials of cimetidine prophylaxis are likely to be disappointing.

As cimetidine does not affect portal pressure in patients with cirrhosis it probably does not reduce splanchnic blood flow. The possibility that it causes simultaneous vasoconstriction in the portal system to maintain portal pressure is highly unlikely. The original report¹ that cimetidine reduces blood flow to the liver in normal subjects has itself been challenged. In that study hepatic blood flow was measured by clearance of indocyanine green and the reduction after cimetidine interpreted as indicating decreased liver blood flow. The reduction in indocyanine green clearance after cimetidine may, however, have been caused not only by a decrease in blood flow to the liver but also by a decrease in extraction of indocyanine green. Such a decrease in extraction of indocyanine green after cimetidine has been shown in two patients with liver disease, in whom hepatic blood flow apparently increased.⁵ This provides further support for our conclusion that cimetidine does not have any effect on portal hypertension in patients with cirrhosis and so is unlikely to be beneficial in preventing recurrent bleeding from gastrooesophageal varices.

- 1 Feely J, Wilkinson GR, Wood AJJ. Reduction of liver blood flow and propranolol metabolism by cimetidine. *N Engl J Med* 1981;304:692-5.
- 2 Lebrech D, Novel O, Bernavay J, Bouygués M, Rueff B, Benhamou J-P. Propranolol in prevention of recurrent gastrointestinal bleeding in cirrhotic patients. *Lancet* 1981;i:920-1.
- 3 Groszmann R, Glickman M, Blei A, Storer E, Conn HO. Wedged and free hepatic venous pressure measured with a balloon catheter. *Gastroenterology* 1979;76:254-8.
- 4 Boyce MJ, Wareham K. Histamine H_1 and H_2 receptors in the cardiovascular system of man. In: Torsoli A, Lucchelli PE, Brimblecombe RW, eds. *H₂ antagonists*. Amsterdam: Excerpta Medica, 1980:280-93.
- 5 Lebrech D, Goldfarb G, Benhamou J-P. Reduction of liver blood flow by cimetidine. *N Engl J Med* 1981;305:3464.

(Accepted 8 January 1982)

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Cyclophosphamide treatment of systemic lupus erythematosus: risk of bladder cancer exceeds benefit

Systemic lupus erythematosus has a variable clinical course, making assessment of treatment difficult. In association with steroids cyclophosphamide has been used to treat the disease for at least 20 years. Cyclophosphamide is claimed to reduce the dose of steroids required but is extremely toxic.

We report on two women who developed bladder cancer after prolonged treatment with cyclophosphamide.

Case 1—A 28-year-old woman developed systemic lupus erythematosus in 1969 after exposure to sunlight. Symptoms included rash, haemolytic anaemia, and proteinuria. Renal biopsy specimens showed proliferative glomerulonephritis. Treatment was started with steroids and with cyclophosphamide 50-100 mg daily, which was given intermittently for six years. In 1981 she presented with symptoms of urinary tract infection. Cultures were sterile. Intravenous urography disclosed a bladder tumour: biopsy specimens showed poorly differentiated keratinising squamous-cell carcinoma with extensive haemorrhage and necrosis. A short course of deep x-ray treatment was followed by total cystectomy and transplantation of ureters into an ileal conduit. Kidney function remained normal with no evidence of recurrence of the systemic lupus erythematosus.

Case 2—A 45-year-old woman presented in 1969 with a five-year history of respiratory symptoms, bilateral pleural effusions, and moderate proteinuria and lupus erythematosus cells on testing. She was three months pregnant. Renal biopsy specimen's showed proliferative glomerulonephritis. She underwent hysterotomy and tubal ligation. Prednisone 50 mg and cyclophosphamide 100 mg daily were started: both were reduced to maintenance dosage but when they were stopped joint swelling recurred.

In 1976, while taking 20 mg cyclophosphamide and 7.5 mg prednisone, she developed left loin pain. Intravenous urography showed a dilated left ureter and calices due to obstruction by bladder tumour. Investigations showed poorly differentiated transitional-cell carcinoma infiltrating muscle. She underwent deep x-ray treatment, total cystectomy, and transplantation of ureters into an ileal conduit. Renal function was normal. Four years after this operation she developed an exacerbation of systemic lupus erythematosus after exposure to sunlight. She responded satisfactorily to steroids alone.

Comment

Carcinoma of the bladder is uncommon in women aged under 40, and invasive carcinoma as found in these two patients is exceptional. Neither had been exposed to any known carcinogen other than cyclophosphamide, but both had received extensive treatment with this drug.

Since the early 1970s evidence has accumulated concerning the carcinogenic properties of cyclophosphamide.¹⁻⁴ Accepting this association, two questions must be answered: Is it justifiable to use the drug? What follow-up should patients receive who have already received the drug? Donadia *et al.*⁵ found no convincing evidence that