activity. In the present case, however, the inhibitory activity was more probably of maternal origin since six exchanges (total of 24 litres) were required to remove it.

We have recently undertaken plasma exchanges on several other women sensitised to anti-D with disappointing results, despite using a more intensive regimen than that reported to be successful elsewhere.[2] Our present findings suggest that the role of plasma exchange in haemolytic disease of the newborn is more complex than simply removing the antibody and that further investigations are required.

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Indium-111 labelled platelets in diagnosis of leg-vein thrombosis: preliminary findings

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Summary and conclusions

Platelets from eight patients thought clinically to have deep venous thrombosis were labelled with indium-111 and reinjected. Subsequent scanning of the patients with a wholebody scanner and imaging with a gammacamera showed focal accumulation of the label at five sites in four legs, which correlated precisely with the sites of venous thrombi identified by ascending venography.

This technique is a useful addition to methods for diagnosing venous thrombosis.

Introduction

Many techniques are used for detecting leg-vein thrombosis.[1] Ascending venography is the yardstick by which all others are measured but it is often uncomfortable and carries a small but definite morbidity.[2 3] The use of fibrinogen labelled with iodine-125 avoids the problem of discomfort and has the major advantage of being performed at the bedside. It has two major disadvantages, however. Firstly, though accuracy is good in detecting calf-vein thrombosis it diminishes in the thigh,[1] and the method is useless for detecting pelvic-vein thrombosis; secondly, its value lies in detecting thrombi as they form, whereas it does not accurately identify already established thrombi.

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Platelets labelled with indium-111 have been used to estimate platelet survival,[4-7] to diagnose renal transplant rejection,[8] and in attempts to detect atherosclerotic plaques.[9 10]

This study was undertaken to determine whether platelets labelled with this radionuclide were useful in detecting established venous thrombosis.

Materials and methods

Platelets were labelled with indium-111 by the method of Hawker *et al.*[6 7 11] A total of 26 ml of venous blood was withdrawn with an 18-gauge needle, 9 ml being added to 1 ml 3·8% trisodium citrate and used for aggregation standards and the production of platelet-poor plasma. The remaining 17 ml was anticoagulated with 3 ml acid citrate and the platelets separated by differential centrifugation, washed, resuspended in Ca^{++}-free Tyrode's solution containing prostaglandin E_1 (Imperial Chemical Industries Ltd), and incubated with 200-250 μCi indium-111 oxine (Radiochemical Centre) at 37°C for 60 seconds. After centrifugation the platelets were suspended in 5 ml of platelet-poor plasma and reinjected into the patient 45-60 minutes after the initial venepuncture.

Scanning at slow speed was performed with an El-Scint wholebody scanner fitted with medium-energy VC-3 collimators, and the data were displayed on a VD2 videoprocessing colour display. Regions of interest were imaged with an Ohio Nuclear series 410 wide-field-of-view gammacamera linked to a Digital Equipment Corporation Gamma-11 computer system.

Ascending venography was performed on all patients after scanning was completed and the findings reported without knowledge of the results of scanning.

Results

Eight patients were studied. Ascending venography was performed on 13 legs, and five thrombi were identified in four. The number, location, and extent of these correlated precisely with the areas in

which abnormal accumulations of the radiolabel had been found when the scans were interpreted. Two representative cases are described.

Case 1—A 61-year-old retired publican admitted to hospital with a three-day history of haemoptysis and left-sided pleuritic chest pain subsequently developed a pleural rub. He had no symptoms or clinical signs in his legs. Chest radiographs and lung scans suggested a pulmonary embolus. Ten days after admission his platelets were labelled with 250 μCi indium-111; figure 1 shows the gammacamera views obtained 20 hours later. There was a major concentration of label in the left leg extending from the iliac to the popliteal vein; this corresponded to the thrombus detected by venography. The scan also suggested the presence of a small thrombus in the right iliac vein; the patient, however, found venography so uncomfortable that he declined to undergo venography of the right leg.

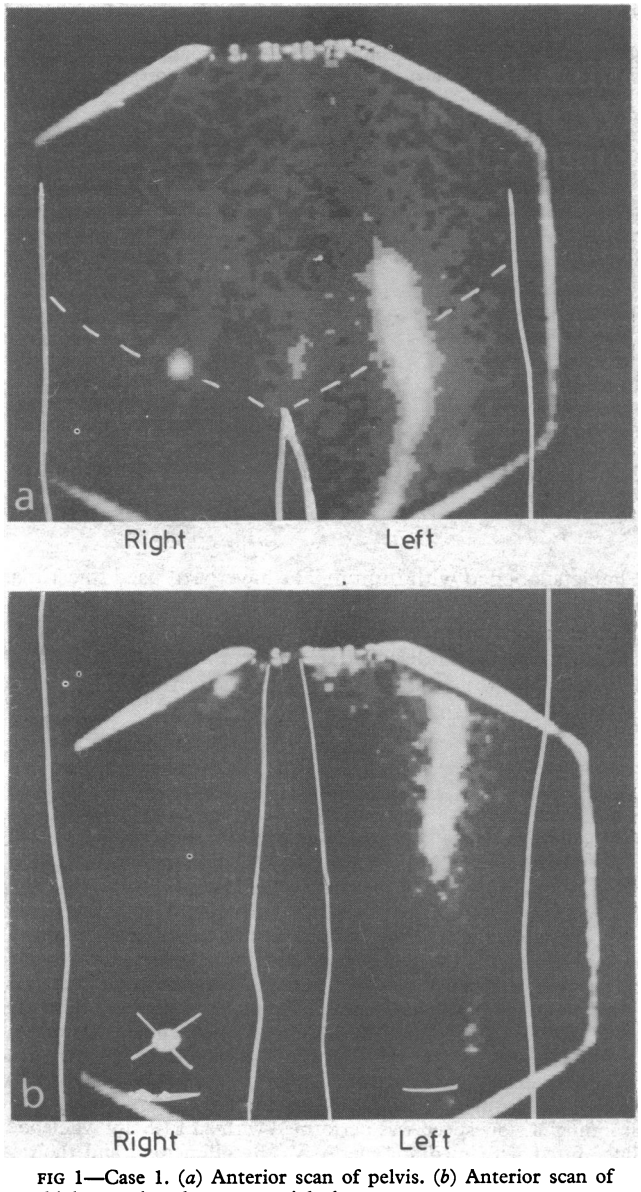

FIG 1—Case 1. (*a*) Anterior scan of pelvis. (*b*) Anterior scan of thighs; marker shown over right knee.

Case 2—A 55-year-old woman undergoing routine ^{125}I-fibrinogen scanning after a gynaecological operation developed a "hot spot" in her left calf four days after a Manchester repair. Her platelets were labelled with 200 μCi indium-111 three days later, and the scans obtained 24 hours after injection showed a major concentration of label in this calf, and suggested that a thrombus was present in the long saphenous vein close to the entry into the femoral vein (fig 2). Both the calf-vein thrombus and the saphenous-vein thrombus were confirmed on venography.

No side effects were experienced by any of the patients studied.

Discussion

This technique offers several advantages over the use of ^{125}I-fibrinogen. It identifies already established thrombi, and in our hands identified thrombi that on clinical grounds were believed to be up to five weeks old. It also identifies thrombi high in the iliofemoral segment. As mobile gammacameras become more widely available, imaging should be possible with

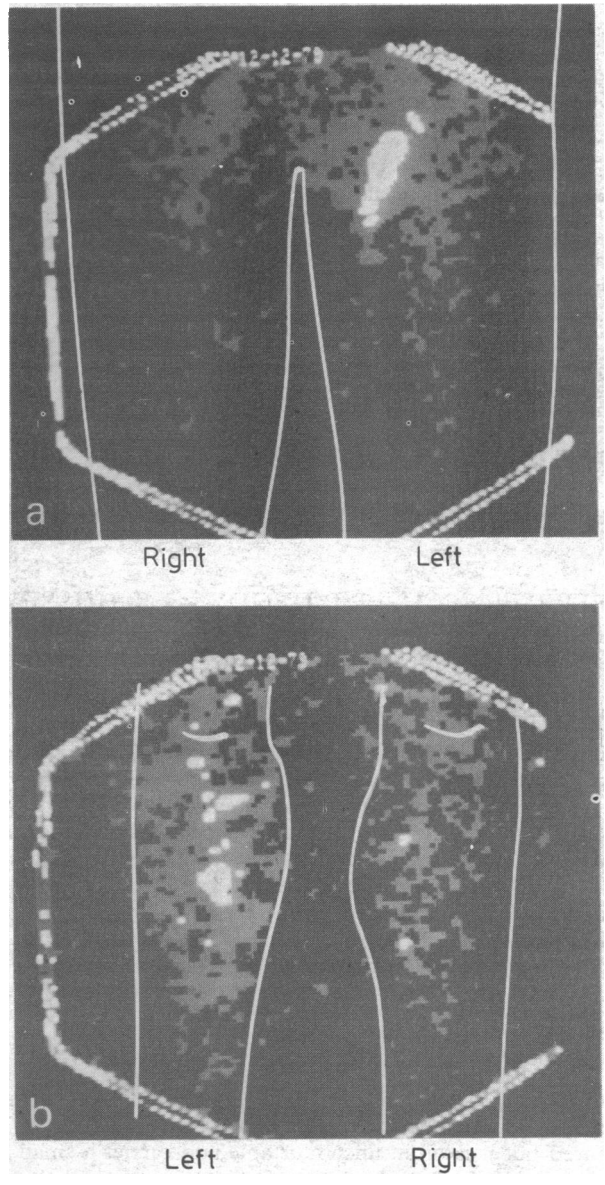

FIG 2—Case 2. (*a*) Anterior scan of thighs. (*b*) Posterior scan of calves.

minimal movement of the patient. The procedure is free of discomfort, which is an advantage over venography. The total dose of radiation to the spleen, which is the target organ in this examination, has been estimated as 4·0-5·5 rads when the stated doses of indium-111 are used.

A detailed comparison of the accuracy of this technique with that of venography in identifying venous thrombi is currently under way. The results of this study suggest that this technique will be a valuable addition to methods for diagnosing leg-vein thrombosis.

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E_1. We are grateful to Joyce Davidson and Lesley Kemp for excellent technical help. Albert Fenech thanks Robert and Linda Hawker for their help and patience in teaching him their technique.

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Atenolol, sustained-release oxprenolol, and long-acting propranolol in hypertension

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Summary and conclusions

The effect of once-daily atenolol, sustained-release oxprenolol (a new formulation of oxprenolol presented as a compressed tablet in a waxed matrix), and long-acting propranolol (a new formulation presented as spheroids in a capsule) was studied in a double-blind crossover trial in 23 carefully selected hypertensive outpatients. After a run-in period with matching placebo each patient received atenolol (100 mg/day), sustained-release oxprenolol (160 mg/day), long-acting propranolol (160 mg/day), and placebo according to a randomised sequence.

After four weeks' treatment with sustained-release oxprenolol blood pressure in the two to four hours before the next dose was not significantly lower than after placebo. The effectiveness of atenolol and of the new formulation of propranolol in reducing blood pressure was confirmed.

These results suggest that the present formulation of sustained-release oxprenolol should be reconsidered.

Introduction

We have compared conventional fixed doses of three beta-adrenoceptor antagonists that are claimed to be suitable for once-daily use in hypertension—namely, atenolol, sustained-release oxprenolol (a compressed tablet in a waxed matrix), and long-acting propranolol (a spheroid formulation).

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Patients and methods

Our procedure for selecting patients with mild hypertension has been described.[1 2] Patients were excluded if their lying diastolic pressure fell below 90 mm Hg after a four-week outpatient run-in period with placebo. Suitable patients were then allocated in a randomised order to four treatment periods (double-blind, within-patient) of four weeks each.

Twenty-three patients were studied (12 men; average age 40·9 years, range 21-59). The drugs were taken once daily at 1800, the doses (atenolol 100 mg, sustained-release oxprenolol 160 mg, long-acting propranolol 160 mg, or matching placebo) being considered to be approximately equivalent in effect.

Blood pressures were recorded with Hawksley random-zero sphygmomanometers (diastolic pressure phase 4) under standard conditions.[1 2] The means of two blood-pressure readings and heart rates were recorded after five minutes' lying and two minutes' standing. A single measurement of heart rate and blood pressure was taken immediately after a two-step exercise test designed to produce a target untreated heart rate of 140/min.[1 2] Measurements were made between 1400 and 1630 (20-22 hours after dosing), at the same time of day on each occasion for each patient. Patients were seen fortnightly. A questionnaire on symptoms was completed by a different observer from the one recording blood pressure.[1 2] Compliance with drug taking, assessed by tablet counts, was satisfactory throughout (> 90%).

Data on blood pressure, heart rate, and weight were analysed separately by analysis of variance after two and four weeks with each treatment. If the overall comparison between treatments, as assessed by the F test, was significant at the 5% level then pairs of adjusted means were compared using a *t* test. The standard deviation used in the *t* test was based on the residual mean square from the analysis of variance.

Results

Table I lists the mean blood pressures, pulse rates, and weights during the run-in and treatment periods, and table II the levels of statistical significance.

After four weeks' treatment systolic and diastolic blood pressures measured lying, standing, and after exercise were significantly lower after atenolol and long-acting propranolol than after placebo, but the same was not true for sustained-release oxprenolol. Atenolol was significantly superior to sustained-release oxprenolol after four weeks' treatment in lowering systolic and diastolic blood pressures and heart rates in each position. Long-acting propranolol was also superior to