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Eligibility for home treatment of deep vein thrombosis: prospective study

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Low molecular weight heparin is safe and effective for the treatment of deep vein thrombosis.¹ We have recently shown in a randomised study that immobilisation is not necessary.² The results challenge the traditional notion that these patients must be treated in hospital. For selected patients, outpatient treatment has been shown to be safe and effective.^{3,4} We determined the proportion of patients who still require admission to hospital and why.

Methods and results

Between 1 November 1998 and 15 August 1999 all patients presenting to the vascular diagnostics unit of the University Hospital Dresden, Germany, as outpatients with acute deep vein thrombosis in the leg were prospectively evaluated regarding eligibility for home treatment. We defined acute deep vein thrombosis as non-compressible deep veins on ultrasonography (UM9 HDI, linear array 4-7 MHz, ATL, Bothell, Washington, DC) and symptoms that had been present for less than two weeks. Written informed consent was obtained from all patients.

On the day of diagnosis patients were started on oral anticoagulation with phenprocoumon (adjusted to a target international normalised ratio of 2-3) and the low molecular weight heparin nadroparin (90 IU/kg body weight twice daily) until a therapeutic ratio was achieved. All patients received class II compression stockings. At presentation, the decision regarding hospital admission was based on medical reasons, home care situation, patients' and general practitioners' rejection of outpatient treatment, and hospital service logis-

tics. The 95% confidence intervals were calculated according to the Wilson procedure.

We assessed recurrent venous thromboembolism (verified by sonography, ventilation-perfusion scan, or pulmonary angiography), major bleeding, and death at clinical follow up of patients treated at home. Assessments were at three and six days and two, four, and 12 weeks after initiation of treatment. The study was approved by the local ethics committee.

A total of 117 consecutive outpatients (48 men, 69 women) were diagnosed as having acute deep vein thrombosis. Of these, 92 received home treatment—that is, they were not admitted at all. The median (range) age was 62.0 (19-95) years. Three patients were admitted to hospital for medical reasons; 11 because of the home care situation; and 11 for reasons of hospital service logistics (table). At the 12 week follow up of the 92 patients, eight had died (six from cancer and two from chronic heart failure; three had recurrent thrombosis; and four had developed minor bleeding. No clinical pulmonary embolism or major bleeding occurred. Safety and efficacy figures are similar to those previously published.⁵

Comment

Most outpatients presenting with acute deep vein thrombosis do not need to be admitted to hospital. The proportion who do require admission depends mainly on factors to do with infrastructure rather than medical reasons. In our study, only 3% of patients were admitted for medical reasons, and in 9% admission was because medication and international normalised ratio

Reasons for admission to hospital in 117 consecutive outpatients with deep vein thrombosis

Reason for admission	No of patients (%; 95% CI)	Details
Medical reason	3/117 (2.6; 0.9 to 7.1)	Massive leg swelling and severe pain (n=2); concomitant pneumonia (n=1)
Home care situation	11/117 (9.4; 5.3 to 16.1)	Self injection with heparin not possible (n=7; poor compliance in 5, social reasons in 2); daily INR testing not possible (n=5)
Patient or general practitioner rejects outpatient treatment	0 (0 to 3.2)	NA
Hospital service logistics	11/117 (9.4; 5.3 to 16.1)	Presented at weekend (n=7) or after 5 pm (n=4)

INR=international normalised ratio.
NA=not applicable.

could not be monitored. Even these patients could have been treated as outpatients if adequate professional care had been available at home. No serious complications were noted in patients treated in an outpatient setting. Another 9% of our patients presented in the emergency room and were already being treated for deep vein thrombosis suspected on clinical grounds alone. They were admitted until ultrasound examination could be performed.

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Contributors: TS and SMS had the original idea for the study, recruited a large number of patients, created the trial database, analysed the data, and wrote the paper. BS conducted statistical analysis and recruited patients. UH advised on data collection and analysed the data. JB recruited patients for the study. HES revised the final version of the manuscript and is the guarantor of the paper. All authors approved the final version of the paper.

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Drug points

Pseudophaeochromocytoma syndrome associated with clozapine

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Clozapine (Clozaril, Novartis), a tricyclic dibenzodiazepine derivative, has an established role in the treatment of refractory schizophrenia. In the United Kingdom the drug may only be prescribed by consultant psychiatrists registered with the Clozaril Patient Monitoring Service; this reflects the serious adverse effect profile of the drug, which includes agranulocytosis. Paradoxical hypertension with increased concentrations of urinary catecholamines has also been reported, albeit rarely and in association with other antipsychotic treatment.¹

We describe four patients with a pseudophaeochromocytoma syndrome associated with clozapine. All had serious refractory psychiatric disturbances. Case 2 presented to a cardiology clinic with hypertension for which she was receiving bendrofluzide 2.5 mg daily, and case 3 was referred to a diabetes clinic with type 2 diabetes (treated with metformin 500 mg twice daily) and dyslipidaemia. Case 4 was initially referred to a renal clinic with hypertension. Profuse sweating, hypertension, and obesity were common to all the patients; intermittent tachycardia was noted in cases 1 to 3 (table). Renal and hepatic function were normal in all the patients, and there was no evidence of alternative causes of secondary hypertension. The interval between the start of clozapine treatment and the development of the clinical features varied (table), being evident within one week in case 1. Urinary catecholamine concentrations, measured in 24 hour collections during clozapine treatment, were increased in all four patients (table). To exclude the possibility of phaeochromocytoma, case 1 underwent computed tomography and cases 3 and 4 underwent isotopic imaging.² In cases 1 and 2, urinary catecholamine concentrations normalised, and clinical features improved or resolved after withdrawal of the drug; these patients also lost several kilograms in body weight. Clozapine was continued at a lower dose in case 3 as the supervising psychiatrist advised against its withdrawal. Treatment was also continued in case 4 because his blood pressure settled spontaneously.

The neuropharmacological actions of clozapine are complex and include affinity for 5-HT₂ receptors and for adrenergic receptors *in vitro*.³ Clozapine has been

reported to cause increases in plasma noradrenaline concentrations, a postulated mechanism being the inhibition of resynaptic reuptake mediated by α_2 adrenergic receptors.⁴ Sulpiride, which blocks presynaptic α_2 adrenoceptors, may have contributed to the clinical features in cases 2 and 4.⁵

We contacted the manufacturer, Novartis, and the Committee on Safety of Medicines about this adverse event.

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Clinical details of patients and catecholamine concentrations

Case No	Age (years)	Sex	Body mass index (kg/m ²)	Clozapine dose (mg/day) and duration of treatment*	Other drugs	Heart rate (beats/min)	Blood pressure (mm Hg)	24 hour urinary catecholamine concentration (µmol) (reference range)
1	27	Male	31	400 for 2 months	Fluoxetine 20 mg daily	110	170/120	Noradrenaline 1.68 (<0.59), vanillylmandelic acid 54 (<35)
2	28	Female	38	700 for 12 months	Bendrofluzide 2.5 mg daily	104	143/112†	Noradrenaline 1.02 (0.08-0.45)
3	38	Male	40	900 for 18 months	Sulpiride 600 mg, venlafaxine 150 mg, and metformin 500 mg twice daily	130	156/100	Noradrenaline 0.53 (0.07-0.48), normetadrenaline 4.3 (0-3.00)
4	22	Male	30	600 for 3 months	Sulpiride 200 mg daily and paroxetine 50 mg daily	NA	180/120	Noradrenaline 0.90 (0.07-0.48), normetadrenaline 4.6 (0-3.00)

NA=not available. *Before measurement of 24 hour urinary catecholamine concentration.

†Average during ambulatory monitoring.