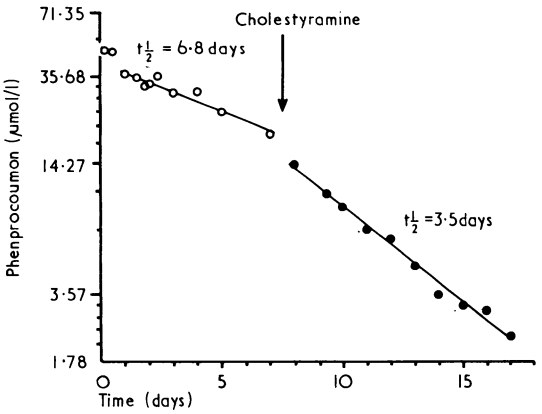
Treatment of phenprocoumon intoxication with cholestyramine

Cholestyramine enhances the elimination of phenprocoumon (Marcoumar) in man by interrupting its enterohepatic recycling.[1] Recently we saw a patient early after an intoxication with phenprocoumon and followed the plasma concentration of the drug before and after cholestyramine treatment. We found that its elimination from the body can be greatly enhanced by giving cholestyramine by mouth.

Case report

A 35-year-old man, treated with phenprocoumon for one year because of thromboangiitis obliterans, needed an average of 3 mg daily to maintain a therapeutic level (prothrombin complex activity of between 15 and 30% of normal). He stated that between midnight and 4 am the previous night he had swallowed 30 to 35 3-mg tablets of phenprocoumon and about 20 tablets of Trivastal (each containing 20 mg 2-(4-piperonyl-piperazin-1-yl)-pyrimidin), intending to commit suicide. We saw the man at noon the next day. We gave him Vitamin K_1 and a commercially available prothrombin complex concentrate (PPSB human, DRK-Blutspendedienst) immediately after prothrombin testing and maintained him on this therapy so long as the prothrombin complex activity was below the therapeutic range. The prothrombin time was determined in a clinical service laboratory, and the plasma concentration of phenprocoumon was measured over a period of 17 days by a fluorometric method (figure).[2] The first measurement of 46 μmol/l (13 μg/ml) 14 to 18 hours after taking the drug confirmed that a large dose of phenprocoumon had been taken. The concentration of 46 μmol/l was partly due to the regular anticoagulant therapy but mostly to the additional 30 to 35 tablets. After a short distribution phase the plasma concentration gradually decreased monoexponentially, the half life being 6·8 days. After seven days, when the plasma concentration had declined to about 20 μmol/l (5·5 μg/ml) (above the therapeutic level), cholestyramine 4 g was given three times daily for 10 days. During this period the phenprocoumon plasma concentration declined with a half life of 3·5 days.



Phenprocoumon plasma concentrations after ingestion of 90-105 mg before (t ½ = 6·8 days) and during treatment with cholestyramine (t ½ = 3·5 days). Time zero indicates time of admission.

Conversion: SI to traditional units: Phenprocoumon: 1 μmol/l ≈ 0·28 μg/ml.

Comment

The clinical findings and the plasma concentrations suggest that most of the dose of 30-35 tablets of phenprocoumon had been absorbed. The half-life of phenprocoumon in the postabsorptive phase corresponds to those previously reported.[1-3] This may indicate that the rate of elimination of phenprocoumon was not greatly affected by the Trivastal taken with it and that there is no capacity-limited elimination of phenprocoumon. The latter has been confirmed by others.[4] When cholestyramine was given in doses of 12 g/day by mouth the elimination rate of phenprocoumon was nearly doubled. This accords with results obtained in healthy volunteers after intravenous administration of phenprocoumon.

The use of cholestyramine in phenprocoumon overdosage and intoxication is recommended because it reduces the gastrointestinal absorption of phenprocoumon in man[5] and it enhances the elimination of phenprocoumon by interrupting its enterohepatic recycling. Since cholestyramine also enhances the elimination of warfarin in healthy people the same therapeutic principle may also apply with that drug.

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[4] Seiler, K, and Duckert, F, *Thrombosis et Diathesis Haemorrhagica*, 1969, **21**, 320.
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24-Hour ambulatory electrocardiographic monitoring on a regional basis

Twenty-four hour ambulatory electrocardiographic (ECG) monitoring is an established technique in the assessment of patients suspected of transient cardiac arrhythmias.[1-3] Suitable recording equipment is relatively cheap, but since a commercial reporting service for 24-hour ECG recordings is lacking in Britain, the technique has been available only to centres that can afford the expensive equipment needed to process the records.

In establishing a 24-hour ECG monitoring service for the Birmingham Region we tried to cover as wide a geographic area as possible by using district general hospitals as satellite recording stations, and by sending records to a central analysis unit.

Methods and results

Recordings were accepted from physicians practising in 10 centres throughout the Midlands and one centre in East Anglia. Recordings were made by ECG technicians at the hospital concerned and were posted to the analysis unit.

Equipment—Recordings were made on standard C120 magnetic tape cassettes[4] using a miniature tape recorder (Oxford Electronic Instrument Company). Tape recordings were analysed with a commercially available automatic replay and analysis system (The Oxford Electronic Instrument Company) based on that originally described by Cashman.[5] The analyser provided 10-second samples of any arrhythmias detected, written out by a

Arrhythmias detected in 124 patients with use of 24-hour ambulatory ECG monitoring service. Figures are numbers (%) of patients

Arrhythmia detected	Clinical presentation	
	Possible Adams-Stokes disease	Palpitations and other symptoms
None	25 (39)	28 (46·6)
Atrial ectopic beats >6/min	3 (4·7)	10 (16·6)
Ventricular ectopic beats >6/min	13 (20·3)	15 (25·0)
Paroxysmal atrial fibrillation	6 (9·4)	5 (8·3)
Paroxysmal atrial flutter	1 (1·6)	
Paroxysmal atrial tachycardia	3 (4·7)	4 (6·6)
Ventricular tachycardia	4 (6·25)	1 (1·6)
Sinus bradycardia	5 (7·8)	4 (6·6)
Sinus arrest	8 (12·5)	2 (3·3)
Atrioventricular block:		
First degree	2 (3·1)	
Second degree	2 (3·1)	1 (1·6)
Complete	5 (7·8)	