Effect of cigarette smoking on subsequent postoperative thromboembolic disease in gynaecological patients

The risk of deep vein thrombosis (DVT) in women taking oral contraceptives is increased if they are also cigarette smokers.¹ On the other hand, cigarette smoking has been said to "protect" against the subsequent development of DVT after myocardial infarction^{2,3} and also after emergency surgery.⁴ Our own study into the relation between cigarette smoking and postoperative DVT was part of a multi-variable study of both clinical and coagulation factors in the prediction of a tendency to postoperative DVT.⁵

Patients, methods, and results

A total of 231 patients undergoing major gynaecological surgery were investigated. Their smoking habits over the month before surgery were established, and their weights and heights were also recorded. All patients underwent preoperative isotopic scanning of the legs using the ¹²⁵I-fibrinogen technique. Routine postoperative scanning was performed on the first, third, and sixth day, unless a significantly high count was obtained, when daily scanning was started. None of the patients in this series received specific prophylaxis for DVT.

There were no patients with preoperative evidence of DVT. Postoperatively 37 (16%) of the 231 patients developed isotopic evidence of DVT. Of the 99 smokers, eight (8.1%) developed DVT, while 29 (22%) of the 132 non-smokers developed DVT (see table). The difference between the two proportions is significant at the 5% level on a χ^2 test. The percentage overweight for height was calculated (Geigy tables) and showed that the mean percentage overweight for height in those with DVT was 13.0 compared with 4.8 in those without ($P < 0.05$). When, however, the smokers and the non-smokers were considered in relation to their percentage overweight for height, we found that the eight patients who smoked and developed postoperative DVT had a mean percentage overweight for height of 18.7%. The 91 smokers without DVT were only 3.7% overweight for height. Of the non-smoking patients, 29 were in the DVT-positive group and were 11.4% overweight for height, compared with 103 in the DVT-negative group, who were only 5.8% overweight.

Comment

We found that cigarette smokers had a decreased incidence of postoperative DVT. Cigarette smoking increases the chances of developing myocardial infarction, but cigarette smokers who do suffer myocardial infarction seem to be less likely to develop complicating peripheral vein thrombosis.³ Our results also show an apparent protective value of cigarette smoking, since only 21% of the DVT-positive group were cigarette smokers compared with 47% of the DVT-negative group. The series differs from that of Pollock,⁴ in that all our patients had surgery performed as an elective procedure.

Deep vein thrombosis must be considered a disease of multifactorial origin. We have reported significant differences in certain clinical features and the results of preoperative coagulation tests between patients who postoperatively did or did not develop DVT.⁵ Our results show that the DVT-positive patients were significantly heavier than the DVT-negative ones. Smoking seemed to "protect" the patient against developing postoperative DVT. The results also show that the cigarette smokers who developed postoperative DVT were grossly overweight. The non-smoking DVT-positive patients were also overweight, but not to the same extent as the smoking group. It is tempting to suggest, therefore, that the overweight cigarette smoker runs a higher risk of developing postoperative DVT compared with the smoker who is close to optimum weight.

The explanation for this "protection" of our smoking patients against postoperative DVT provided they are lean remains obscure. No data exist to suggest that this is a direct function of cigarette

smoking; it may be that the low incidence of postoperative DVT in non-obese cigarette smokers reflects resistance to venous thrombosis as a constitutional feature, which correlates with but is not due to a predilection to smoke cigarettes.

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Joint hypermobility mimicking pauci-articular juvenile polyarthritis

Patients with generalised joint hypermobility may develop premature osteoarthritis and chondrocalcinosis.¹ Nevertheless, symptoms from hypermobile joints occur as early as childhood,² when the synovitis associated with hypermobility may be confused with juvenile polyarthritis.³ We describe a patient in whom symptoms initially attributed to chronic polyarthritis are more likely to be related to hypermobile joints.

Case report

A 13-year-old girl experienced pain and swelling, acute in onset, in the right knee after a race at school. She was talented at sports and dancing. A few weeks later the proximal interphalangeal joint of her right middle finger became swollen and a month later she had swelling at the interphalangeal joint of the right thumb. She was referred to hospital within three months, when the presence of swelling was confirmed in these joints though of these only the right knee was hot, with a small effusion and some synovial thickening. The effusion was not aspirated. Haemoglobin concentration was 12.4 g/dl, WBC 6000 $\times 10^9$ /l, and ESR 9 mm/hour. X-ray films of the hands, cervical spine, and knees were normal and the latex fixation test result was negative. There was no history of sore throat and ASO titre was 1/50. There was no evidence of carditis or systemic upset.

She was treated with soluble aspirin and rest and over three months all symptoms and signs disappeared. They have not recurred over the two years of follow-up in spite of return to normal activities. Her ESR has been consistently normal, the ANF test result is negative, and findings on ophthalmological examination have been normal. The results of tissue typing were HLA A2,3; B7, 15.

The patient had always considered herself "double-jointed." She had a Carter and Wilkinson score (modified by Beighton⁴) of 9/9 denoting generalised joint laxity. All her fingers hyperextended and both knees hyperextended by 15 degrees. In addition, she could place the soles of her feet together, extend both elbows backwards in the horizontal plane to 110°, and had lax feet and hands. Three siblings, none of them loose-jointed, had been free of rheumatic complaints. Nevertheless, the mother who had experienced very similar symptoms to her daughter at the age of 14, had been loose-jointed and still retained this feature in her hands and feet. She had also had severe varicose veins and crepitus in both knee joints at the age of 40. A maternal cousin and her daughter also considered themselves "double-jointed."

DVT in smokers and non-smokers

	DVT-positive						DVT-negative					
	Smoker			Non-smoker			Smoker			Non-smoker		
	Mean	SE	No	Mean	SE	No	Mean	SE	No	Mean	SE	No
% Overweight	18.7	8.5	8	11.4	3.2	29	3.7	1.5	91	5.8	1.3	103

Comment

We consider that a hypermobility syndrome is a more plausible explanation for this patient's symptoms than a pauci-articular juvenile polyarthritis. We suggest that joint laxity deserves more recognition as a cause of chronic synovial thickening. The distinction from juvenile polyarthritis is important since hypermobile patients may be spared the uveitis of this condition and may be at risk of premature osteoarthritis.

The nature of the effusion that may occur in hypermobile joints has not been adequately explained. Since joint laxity has now been linked with chondrocalcinosis,¹ it remains a possibility that it might be the first sign of crystal deposition disease in joints that will subsequently develop premature osteoarthritis.

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High-density lipoprotein cholesterol and antihypertensive drugs: the Oslo study

Thiazides and beta-blockers induce changes in serum lipid concentrations.^{1 2} Thiazides increase triglyceride and urate concentrations, and propranolol seems to accentuate these effects.³ Because of the increased risk of coronary heart disease associated with reduced serum concentrations of high-density lipoprotein cholesterol,⁴ we studied the effects of various antihypertensive regimens on serum HDL cholesterol concentrations.

Patients, methods, and results

The patients were selected from among men aged 40-49 with mild, symptom-free hypertension who were taking part in a controlled drug trial. The regimens and laboratory methods for determining total cholesterol, triglycerides, and urate have been described.^{1 3}

From September to December 1977 HDL cholesterol was analysed in fresh sera at routine follow-up. The same analysis was performed on non-fasting pretreatment sera (from the same men) which had been stored at -20°C since 1973. HDL cholesterol was determined as follows: low density lipoproteins and very low density lipoproteins were precipitated with a heparin-manganese reagent⁵ to final concentrations of 200 IU/ml heparin and 50 mmol/l Mn⁺⁺. After centrifugation at 4°C cholesterol was determined

enzymatically in the supernatant (CHOD-PAP Boehringer Mannheim kits). Cholesterol determination was standardised and controlled with 1.29 mmol/l (50 mg/100 ml) cholesterol and 2.20 mmol/l (85 mg/100 ml) cholesterol standards (Preciset, Boehringer Mannheim and Seronorm, Nyco), and control sera (inter-series variation coefficient <2%) were included in all series. In frozen sera from the untreated controls HDL cholesterol concentrations were about 38% lower than in fresh sera, but there was a fair correlation between the individual values in frozen and fresh sera ($r=0.60$; $P<0.001$). In this study we used the HDL cholesterol values from frozen sera only for selecting groups. The patients on different drug regimens were selected so that they had the same means and distribution of pretreatment HDL cholesterol concentrations. Pretreatment triglyceride concentrations were also comparable in patients treated with hydrochlorothiazide and methylodopa, hydrochlorothiazide and propranolol, and hydrochlorothiazide alone and in the untreated controls. The lower pretreatment triglyceride value of the group given hydrochlorothiazide alone was not significant ($P>0.05$); differences between means were tested by a modified t test accounting for unequal variances in groups.

During treatment mean HDL cholesterol concentrations were significantly lower in patients treated with thiazide-propranolol than in those treated with thiazide-methylodopa ($P<0.01$) or thiazide alone ($P<0.01$) or the untreated controls ($P<0.01$). Total serum cholesterol concentrations did not change significantly on the various regimens. The hydrochlorothiazide-propranolol combination also induced a significant increase in triglyceride concentrations ($P<0.01$), while values were increased only slightly on hydrochlorothiazide and methylodopa and fell slightly in the controls and patients treated with a thiazide alone (see table). After hydrochlorothiazide-propranolol treatment urate concentrations were significantly higher than pretreatment values or values after either of the other two treatment regimens ($P<0.05$). Urate concentrations fell over the four years in the controls ($P<0.01$).

Comment

Our results have shown that treatment with a thiazide and propranolol in combination reduces serum HDL cholesterol concentrations and increases triglyceride and urate concentrations. The results are consistent with the reported inverse correlation between HDL cholesterol and triglycerides.⁴ The effect of this drug combination on serum lipid concentrations may counteract the beneficial effect of blood pressure lowering. As the patient groups were small and not randomised, however, the results need to be confirmed in future studies.

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Mean ($\pm$ SE of mean) values before and after four years of treatment in patients on different drug regimens and in controls

	HDL cholesterol (mmol/l)		Triglycerides (mmol/l)		Urate (μ mol/l)		Total cholesterol (mmol/l)		Relative body weight (weight (kg)/height ² (m))		Diastolic blood pressure (mm Hg)	
	Before*	After	Before	After	Before	After	Before	After	Before	After	Before	After
Hydrochlorothiazide and propranolol (n=33)	0.85 $\pm$ 0.05	1.09 $\pm$ 0.05	1.87 $\pm$ 0.14	2.68 $\pm$ 0.26	324.2 $\pm$ 9.9	395.0 $\pm$ 13.9	6.76 $\pm$ 0.18	7.07 $\pm$ 0.18	24.6 $\pm$ 0.55	25.3 $\pm$ 0.55	97.0 $\pm$ 1.34	87.5 $\pm$ 0.72
Hydrochlorothiazide and methylodopa (n=33)	0.87 $\pm$ 0.06	1.28 $\pm$ 0.05	1.72 $\pm$ 0.12	1.92 $\pm$ 0.21	324.2 $\pm$ 10.4	349.7 $\pm$ 15.0	7.04 $\pm$ 0.22	7.15 $\pm$ 0.24	25.4 $\pm$ 0.39	25.8 $\pm$ 0.39	98.0 $\pm$ 1.12	87.7 $\pm$ 0.81
Hydrochlorothiazide alone (n=26)	0.85 $\pm$ 0.07	1.35 $\pm$ 0.07	1.61 $\pm$ 0.10	1.35 $\pm$ 0.06	306.9 $\pm$ 11.5	316.4 $\pm$ 16.1	6.97 $\pm$ 0.20	7.00 $\pm$ 0.18	24.4 $\pm$ 0.41	24.0 $\pm$ 0.39	92.4 $\pm$ 1.38	82.7 $\pm$ 0.97
Controls (n=33)	0.85 $\pm$ 0.05	1.37 $\pm$ 0.06	1.91 $\pm$ 0.14	1.56 $\pm$ 0.11	334.9 $\pm$ 9.8	277.8 $\pm$ 8.5	7.12 $\pm$ 0.21	7.17 $\pm$ 0.24	24.8 $\pm$ 0.45	25.0 $\pm$ 0.45	95.8 $\pm$ 1.14	97.2 $\pm$ 1.55

*Samples kept frozen for four years (38% reduction—see text).

Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 39 mg/100 ml. Triglycerides as triolein: 1 mmol/l $\approx$ 89 mg/100 ml. Urate: 1 μ mol/l $\approx$ 0.017 mg/100 ml.