SHORT REPORTS

Do sex hormones affect colorectal cancer?

Reproductive factors have been implicated in the aetiology of cancer of the colon. The influence of sex hormones on bowel cancer, particularly cancer of the right side of the colon,¹ is suggested by a higher than expected incidence of cancer of the colon in nuns; a strong correlation between cancer of the breast and of the colon in international mortality statistics; a direct association between nulliparity and risk of cancer of the colon; increased survival from colorectal cancer in parous compared with nulliparous women; and higher age specific incidences of cancers of all sites in the colon in premenopausal women compared with men, which persist for right sided sites in older women. The effect of oral contraceptives on the risk of cancer of the colon has been inconsistent.¹ We reasoned that the influence of exogenous oestrogen might be more clearly assessed in men.

Patients, methods, and results

We studied the distribution of sites of primary cancers of the colon in men who had previously had primary cancers of the prostate, which often require treatment with exogenous oestrogens. The Hawaiian tumour registry yielded 3084 men with prostatic cancer during 1960-83, of whom 1172 had received hormonal treatment and 26 had developed a primary adenocarcinoma of the large bowel six or more months later. These men were grouped according to whether they had received at least six months' treatment with stilboestrol. Sites within the large bowel were grouped into four categories: ascending (ICDO codes 153·4-153·6), transverse (153·0, 153·1, 153·7), descending (153·2, 153·3), and rectal (154·0, 154·1).

An exact test for trends in ordered contingency tables² showed that the proportion of patients with cancer of the colon who had received stilboestrol showed a significant ($p=0.01$) increasing trend from the left to the right side of the colon (table). A further analysis indicated that the proportion

Distribution of cancer of colon in men with initial primary cancer of prostate according to treatment

Treatment	Site				p*
	Ascending	Transverse	Descending	Rectum	
Stilboestrol	5	2	2	1	0.01
No stilboestrol	3	1	7	7	
Stilboestrol and orchidectomy	3	0	0	0	0.02
Neither stilboestrol nor orchidectomy	2	1	5	5	

*Exact test for trend, one sided.

of patients who had both received stilboestrol and undergone orchidectomy showed a significantly ($p=0.02$) increasing trend from the left to the right side when compared with those who had not received either treatment. The mean ages of the patients were similar in all treatment groups, and there was no overall increase in cancer of the colon in the men who had had hormonal treatment. The mean interval between the diagnoses of the two primary cancers was shorter for patients treated with stilboestrol (39.6 months) than for untreated patients (49.6 months) but not significantly different ($p=0.45$).

Comment

Possible mechanisms for an oestrogenic effect on colorectal cancer include a lowering of total plasma cholesterol concentration and an increase in production of bile acid,¹ and a direct influence of oestrogens on the late stages of cancer of the colon, suggested by the presence of oestrogen receptors in cancers but not adenomatous polyps of the colon.³

An alternative explanation for this distribution of colorectal cancer is androgenic stimulation of cancer of the left side of the colon relative to that of the right side. Although one study reported that androgens and not oestrogens increased the incidence of cancer of the colon in rats,⁴ this has no basis in man. Our observations are unlikely to have been the result of non-random assignment of patients to treatment with oestrogen as preferential selection of patients with advanced prostatic cancer for stilboestrol treatment and orchidectomy is unrelated to known variables of cancer of the colon. Moreover, a recent report

associated relative physical inactivity, which is more likely to be found in our patients with advanced disease, with cancer of the left side of the colon.⁵ Our findings are consistent with an effect of oestrogens on cancer of the right side of the colon but are based on a small number of cases. Certainly, ineffective chemotherapy for cancer of the colon and the availability of effective oestrogen inhibitors indicate that further exploration of this possible oestrogenic influence in a larger study is warranted.

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Epidemiology Programme, Cancer Research Centre, University of Hawaii, Honolulu, Hawaii 96813

MICHAEL DAVIDSON, MD, MPH, epidemiologist and adjunct associate professor of public health and medicine

CARL N YOSHIZAWA, PHD, biostatistician and adjunct associate professor of public health

LAURENCE N KOLONEL, MD, PHD, director and professor of public health

Correspondence to: Dr M Davidson.

Risk profile of soldiers aged under 40 with coronary heart disease

Junior ranks in the British army have a higher mortality from coronary heart disease than comparable British civilians.¹ This report examines the conventional coronary risk profile of young soldiers with coronary heart disease.

Subjects, methods, and results

Forty five men in the British army who survived a coronary event took part in a cardiac rehabilitation programme between 1979 and 1983. The mean age at presentation was 34.5 (SD 3) years and the mean interval between the initial event and rehabilitation 2.3 (2.4) years. Very few men with coronary heart disease, particularly those aged under 40, did not take part or were medically discharged before rehabilitation. All patients had a minimum of 70% stenosis of at least one coronary artery as defined by coronary angiography. Height and weight were measured on entry to the programme, and relative body weight was calculated using Quetelet's formula (weight (kg)/height (cm)² × 100). Obesity was defined as a relative body weight of 0.28 or more; this represents a 20-25% increase over ideal body weight.

A positive family history was recorded when myocardial infarction or angina had occurred under the age of 60 in a member of the patient's family, his parents' family, or his grandparents' family. Smoking habit was taken as that before the presenting event and blood pressure as that recorded at the start of rehabilitation (one patient was being treated for hypertension). Plasma lipid and uric acid concentrations and glucose tolerance were measured on a fasting specimen at the start of rehabilitation (32 patients also had a repeat estimation of glucose tolerance two hours after 100 g glucose load).

The mean height and weight were 171 (SD 6) cm and 78.7 (10) kg, giving a mean relative body weight of 0.267; 13 patients were obese. Forty two patients smoked cigarettes, on average 28 daily; 34 smoked 20 or more daily, 18 smoked 30 or more, and 11 smoked 40 or more. The mean serum total cholesterol concentration was 6.83 mmol/l (264 mg/100 ml), and 10 patients had a concentration in excess of 8 mmol/l (309 mg/100 ml). The mean serum triglyceride concentration was 2.18 mmol/l (193 mg/100 ml), and the mean high density lipoprotein cholesterol concentration was 1.32 mmol/l (51 mg/100 ml). The mean fasting glucose concentration was 4.28 mmol/l (77 mg/100 ml), and only one patient had abnormal glucose tolerance. The mean uric acid concentration was 426 μmol/l (72.8 mg/100 ml) and nine patients had concentrations over 500 μmol/l (84 mg/100 ml). None

had a blood pressure persistently greater than 140/90 mm Hg except the one patient being treated for hypertension. A family history of coronary heart disease was obtained in 22 cases.

Comment

High consumption of cigarettes, high serum cholesterol concentration, and high relative body weight appear to be the main risk factors for coronary heart disease in young soldiers. The low prevalence of hypertension and glucose intolerance may reflect the fact that these two risk factors, and possibly gross obesity, preclude recruitment. Only insulin dependent diabetes results in premature discharge from the service; other risk factors are managed in the normal way. A positive family history is no more common in soldiers than civilians. The table shows the high cigarette consumption of young soldiers with coronary heart disease compared with healthy soldiers and healthy civilians.

Smoking habit of young soldiers with coronary heart disease, healthy soldiers, and healthy civilians

	% Of smokers	Average No of cigarettes smoked/day	Percent consuming:		
			≥20/day	≥30/day	≥40/day
Soldiers with coronary heart disease	95	28	85	45	28
Healthy soldiers ^{3*}	60	21	52	12	
Healthy civilians ¹	45	18	21		

*Data available from department of preventive medicine, Royal Army Medical College, London SW1.

Few studies on the risk profile of young men with coronary heart disease have been carried out, but heavy smoking and high blood cholesterol concentrations are more prevalent in young than middle aged patients with coronary heart disease.² High cholesterol concentrations may be due to bias induced by familial hypercholesterolaemia. The disproportionately high mortality from coronary heart disease in junior soldiers seems to be due to the high prevalence of heavy cigarette smoking in the British army. British soldiers probably take advantage of the very low costs of cigarettes in some parts of the world. In the British army the expected protective effect of physical fitness is overwhelmed by the deleterious effect of high consumption of cigarettes.

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Cardiac Department, Queen Elizabeth Military Hospital, London SE18

PETER LYNCH, MD, MRCP, consultant physician
NEIL INESON, MRCP, senior registrar
K P JONES, MB, registrar
A W SCOTT, MB, registrar
I C CRAWFORD, CBE, FRCP, consultant physician

Correspondence to: Lt Col P Lynch.

Tolerance of elemental diet administered without starter regimen

An important aim of nutritional support is to achieve an overall positive nitrogen balance. In practice, we have found that this is not achieved in up to 40% of patients fed enterally.¹ One reason for this is the use of starter regimens—that is, feeding a dilute diet for several days to minimise possible gastrointestinal side effects.^{2 3} Over a short period of enteral feeding this can result in inadequate administration of nitrogen. In a recent controlled trial we showed that gastrointestinal side effects were not increased when a full strength polymeric diet

was infused nasogastrically from the outset of feeding to patients with normal gastrointestinal function. Because the starter regimen was omitted nitrogen intake increased and nitrogen balance improved.⁴

Elemental diets have a higher osmolality than polymeric diets as they contain predigested nutrients. Their use has been suggested in patients with impaired gastrointestinal function.⁵ We undertook this study to investigate whether starter regimens could also be abandoned when an elemental diet is used.

Patients, methods, and results

Fourteen patients with impaired gastrointestinal function entered the study (one on two occasions). All were anorectic and judged to require nasogastric feeding as the sole source of nutrition. Twelve patients were admitted with acute exacerbations of inflammatory bowel disease (Crohn's disease, seven; ulcerative colitis, three; indeterminate inflammatory colitis, two), and two had the short bowel syndrome. All received standard medical treatment in addition to enteral nutrition.

Our aim was to administer a daily minimum of 2.1 litres of a chemically defined elemental diet (Vivonex TEN, Norwich-Eaton Pharmaceuticals). The diet (osmolality 630 mmol(mOsm)/kg) was infused continuously at 87 ml/h through a fine bore nasogastric feeding tube. The full prescribed volume or more of full strength diet was given in nine cases. In the remaining six cases either an unexplained disparity between prescription orders and the volume of diet administered or a technical problem with the feeding tube was responsible for reduced intake (table).

Details of intake of nutrients by 14 patients

Case No	Days on which patient fed	Volume fed* (l/24 h)	Total energy (MJ/24 h)	Infused load (mmol/min)	Nitrogen (g/24 h)
1	7	2.1	8.8	0.91	12.0
2	1-6	2.1	8.8	0.91	12.0
	7-15	2.5	12.6	1.31	17.1
3	1-7	2.1	8.8	0.91	12.0
	8-10	2.1	11.3	1.18	15.4
4	21	1.6	6.7	0.70	9.0
5	7	2.1	8.8	0.91	12.0
6 (admission 1)	21	1.4	5.9	0.61	8.0
6 (admission 2)	17	2.1	8.8	0.91	12.0
7	10	2.1	8.8	0.91	12.0
8	12	1.7	7.1	0.74	9.7
9	8	1.7	7.1	0.74	9.7
10	4	2.1	8.8	0.91	12.0
11	15	2.1	8.8	0.91	12.0
12	7	1.3	5.5	0.56	7.4
13	7	2.0	6.3	0.65	8.5
14	7	2.1	8.8	0.91	12.0
Mean (SEM)	11.2 (1.4)	1.9 (0.07)	8.4 (0.4)	0.86 (0.04)	11.3 (0.6)

*Mean daily intake during treatment.

Conversion: SI to traditional units—Total energy: 1 MJ ≈ 238 kcal. Infused load: 1 mmol = 1 mOsm.

Upper gastrointestinal symptoms, graded 0 (absent) to 3+ (severe), occurred in only five of the 14 patients at some stage during enteral feeding. Three patients developed mild (1+), transient nausea, and two developed moderate (2+) nausea that persisted for two to four days. Abdominal bloating did not occur. One patient experienced mild (1+) colicky pain that lasted three days, and one experienced moderate (2+) colicky pain that lasted six days. These symptoms did not slow down the rate of infusion.

Stool wet weights decreased significantly during the study from 545 (SEM 330) g/24 h to 131 (70) g/24 h ($p < 0.01$, $n = 7$), as did the ileostomy effluent volume in one patient with the short bowel syndrome.

Comment

This study shows that an undiluted, hypertonic elemental diet, administered by continuous nasogastric infusion over 24 hours, was well tolerated by patients with impaired gastrointestinal function due to inflammatory bowel disease and the short bowel syndrome. The diet contained predigested, hypoallergenic nutrients.⁵ The incidence of gastrointestinal symptoms was probably normal for patients with acute inflammatory bowel disease. We did not have to reduce the rate of administration of the diet because of the patients' symptoms. Moreover, for clinical reasons the volume was successfully increased in two patients after several days of feeding.

These findings are similar to those of our previous controlled study, which showed that the incidence of gastrointestinal side effects was not increased when undiluted, hypertonic polymeric diet was given to patients with normal gastrointestinal function.⁴ When starter regimens, in which a full strength diet is not started until day three or four, are omitted patients benefit by receiving an estimated 60% or more additional nitrogen during the first three days of enteral nutrition.