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Hemoccult screening for colorectal carcinoma in general practice

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Summary

A collaborative general practice study to test for colorectal carcinoma is described. All patients who were asymptomatic for gastrointestinal complaints above the age of 40 years and who presented to practices in five coastal towns in the Cape Province, SA, were offered entry. Several pre-malignant and early malignant lesions were found. General practice is regarded as the ideal arena for this screening test.

For a 'screening test' to be introduced into general practice certain accepted criteria should be fulfilled.[1,2,3]. These criteria are:

1. The disease in question should be a serious health problem
2. There should be a pre-symptomatic or latent phase of the disease whose natural history is known, during which treatment can change the course of the disease more successfully than in the symptomatic phase
3. The screening procedure and the ensuing treatment should be acceptable to both the public and the doctor
4. The screening procedure should have acceptable sensitivity and specificity (ie not produce too many false positives or negatives)
5. The screening procedure and ensuing treatment should be cost-effective
6. Adequate facilities for diagnosis and treatment should be available

Before general practitioners (GPs) effect the necessary behavioural change both in themselves and their patients there must be convincing evidence in support of the test. Occult blood screening has been advocated by several authors[4] but as yet no major study has been reported on where general practitioners 'case find' as part of their normal day to day routine. Sangster and Gerace reported on 355 patients who were screened in a Canadian family practice[5]. All patients who were asymptomatic for gastrointestinal complaints above the age of 40 years, and who presented to the practice were offered entry into the study[5]. The overall compliance rate was 80%[5] and several premalignant lesions as well as other colonic lesions were found[4]. It thus appeared appropriate to initiate a collaborative general practice study to test for colorectal carcinoma.

HEALTH PROBLEM

Colorectal carcinoma is the second most common malignancy in both sexes in North America[6]. The disease is more common in Western countries with an incidence of approximately 3-4%. Its incidence begins to rise significantly above the age of 40 years and increases twofold in each succeeding decade reaching a peak at the age of 75 years[7]. It thus constitutes a serious health problem. Winawer found an incidence of 22 per 10 000 in a mass screening study which was five times higher than predicted[4].

Colorectal carcinoma is the second most common malignancy in both sexes in North America. Incidence rises significantly above the age of 40 years.

NATURAL HISTORY AND TREATMENT

There appears to be an asymptomatic phase of the disease during which, if the disease is detected and treated, a significantly better prognosis results[8].

If the cancer is limited to the wall, the corrected 5-year survival rate is about 90% as opposed to a 30% 5-year survival rate in those who have lymphatic spread[8]. Moreover, colorectal adenocarcinomas pass through a benign adenomatous stage and removal of these may reduce the risk of development of invasive carcinomas[9]. Patients at high risk include those with ulcerative colitis, polyposis coli and colorectal carcinoma in families.

In spite of therapeutic developments the overall survival rate has improved only slightly over the past thirty years[10,11]. Thus the only logical way to treat this disease would be by early detection in the pre-malignant phase or where the tumour is still localised.

General practice would be the appropriate arena for introducing a screening test as patients are seen on a continuing basis and present to their practitioners for all complaints. At least 70% of patients consult their GPs in one year[12] and at least one member of a family will consult within 1-year giving the GP access to all his patients.

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PATIENTS AND METHODS

The screening programme was performed in five coastal towns in the Cape Province, Republic of South Africa (Cape Town, Mossel Bay, George, Knysna and Plettenberg Bay). Ninety five GPs, under the aegis of the research group of the SA Academy of Family Practice/Primary Care took part in the study. Doctors were asked to invite only asymptomatic patients between 40 and 75 years of age who were not on analgesics or anti-inflammatory agents. Each participant was informed that there were no dietary restrictions. They were then asked to collect a stool sample, open the Hemoccult test card, smear faeces on the filter paper with a cardboard spatula and then reseal the test card. After 6 tests (3 cards) on 3 consecutive days had been completed the cards were returned in a prepaid and pre-addressed envelope. The cards were tested in the Groote Schuur Hospital Gastro-Intestinal Clinic by one of the authors or a trained research assistant who added a stabilised hydrogen peroxide agent. A blue discoloration occuring at 30 seconds was regarded as positive.

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All patients with a positive result were contacted immediately and were asked not to eat red meat or to take vitamin C tablets prior to further collections of faecal samples. Each patient was then given 6 further Hemoccult test cards and was asked to repeat the sampling for 6 consecutive days.

Those patients with a positive test had a full history taken, and a clinical examination, including digital rectal examination, proctoscopy and rigid sigmoidoscopy. All patients subsequently had a double contrast barium enema and a colonoscopy. Nearly all investigations were conducted and all treatment carried out at the Groote Schuur Hospital.

Those patients who were positive only on the first testing and were negative on the second testing were to be followed up with a further hemoccult test to be repeated within a year.

Hemoccult slides were supplied by Noristan Laboratories, Pretoria. Each kit contained slides for three stool specimens, three test cards with two areas for testing, three spatulas and an envelope with clear instructions.

RESULTS

Of the 5 012 patients of white and mixed races on a normal diet who were invited to participate, 3 422 completed and returned their Hemoccult tests (an overall compliance rate of 67%). Ninety-nine patients had a positive result (3%).

All these patients who had a positive result underwent the second 6-day test on a restricted diet (compliance rate 100%). Thirty-two (1%) of these patients had a positive result.

Examination of these 32 patients revealed neoplastic bowel disease in 27 (84%). Twelve patients had adenocarcinomas of the large bowel (9 Dukes A, 2 Dukes B, 1 Dukes C). This represents the high incidence rate of 35 per 10 000 — of which 92% (11 of 12) could be said to be early disease. In addition six of these 12 patients were found to have a further 10 adenomas. The remaining 15 patients had 27 adenomas (one patient had 10 adenomas).

Four of the twelve patients with adenocarcinoma were found to have symptoms on close questioning. Four of the patients with adenomas were also symptomatic.

All patients who were found to be negative after the second Hemoccult test are being followed up. Follow-up at present varies between 3 and 11 months. All patients are asymtomatic. Thirty of the sixty-seven patients have undergone a further Hemoccult test on a restricted diet six months after the initial test. All have been negative.

INVESTIGATIONS

None of the carcinomas were identified by digital examination. Rigid sigmoidoscopy demonstrated two of the 12 adenocarcinomas (17%) and three of the 37 adenomas (8%). Double contrast barium enema identified 9 of the 12 carcinomas (75%) and only 16 of the 37 adenomas (43%).

Of the 32 patients investigated, 28 (88%) were colonoscoped through to the caecum. The remaining 4 patients had already been diagnosed as carcinoma at barium enema and preferred not to undergo an additional investigation prior to surgery. Colonoscopy identified the three carcinomas that were missed at double contrast barium enema. These were all polypoid Dukes A lesions and were situated in the caecum, transverse colon and sigmoid colon respectively. Twenty-one of the 37 adenomas (57%) were also identified at colonoscopy only.

NEOPLASMS

Nine of the twelve carcinomas were Dukes A lesions (75%) of which 4 showed no invasion beyond the submucosa. Two patients had a Dukes B lesion and 1 patient a Dukes C lesion. Eleven of the patients were treated by bowel re-section and one by colonoscopic polypectomy. Eight of the carcinomas were situated in the sigmoid colon, three were in the caecum and one in the transverse colon.

Thirty-seven adenomas (5 mm or greater in size) were found in 21 patients. Thirty-three of the 37 adenomas were situated distal to the splenic flexture (89%). Thirty-five of the adenomas were removed by colonoscopic polypectomy and two by colonoscopic re-section.

Ten of the adenomas were greater than 2 cms in size. Severe atypia was present in three adenomas (2 tubulovillous, 1 tubular adenoma).

DISCUSSION

It appears that the screening programme was acceptable to both doctor and patient. The overall compliance rate of 67% compares favourably to other large studies[13,14]. Nevertheless it was disappointing for a general practitioner study. The compliance rate for individual practitioners varied from 9-100% and the numbers of patients entered by individual practitioners ranged from 1 to 160 patients. It was interesting to note that of the 60 GPs who entered more than fifty cases, the compliance rate was approximately 74% as opposed to about 62% in those practitioners who entered 50 or less. It would appear that those who made the greatest effort to enter cases also had the highest compliance rate.

The importance of doing several tests is emphasized by the number of positive results found on testing. (Table I). Three of the adenocarcinomas only had one positive out of 6 on intitial testing.

As bleeding is intermittent every effort was made not to have any false negatives in the second phase of the study, hence double the number of specimens (12) were asked for. As indicated a follow-up of almost half the patients found to be negative in the second stage of the original study have been re-tested and still found to be negative.

With the two stage design very few false positive results occurred since 84% of the patients investigated had either malignant and/or pre-malignant conditions. This means 5 of 3 422 asymptomatic patients were subjected to unnecessary investigation.

TABLE I
NUMBER OF HEMOCCULT POSITIVE SLIDES ON NORMAL AND RESTRICTED DIETS. (Mean)

ADENOMAS	No. OF PATIENTS	1ST TEST (Normal Diet)	2ND TEST (Restricted Diet)
Less than 1 cm	6	2/6 (range 1-3/6)	3/12 (range 2-7/12)
1-2 cm	8	4/6 (range 3-6/6)	5/12 (range 3-8/12)
Greater than 2 cm	7	5/6 (range 4-6/6)	5/12 (range 3-9/12)
ADENOCARCINOMAS			
Dukes A	9	3/6 (range 1-6/6)	9/12 (range 1-12/12)
Dukes B	2	4/6 (range 3-5/6)	9/12
Dukes C	1	2/6	5/12

It must be accepted, however, that this is a new test and an effort will have to be made by GPs to introduce it into their preventive approach. A positive effort will have to be made to educate patients as well since, often, the test cannot be done immediately after the visit as the patient may well be on analgesic or anti-inflammatory agents.

The compliance rate for individual practitioners varied from 9-100%.

The two-stage design of the study was implemented in order to gain compliance. It was thought that patients would more readily perform the test if they did not have their diets restricted. Thus only 99 of the 3 422 had to repeat the test with dietary restrictions. Conversely, it could be argued that we induced unnecessary anxiety in 67 patients who had negative tests on retesting. GPs were told to explain the possible incidence of false positives in the first stage of the test.

Great emphasis in this study was placed on the use of colonoscopy[15]. It was shown that 3 of 12 adenocarcinomas and 21 of the 37 adenomas would have been missed, had it not been for colonoscopy. It is argued that double contrast barium enemas and colonoscopy compliment each other.

It is hoped that an appropriate number of specialists will become skilled enough in colonoscopy investigation should the occult test become a regular screening procedure.

An effort will have to be made by GPs to introduce this test into their preventive approach and to educate patients.

COST-EFFECTIVENESS

Cost-effectiveness is a difficult concept to measure. In this study to screen 3 422 patients the "unnecessary" financial costs, calculated at medical aid tariffs, was approximately R11 800. (Table II). This is made up of 3 395 subsequently 'negative' pts. at R3,03 (1st Stage) and 72 negative hemoccult tests at R6,06 (2nd Stage) giving a total cost of approximately R10 720. "Unnecessary" special investigations and specialist consultations for the 5 negatively investigated patients would have cost approximately R1 060. The retun for this was 12 diagnosed carcinomas of which 11 were diagnosed in early phases. The cost of an operation in late phases is at least double. So assuming about half of these (5) would have been diagnosed late (ie Dufkes C and D) the cost of their operations and immediate after-care in hospitals would have been at least R20 000 extra — not to mention their expensive follow-up treatment and subsequent hospitalisation. If only one of the 15 pre-malignant adenomas would have gone onto a later phase carcinoma, the immediate costs of operation and after-care would have been R8 000. So even on this initial hospital costing, the financial outlay seems well worth it.

TABLE II

ADDITIONAL FINANCIAL COSTS

"Immediate"

3 395 negative tests (1st Stage) at R3,03	10 286,85
72 negative tests (2nd Stage) at R6,06	436,32
5 patients "unnecessarily investigated"	1 068,00
	R11 791,17

This costing does not take into account loss of productivity and medical costs of those who would have inevitably diagnosed late. Dukes Stage C has a 5 year survival rate of 32% and Stage D, 1,2%. Furthermore, the state aid, pensions and insurance that would have to be paid out to the spouse are not included as well as the medical costs for the increased morbidity and even mortality in the bereaved. Finally, the pain and suffering to both patient and family is drastically reduced and this is, ultimately, why society pays such a heavy cost for medical care.

CONCLUSION

The high incidence of malignant and pre-malignant conditions (1%) obviously justifies the introduction of occult blood screening in patients over the age of 40 years. This is especially so in the light of the fact that 11 of the 12 carcinoma patients had relatively confined carcinomas. It is obvious, however, that GPs will have to make the effort and organisational arrangements to perform the test on an annual basis. Attempts to educate patients must be introduced both on a mass and individual level.

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The following general practitioners took part in the study:-

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GJ Budow
CG Coetzee
MM Cohen
HW Cox
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J Davey
B de Bruijn
J de Kock
J Dhansay
AS Dodds
G Dommisse
D Douglas-Henry
PR Dower
G Dreyer
MS Druker
S Dubb
GC van Hoorn
NW Wells
JC Weideman
HJ Zietsman
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