

Immunochemical Fecal Occult Blood Testing for Early Gastrointestinal Bleeding Detection in Patients Using Warfarin

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ABSTRACT

Background: Warfarin is an effective drug for treatment and prevention of thromboembolic disorders; however, acute gastrointestinal bleeding is a life-threatening complication of warfarin therapy. Immunochemical fecal occult blood testing is widely recommended as a screening test for occult gastrointestinal bleeding. Thus we used the immunochemical fecal occult blood testing to early detect gastrointestinal bleeding in patients using warfarin.

Objective: To determine the role of immunochemical fecal occult blood testing for detection of gastrointestinal bleeding in patients who are on warfarin treatment.

Patients and Methods: 22 patients who have indications to be on warfarin were enrolled in this study, FOBT was tested before and followed up during warfarin-fecal occult blood protocol. All patients that fecal occult blood test was positive underwent esophagogastroduodenoscopy (EGD). Colonoscopy was performed in patient with a negative EGD.

Results: 4 of 22 patients had positive fecal occult blood testing positive, 3 of 4 patients have positive EGD finding; one patients had gastric ulcer, two had haemorrhagic gastritis. One of 4 patients had colonoscopy, which findings revealed diverticulitis. Fecal occult blood testing was negative in 18 of 22 patients. No patients developed overt gastrointestinal bleeding and still had fecal occult blood testing negative at the end of study.

Conclusion: This is the first study of immunochemical fecal occult blood testing for detection of gastrointestinal bleeding under warfarin. The result showed that immunochemical fecal occult blood testing may have benefit for early detection of gastrointestinal bleeding under warfarin.

Key words : Immunochemical Fecal Occult Blood Testing, Gastrointestinal Bleeding, Warfarin

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INTRODUCTION

Warfarin is an effective drug in the treatment and prevention of thromboembolic disorders but major side effect is bleeding. The recent reports showed the incidence of hemorrhagic complication in the patients treated with anticoagulant drugs ranged from 12-40 % per year⁽¹⁾, severe bleeding 0.2-2.2 % per year⁽²⁾ and death 1% per year due to uncontrolled bleeding⁽³⁾. During the first year of anticoagulant patients, who take warfarin, have is greater risk of bleeding⁽¹⁾. Warfarin does not cause bleeding by itself but the patients usually have underlying diseases in the gastrointestinal tract and warfarin provokes bleeding in gastrointestinal tract⁽⁴⁾.

In present day, the physicians follow up the patients, who are on warfarin therapy by history, symptoms and signs to ruled out gastrointestinal bleeding but many patients do have gastrointestinal bleeding occurred during therapy. The fecal occult blood test has been widely recommended as a screening test for occult gastrointestinal bleeding and the sensitivity of immunochemical fecal occult blood is 89% and specificity 94%⁽⁵⁾, which is higher than guaiac, based fecal occult blood test. Thus this research aims to determine that fecal occult blood testing can early detect and prevent major bleeding from gastrointestinal tract in the patients using warfarin.

PATIENTS AND METHODS

Study Design

Both inpatients and outpatients who had indications for warfarin at the Department of Medicine, Vajira hospital between March 1st, 2006 and February 28th, 2007 were enrolled in this study. All patients were older than 15 years, written informed consents were obtained from participated volunteer. The patients were excluded, if they had history of gastrointestinal bleeding or contraindication for upper gastrointestinal endoscopy or colonoscopy.

Patient Data

22 enrolled patients underwent immunochemical fecal occult blood test (FOBT), upper gastrointestinal endoscopy and colonoscopy. The clinical data were recorded which included sex, age, alcohol consumption, aspirin and/or nonsteroidal anti-inflammatory agents used, history of dysphagia, heart burn, bowel

habit change, family history of cancer, indications for warfarin and laboratory data of complete blood count (CBC) especially hematocrit and platelet count, prothrombin time and INR, creatinine level, immunochemical fecal occult blood testing before starting warfarin and after being on warfarin for six months, upper gastrointestinal endoscopy findings and colonoscopy findings.

The definition of anemia was Hb in male < 13 g/dl or Hb in female < 12 g/dl. Thrombocytopenia was platelet count < 150,000 μ l. The definition for significant drop of hematocrit was >3%.

FOBT

We performed a 1-day immunochemical FOBT⁽⁶⁾. Participants were asked to prepare a fecal sample from stool specimen by using the collection kit provided by the manufacturer (EI KEN Chemical Co., Ltd.). The participants received collection kit and were tested before they were started warfarin, at the time hematocrit drop significantly and the end of study. The participants collected stool sample themselves, keeping the sample dry during collection (without touching the water in the toilet bowl). Participants were instructed to bring the collection tubes to the hospital or clinic on the day of follow up and stool samples were tested immediately.

Upper Gastrointestinal Endoscopy (EGD) and Colonoscopy

The participants who had positive FOBT would be sent for EGD. If EGD result was normal the participants would be scheduled for colonoscopy. Patients were excluded if endoscopic examinations were incomplete. When found the overt GI bleeding, the study was stopped.

Statistical Analysis

Patient characteristics were analyzed by descriptive statistics and reported as median, range and percent.

RESULTS

Patient characteristics were shown in Table 1, the median age of the 22 anticoagulant patients was 56 years (range 42-79 years), 7 were men and 15 were women. The indications for anticoagulant were valvular heart diseases (10), atrial fibrillation (8), valvu-

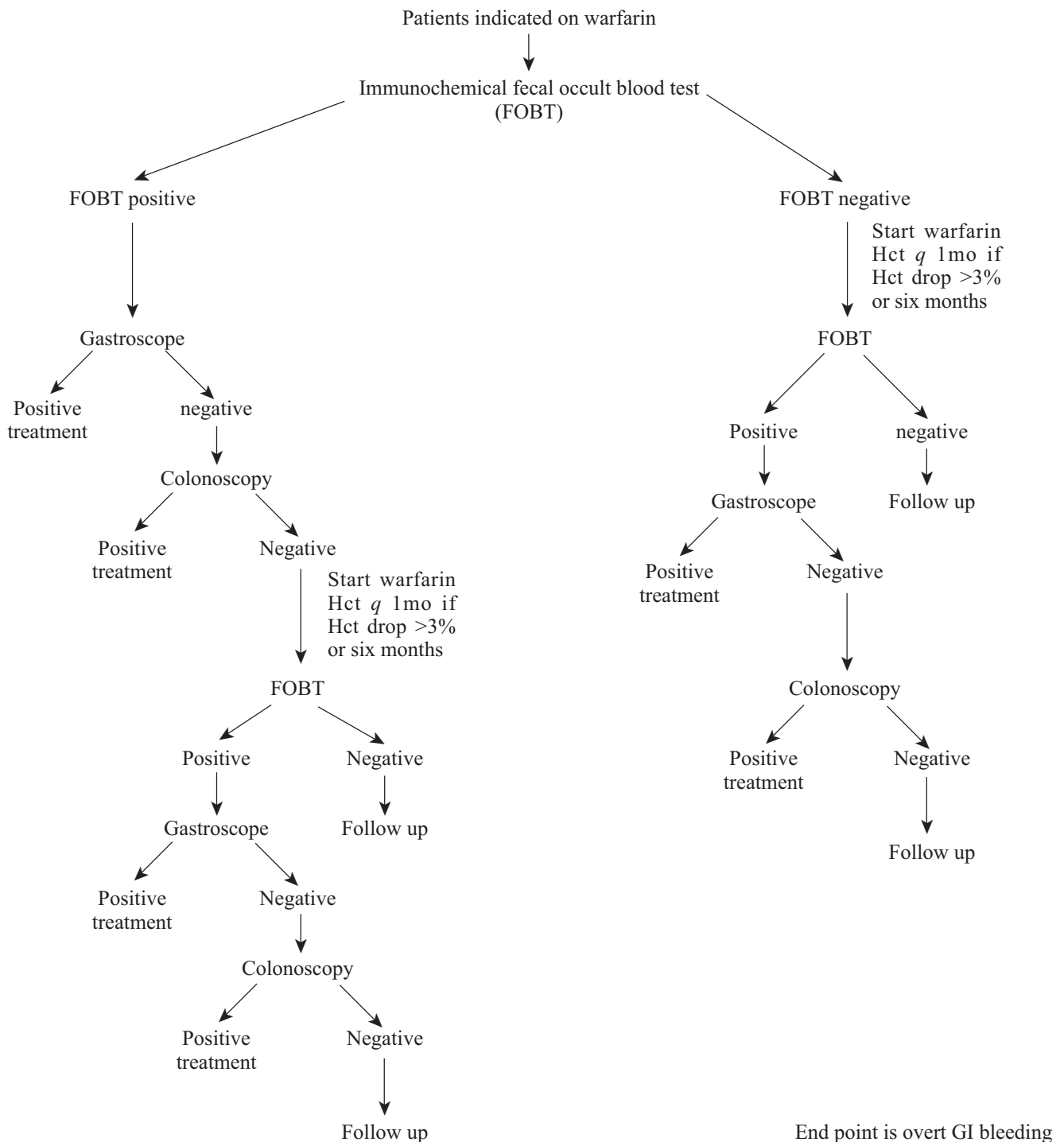


Figure 1 Protocol

lar heart diseases and atrial fibrillation (2), cerebrovascular disease (2). Another recorded clinical information were history of alcohol consumption (1), NSAIDs (3), dysphagia (1), heartburn (2), bowel habit change (0), family history of cancer (2), anemia (11), thrombocytopenia (1), and renal insufficient (4). Immunochemical fecal occult blood test was positive in 4

patients (18.18%) before under warfarin, whose age were between 72-76 years. 3 patients had history of anemia. 2 had history of NSAIDs used and one had family history of cancer. EGD were done in 4 patients that fecal occult blood was positive, findings were gastric ulcer (1), hemorrhagic gastritis (2) and negative finding (1). Colonoscopy was performed in patient

with negative EGD and finding revealed diverticulitis (1). These patients had been treated. No patients developed overt gastrointestinal bleeding and fecal occult blood testing is negative at the end of study.

In 18 patients (81.82%), the fecal occult blood test was negative before starting warfarin. They received warfarin and followed the fecal occult blood testing program, no patients had hematocrit drop greater than 3%. No patients developed overt gastrointestinal bleeding even the patients who had supratherapeutic level of warfarin. At the end of study all patients remained fecal occult blood testing negative as Table 1. No overt GI bleeding was found in this study.

DISCUSSION

The results of this study show that the patients who have indication for anticoagulant therapy and follow up screening with immunochemical fecal occult blood testing is benefit because all the patients that fecal

occult blood testing is positive before anticoagulant therapy with risk factor old age , anemia , NSAIDs used, history family cancer can find gastrointestinal lesion such as gastric ulcer (1), hemorrhagic gastritis (2), diverticulitis (1). Thus we can treat the diseases and these patients had not developed overt gastrointestinal bleeding during times of the study and the anemic patients were improved.

But the study has some defects because short duration and small number of patients were enrolled. No patients in the arm of fecal occult blood testing positive that can not identify lesions and find overt gastrointestinal bleeding to compute statistical significant.

In the fecal occult blood testing is negative patients before and after anticoagulant therapy. Screening with immunochemical occult blood test is benefit because no patient in this arm developed overt gastrointestinal bleeding, no hematocrit drop >3% despite the patients had co-morbid diseases such as old age , alcoholic consumptions, smoking , aspirin and NSAIDs

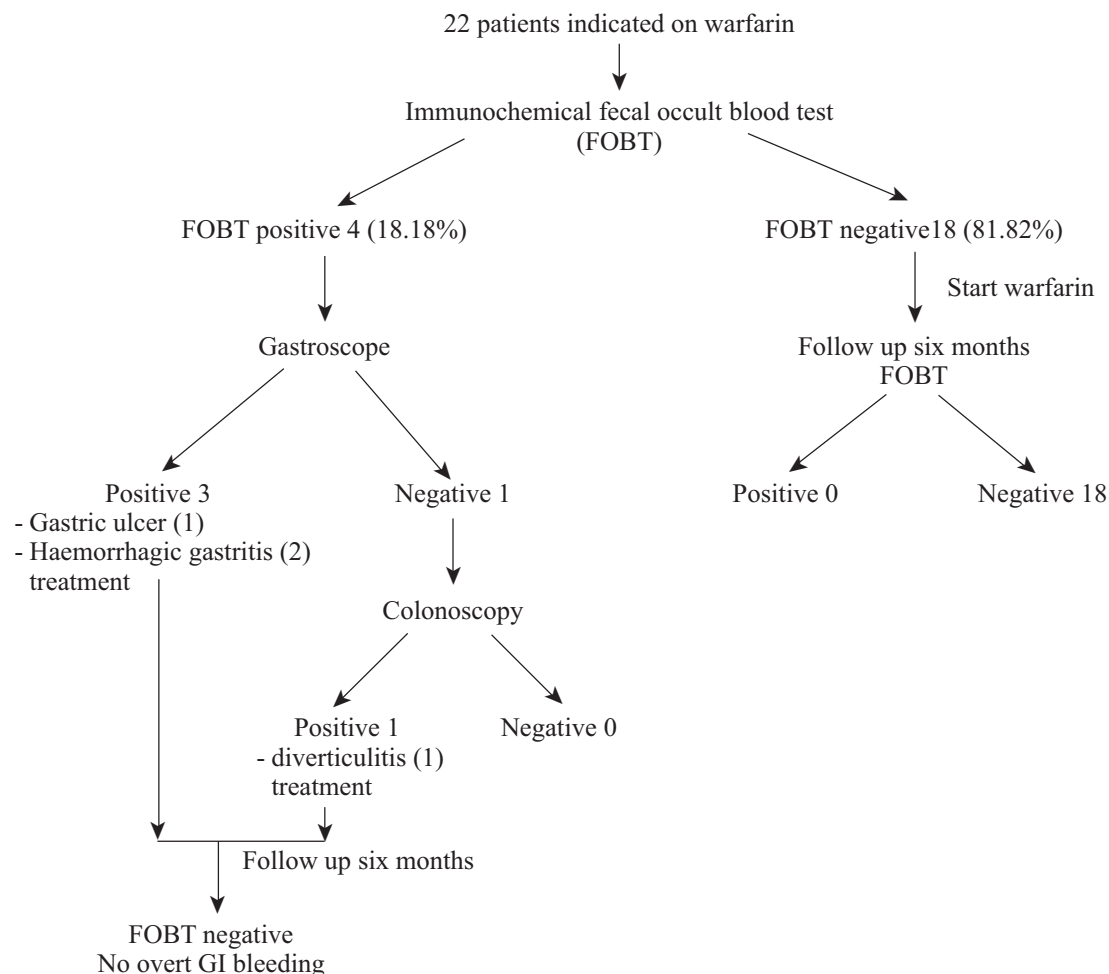


Figure 2

Table 1 Patient characteristics

Variable	Number of patients (%) Patients at enrollment, n = 22
Sex	
male	7 (31.82%)
female	15 (68.18%)
Age	
40-49 year	4 (18.18%)
50-59 year	7 (31.82%)
60-69 year	2 (9.09%)
70-79 year	9 (40.91%)
Alcohol consumption	1 (4.55%)
Smoking	1 (4.55%)
NSAIDs used	3 (13.64%)
Dysphagia	1 (4.55%)
Bowel habit change	0 (0%)
History family cancer	2 (9.09%)
Indication for warfarin	
Atrial fibrillation	10 (45.45%)
Cerebrovascular disease	2 (9.09%)
Heart valve disease	12 (54.55%)
Anemia	11 (50%)
Thrombocytopenia	1 (4.55%)
Hematocrit drop >3%	0 (0%)
Renal insufficiency	3 (13.64%)
INR	
below therapeutic level	60 (45.45%)
therapeutic level	40 (30.30%)
high therapeutic level	32 (24.25%)
Stool occult blood positive	4 (18.18%)
Stool occult blood negative	18 (81.82%)
Overt gastrointestinal bleeding	0 (0%)

used, anemia, renal insufficiency even though supratharapeutic level of INR. But the results in this arm has some defects because no patients in the arm that fecal occult blood testing negative were not developed overt gastrointestinal bleeding to compute statistical significant with the arm of fecal occult blood testing negative were developed overt gastrointestinal bleeding, and no patients in the arm that fecal occult blood testing is negative and took warfarin after follow up fecal occult blood testing positive to compare.

Limitation

There are many limitations in our study, notably; the study period was only twelve months the number of patients enrolled was small that could not represent the benefit of fecal occult blood testing in early detec-

tion of gastrointestinal tract bleeding. Further study needs to be performed to confirm our finding.

CONCLUSIONS

This was the first study with a small number of patients. We are continuing our study to collect more samples, although the statistic results may be changed at the end of the study. There is possible for FOBT to be used for early detection of gastrointestinal bleeding in patients using warfarin.

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