

Research papers

Patients referred from primary care with iron-deficiency anaemia: analysis of a nurse-led service. An improvement for both doctor and patient?

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ABSTRACT

Iron-deficiency anaemia (IDA) is a very common disorder. In 1998, an analysis of historical data revealed that 20 patients harbouring gastrointestinal cancer who were initially referred with IDA had an average wait of 11 weeks from referral to diagnosis. Recent government recommendations have brought this subject to the fore and are driving change in an already pressured service by insisting that IDA should be included in the indications for urgent referral as part of the two-week wait rule. With the paucity of diagnostic symptoms and clinical signs seen in most patients with IDA, a wait for consultant outpatient review prior to endoscopic evaluation seemed an unnecessary delay. In December 1998 a fast track protocol-directed nurse-led IDA clinic was established and here we evaluate the results of the first consecutive 100 patients. All 100 patients referred over 15 months were seen within two weeks. A nurse specialist

followed an established protocol to elicit a structured medical history and undertake a limited physical examination. The presence of alarm symptoms or signs led to rapid investigation within two weeks. Nineteen patients were found to have gastrointestinal cancer (17 colonic, two oesophageal). In these 19 patients the mean time from general practitioner referral letter to diagnosis was four weeks and 79% had a diagnosis within three weeks. In conclusion, this nurse-led open access IDA clinic attracted appropriate referrals from primary care and greatly improved the referral-to-diagnosis time for patients harbouring gastrointestinal malignancy. In all cases it was apparent that a clinical nurse specialist was entirely capable of safely assessing these patients and planning appropriate investigations.

Keywords: anaemia, colonic neoplasm, iron deficiency, nurse practitioner

Introduction

Iron deficiency is the commonest cause of anaemia in the United Kingdom.¹ Estimates suggest that 3–5% of men and post-menopausal women have iron-deficiency anaemia (IDA) with the level rising to 7% in elderly hospital inpatients.^{2–4} Unless there is a clinically obvious cause, occult gastrointestinal bleeding should always be considered, with studies

demonstrating gastrointestinal abnormalities in 50–90% of IDA patients.^{2,5–9} The incidence of carcinoma (oesophageal, gastric or colonic) in these studies is consistently reported to be greater than 10% and even as high as 50%.⁶ This has been influential, with government recommendations aimed at improving the diagnosis of colorectal cancer suggesting that IDA should be included in the indications for urgent referral as part of the two-week wait rule.

Traditionally IDA patients have been referred to a number of different specialities including surgeons, gastroenterologists, haematologists and geriatricians. Waiting times for clinic appointments and the urgency of subsequent investigation are likely to have varied considerably. In 1998, an analysis of historical data from this hospital revealed that 20 consecutive patients specifically harbouring gastrointestinal cancer, who were initially referred with IDA, had an average wait of 11 weeks (median eight weeks) from referral to diagnosis. With the relative paucity of diagnostic symptoms and clinical signs found in patients presenting with IDA, a wait for consultant outpatient review prior to endoscopic evaluation seemed an unnecessary delay. In December 1998, in collaboration with consultant colleagues who frequently saw IDA patients, we established a fast track protocol-based nurse-led IDA clinic. This clinic had open access to the local primary physicians and was widely advertised. This paper reports the findings of the first 100 referred patients.

Methods

In October 1998 the local primary physicians received notification of the new IDA clinic and were encouraged to use the facility. Between December 1998 and March 2000, 100 new cases of IDA were referred for evaluation. All patients were assessed by a clinical nurse specialist using a specially developed protocol focusing on the relevant medical history and a basic clinical examination (see Appendix 1). The nurse had attended the consultant clinic and observed and been taught basic examination for a three-month period. Structured questioning was used to identify alarm symptoms. The clinic was run in parallel with the gastroenterology outpatient clinic and all patients were discussed with the consultant or specialist registrar (SpR) and a management plan decided upon.

Confirmation of IDA was obtained (haemoglobin [Hb] < 13.0 g/dL and ferritin < 30 µg for males, Hb < 11.5 g/dL and ferritin < 14 µg for females with a mean corpuscular volume [MCV] < 80 fL) and subsequent management was based on the recently published British Society of Gastroenterology guidelines.¹⁰ If any alarm symptoms or signs were elicited (e.g. dysphagia, weight loss, abdominal mass) then the aim was to perform appropriate investigations within two weeks. For other patients with no such features, investigations were booked within the following six weeks. Provision was made in the endoscopy department for two extra cases per week. If a likely source of significant bleeding other than the gastrointestinal tract was apparent (e.g. menorrhagia),

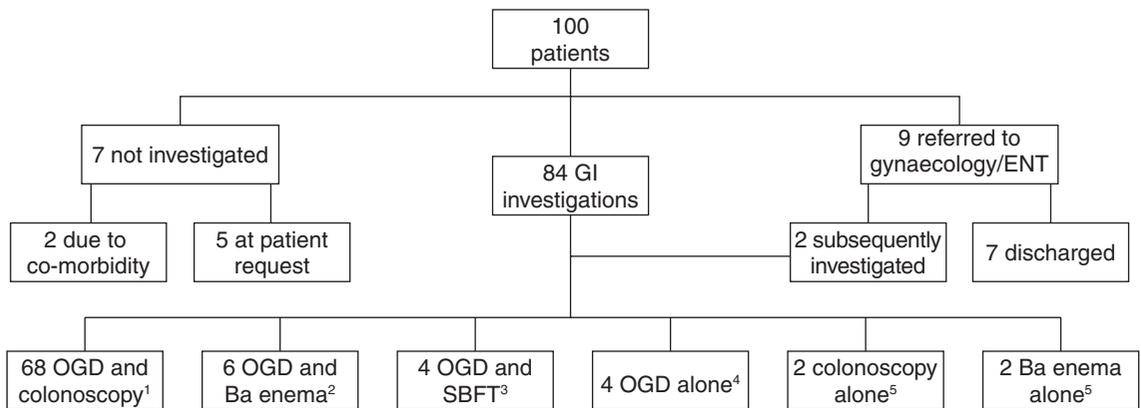
then the patient was referred to the appropriate speciality. Most asymptomatic patients were booked for outpatient combined oesophagogastroduodenoscopy (OGD) and colonoscopy at the same session. A minority of patients with significant co-morbidity who were felt to be at risk from colonoscopy had a barium enema instead. Patients with definite localising symptoms to the upper or lower gastrointestinal tract (e.g. dysphagia, altered bowel habit) had that area investigated first. Endoscopic findings taken to be significant causes of anaemia were grade 3 or 4 oesophagitis, portal hypertensive gastropathy, haemorrhagic gastritis, chronic peptic ulceration, coeliac disease, colonic polyps >1 cm, colonic angiodysplasia and carcinoma of the oesophagus, stomach and colon.

Results

Between one and four patients were referred each week and all 100 consecutive patients were seen within one to two weeks of receiving the referral letter. There was generally spare capacity in the clinic and it was envisaged that up to six patients could have been seen and investigated without a major impact on endoscopy provision.

The median age was 66 years (range 29–88) with a female predominance (63% female vs 37% male) and a mean haemoglobin of 9.4 mmol/l (range 5.7–12.0). The outcome for these 100 patients and the investigations performed are shown in Figure 1. Two patients were admitted as emergencies prior to their outpatient investigations. The first had a haematemesis and at OGD a large duodenal ulcer was found. The second was admitted with abdominal pain and had an inpatient OGD and colonoscopy. Both procedures were normal and subsequent investigations revealed an acute promyelocytic leukaemia. Two elderly patients had such significant co-morbidity that they were too unfit for further investigation. Following discussion and against our recommendation five patients declined further investigation. One patient was referred to the ear, nose and throat surgeons for treatment of recurrent epistaxis, and eight young females with no gastrointestinal symptoms were referred for gynaecological assessment of possible menorrhagia. Six of these patients were felt to have menorrhagia sufficient to account for their anaemia and the other two returned for OGD and colonoscopy.

At the initial assessment, 15 patients were thought to have alarm symptoms and were investigated 'urgently' within two weeks. The other patients had initial investigations within six weeks with an overall mean time from referral to diagnosis of five weeks. In no patients were relevant clinical signs elicited at the



¹One patient required subsequent barium enema due to incomplete colonoscopy.

²Barium enema chosen as unfit for double endoscopic approach (predominantly due to respiratory disease).

³Initial symptoms suggestive of small bowel disease.

⁴Definite upper gastrointestinal symptoms (e.g. dysphagia) and significant pathology found at OGD.

⁵Colonic symptoms and significant pathology found at colonoscopy/barium enema.

OGD: oesophagogastroduodenoscopy; SBFT: small bowel follow-through; GI: gastrointestinal; Ba: barium; ENT ear, nose and throat department

Figure 1 Outcome for 100 consecutive cases of IDA

initial nurse examination or subsequently by the attendant physician in those cases with malignancy.

Results of the investigations are shown in Table 1. Of the 86 patients who had gastrointestinal investigations, 45 (52%) had significant abnormalities detected. Nineteen cancers were found, and all patients thought initially to have alarm symptoms were found to have

neoplastic disease. For these patients the mean time from referral letter to diagnosis was four weeks (range 2–8) with 79% diagnosed within three weeks. It is noteworthy that of the 17 patients with colonic cancer, seven patients had Dukes stage D disease. Only one patient had both an upper and lower gastrointestinal cause for their IDA (gastritis and colonic cancer).

Table 1 Findings and treatment in the 86 patients having gastrointestinal investigation

Lesion	Patients <i>n</i>	Treatment
Oesophagitis (grade 3 or 4)	6	PPI
Oesophageal cancer	2	50% surgery ^a
Haemorrhagic gastritis	6	NSAID avoidance, HP eradication, PPI
Chronic peptic ulceration	3	NSAID avoidance, HP eradication, PPI
Coeliac disease	5	Gluten-free diet
Small bowel Crohn's disease	3	Medical management
Colonic polyp	3	Successful polypectomy
Angiodysplasia	1	Successful diathermy
Colonic cancer	17	94% surgery ^b

^aOne patient aged 78 declined oesophageal surgery.

^b16 patients had surgery (2 Dukes stage A, 8 stage B, 1 stage C, 6 stage D) and one patient had pre-operative liver metastasis and was treated with palliative care.

PPI: proton pump inhibitor; NSAID: non-steroidal anti-inflammatory drug; HP: *Helicobacter pylori*

Discussion

It has been known for many years that IDA is a marker for gastrointestinal malignancy and should prompt urgent assessment of iron-deficient patients. The establishment of a rapid access nurse-led clinic enabled the assessment of IDA patients within two weeks of referral and more importantly resulted in the majority of cases (80%) of malignant disease being diagnosed within three weeks. This clearly compares very favourably with the historical data from this hospital when the mean time from referral with IDA to diagnosis of cancer was 11 weeks. Retrospective analysis of data is fraught with the problems of case selection and bias. However, comparison with historical cancer cases is probably more reliable than a comparison with retrospective endoscopy patients, who undoubtedly would represent a selected population. We were unable to find data in the literature looking specifically at waiting times for IDA, although these may become available as the two-week wait recommendations are audited.

There is the potential for delay in the diagnosis of neoplasia in IDA patients, as the importance placed on investigation of such patients seems to vary enormously. This hospital serves a population of 235 000 and examination of the haematology computer database revealed that over a year 1651 individuals (993 females, 658 males) had results suggestive of IDA (low Hb and low MCV) and yet only 100 patients were referred to this clinic over 15 months. The clinic was new at that time and referral numbers have increased since then, but it still seems likely that many patients with IDA are managed solely in the community. Recent published data suggest that 50% of IDA patients in the community have either no investigations at all or just testing for faecal occult blood.¹¹ Furthermore, faecal occult blood testing in IDA patients may have a sensitivity of only 50% for detecting significant pathology compared to endoscopic evaluation.^{8,12} It is possible that general practitioners only refer patients to hospital who they perceive to be at high risk of malignancy due to their symptoms or clinical signs. However, 21% of the patients with malignancy detected in this study were entirely asymptomatic, and several studies have documented a poor correlation between symptoms and endoscopic findings.^{5,9} Despite this documented poor correlation, alarm symptoms did appear to be a very reliable predictor of malignancy in this patient cohort.

Delay in diagnosis may also result from lack of centralisation of referrals, with patients referred to different specialities each with variable clinic waiting times and variable access to investigation. This study suggests that if referral patterns are centralised then

prompt investigation can be ensured. The costs of this clinic are difficult to ascertain exactly, as it was run as an adjunct to the high-throughput parallel consultant clinic. Minimal receptionist and clerical support were required and the only major cost was the nurse specialist's time (£11/h, H grade of payscale).

It could be argued that all IDA patients should be sent directly for investigation without an initial assessment. However, the advantage of an outpatient review are several-fold: 1) investigations can be targeted (e.g. small bowel studies if the history suggests Crohn's disease); 2) investigations can be instigated urgently if alarm symptoms are present. Conversely, patients with long-standing but not previously investigated anaemia could have more leisurely investigations; 3) patients with other causes of IDA can be directed to the appropriate specialist; 4) investigations can be discussed and the consent process begun and 5) patients' co-morbidity can be assessed to establish the most appropriate investigation. We found that a clinical nurse specialist using a specially developed protocol was entirely capable of assessing these patients and planning their investigations. Certainly patient satisfaction appeared to be high, probably in part because of the time available for the nurse to explain the investigations and to begin the consent process (average consultation 30 min). Because the overall number of patients requiring investigation was small (<2/week), and only a minority needed investigation within two weeks, the impact on endoscopy provision was minimal.

The findings at investigation of this group of IDA patients were similar to those of previous series.^{2,5-9} In the 86 patients investigated, significant abnormalities were found in 52%, with malignancy in 22% and coeliac disease in 6%. A degree of variation in the frequency of abnormalities reported in studies may represent differences in the patient cohort, criteria taken for a significant positive finding and the method of investigation employed. Barium enema, for example, can miss small polyps or angiodysplasia, but it appears to be comparable to colonoscopy at demonstrating colonic carcinoma in IDA patients.¹³ All patients having an OGD had duodenal biopsies taken to look for coeliac disease and five cases had typical histological features. It is interesting to note that the endomysial antibody test was positive in only two of these patients. This apparent low sensitivity of the endomysial antibody test is at variance with most published studies, although in partial villous atrophy the sensitivity may be only 30%.^{14,15} It is possible that the low endomysial antibody sensitivity may have related to a problem with the local assay, and screening for coeliac disease is now done using the tissue transglutaminase antibody.

Conclusion

In this study a nurse-led open access protocol-based IDA clinic greatly improved the referral-to-diagnosis time for patients harbouring gastrointestinal malignancy. It is hoped that initiatives towards earlier cancer diagnosis and treatment will result in enhanced long-term survival. Certainly, a reduced waiting time for investigation will help to allay many patients' anxiety regarding their possible occult malignancy and allow non-malignant conditions (e.g. peptic ulceration, severe oesophagitis) to be treated before complications ensue. This clinic was a safe efficient clinical pathway that centralised the referral of patients from primary care and freed consultant clinic space. As recent recommendations include IDA as an indication for urgent referral (i.e. within two weeks), the development of this type of clinic may be one useful approach to service provision.

REFERENCES

- 1 Weatherall DJ. Anaemia: pathophysiology, classification and clinical features. In: Weatherall DJ, Ledingham JCG and Warrell DA (eds). *Oxford Textbook of Medicine*. Oxford: Oxford University Press, 1996, pp. 3457–62.
- 2 Calvey HD and Castleden CM. Gastrointestinal investigations for anaemia in the elderly: a prospective study. *Age and Ageing* 1987;16:399–404.
- 3 Wroblewski M and Ostberg H. Ulcer disease among geriatric inpatients with faecal occult blood test and/or iron deficiency anaemia. *Scandinavian Journal of Gastroenterology* 1990;25:489–95.
- 4 Sayer JM and Long RG. A perspective on iron deficiency anaemia. *Gut* 1993;34:1297–9.
- 5 Cook IJ, Pavli P, Riley JW, Goulston KJ and Dent OF. Gastrointestinal investigation of iron deficiency anaemia. *British Medical Journal* 1986;292:1380–2.
- 6 Hardwick RH and Armstrong CP. Synchronous upper and lower gastrointestinal endoscopy is an effective method of investigating iron-deficiency anaemia. *British Journal of Surgery* 1997;84:1725–8.
- 7 Rockey DC and Cello JP. Evaluation of the gastrointestinal tract in patients with iron-deficiency anaemia. *New England Journal of Medicine* 1993;329:1691–5.
- 8 Kepczyk T and Kadakia SC. Prospective evaluation of gastrointestinal tract in patients with iron-deficiency anaemia. *Digestive Diseases and Sciences* 1995;40:1283–9.
- 9 McIntyre AS and Long RG. Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut* 1993;34:1102–7.
- 10 Goddard AF, McIntyre AS and Scott BB, for the British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. *Gut* 2000;46(Suppl 4):(iv)1–5.
- 11 Lucas CA, Logan ECM and Logan RFA. Audit of the investigation and outcome of iron-deficiency anaemia in one health district. *Journal of the Royal College of Physicians of London* 1996;30:33–5.
- 12 Simon JB. Occult blood screening for colorectal carcinoma: a critical review. *Gastroenterology* 1985;88:820–7.
- 13 Sayer JM, Donnelly MT, McIntyre AS *et al.* Barium enema or colonoscopy for the investigation of iron deficiency anaemia. *Journal of the Royal College of Physicians of London* 1999;33:543–8.
- 14 Ferreira M, Davies SL, Butler M *et al.* Endomysial antibody: is it the best test for coeliac disease? *Gut* 1992;33:1633–7.
- 15 Rostami K, Kerckhaert J, Tiemessen R *et al.* Sensitivity of antiendomysial and antigliadin antibodies in untreated celiac disease: disappointing in clinical practice. *American Journal of Gastroenterology* 1999;94:888–94.

CONFLICTS OF INTEREST

None.

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Appendix 1

Iron-deficiency anaemia clerking sheet

Height Date.....

Weight.....

Urine.....

Insert addressograph label

Hospital no:

Name:

Address:

DOB:

GP:

Source of referral.....

Blood results:

Hb.....

MCV.....

WCC.....

MCH.....

PLTS.....

Serum iron.....

Ferritin.....

Transferrin: % saturation.....

B12.....

Folate.....

Iron deficiency confirmed:

Yes: continue

No: discuss with consultant

Smoker:

Yes/no

Number per day

Alcohol:

Yes/no

Units per week

Current medication:

Anticoagulants

NSAIDS

Other:.....

Allergies:

HISTORY

Previous anaemia:

Yes/no

When.....

Treatment.....

Transfused in past:

Yes/no

Why.....

Current anaemia:

Asymptomatic

Tiredness/lethargy/SOB/chest pain

Blood loss:

No blood loss seen

Haematemesis/melaena/rectal bleeding

Haematuria

Periods:

Yes/no

Age of menarche

Length of cycle

Light/moderate/heavy

Number of towels

Passage of clots

Malabsorption:

Diarrhoea

Yes/no

Features of steatorrhoea

Yes/no

General:

Weight loss/gain

Specify.....

Appetite.....

Mouth ulcers

Yes/no

Number of pregnancies.....

Number of live births.....

PAST MEDICAL HISTORY

Previous GI surgery: Yes/no Specify:

Other relevant history:

Family history:

IBD	Yes/no
Coeliac	Yes/no
CA colon	Yes/no
Iron deficiency (History in family)	Yes/no
Thalassaemia	Yes/no

RISK ASSESSMENT FOR INVESTIGATION

Cardiac: Angina/MI/valvular problems
or replacements Specify:

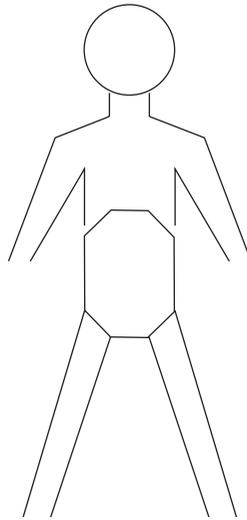
Respiratory: Asthma/COPD. Exercise tolerance:

Other information:

EXAMINATION FINDINGS

Indicate masses/draw scars/shade tender areas

Cyanosis
Anaemia
Jaundice
Mouth ulcers
Telangiectasia
JVP
Nodes
Pulse
BP
Heart sounds
Chest
Liver
Spleen
Kidneys
PR
Sigmoidoscopy
General physical condition

**PLAN**

ODG and colonoscopy booked: Yes/no Date
If no specify reason (i.e. unfit, refused, etc)

Other investigations requested: (discuss with consultant)

Next appointment.

Results:

OGD
Colonoscopy
Histology
Other

Other comments