Monitoring is key in Crohn's disease

Maeve M Skelly, Emma Tobin, Masood Iqbal

Crohn's disease is a chronic relapsing and remitting disease that presents in all age groups but has two peaks of incidence – in the teenage years and again in the sixth decade. Treatment involves the use of long established drugs, dietary manipulation, lifestyle changes (e.g. stopping smoking), the involvement of a multidisciplinary team and the rapidly developing field of biological agents.

Given the peak incidence in young life, many individuals have to negotiate study, job-seeking, marriage and starting a family while trying to come to terms with a new diagnosis and management of a relapse.

This short review will give an overview of the role of monitoring in a patient with Crohn's disease. The monitoring role manifests in a number of ways. There is the monitoring that specific diets and drug treatments require and there is the unique role of ensuring that the patient's health and wellbeing is maintained as they grow through different life stages, transfer from one hospital-based specialty to another and experience particular events such as conception or pregnancy.

The patient and their team need to know what services are available locally for those with Crohn's disease. Some patients are fortunate to be cared for in an area with a hospital-based dedicated inflammatory bowel disease (IBD) nurse. These individuals are a great resource for patients, consultants and GPs. Where IBD nurses are not available, many consultants try to maintain a 'next clinic' policy for Crohn's patients who run into trouble. Many of these patients will be equally well-known to the GP and the gastroenterologist, with the result that a telephone call from primary care for advice may sort out a significant number of problems. Shared care protocols between primary and secondary care in addition to patient-initiated treatment protocols could be a useful locally-agreed resource.

Dietary monitoring

Nutrition plays an important role in many chronic illnesses. Nutrition is especially important in Crohn's disease as weight loss is a common symptom of disease activity, and correction of malnutrition improves outcome of small bowel disease, helps attainment of growth milestones in children and reduces post-operative complications if surgery is required.

Many patients with Crohn's disease experiment with their diet in the hope that it will alter disease behaviour. This may lead patients to exclude major food groups, dairy products being a frequent example. There is no evidence for empirical food exclusion in Crohn's disease and foods from all elements of the food pyramid are recommended. A 'brief intervention' strategy to check that the patient is eating a balanced diet and maintaining a steady weight is useful.

An additional record of height trajectory in children is important as growth failure is common in children with Crohn's and appears to be due to subtle disease-related malnutrition.

Patients may be prescribed dietary supplements or even have a percutaneous endoscopic gastrostomy (PEG) feeding tube inserted. Patients on such diets may require regular blood tests and may present in primary care with particular problems with their PEG tubes. Primary care professionals need to be familiar with the local arrangements for 'trouble shooting' PEG tubes, e.g. via the gastroenterology team or the hospital-based IBD nurse if one is in post.

Medication monitoring

Typically, a patient with Crohn's disease will be started on an aminosalicylate, take a corticosteroid if they have a relapse and move to an immunosuppressant if they have more than two relapses requiring steroids in a 12-month period. This approach is termed 'step up' and is now being challenged by proponents of early use of biological agents, perhaps at disease onset or instead of starting an immunosuppressant. This approach of early use of biologics such as infliximab or adalimumab is termed 'top down'. To ensure the safe and effective use of all these drugs, the patient must be regularly monitored.

Patients may fail to take their prescribed medication regularly; factors involved include forgetfulness, limited literacy, unstable lifestyle or disease denial. The primary care team are often the first people to detect problems with drug compliance and are also often the people best placed to work through the issues surrounding it. In addition to responsibility for repeat prescriptions of maintenance drugs, primary care is the first port of call for patients with exacerbations of Crohn's disease. Patients who require more than two courses of steroids in a year should be referred to secondary care to discuss alternatives.

Aminosalicylates can cause haematological problems and it is becoming increasingly known that interstitial nephritis can complicate the use of these drugs. For this reason an annual check of FBC, U+E and LFTs would be reasonable, as well as opportunistic testing if the clinical situation merits it, e.g. bruising or febrile illness. Patients who are diabetic will require particular monitoring if they are prescribed a course of steroids and may need to alter their glycaemic control strategy.

Patients who regularly take courses of steroids for their Crohn's disease also often the people best placed to work through the issues surrounding it. In addition to responsibility for repeat prescriptions of maintenance drugs, primary care is the first port of call for patients with exacerbations of Crohn's disease. Patients who require more than two courses of steroids in a year should be referred to secondary care to discuss alternatives.
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disease are at an increased risk of osteoporosis. Guidance suggests that such patients should be co-prescribed a calcium supplement and may need a DXA scan.

Azathioprine and 6-mercaptoapurine are the most commonly used immunosuppressants. Side-effects include bone marrow suppression, pancreatitis or liver dysfunction in addition to the more commonly experienced nausea, headache or rash. There is no evidence that regular monitoring of the FBC or U+E prevents the development of bone marrow or renal failure. However, it is intuitive that regular monitoring should detect at least some of the cases before they progress.

On a more legalistic basis, the drug manufacturers and the British National Formulary recommend regular monitoring and it might be harder to mount a defence if a patient who developed drug side-effects was regularly given repeat prescriptions without any record of regular blood tests.

Monitoring regimes

Monitoring regimes vary, but a typical one involves weekly FBCs for the first month, then monthly for three months, then every three months thereafter. LFTs could be checked every three to six months. Patients typically present initially to their GP with drug side-effects and vigilance is the by-word when monitoring patients on immunosuppressants.

A particular issue can arise where the immunosuppressed patient reports contact with an infectious disease, eg. varicella. If the patient has not previously been exposed to varicella, serious illness can result. When immunosuppressed patients report such exposure and it is not known if they are immune, it would be reasonable to tell the patient to stop their immunosuppression, have bloods checked (including serology for the virus in question) and make contact with the responsible team. GPs may wish to prescribe empirical acyclovir while referring back to secondary care.

Methotrexate is a less commonly used immunosuppressant. It requires FBC and LFT monitoring, not because this has been shown to reduce the incidence of toxicity but because the manufacturers recommend it and it would be considered a basic component of patient care. Liver toxicity is a well recognised problem with methotrexate. Some gastroenterologists do a liver biopsy on all patients who have received more than 1g in total of the drug but there is no evidence to support this, and so many rely on regular blood tests to detect liver dysfunction.

Caution in conception

There are two other well-recognised problem areas with methotrexate that require careful monitoring in primary care. The drug is teratogenic, and both males and females taking it are advised to avoid conception while on the drug and for six months after stopping it. This message should be emphasised along with advice on effective contraception.

Methotrexate is a drug that should only be taken weekly and is available in different doses. It is well recognised that patients may take it daily by accident or may continue to take ‘four tablets’ without appreciating that they have been dispensed a different formulation with a higher total milligram content. Timely intervention may avert a dangerous situation with this potent drug.

Infliximab and adalimumab are new agents that target TNF alpha (tumor necrosis factor). Collectively they are referred to as biological agents or biologics. They are powerful drugs which can have great effects on disease outcome; they have been shown to induce mucosal healing, an endpoint not commonly seen in the treatment of Crohn’s disease. However, there is a well-recognised risk of infection with regular, aggressive or atypical microbes in patients on biological agents and some large series have reported a drug-related death rate of 1%, making careful patient selection and monitoring crucial.

Reactivation of latent TB while on biological agents is a particular concern. Patients are screened for TB before starting these drugs and if they are found to have evidence of previous TB, will be put on anti-TB treatment before starting the biological agent. Biologics must not be given if there is any evidence of active infection. If patients on biological therapy develop symptoms or signs of infection, careful clinical assessment is necessary. The patient should be referred for blood work up, chest radiograph, blood and urine culture and other investigations of infection as becomes apparent. These patients can develop serious infection despite an adequate white cell count.

Monitoring in pregnancy

The ‘whole patient’ is particularly important in relation to planning a pregnancy where the patient has Crohn’s. Patients of either gender should not conceive while on methotrexate or for six months after stopping the drug. All female patients with Crohn’s should be actively counselled to conceive during remission.

Before conception, female patients should be well nourished and take folate supplements. Most women who plan a pregnancy wish to stop medication; this is inadvisable where aminosalicylates, 6-mercaptopurine or azathioprine are keeping their disease in remission. Active Crohn’s which flares up during pregnancy is a greater risk to foetal outcome than continuing these prescribed medications.

Provided that they have inactive disease, women with Crohn’s disease can expect to have a normal pregnancy outcome. There are emerging data on the use of biologics during pregnancy; the drugs used do not appear to be teratogenic and foetal outcomes have been good, albeit in small case series. Again, the key issue appears to be keeping the disease in remission and if they are necessary, then biologics can be continued. Women with active perianal disease should be advised they can expect to have a Caesarean section rather than vaginal delivery.

Monitoring cancer risk

Crohn’s colitis of more than eight years duration appears to increase the relative and absolute risk of colon cancer. In addition, having Crohn’s disease per se may increase the risk of the patient developing lymphoma. A strategy has emerged whereby patients who have Crohn’s colitis for eight years are offered colonoscopy every year to 18 months. The risk of bowel cancer increases the longer the patient has colitis, so older age should not be a reason to cease colonoscopic surveillance, as older patients who have the disease longest are at the greatest risk of developing bowel cancer.

Patients with Crohn’s disease are more likely to have primary sclerosing cholangitis (PSC), and the development of PSC has been shown to increase the risk of developing both bowel and biliary cancer. No effective strategy exists for monitoring the risk of malignant transformation in the bile ducts of patients with PSC, but regular colonoscopic surveillance is recommended as soon as a diagnosis of PSC is made.

Maeve M Skelly is consultant gastroenterologist, Emma Tobin is senior house officer in gastroenterology and Masood Iqbal is registrar in gastroenterology at the Mid-Western Regional Hospital, Limerick.