Inflammatory bowel disease

Prohibited substances: Glucocorticoids

1. Introduction

Inflammatory Bowel Disease (IBD) specifically includes Crohn's disease (CD) and ulcerative colitis (UC) but also includes IBD unclassified (IBDu), seen in about 10% of cases. These are chronic intermittent diseases, predominantly affecting the gastrointestinal tract, but with the potential to cause extra-intestinal manifestations such as arthralgia and skin disease. These conditions may have a familial tendency and affect people of all ages but usually begin before the age of 30, with peak incidence from 14 to 24 years. Both CD and UC, but mainly UC, have a second smaller peak between the ages of 50 and 70 years; consequently, it is not uncommon for active young athletes to seek an exemption to use prohibited substances including glucocorticoids (GCs). However, good management dictates that these medications should only be used short-term (up to 3 months at a time), to treat an acute flare-up of disease and if their use is necessary more frequently, "steroid-sparing" maintenance medication should be initiated to keep patients in remission.

2. Diagnosis

a. Medical history

IBD carries a characteristic medical history that may include altered bowel habit, usually diarrhea that can be bloody, fever, abdominal pain, anorexia, and weight loss. While UC only affects the large intestine and the inflammation is often more superficial, transmural inflammation in CD can affect the entire gastrointestinal tract and in the very young there may be a history of growth retardation, especially if small bowel disease leads to malabsorption. Complications are common and especially in CD, may lead to perianal disease, fistula formation, abscesses, and perforation.

b. Diagnostic criteria

Given a suspicious medical and family history, the definitive diagnosis of IBD demands specific investigations carried out under the supervision of a specialist-gastroenterologist. Stool tests should be requested to confirm the absence of infection and the presence of inflammation while routine laboratory screening investigates for anemia, iron deficiency, chronic inflammation, and malabsorption. Assessment of the gastrointestinal tract is required to investigate the extent, distribution, and severity of IBD. A single diagnostic gold standard is not available, but diagnosis should not rely exclusively on radiological imaging. In CD, direct visualization of the entire gastrointestinal tract by a combination of one or more of gastroscopy, colonoscopy, wireless capsule endoscopy or by CT, MR and US imaging +/- biopsies to demonstrate specific pathological features at selected sites. In UC, colonoscopies are often sufficient. In general, a combination of clinical, histological, radiological and biochemical markers usually confirms the diagnosis of IBD.

For the identification of complications such as abscesses, computerized tomography (CT) or magnetic resonance (MRI) scanning may also be employed.

c. Other relevant medical information

The primary care/family physician frequently obtains a relevant medical history of bowel habit disturbance, weight loss, anorexia, and inappropriate fatigue. Where the patient is also an elite athlete, there is added urgency to seek specialist opinion and diagnostic confirmation as outlined above. However, despite the intermittent and relapsing nature of the disease, it should not be forgotten that common IBD symptoms such as abdominal pain and diarrhea might be due to causes other than active disease and necessitate thorough investigation prior to treatment initiation.

3. Treatment

IBD represents life-long, relapsing disorders and while flare-ups are usually associated with significant symptoms, during periods of remission the patient may remain totally asymptomatic. However, the frequency of flare-ups and the endoscopic appearance of the mucosa dictate the use of maintenance medication to keep the patient in remission.

Several scoring systems have been developed to help monitor disease and recognize a flare-up as early as possible to initiate treatment. In UC, the Simple Chronic Colitis Activity Index (SCCAI) has been established, while for CD the Harvey-Bradshaw-Index (HBI) or the Crohn's Disease Activity Index (CDAI) is often used. These indices each have validated thresholds to distinguish between remission and active disease. Calculators for these indices are available on the internet and combine patient data, laboratory, and examination findings to produce scores that assist in deciding whether treatment with GCs is appropriate. However, a well-known limitation to the use of these scoring systems is the fact that there is no robust correlation with findings on endoscopy.

IBD treatment includes medications for managing acute flare-ups (e.g., GCs and in UC also 5-ASA preparations) and medications to maintain remission (e.g., immunomodulators and biologicals). Furthermore, especially in UC, knowledge of the location and extent of the disease is crucial to make maximum use of topical treatment. GCs are a critical adjunct in the treatment of IBD acute flares but should not be used for maintenance of remission,

a. Systemic glucocorticoids

As of the 2022 Prohibited List, oral, rectal or any injectable routes of administration of glucocorticoids (GCs) are prohibited in-competition only. However, an In-Competition urine sample may show GC levels above the established laboratory reporting levels even though administration occurred Out-of-Competition. In accordance with the Code, a resulting positive doping test, known as an adverse analytical finding (AAF), could render the athlete liable to a sanction under the concept of Strict Liability. However, as per ISTUE Article 4.1e, the athlete is permitted to apply retroactively for a TUE if there is an In-Competition AAF from Out-of-Competition use.

b. Route of administration

GCs may be administered via oral, intravenous, or rectal routes in the treatment of IBD.

c. Dosage and frequency

The use of GCs should be limited to the treatment of an acute flare-up and should not be used prophylactically. Rather, an increase in disease activity should be recognized early and treated promptly to avoid unnecessarily high doses and prolonged GC administration to limit complications. Despite this, doses of oral prednisone (max. 1mg/kg body weight per day, usually 40-60mg per day) may be necessary in the acute management of IBD, tapering over a period of several weeks to a maximum of three months. A too-cautious tapering regime will lead to unnecessary side effects while tapering too fast carries the risk of a relapse.

Intravenous hydrocortisone 400 mg/day or methylprednisolone 60-80mg/day by continuous drip or in divided doses may be used for severe disease and normally requires hospital admission. GC doses are individualized and demand specialist oversight in combination with other appropriate therapeutic agents. A small proportion of patients with IBD, especially after frequent and/or prolonged GC exposure, become corticoid dependent which is normally avoided by appropriate escalation of advanced therapies (immunomodulators, biologics and small molecules)

d. Duration of treatment

Given the chronic nature of IBD, duration of treatment for athletes is likely to be lifetime or at least for the life of their exposure to high performance sport. However, GCs should only be given during periods of acute disease and according to international guidelines, with effort made to minimize GC exposure in IBD. If GC administration becomes a frequent necessity, maintenance therapy with immunomodulators, biologics or small molecules should be initiated.

4. Non-prohibited alternative treatments

Permitted agents to maintain remission and shorten GC exposure include immunomodulating drugs (such as azathioprine, 6-mercaptopurine, methotrexate), 5-aminosalicylates, analgesics and antibiotics. Lately, so-called biologics such as the anti-TNF agents (e.g., infliximab, adalimumab), anti-integrins (e.g., vedolizumab) and anti-IL-12/23 antibodies (e.g., ustekinumab), and the small molecules JAK inhibitors (Tofacitinib, Filgotinib, Upadacitinib) and S1P modulators (Ozanimod, Etrazimod) have been used to induce and maintain remission in IBD.

5. Consequences to health if treatment is withheld

If untreated, IBD may run a relapsing and remitting disease course with a potentially life-threatening outcome.

6. Treatment monitoring

During periods of IBD remission, the athlete may be totally asymptomatic and does not need much monitoring. Treatment usually requires routine oversight from the family physician with recommended

review by the specialist (gastroenterologist) at least annually or as clinically indicated. Monitoring might consist of regular blood tests if the patient is treated with a thiopurine and/or measurement of drug levels and periodic imaging and/or colonoscopy to optimize individual treatment.

As indicated, indices exist for scoring the activity of IBD (SCCAI, HBI, CDAI) and these may be applied to initial assessment of acute exacerbations. Fecal calprotectin, a stool test measuring intestinal inflammation, correlates well with endoscopic findings and is recommended for assessment.

7. TUE duration

Documented medical conditions requiring long tapering courses or intermittent recurrent courses of oral GCs could initially be granted TUEs for up to 12 months, conditions should be attached to the approval outlining the need for either notification of use throughout the 12 months or a summary of use, from the treating practitioner prior to reapproval. The TUE Committee should reserve the right to request relevant medical records during the time of approval to confirm TUE conditions are met. It is recommended that caution should be applied to athletes from sports with historic, high-risk GC abuse profile (e.g., cycling) and long-term approvals may be inappropriate for these groups.

In certain cases, with long-established remitting disease, the recommended TUE duration for IBD could be extended to up to 4 years with annual specialist review. Common sense should always apply to athletes with IBD, given varying GC requirement during acute crises or periods of remission. Athletes, supported by their attending physician, must provide documentation of acute crises requiring GC treatment to avoid indiscriminate use.

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