INFLAMMATORY BOWEL DISEASE

1. Medical Condition

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. These conditions may have a familial tendency and affect people of all ages but usually begin before age 30, with peak incidence from 14 to 24 years. Both CD and UC, but mainly UC, have a second smaller peak between ages 50 and 70 years; consequently it is not uncommon for active young athletes to seek exemption to use prohibited substances including glucocorticoids (GCs). However, good management dictates that these medications should only be used short-term 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 diarrhoea, 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 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. Apart from routine laboratory screening including stool tests to confirm the absence of infection and the presence of inflammation and anaemia, 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 visualisation of the entire gastrointestinal tract by gastroscopy, enteroscopy and colonoscopy permits biopsy to demonstrate specific pathological features at selected sites. In UC, colonoscopy is often sufficient. In general, the diagnosis of IBD is usually confirmed by a combination of clinical, histological, radiological and biochemical markers.

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

C. Relevant medical information

A relevant medical history of bowel habit disturbance, weight loss, anorexia and inappropriate fatigue is frequently obtained by the primary care/family physician. 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 diarrhoea may be due to causes other than active disease and necessitate thorough investigation prior to treatment initiation.

3. Medical Best Practice 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 recognise a flare-up as early as possible to initiate treatment. In UC, the Simply 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 GC is appropriate.

IBD treatment includes medications for managing acute flare-up (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.

A. Name of prohibited substance

Glucocorticoids (GCs) are a critical adjunct in the treatment of IBD.

B. Route

All forms of systemic GC administration (intravenous, oral, rectal and intramuscular) are prohibited.

C. 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 to four months. A too-cautious tapering regime will lead to unnecessary side-effects while tapering too fast carries the risk of a relapse.

Intravenous hydrocortisone 300mg/day or methylprednisolone 60-80mg/day by continuous drip or in divided doses may be used for severe disease and normally requires hospital admission. It should be remembered that GCs are only prohibited during the in-competition period and that intravenous infusions or injections are prohibited at all times (unless part of a hospital admission, clinical investigation, or a surgical treatment, or is given in less than 50 mL q. 6 hours). 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.

D. Recommended duration of treatment

Given the chronic nature of IBD, the 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 treatment becomes a frequent necessity, maintenance therapy with immunomodulators or biologicals should be initiated.

4. Other Non-Prohibited Alternative Treatments

Permitted agents to maintain remission and to 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-TNFα agents (e.g. infliximab, adalimumab), anti-integrins (e.g. vedolizumab) and anti-IL-12/23 antibodies (e.g. ustekinumab) have been used to induce and maintain remission in IBD.

5. Consequences to Health if Treatment is Withheld

If untreated, IBD may run an undulating, unremitting course with a potentially life-threatening outcome.

6. Treatment Monitoring

During periods of remission from IBD, the athlete may be totally asymptomatic and does not need much monitoring. Treatment usually requires monitoring routinely facilitated by the family physician with recommended review by the specialist - gastroenterologist at least annually or as clinically indicated.

As pointed out above, indices exist for scoring the activity of IBD (SCCAI, HBI, CDAI) and these may be applied to the initial assessment of acute exacerbations of the disease. Faecal calprotectin, a stool test measuring intestinal inflammation has been shown to correlate well with endoscopic findings and is recommended for assessment.

Well documented medical conditions requiring long tapering courses or intermittent recurrent courses of oral glucocorticoids (GCS) could be granted TUEs for up to 12 months. In these cases, 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 consideration of reapproval. The TUEC should reserve the right to request relevant medical records during the time of approval to confirm the TUE conditions have been met. It is recommended that a more cautious approach should be used with athletes from sports with a high risk of GC abuse (e.g. cycling) and longer term approvals may not be appropriate for these groups.

7. TUE Duration and Recommended Review Process

The recommended duration of a TUE for Inflammatory Bowel Disease is 4 years with an annual review by a specialist physician. A common sense approach should always be adopted with respect to IBD, given the altered requirements of glucocorticoids during acute crises or periods of remission. Athletes must be able to provide documentation for any acute crises that require the use of a prohibited substance to avoid indiscriminate use of glucocorticoids.

8. Any Appropriate Cautionary Matters

The sustained use of systemic glucocorticoids carries well-documented long-term risks.

References

1. Dignass A, van Asche G, Lindsay JO, et al. “The second European evidence-based Consensus on the diagnosis and management of Crohn’s disease: Current management.” JCC 4:28-62, 2010.

2. Van Asche G, Dignass A, Panes J, et al. “The second European evidence-based Consensus on the diagnosis and management of Crohn’s disease: Definitions and diagnosis.” JCC 4:7-27, 2010.

3. Dignass A, Eliakin E, Magro F, et al. “The second European evidence-based Consensus on the diagnosis and management of ulcerative colitis Part 1: Definitions and diagnosis.” JCC 6: 965-990, 2012.

4. Dignass A, Lindsay JO, Sturm A, et al. “The second European evidence-based Consensus on the diagnosis and management of ulcerative colitis Part 2: Current management.” JCC 6: 99101030, 2012.

5. Baumgart DC, Sandborn WJ, Inflammatory bowel disease: clinical aspects and established and evolving therapies.” Lancet 369:1641-57, 2007.

6. Best WR, et al., "Development of a Crohn's disease activity index." Gastroenterology; 70:439-444, 1976.

7. Carter MJ, A J Lobo, Travis SPL, “Guidelines for the management of inflammatory bowel disease in adults.” Gut; 53: v1 - v16, 2004.

8. Walmsley RS, Ayres RCS, Pounder RE, Allan RN, “A simple clinical colitis activity index.” Gut; 43:29-32, 1998.

9. Sachar, DB, Walfish, AE, “Overview of Inflammatory Bowel Diseases.” Revision February 2010 Merck Manual 19Th Ed.