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Biologic agents in inflammatory arthritis

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INTRODUCTION

The term 'inflammatory arthritis' (IA) encompasses a spectrum of diseases, of which the most common forms are rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). Over the past decade, the advent of immunomodulatory biological therapies has dramatically changed the management of such diseases, and offers alternatives for patients with a poor response to the more conventional disease-modifying anti-rheumatic drugs (DMARDs).

Over recent years, more emphasis has been placed on the concept of shared care between specialist and primary care physicians for many chronic conditions once on a stable treatment regime, in order to improve hospital workload and enable more flexibility for patients. This brief review highlights the key points relevant to primary care physicians involved in the care of patients with IA on biologic agents.

IMMUNOMODULATORY BIOLOGIC AGENTS IN INFLAMMATORY ARTHRITIS

Immunomodulatory biologic agents (Table 1) are proteins derived from human genes that are genetically engineered to inhibit precise components of the immune system.[1] By doing so, they suppress specific pathways that play a pivotal role in IA pathogenesis and, hence, differ from the more commonly used DMARDs, which have broader targets.[1] If tolerated, biologic agents are used in combination with methotrexate, or an alternative DMARD, in view of enhanced efficacy.

Biologic agents are initiated and monitored by the specialist rheumatology team and, in general, their use is recommended following either poor response or intolerance to conventional treatment options.[2] Patients may be switched from one biologic to another due to intolerance (side effects or abnormal blood parameters) or poor efficacy.

Prior to prescription, patients will have been screened for history of recurrent infection or symptoms/signs of malignancy, tuberculosis (TB) risk (chest X-ray and immune test according to local protocol), and virology (hepatitis B and C/HIV/varicella IgG) due to reactivation risk.[3] Screening blood tests are also performed for full blood count (FBC), liver function tests (LFTs), and lipids[3] (Table 1) as biologic agents can affect these parameters.[2] Guidelines recommend that all patients are up to date with varicella zoster, hepatitis B, and measles, mumps, rubella (MMR) vaccinations prior to use of biologic agents.[3]

'Biosimilars'

Biosimilars are medications almost identical in structure to biologic agents produced by different pharmaceutical companies. Due to a lower production cost, biosimilars are now recommended ahead of biologic agents.

Studies thus far have shown that biosimilars have a similar mechanism of action and safety/side effect profile to the standard biologic agents.

RECOMMENDATIONS FOR BIOLOGIC AGENT MONITORING AND GENERAL ADVICE IN SHARED CARE

The most common side effect experienced by patients on biologic agents is irritation at the injection site (affecting ≤30% of patients). Allergic reactions following intravenous infusions have been reported but are infrequent.[4]

A flu-like illness or upper respiratory tract or gastrointestinal (GI) tract symptoms (nausea, diarrhoea) may occur. Headache has also been noted in some patients.[1]

As with any immunomodulatory agent, the main risk of biologic use is infection due to immunosuppression; this includes TB and fungal infections, as well as common bacterial infections.[5]

Key points in the care of a patient on an immunomodulatory biologic agent are summarised as follows.

Table 1. Summary of biologic agents licensed for the treatment of inflammatory arthritis[3,4]

Drug name	Brand name	Mechanism of action	Licensed indication for IA	Route of administration	Specific cautions
Infliximab[a]	Remicade® Inflectra®[b] Remsima[b]	Anti-TNF	RA, PsA, AS	IV	FBC and LFT monitoring Risk of TB reactivation
Etanercept[a]	Enbrel® Benepali®[b]	Anti-TNF	RA, PsA, AS	S/C	
Adalimumab[a]	Humira®	Anti-TNF	RA, PsA, AS	S/C	
Certolizumab Pegol	Cimzia	Anti-TNF	RA, PsA, AS	S/C	
Golimumab	Simponi®	Anti-TNF	RA, PsA, AS	S/C	
Tocilizumab	RoActemra	Anti-IL-6	RA	IV or S/C	Lipid monitoring Reduced CRP response to infection
Abatacept	Orencia®	Anti-CD28	RA	IV or S/C	
Rituximab	Mabthera	Anti-CD20	RA	IV	Rarely can cause PML — alert specialist if neurological symptoms develop

[a]Most commonly used. [b]Biosimilar drugs that are licensed in the UK — see text. AS = ankylosing spondylitis. CD = cluster of differentiation. CRP = C-reactive protein. FBC = full blood count. IL = interleukin. IV = intravenous. LFT = liver function test. PML = progressive multifocal leukoencephalopathy. PsA = psoriatic arthritis. RA = rheumatoid arthritis. S/C = subcutaneous. TNF = tumour necrosis factor.

General points

- Patients should be advised to seek medical attention urgently if symptoms of infection develop.
- Patients with symptoms of infection should stop their biologic treatment until medical advice is sought.
- Advice should be given to avoid contact with those suffering from chickenpox or shingles.
- Regular influenza and pneumococcal immunisations are advised.
- Live vaccinations should be avoided; if clinically indicated, specialist advice should be sought.
- With regards to travel, patients must ensure they are up to date with appropriate vaccinations, and caution must be taken regarding storage of biologic drugs (certain drugs need refrigeration and can only be kept at room temperature for short time durations).
- Long-term use of certain biologic agents can increase malignancy risk, such as lymphoma and skin cancers, so a high index of suspicion is needed for timely diagnosis.
- If LFTs are within normal limits, low-to-moderate alcohol consumption is permitted (but caution should be taken if the patient is also taking methotrexate).
- Smoking cessation advice and support is advised because studies have shown improved efficacy of biologic agents following smoking cessation.

Holding therapy and seeking specialist advice

- If the patient develops symptoms (for example, flu-like illness or gastrointestinal upset) following biologic dosing, this should be discussed with the specialist team if there are concerns regarding potential side effects.
- If a patient has evidence of active infection requiring antibiotic/antifungal therapy (regardless of severity), the GP should hold the biologic agent and treat the infection urgently; advice should be sought from the specialist rheumatology team regarding when the biologic agent can be restarted.
- Note that patients on immunosuppressive therapies may not respond to the standard short course of antibiotics and may require a longer treatment duration (refer to local antibiotic guidelines for antibiotic choice and duration).
- If there are symptoms of viral illnesses, consider holding the biologic agent if dose is due imminently and seek advice from the rheumatology specialist team.
- The frequency of blood monitoring should be specified by the specialist rheumatology team; if there are any relevant abnormal parameters in the blood results (such as neutropenia or elevated LFTs), advise the patient to hold their treatment and contact the specialist team for advice.
- Biologic agents should be stopped in a timely manner prior to elective surgery, according to drug half-life, as they can impair wound healing and increase infection risk — this should be a joint decision between the surgical and rheumatology teams.
- Some biologic agents are contraindicated in pregnancy; advice regarding pregnancy should be discussed with the specialist rheumatology team.

CONCLUSION

Primary care physicians are usually the first point of access for patients with chronic conditions. Over recent years there have been significant changes to the way IA is managed. The advent of biologic agents has provided an effective therapy for patients with poorly controlled disease on more conventional DMARDs. An understanding of biologic agents by primary care physicians is vital for a successful 'shared care' model for such diseases, especially with regards to identifying comorbid signs and symptoms in patients already established on treatment.

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