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REVIEW PAPER

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Infliximab in therapy of inflammatory bowels diseases

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ABSTRACT

Introduction. Infliximab is a monoclonal antibody that acts against tumor necrosis factor TNF-α. The drug is used in the treatment of autoimmune diseases.

Aim. This article reviewed the efficacy and safety of infliximab for the treatment in severe ulcerative colitis. This review included studies that evaluated the clinical use of infliximab.

Material and methods. This meta-analysis was performed according to systematic literature search of three major bibliographic databases (Scopus, PubMed, and Cochran).

Results. Infliximab has been approved by the US Food and Drug Administration (FDA) as a medicine to treat Leśniowski and Crohn's disease, ulcerative colitis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and rheumatoid arthritis. However, further trials are required to compare other parameters of efficacy such as the clinical response with infliximab.

Conclusion. In patients suffering from Crohn's disease or ulcerative colitis under infliximab maintenance therapy, sustained good trough levels are associated with: better response and remission rates, more mucosal healing and less loss of response.

Keywords. infliximab, TNFα, ulcerative colitis

Introduction

There is still a need to develop new effective medications for the treatment of ulcerative colitis, particularly for patients who are intolerant or resistant to first line therapies.[1-5] Current pharmacotherapy for inflammatory bowel diseases are: derivatives of 5-aminosalicylic acid; glucocorticoids; purine analogs; antibiotics, metronidazole, quinolones and biological treatment anti-TNFα antibodies (infliximab, adalimumab, certolizumab). Infliximab is a chimeric immunoglobulin G1 (IgG1κ monoclonal antibody), monoclonal antibody which contains a human constant region and a mouse-derived murine variable region. Infliximab (molecular weight of approximately 149.1 kilodaltons) is specific for hu-

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Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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man tumor necrosis factoralpha (TNFα).[6-8] Infliximab is clinically used as lyophilized concentrate for injection and get approval in 1998. The drug cannot be administered orally, because the digestive system destroys the active part of the drug. Infliximab is administered by intravenous infusion.[9-12] Tumor necrosis factor α; TNF-α, is one of the main mediators in inflammatory processes and plays an important role in the pathogenesis of many chronic inflammatory diseases - rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis or juvenile idiopathic arthritis.[13-17] The introduction of anti-TNF-α drugs into clinical practice has opened a new era in the treatment of chronic inflammatory diseases.[18-23]

Material and methods

Major bibliographic databases (Scopus, PubMed, and Cochran) were searched for the newest information about infliximab.

Results

A group of biological drugs that are known as TNF antagonists include human anti-TNF-α (adalimumab), chimerized, mouse-human anti-TNF-α (infliximab) antibodies, as well as fusion proteins that competitively bind to the TNF-membrane receptor α (etanercept).[24-27] TNF promotes the inflammatory response in rheumatoid arthritits, ankylosing spondylitis, Crohn's disease, ulcerative colitis and psoriasis. Inflammatory Bowel Disease (IBD) Infliximab neutralizes the biological activity of TNFα by binding to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors. Anti-TNF drugs such as infliximab also induce the formation of anticardiolipin antibodies (aCL).[28-32] Both of these drugs have approximately similar capacity to induce these antibodies. Inflammatory response has been shown to be ineffective in patients with aCL. Infliximab is approved for severe cases of rheumatoid arthritis, together with methotrexate, for pronounced psoriasis and psoriasis-arthritis, ankylosing spondylitis as well as for chronic inflammatory bowel disease.[33-43]

Generally, it is advantageous that infliximab be dosed with concomitant methotrexate to inhibit the formation of antidrug antibodies.[32-35] It is also thought that the concurrent dosing of methotrexate during the study reduces such immunogenicity. Infliximab has negative side effects, some are life-threatening, they are common to all drugs in the immunosuppressive class of TNF. Some of the most severe side effects are: serious infections, reactivation of hepatitis B reactivation of tuberculosis, lethal liver lymphoma (usually only in combination with 6-mercaptopurine), lupus, demyelination of the central nervous system, psoriasis and skin changes and new cases of vitiligo. Studies in both psoriatic arthritis and rheumatoid arthritis have established better patient outcomes using combination therapies with methotrexate. Lower doses of TNF-α antagonists are also more cost-effective for the patient. Infliximab has been associated with hepatosplenic T-cell lymphoma in inflammatory bowel disease patients treated concurrently with azathioprine. Thus, caution should be taken in using combination treatment and should not be first line because larger clinical trials are needed. Patients receiving infliximab are more susceptible to serious infections, including mycobacterial infections. Concomitant treatment with glucocorticoids was the only independent susceptibility factor for infections in patients with inflammatory bowel disease treated with infliximab.

Table. 1 Dose of infliximab and disease[33-43]

Disease	Dose
Crohn's Disease	5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks
Pediatric Crohn's Disease	5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.
Ulcerative Colitis	5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks
Pediatric Ulcerative Colitis:	5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks. Rheumatoid Arthritis: In conjunction with methotrexate
Rheumatoid Arthritis	3 mg/kg at 0, 2 and 6 weeks, then every 8 weeks. Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks
Ankylosing Spondylitis	mg/kg at 0, 2 and 6 weeks, then every 6 weeks. Psoriatic Arthritis and Plaque Psoriasis: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks

Conclusion

In patients suffering from Crohn's disease or ulcerative colitis under infliximab maintenance therapy, sustained good trough levels are associated with: better response and remission rates, more mucosal healing and less loss of response.

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