





# Indications, response, and side effects of biologic treatment in Behçet's disease: an 8-year study with follow-up

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## Abstract

**Introduction:** The treatment of Behçet's disease has improved significantly with the introduction of biologic therapies. However, there is still a need for more information about their use. This study aimed to evaluate the indications, response, and side effects of biologic agents in patients with refractory or severe Behçet's disease in the south of Iran, their follow-up and reasons for changing the biologics.

**Material and methods:** A retrospective analysis was conducted on 44 patients aged 16–65 years who were prescribed biologic agents for at least 6 months. The clinical history, partial and complete remission at 6 and 12 months, occurrence of side effects, and need for switching to a second or third biologic agent were recorded.

**Results:** The most common indications for starting biologic agents were ophthalmic (68.2%), parenchymal brain involvement (15.9%), and arthritis (11.4%). Improvement was observed in various manifestations of Behçet's disease, with complete remission in 86, 51.6, 92.8, 66.7, 42.9, 33.3, and 80.0% of oral aphthous lesions, ophthalmic activity, genital aphthous lesions, skin activity, arthritis, brain parenchymal lesions, and vascular activity, respectively, 6 months after starting biologic agents. These rates were unchanged or increased at the 12-month follow-up. In 25.0% of patients, a switch to a second biologic agent was necessary due to severe disease, side effects, or refractory disease. Side effects occurred in 16.3% and 33.3% of patients on the first and second biologic agents, respectively. The majority of side effects were not serious.

**Conclusions:** We found a promising improvement at 6-month and 12-month follow-ups with various biologic agents in treating Behçet's disease with an acceptable safety profile.

**Key words:** Behçet's disease, biologics, anti-TNF, TNF- $\alpha$  inhibition.

## Introduction

Behçet's disease is a systemic vasculitis that presents with various unpredictable symptoms such as recurrent oral and genital aphthae, neurological disease, relapsing uveitis, and other manifestations [1, 2]. The disease can cause blindness, and the therapeutic management focuses on suppressing inflammatory exacerbations and preventing relapses [3, 4].

Severe manifestations require aggressive management with immunosuppressive and biologic agents,

alone or in combination with conventional therapies [1, 2, 5]. Some studies have shown the effectiveness of infliximab (IFX), adalimumab (ADA), and rituximab (RTX) for ocular and neurological manifestations of Behçet's disease [6–10].

However, anti-TNF agents can cause serious side effects such as bacterial infection, viral hepatitis reactivation, hypersensitivity and injection site reactivation, autoimmune disease, and neoplasm [3].

Here, we report our 8-year experience with biologic treatments in Behçet's disease patients, including the in-

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Another Japanese study showed that IFX use decreased the rates of cyclosporine, GC, and colchicine use in Behçet's patients, potentially reducing the risk of related side effects [30]. Therefore, biologic agents can efficiently decrease the need for GCs, thereby preventing their side effects, such as secondary cataracts, secondary glaucoma, and diabetes [14].

In our study, 11.4% of patients experienced blindness and 2.3% died, but these events were not caused by biologic agent failure. Rather, these patients had serious pre-existing ophthalmologic damage and poor compliance with biologic treatment.

One of the strengths of the study was the reporting of the effectiveness results for several types of involvement. Similarly to most previous studies in the literature [13–17], ophthalmic activity of Behçet's disease was the most common reason for starting biologic therapy in this study, followed by CNS parenchymal involvement. In addition, our study had limitations, including a short follow-up period and a small sample size. Additionally, we did not measure anti-biologic agent antibodies.

Due to the differences in the study design, treatment protocols, and patient characteristics, we were unable to compare the effectiveness of different biologic agents. However, we did observe the effectiveness of anti-biologic agents in inducing remission in refractory or severe Behçet's patients who were unresponsive to conventional immunosuppressive therapy.

## Study limitations

Nevertheless, the limitations of our study, including a short follow-up period and a modest sample size, underscore the need for extensive randomized controlled trials to further assess the effectiveness and safety of these agents in Behçet's disease and compare different biologics and treatment protocols.

## Conclusions

Our study suggests that biologic agents can be an effective treatment option for patients with refractory or severe Behçet's disease, with the potential to induce remission and decrease the need for GCs and other immunosuppressive agents.

Side effects were observed with both first and second biologic agents, but most were not serious. A quarter of patients required switching to a second biologic agent due to severe disease or side effects.

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