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INVITED REVIEW

The use of glucocorticoids in Behçet's disease

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ABSTRACT

Behçet's disease (BD) is a chronic, multifactorial inflammatory disorder characterized by episodic involvement of multiple systems, including mucocutaneous, ocular, vascular, gastrointestinal, joint, and neurological domains. Glucocorticoids (GC) play a pivotal role in managing BD, especially during acute flares and severe organ involvement. This review highlights the tailored use of GC across various manifestations of BD. For mucocutaneous lesions, topical GC are effective, where as short-term low-dose systemic GC are reserved for colchicine-resistantcases. In ocular BD, systemic GC are in dispensable for sight-threatening conditions, often combined with disease-modifying anti-rheumatic drugs (DMARDs) or biologics to minimize GC dependency. In vascular involvement, particularly pulmonary artery aneurysms, high-dose or pulse GC are essential to control vessel wall inflammation, often alongside immunosuppressive agents like cyclophosphamide. Neurological BD necessitate surgent high-dose GC therapy, complemented by DMARDs for sustained control. Joint involvement can be managed with intraarticular GC, reducing systemic exposure. In gastrointestinal BD, GC use is limited due to potential mucosal irritation, with biologics and DMARDs serving as adjunctive options. Across all manifestations, GC tapering is prioritized to mitigate adverse effects, while combination therapy with DMARDs or biologics ensures comprehensive disease control. This comprehensive review underscores the critical role of GC in BD management, advocating for individualized treatment strategies to balance efficacy and safety.

Keywords: Behçet's disease, glucocorticoids, anti-inflammatory agents, mucocutaneous lesions, vascular, ocular, systemic inflammation, immunomodulatory treatment.

Introduction

Behçet's disease (BD) is a multifactorial, chronic inflammatory disease with an unknown etiopathogenesis, characterized by recurrent manifestations of oral and genital aphthousulcers, uveitis, erythema-nodosum-like lesions, arthritis, and involvement of major vessels, gastrointestinal, and central nervoussystems [1,2]. Given its natural course as a relapsing and remitting disease, the primary goal of treatment is to suppress flare-ups and prevent long-term damage. Treatment options include immunomodulatory agents, primarilyglucocorticoids (GC), disease-modifying anti-rheumaticdrugs (DMARDs), and biologics. The treatment regimen should be tailored to the patient's characteristics (such as gender, age, fertility expectations, comorbidities, and major organ involvement), as well as prognostic factors and the disease's activity and severity [3]. Major organ involvement serves as a warning sign of BD, with ocular, vascular, neurologic, and gastrointestinal involvement associated with a poor prognosis, requiring the administration of immunosuppressive therapy [4,5].

Glucococorticoids are available in several forms, including topical, oral, and systemic routes. The choice of type and dosage of GC should be individualized, and the lowest effective dose should be used for the shortest possible duration to minimize adverse effects. In Figure 1, we summarize the EULAR treatment guidelines based on organ involvement and the forms of GC used [6,7].

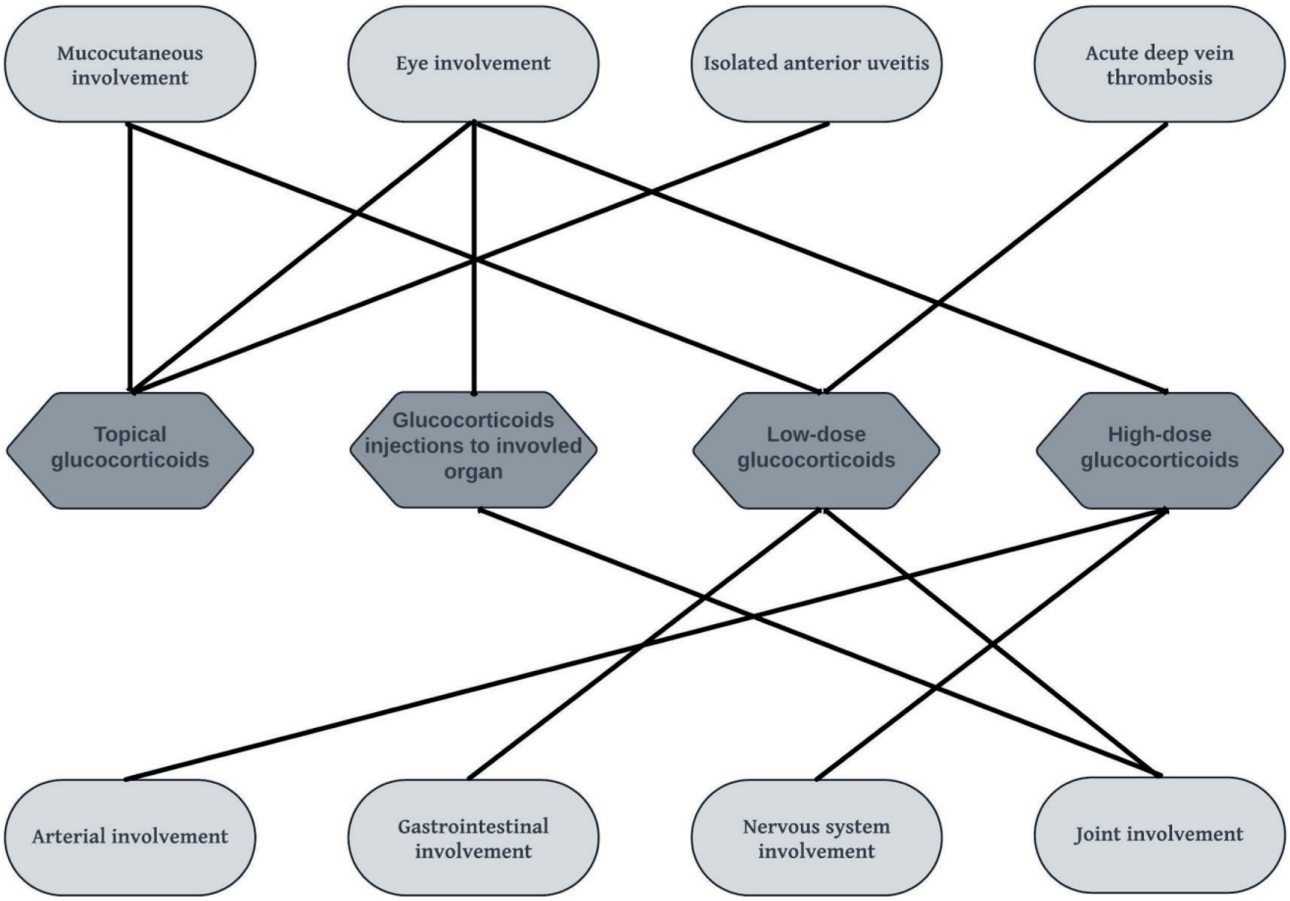

Figure 1. The main disease manifestation groups and used of glucocorticoids according to administration route and dose [7].

Glucocorticoids treatment in mucocutaneous involvement

Mucocutanous involvement includes oral aphtae, genital ulcers, papulopustular and acne-like lesions, erythema nodosum. Although colchicine is the main treatment agent for mucocutaneous involvement, glucocorticoids may also be used in various forms. For oral aphthae, genital ulcers, and papulopustular lesions, topical GC can be used without the risk of systemic adverse effects. In colchicine-resistant or intolerant patients, short-term, low-dose GC can be effective in all manifestations of mucocutaneous involvement, particularly erythema nodosum [8].

Glucocorticoids treatment in eye involvement

The prototype lesion of eye involvement in BD is uveitis, particularly affecting the posterior segment. Uveitis is more common in younger patients and males, and timely, effective treatment is crucial to suppress inflammation, prevent recurrence, and avoid permanent decrease in visual acuity or vision loss. The use and dosage of GC should be determined based on the severity of eye involvement and the presence of sight-threatening conditions. It is highly recommended to combine GC with systemic DMARDs or biologics to reduce GC dependency, and they never be used as a monotherapy [9].

Isolated anterior uveitis, on the other hand, can be managed with topical agents alone [10]. Intravitreal injections of GC may be used as an adjunctive treatment option to systemic treatment, especially in case of single-eye involvement [7]. High-dose systemic GC are employed for rapid control of acute-attacks but should be tapered as soon as the effects of concomitantly used immunosuppressive agents become apparent.

Glucocorticoids treatment in acute deep vein thrombosis

In BD patients, thrombosis is considered a result of inflammation rather than hypercoagulability. Therefore, anti-inflammatory treatment is the cornerstone of management rather than anticoagulation. The primary goals are the early and effective control of thrombosis, the preservation of vascular flow, or the achievement of re-canalization,

all of which are crucial to preventing chronic leg ulcerations and post-thrombotic syndrome. In most cases, low-dose GC and DMARDs combination is recommended and successful, but in refractory cases biologics and addition of anti-coagulant can be needed [11].

Glucocorticoids treatment in arterial involvement

The most frequent arterial involvement in BD is pulmonary artery aneurysms and thrombosis, both of which carry a high risk of increased morbidity and mortality. Aortic and peripheral aneurysms as well as rare instances of thrombosis, are also observed. In selected cases, surgical or endovascular repair, in addition to systemic treatment, may be considered. In all cases, high-dose GC should be initiated to control vessel wall inflammation and prevent complications. For pulmonary artery involvement, initial pulse GC are administered. For invasive procedures, preoperative administration of GC is crucial to enhance perioperative success and prevent postoperative complications and recurrences. Given the severity of the disease manifestations and the need for long-term immunosuppression, the addition of potent systemic agents like cyclophosphamide or TNF-alpha blockers, along with adjunctive DMARDs, should be initiated as soon as possible [12].

Glucocorticoids treatment in gastrointestinal involvement

Gastrointestinal involvement is a less common but significant manifestation of BD, requiring careful diagnostic evaluation to exclude other inflammatory and infectious causes. For the rapid healing of ulcers and control of acute exacerbations, GC can be used. However, due to their mucosal irritation effects, high-dose GC use is not recommended, particularly in cases where there is a risk of perforation. In managing these cases, a combination of locally effective agents, DMARDs, and biologics should be included in the treatment plan [13].

Glucocorticoids treatment in joint involvement

In cases of acute monoarthritis, intra articular GC can be administered after the aspiration of excess synovial fluid, there by reducing the need for systemic immunosuppressive therapy and GC. However, in cases of recurrent monoarthritis or oligo/polyarthritis that are refractory to colchicine, low-dose GC can be used in conjunction with DMARDs, for the shortest duration possible [14,15].

Glucocorticoids treatment in nervous system involvement

In both types of acute central nervous system involvement—parenchymal involvement and cerebral venous thrombosis—urgent treatment with high-dose GC is required. To better control inflammation and facilitate GC tapering, at least one DMARD should be initiated alongside GC [16].

Conclusion

In summary, for mucocutaneous involvement, topical GC are typically sufficient, with short-term low-dose GC reserved for rare, resistant cases. In joint involvement, intra articular or low-dose GC can be used as well. However, in acute flares involving the ocular, vascular, gastrointestinal, and nervous systems, GC remain the primary and life-saving initial therapy. Long-term and high-dose GC should be avoided due to their adverse effects, and the use of combinations with DMARDs and biologics, along with careful tapering, can help minimize these effects and reduce the cumulative GC dose.

Author contribution

Study conception and design: RD, CB; draft manuscript preparation: RD, CB. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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