From the Medical Board of the National Psoriasis Foundation: Perioperative management of systemic immunomodulatory agents in patients with psoriasis and psoriatic arthritis

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Treatment with systemic immunomodulatory agents is indicated for patients with moderate to severe plaque psoriasis and psoriatic arthritis. In these patients, surgery may confer an increased risk of infectious or surgical complications. We conducted a literature review to examine studies addressing the use of methotrexate, cyclosporine, and targeted immunomodulatory agents (tumor necrosis factor-alfa inhibitors, interleukin [IL]-12/23 inhibitors, IL-17 inhibitors) in patients undergoing surgery. We examined 46 total studies; the majority were retrospective studies in patients with rheumatoid arthritis and inflammatory bowel disease. One study in patients with psoriasis and psoriatic arthritis reviewed 77 procedures and did not find an elevated risk of postoperative complications with tumor necrosis factor-alfa and IL-12/23 inhibitors even with major surgeries. Based on level III evidence, infliximab, adalimumab, etanercept, methotrexate, and cyclosporine can be safely continued through low-risk operations in patients with psoriasis and psoriatic arthritis. For moderate- and high-risk surgeries, a case-by-case approach should be taken based on the patient's individual risk factors and comorbidities. (J Am Acad Dermatol 2016;75:798-805.)

Key words: biologic; cyclosporine; immunosuppressant; methotrexate; perioperative; psoriasis; psoriatic arthritis; tumor necrosis factor-alfa inhibitor.

Immunomodulatory agents are the hallmark of therapy for psoriasis and psoriatic arthritis (PsA). They include oral methotrexate (MTX) and cyclosporine along with the currently 8 Food and Drug Administration–approved targeted immunomodulatory drugs for psoriasis, PsA, or both: etanercept, adalimumab, infliximab (IFX), golimumab, secukinumab, ustekinumab, certolizumab

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pegol, and ixekizumab. The risk of infection with systemic immunomodulatory agents may be compounded in patients undergoing surgery, as surgical stress has been shown to induce widespread immune suppression and reduction in cell-mediated immunity.[1] Studies have also shown that tumor necrosis factor (TNF)-alfa promotes angiogenesis and endothelial cell and fibroblast proliferation, which are critical components of wound healing.[2]

This article, from the Medical Board of the National Psoriasis Foundation, aims to provide a comprehensive review of the literature in regards to the perioperative management of systemic immunomodulatory agents for psoriasis and PsA.

CAPSULE SUMMARY

- Surgery induces immunosuppression, which may be compounded by immunomodulatory therapy.
- The evidence supports that infliximab, adalimumab, etanercept, methotrexate, and cyclosporine can be safely continued through low-risk surgery.
- For intermediate and high-risk surgery, a case-by-case approach should be taken based on individual risk factors and comorbidities.

METHODS

Given the paucity of studies in patients with psoriasis and PsA, our review included relevant studies in other chronic inflammatory disorders, namely, rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). A systematic search of the MEDLINE PubMed database was performed during the period covering January 1, 1970, to November 27, 2015, using the medical subject headings (MeSH) search ("Psoriasis/surgery"[MeSH] OR "Arthritis, Rheumatoid/surgery"[MeSH] OR "Inflammatory Bowel Diseases/surgery"[MeSH] OR "Colitis, Ulcerative/surgery"[MeSH] OR "Crohn disease/surgery"[MeSH] OR "Spondylitis, Ankylosing/surgery"[MeSH]) AND ("Tumor Necrosis Factor-alpha/antagonists and inhibitors"[MeSH] OR "Antibodies, Monoclonal"[MeSH] OR "Biological Products"[MeSH] OR "Immunosuppressive Agents"[MeSH] OR "Anti-Inflammatory Agents"[MeSH] OR "Antirheumatic Agents"[MeSH] OR "Perioperative Care"[MeSH] OR "Postoperative Complications"[MeSH]). For articles not MeSH indexed another search was performed using the general search terms "perioperative" and "biologic," "methotrexate," "cyclosporine," "TNF-inhibitor," "tumor necrosis factor-alpha inhibitor," "IL-17 inhibitor," "IL-23 inhibitor," "etanercept," "adalimumab," "infliximab," "ustekinumab," "golimumab," "secukinumab," "certolizumab pegol," "apremilast," "psoriasis," "psoriatic arthritis," "rheumatoid arthritis," "Crohn's disease," "ulcerative colitis," "inflammatory bowel disease," and "ankylosing spondylitis." All original studies regarding the perioperative use of MTX, cyclosporine, or biologics were included.

The categorization and grading of evidence were based on guidelines by Shekelle,[3] with category Ia evidence being meta-analysis of randomized controlled trials; category Ib being at least 1 randomized controlled trial; category IIa being at least 1 controlled study without randomization; category IIb being at least 1 other type of quasiexperimental study; category III being nonexperimental descriptive studies; and category IV being expert committee reports or clinical experience from respected authorities. Grading the strength of recommendation is then based on categories of evidence, with grade A being based on category I evidence; grade B based on category II evidence or extrapolation from category I evidence; grade C based on category III evidence or extrapolation from category I or II evidence; and grade D based on category IV evidence or extrapolation from category I, II, or III evidence.

RESULTS

Our search yielded 5444 results; 5398 articles were excluded as they were not original studies addressing the perioperative complications of MTX, cyclosporine, or targeted immunomodulatory agents in patients with psoriasis, PsA, RA, or IBD (Fig 1). We examined 46 total studies; nearly all were retrospective studies for patients with IBD and RA, supporting grade C recommendations. In this review, we specifically discuss the studies for patients with psoriasis and RA. The data from patients with IBD were also included in the formulation of our recommendations and included in separate tables.

TNF-alfa inhibitor or interleukin-12/23 inhibitor therapy: Evidence from psoriasis

There are 3 studies (240 patients) to date regarding the perioperative use of TNF-alfa inhibitors or interleukin (IL)-12/23 inhibitors in patients with psoriasis. Reinstadler et al[4] performed a retrospective chart review of 19 elective surgeries (6 major, 13 minor) in patients with psoriasis receiving a TNF-alfa inhibitor. None of the patients were recipients of any other immunosuppressive medications. Of 5 operations in which the TNF-alfa inhibitor therapy was discontinued 1 to 2 weeks