Considerations for the Use of Biologics in Pregnancy

Marita Yaghi, MD; Emi M. Murase; Jenny E. Murase, MD

Biologics have revolutionized dermatologic treatment, offering substantial relief from chronic and debilitating skin conditions such as psoriasis, hidradenitis suppurativa, atopic dermatitis (AD), chronic urticaria, and immunobullous diseases (eg, pemphigus vulgaris, bullous pemphigoid). By drastically decreasing symptom burden, biologics have the potential to transform patients' lives by improving their overall quality of life (QOL). However, the use of biologics during pregnancy raises critical considerations, especially regarding safety.

Biologics for Cutaneous Conditions

Biologics—tumor necrosis factor (TNF) α inhibitors; IL-17, IL-23, IL-12, and IL-36 inhibitors; and agents such as omalizumab and dupilumab—have shown remarkable efficacy in controlling severe or recalcitrant dermatologic conditions and typically are more effective than traditional systemic therapies.[1] For instance, randomized clinical trials (RCTs) and real-world data have shown that patients with psoriasis can achieve considerable skin clearance with biologics, greatly enhancing QOL.[2] Adalimumab and secukinumab, which have been approved for use in moderate to severe cases of hidradenitis suppurativa, reduce the frequency of painful nodules and abscesses, thereby decreasing pain and improving QOL. Dupilumab, an IL-4/13 receptor antagonist, has revolutionized the treatment of AD by drastically reducing itch and skin lesions and improving QOL.[3] For chronic urticaria, the anti-IgE antibody omalizumab has effectively reduced the incidence of hives and itching, providing pronounced symptom relief when traditional antihistamines fail.[4] Use of rituximab, an anti-CD20 monoclonal antibody, has led to remission in severe cases of pemphigus vulgaris and bullous pemphigoid.[5]

Impact of Untreated Cutaneous Conditions in Pregnancy

When treating patients who are pregnant, dermatologists must consider the health of both the expectant mother and the developing fetus. This dual focus complicates decision-making, particularly with the use of biologics. Untreated cutaneous conditions can profoundly impact a pregnant patient's health and QOL as well as lead to pregnancy complications affecting the fetus, such as preterm birth or low birth weight. In some studies, moderate to severe psoriasis has been associated with increased risk for complications during pregnancy, including preeclampsia and intrauterine growth restriction.[6] Although specific data on hidradenitis suppurativa are lacking, the highly inflammatory nature of the condition suggests similar adverse effects on pregnancy.[7] Atopic dermatitis can be exacerbated during pregnancy due to a shift in the immune system to become more allergic dominant.[8] Generalized pustular psoriasis manifests with widespread pustules, fever, and systemic inflammation, posing serious risks to both the mother and the fetus if left untreated[9]; in such a life-threatening scenario, the use of potent treatments such as spesolimab, an IL-36 receptor antagonist, may be warranted. Therefore, managing these conditions effectively is crucial not only for the mother's health but also for fetal well-being.

Dr. Yaghi is from the Department of Internal Medicine, Mount Sinai Medical Center, Miami Beach, Florida, and the Department of Dermatology, Larkin Community Hospital, South Miami, Florida. Emi M. Murase is from the Department of Genomics, University of California, Davis. Dr. Murase is from the Department of Dermatology, University of California, San Francisco, and the Palo Alto Foundation Medical Group, Mountain View, California.

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Correspondence: Marita Yaghi, MD, Mount Sinai Medical Center, 4300 Alton Rd, Miami Beach, FL 33140 (maritayaghi@outlook.com).

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Which Biologics Can Dermatologists Safely Prescribe?

Despite the benefits, many dermatologists are hesitant to prescribe biologics to pregnant patients due to the lack of understanding and definitive safety data.[10,11] Although there are no RCTs that involve pregnant patients, current evidence suggests that several biologics are not teratogenic and do not cause fetal malformations. Extensive postexposure data support the safety of TNF-α inhibitors during pregnancy.[12] Research has shown that children exposed to these agents in utero have normal development, infection rates, and vaccination outcomes comparable to nonexposed children. For example, a systematic review and meta-analysis found no significant increase in the risk for major congenital malformations, spontaneous abortions, or preterm births among patients exposed to anti–TNF-α agents during pregnancy.[2] The Organization of Teratology Information Specialists Autoimmune Diseases in Pregnancy Project has provided valuable real-world data indicating that the use of TNF-α inhibitors in pregnancy, particularly during the first trimester, does not substantially elevate the risk for adverse outcomes.[13] These findings have been corroborated by several other registry studies and RCTs, providing a robust safety profile for these agents during pregnancy.[14]

Similarly, postexposure data on IL-17 and IL-12/23 inhibitors indicate a favorable safety profile, though the sample sizes are smaller than those for anti–TNF-α agents.[12,14] Studies of drugs such as secukinumab (IL-17 inhibitor), guselkumab (IL-23 inhibitor), or ustekinumab (IL-12/23 inhibitor) have shown no association with teratogenic effects or increased risk for miscarriage.[14] However, agents such as spesolimab (IL-36 inhibitor) are relatively new, and ongoing studies are expected to provide more comprehensive safety data.[15] Similarly, omalizumab and dupilumab have not been associated with increased risk for fetal malformations or adverse pregnancy outcomes. Omalizumab, indicated for chronic urticaria, has a good safety profile in pregnancy, with no significant increase in adverse outcomes reported in studies and registries.[16] Dupilumab, used for AD, has demonstrated safety in pregnancy, with ongoing studies continuing to monitor outcomes.[17]

Conversely, rituximab (an anti-CD20 antibody for autoimmune bullous diseases) has shown evidence of adverse pregnancy outcomes, including fetal harm.[18] Its use generally is discouraged unless deemed absolutely necessary, and no safer alternatives are available. Rituximab can cross the placenta, especially in the second and third trimesters, and has been associated with B-cell depletion in the fetus, leading to potential immunosuppression and increased risk for infections.[5]

Although the data on the safety of biologics in pregnancy are largely reassuring, it is essential to recognize that potential risks have not been ruled out entirely. There are extensive safety data for anti–TNF-α inhibitors, which provides a level of confidence; although newer agents such as IL-17 and IL-23 inhibitors have shown promising early results, further research is required to solidify their safety profiles during pregnancy.

Dermatologists must balance the risks and benefits of using biologics in pregnant patients. This decision-making process involves careful consideration of the severity of the mother's condition, the potential risks to the fetus, and the availability of alternative treatments. For many severe dermatologic conditions, the benefits of biologics in controlling disease activity and improving QOL may outweigh the potential risks, especially when other treatments have failed or are not suitable.

Final Thoughts

The increasing use of biologics in dermatology has undoubtedly improved the management of severe skin conditions, substantially enhancing patients' QOL. As more data become available and clinical guidelines evolve, health care providers will be better equipped to make informed decisions about the use of biologics, particularly in pregnant patients. Collaborative efforts between dermatologists, obstetricians, and researchers will help refine treatment guidelines and ensure that pregnant patients with severe dermatologic conditions receive the best possible care.

For now, although the current evidence supports the safety of many biologics during pregnancy,[10,11] individualized care and informed decision-making remain paramount. Careful management and adherence to current guidelines make it possible to navigate the complexities of treating severe dermatologic conditions in pregnant patients, ensuring the best outcomes for both mother and child.

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