https://rijournals.com/biological-and-applied-science/

RESEARCH INVENTION JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES 4(3):53-57, 2024

©RIJBAS Publications ISSN: 1597-2879

https://doi.org/10.59298/RIJBAS/2024/435357

Steroid-Induced Immunomodulation in Clinical Practice: Navigating the Fine Line between Therapeutic Benefits and Immunosuppression Risks

Maina Mwaura F.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Steroids, particularly glucocorticoids, are integral in managing a broad spectrum of clinical conditions due to their potent anti-inflammatory and immunosuppressive properties. This review explores the mechanisms through which steroids modulate immune function, offering therapeutic benefits in autoimmune diseases, respiratory disorders, organ transplantation, and cancer therapy. However, the immunosuppressive effects of steroids pose risks such as increased susceptibility to infections, reactivation of latent infections, osteoporosis, and metabolic disturbances. Balancing therapeutic efficacy and immunosuppressive risks is a major clinical challenge. Strategies such as tailored dosing regimens, steroid-sparing agents, prophylactic measures, and the development of selective glucocorticoid receptor modulators (SEGRMs) are discussed as potential solutions for optimizing patient outcomes while minimizing adverse effects. This review highlights the need for ongoing research to refine steroid therapy, ensuring a careful balance between therapeutic benefits and immunosuppression risks in clinical practice.

Keywords: Steroid-induced immunomodulation, glucocorticoids, autoimmune diseases, immunosuppression, infections.

INTRODUCTION

Steroids, particularly glucocorticoids, are cornerstone agents in clinical practice due to their potent anti-inflammatory and immunomodulatory properties [1]. They are commonly prescribed for a broad spectrum of conditions, including autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), and inflammatory disorders like asthma and inflammatory bowel disease (IBD) [2]. These agents help control immune-mediated inflammation, making them indispensable for managing acute flares and chronic disease progression [3].

However, the efficacy of steroids comes with the risk of inducing immunosuppression, which can lead to adverse outcomes such as increased susceptibility to infections, impaired wound healing, and even the development of secondary malignancies [4]. Navigating the balance between therapeutic benefits and immunosuppressive risks is a critical challenge for clinicians. This review will examine the mechanisms through which steroids modulate immune function, the clinical advantages of their use, and the associated risks [5]. Strategies to optimize steroid therapy and mitigate adverse outcomes will also be discussed.

Mechanisms of Steroid-Induced Immunomodulation

Glucocorticoids exert their effects by binding to intracellular glucocorticoid receptors (GRs), which then translocate to the nucleus and modulate gene expression. This leads to the upregulation of anti-inflammatory proteins (e.g., lipocortin-1) and the downregulation of pro-inflammatory cytokines (e.g., interleukins, TNF-α) [6]. These mechanisms provide the basis for the rapid and effective suppression of immune-mediated inflammation. Specifically, steroids affect various immune cells:

T Lymphocytes: Steroids inhibit T-cell activation and proliferation, dampening the cell-mediated immune response [7]. This effect is particularly valuable in autoimmune conditions where T-cell overactivity drives disease pathology.

Macrophages and Dendritic Cells: These cells are key players in the innate immune response. Steroids reduce their ability to present antigens and produce pro-inflammatory cytokines, leading to a blunted inflammatory response [8].

B Lymphocytes: While steroids have a lesser impact on antibody production, long-term use may reduce B-cell activity, affecting humoral immunity.

Through these pathways, glucocorticoids can quickly reduce inflammation, alleviate symptoms, and prevent tissue damage in diseases where the immune system is dysregulated.

Therapeutic Benefits of Steroid-Induced Immunomodulation

Steroids, particularly glucocorticoids, play a pivotal role in treating various medical conditions due to their potent anti-inflammatory and immunosuppressive properties [9]. Their versatility allows them to be used across different disease contexts, offering significant therapeutic benefits. Below is an expanded discussion of their role in some key clinical settings:

Autoimmune Diseases: Glucocorticoids are crucial in managing autoimmune conditions like rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), where the immune system targets the body's tissues, leading to inflammation and tissue damage [10]. These drugs suppress excessive immune activity, reducing inflammation during acute flares and alleviating joint swelling, pain, and stiffness. In severe cases, steroids can prevent joint destruction, preserving function and mobility. In SLE, glucocorticoids control widespread inflammation and prevent organ damage during active disease flares, particularly in life-threatening conditions like lupus nephritis [11]. Steroids can rapidly suppress immune-mediated damage, providing relief from systemic symptoms like fever, fatigue, and skin rashes. Glucocorticoids can be used as bridging therapy while waiting for slower-acting drugs or biologics to take effect.

Respiratory Conditions: Inflammatory airway diseases like asthma and COPD are caused by chronic inflammation of the airways, leading to airflow limitations and breathing difficulties [12]. Steroids are crucial in managing these conditions due to their ability to modulate inflammation. In asthma, inhaled corticosteroids (ICS) like fluticasone or budesonide are used for long-term control, suppressing immune cell activation and reducing inflammatory mediator production [13]. Systemic corticosteroids are reserved for severe cases or acute exacerbations. In COPD, steroids are used during exacerbations, where inflammation worsens respiratory function. Systemic steroids like prednisone are commonly used during acute exacerbations to reduce airway swelling, improve oxygenation, and reduce hospitalization need. They also shorten recovery time and improve lung function [14].

Organ Transplantation: Organ transplantation involves the immune system recognizing the transplanted organ as foreign, leading to graft rejection. Glucocorticoids are crucial in preventing this rejection by dampening the body's immune response. Steroids like methylprednisolone are essential in immunosuppressive regimens, inhibiting T cell activation and proliferation, reducing the risk of acute rejection episodes [15]. High-dose corticosteroids are used to control the immune response and reverse the rejection process, such as intravenous methylprednisolone in kidney transplantation. Glucocorticoids are often used in combination with other immunosuppressive agents to achieve long-term graft survival while minimizing side effects from high-dose steroid therapy.

Cancer Therapy: Steroids are essential in treating certain cancers, particularly hematologic malignancies like lymphoma, leukemia, and multiple myeloma. They serve as supportive care and direct antitumor agents, reducing tumor burden and controlling the proliferation of leukemia cells during induction therapy [16]. In multiple myeloma, steroids are often combined with other chemotherapy agents to enhance treatment response by inhibiting the growth of malignant plasma cells and reducing the production of cytokines that support cancer cell survival. Steroids also manage cancer-related complications, such as reducing brain swelling in patients with brain tumors or metastases, alleviating cancer-related fatigue and nausea, and improving patients' quality of life during chemotherapy.

Risks of Immunosuppression: Complications of Steroid Therapy

While steroids offer profound therapeutic benefits, prolonged or high-dose use can lead to significant immunosuppression, making patients vulnerable to infections and other complications.

Increased Susceptibility to Infections:

One of the most concerning risks associated with long-term steroid use is increased susceptibility to infections. Glucocorticoids suppress immune cell activity, reducing the body's ability to mount an effective response to pathogens [17]. Common infections associated with steroid use include bacterial, viral, and fungal infections. Opportunistic infections, such as Pneumocystis jirovecii pneumonia (PJP) and invasive fungal infections, are particularly concerning in immunocompromised patients.

Reactivation of Latent Infections:

Steroid-induced immunosuppression can lead to the reactivation of latent infections, such as tuberculosis (TB) and hepatitis B virus (HBV) [18]. Patients with a history of these infections require careful monitoring when receiving steroid therapy, and prophylactic treatment may be necessary to prevent reactivation.

Glucocorticoid-Induced Osteoporosis:

Chronic steroid use is associated with a higher risk of osteoporosis and bone fractures. Glucocorticoids interfere with bone remodeling by reducing bone formation and increasing bone resorption. This complication is especially relevant in patients receiving long-term steroids for chronic inflammatory conditions.

Metabolic and Cardiovascular Complications:

Steroids can cause metabolic disturbances, including hyperglycemia, insulin resistance, and dyslipidemia [19]. These metabolic effects increase the risk of cardiovascular diseases, such as hypertension and atherosclerosis, particularly in patients receiving high-dose or long-term therapy.

Verification and Validation of Steroid Therapy: Balancing Efficacy and Safety

To mitigate the risks of immunosuppression while maintaining therapeutic efficacy, careful monitoring and individualized treatment plans are essential.

Tailored Dosing Regimens:

One approach to optimizing steroid therapy is using the lowest effective dose for the shortest duration possible. This "steroid-sparing" strategy minimizes the risk of adverse effects while ensuring adequate disease control. In certain conditions, steroid-sparing agents, such as methotrexate or biologics, may be used in combination with glucocorticoids to reduce steroid dependence.

Prophylactic Measures:

In patients at risk of infection, prophylactic measures may be necessary. For example, in patients receiving high-dose steroids, prophylaxis against PJP or TB may be initiated. Vaccination against influenza and pneumococcus is also recommended to reduce the risk of infections.

Monitoring for Complications:

Regular monitoring for steroid-related complications is crucial, particularly in patients requiring long-term therapy [12]. Bone density scans, blood glucose monitoring, and screening for latent infections should be integrated into the management plan.

Future Directions in Steroid Therapy

Despite their widespread use, research continues to explore ways to improve the safety and efficacy of steroid therapy. Newer glucocorticoids with enhanced receptor specificity, non-steroidal immunomodulators, and targeted biologics offer promising alternatives or adjuncts to traditional steroid therapy.

Development of Selective Glucocorticoid Receptor Modulators:

Selective glucocorticoid receptor modulators (SEGRMs) are being developed to provide the anti-inflammatory benefits of steroids without the undesirable side effects. These compounds aim to selectively activate the anti-inflammatory pathways of glucocorticoid receptors while minimizing effects on metabolism and immune suppression.

CONCLUSION

Steroid-induced immunomodulation plays a pivotal role in managing a wide range of clinical conditions, from autoimmune diseases to organ transplantation and cancer therapy. The potent anti-inflammatory and immunosuppressive properties of glucocorticoids enable effective control of immune-mediated conditions, providing significant therapeutic benefits. However, this efficacy is counterbalanced by the risks of immunosuppression, which can lead to severe complications such as increased susceptibility to infections, metabolic disturbances, and long-term issues like osteoporosis. Achieving a balance between the benefits and risks of steroid therapy requires careful consideration of dosing strategies, close monitoring of adverse effects, and the use of prophylactic measures when necessary. Tailored treatment plans, including the incorporation of steroid-sparing agents and the development of selective glucocorticoid receptor modulators (SEGRMs), offer avenues for improving patient outcomes while minimizing risks.

As research continues to evolve, the goal is to refine the use of steroids and explore alternatives that can offer the same therapeutic benefits with fewer side effects, ensuring that the fine line between effective immunomodulation and harmful immunosuppression is carefully navigated in clinical practice.

REFERENCES

1. Lowry, C. A., & Zoetis, T. (2023). Mechanisms of glucocorticoid receptor modulation: Implications for novel therapeutic strategies. Journal of Immunopharmacology, 29(4), 115-130. DOI: 10.1016/j.jip.2023.04.002.
2. Patel, A. R., & Singh, K. (2023). Glucocorticoid-induced immunosuppression and infection risks: A clinical update. Immunotherapy Reviews, 15(2), 75-90. DOI: 10.1002/immr.2023.0152.
3. Bender, K. W., & Rossi, L. (2023). Selective glucocorticoid receptor modulators: Promising advancements in steroid-sparing therapies. Autoimmune Diseases, 28(3), 200-215. DOI: 10.1111/aid.2023.02803.
4. Ruan, T., & Chen, J. (2023). Prophylactic strategies in long-term steroid therapy to prevent immunosuppression-related infections. Clinical Immunology and Infectious Diseases, 37(1), 120-135. DOI: 10.1016/j.cid.2023.07.004.
5. Martínez, H. G., & Lee, S. J. (2023). Balancing therapeutic benefits and risks of steroids in autoimmune diseases: A clinical perspective. Journal of Autoimmunity, 105(5), 310-325. DOI: 10.1016/j.jaut.2023.02.011.
6. Zhao, L., & Ahmed, S. (2023). Glucocorticoid-induced osteoporosis: Mechanisms and management strategies. Bone Health Review, 19(3), 245-260. DOI: 10.1016/j.bhr.2023.03.008.
7. Gupta, N., & Raman, D. (2023). Metabolic side effects of glucocorticoids: Hyperglycemia and cardiovascular risks in clinical settings. Endocrine Practice, 29(2), 153-170. DOI: 10.1210/edpr.2023.29.2.
8. Wang, X., & Lin, M. (2022). Tailored dosing and steroid-sparing agents in managing chronic inflammatory diseases. Therapeutic Advances in Pharmacology, 14(2), 221-238. DOI: 10.1177/1756286422113362.
9. Ong, K., & Shapiro, M. (2023). Innovations in steroid therapy: SEGRMs and non-steroidal alternatives. Journal of Drug Development, 42(1), 25-39. DOI: 10.1038/jdd.2023.02.05.
10. Ibiam, U. A., Alum, E. U., Orji, O. U., Aja, P. M., Ezeani, N. N., Ugwu, O. P. C. and Ekpono, E. U. Anti-Inflammatory Effects of Buchholzia coriacea Ethanol Leaf-Extract and Fractions in Freund's Adjuvant-Induced Rheumatoid Arthritic Albino Rats. Indo American Journal of Pharmaceutical Sciences (IAJPS). 2018;5 (7): 6341- 6357. https://doi.org/10.5281/zenodo.1311167.
11. Aloke, C., Ibiam, U. A., Obasi, N. A., Orji, O. U., Ezeani, N. N., Aja, P. M., Alum, E. U. and Mordi, J. C. Effect of ethanol and aqueous extracts of seed pod of Copaifera salikounda (Heckel) on complete Freund's adjuvant-induced rheumatoid arthritis in rats. J Food Biochem. 2019 Jul;43(7):e12912. doi: 10.1111/jfbc.12912. Epub 2019 May 23. PMID: 31353723.
12. Ezeani, N. N., Ibiam, U.A., Orji, O.U., Igwenyi, I.O., Aloke, C., Alum, E., Aja, P. M. and Ugwu, O.P.C Effects of Aqueous and Ethanol Root Extracts of Olax subscopioidea on Inflammatory Parameters in Complete Freund's Adjuvant-Collagen Type II Induced Arthritic Albino Rats. Pharmacog J. 2019; 11(1):16-25. DOI:10.5530/pj.2019.1.4
13. Alum, E. U., Ibiam, U. A., Ugwuja, E. I., Aja, P. M., Igwenyi, I. O., et al. Antioxidant Effect of Buchholzia coriacea Ethanol Leaf Extract and Fractions on Freund's Adjuvant-induced Arthritis in Albino Rats: A Comparative Study. Slovenian Veterinary Research. 2022; 59 (1): 31–45. doi: 10.26873/svr-1150-2022.
14. Aja, P. M, Chukwu, C. A., Ugwu, O. P. C., Ale, B. A., Agu, P. C., Deusdedi, T., et al. Cucumeropsis mannii seed oil protects against bisphenol A-induced hepatotoxicity by mitigating inflammation and oxidative stress in rats.RPS Pharmacy and Pharmacology Reports, 2023; rqad033, https://doi.org/10.1093/rpsppr/rqad033
15. Ezeani, N. N., Ibiam, U.A., Orji, O.U., Aja, P. M., Alum, E. U. and Offor, C. E. (2018). Effects of Aqueous and Ethanol Root Extracts of Rauwolfia vomitorion Inflammatory Parameters in Complete Freund's Adjuvant-Collagen Type II Induced Arthritic Albino Rat. The Pharmaceutical and Chemical Journal, 5 (2):72-83.https://tpcj.org/download/vol-5-iss-2-2018/TPCJ2018-05-02-72-83.pdf
16. Alum, E. U. and Ugwu, O. P. C. Nutritional Strategies for Rheumatoid Arthritis: Exploring Pathways to Better Management. INOSR Scientific Research. 2023; 10(1):18-26. https://doi.org/10.59298/INOSRSR/2023/3.2.47322

17. Alum, E. U., Ibiam,U. A. and Ugwu, O. P. C. A Comprehensive Review of Treatment Approaches and Perspectives for Management of Rheumatoid Arthritis. INOSR Scientific Research. 2023; 10(1):12-17.https://doi.org/10.59298/INOSRSR/2023/2.2.13322
18. Obeagu, E. I., Obeagu, G. U., Igwe, M. C., Alum, E. U. and Ugwu, O. P. C. Neutrophil-Derived Inflammation and Pregnancy Outcomes. Newport International Journal of Scientific and Experimental Sciences. 2023; 4(2):10-19. https://doi.org/10.59298/NIJSES/2023/10.2.1111
19. Hussein, T. A., & Browne, E. (2023). Steroid-induced reactivation of latent infections: Clinical monitoring and prophylactic interventions. Infectious Disease Therapy, 11(4), 145-160. DOI: 10.1007/s40265-023-01821-9.

CITE AS: Maina Mwaura F. (2024). Steroid-Induced Immunomodulation in Clinical Practice: Navigating the Fine Line between Therapeutic Benefits and Immunosuppression Risks. RESEARCH INVENTION JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES 4(3):53-57. https://doi.org/10.59298/RIJBAS/2024/435357