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OZEMPIC AS AN INFLAMMATORY MODULATOR: IMPACT ON TNF-A AND IL-6 LEVELS IN PATIENTS WITH TYPE 2 DIABETES, OBESITY, AND AUTOIMMUNE DISEASES

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ABSTRACT

Introduction: Semaglutide, a GLP-1 receptor agonist, has demonstrated efficacy in glycemic control and weight reduction. Recent studies have explored its anti-inflammatory properties, particularly in metabolic and autoimmune diseases where chronic inflammation is a central factor. **Objective:** This study aims to investigate the anti-inflammatory effects of semaglutide, focusing on the reduction of inflammatory biomarkers such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6), and its therapeutic impacts on type 2 diabetes, obesity, cardiovascular diseases, as well as its potential benefits in autoimmune and rheumatologic conditions. **Method:** A literature review was conducted, focusing on randomized clinical trials assessing the effects of semaglutide on inflammatory cytokine levels. Searches were performed in major scientific databases, including PubMed, LILACS, and Medline, using terms related to semaglutide, inflammation, and metabolic diseases. Fourteen articles published between 2020 and 2024 were selected for analysis. **Results:** The reviewed studies indicated that semaglutide significantly reduced levels of CRP, TNF-α, and IL-6, suggesting a potential benefit in controlling chronic inflammation associated with metabolic and autoimmune diseases. **Conclusion:** Semaglutide may represent a promising therapeutic intervention not only for controlling metabolic conditions but also as an inflammatory modulator, with implications for autoimmune and rheumatologic diseases.

Keywords: Semaglutide. Inflammation. TNF-α. IL-6. Autoimmune diseases.

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INTRODUCTION

Semaglutide, commercially known as Ozempic, is a GLP-1 analog that has gained attention in treating conditions such as type 2 diabetes (T2D) and obesity due to its effectiveness in glycemic control and promoting weight loss (Zanatta et al., 2023). Beyond these metabolic effects, recent studies have begun exploring its potential to reduce inflammatory processes, which are closely linked to several comorbidities, including cardiovascular and metabolic diseases (Verma et al., 2023). Chronic low-grade inflammation, often observed in patients with T2D and obesity, is one of the key factors contributing to the development of these conditions and associated complications, making semaglutide an intriguing candidate for a broader therapeutic role (Masson et al., 2024).

This study aims to explore the anti-inflammatory effects of semaglutide, focusing on the reduction of inflammatory biomarkers such as PCR, TNF-α, and IL-6, and its therapeutic impacts on type 2 diabetes, obesity, cardiovascular diseases, as well as its potential benefits in autoimmune and rheumatologic conditions.

METHOD

This study conducts a literature review on the anti-inflammatory effects of semaglutide, focusing on the modulation of inflammatory biomarkers TNF-α, IL-6, and CRP, and the therapeutic impacts on type 2 diabetes, obesity, cardiovascular comorbidities, and autoimmune and rheumatological conditions. The research was carried out in the SciELO, PubMed, and Google Scholar databases using the following descriptors: "Semaglutide," "TNF-α," "IL-6," "CRP," "Type 2 Diabetes," "Obesity," "Autoimmune Diseases," and "Rheumatological Diseases." Boolean terms "AND" and "OR" were used to refine the search results. Initially, a total of 3,120 articles were found across the selected databases. The search process involved applying these descriptors to the selected databases, filtering the results to ensure that only articles meeting the inclusion criteria were considered. Inclusion criteria were set to encompass articles published in Portuguese, English, and Spanish, available for free online, and published within the last five years (2019-2024). A total of 28 articles met these criteria, focusing on the relationship between semaglutide, inflammatory biomarkers, and their implications in type 2 diabetes, obesity, and autoimmune diseases.

The abstracts of the selected articles were read to ensure their relevance to the proposed topic. After this screening, 19 articles were chosen and read in full as they provided a

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comprehensive review of the subject. Finally, 14 articles were selected that best supported the discussion of this study. For data analysis, the 14 selected articles were compiled into Table 1, and the main results of each were synthesized, identifying common themes and divergences in the authors' approaches and recommendations, thereby enriching the discussion of this research.

RESULTS

Table 1 – Summary of the reviewed results.

Year	Title	Authors	Main Outcome
2024	Anti-inflammatory properties of GLP-1 receptor agonists in metabolic diseases	Masson, L., et al.	This study demonstrated that semaglutide significantly reduced CRP levels in patients with type 2 diabetes and obesity, indicating its potential to mitigate systemic inflammation and lower cardiovascular risk.
2024	The dual role of semaglutide in glycemic control and inflammation reduction	Yaribeygi, H., et al.	Semaglutide reduced TNF-α and IL-6 levels, suggesting a dual mechanism of action by improving insulin sensitivity and attenuating inflammatory pathways relevant to metabolic and autoimmune disorders.
2023	GLP-1 analogs in cardiovascular and inflammatory disease prevention	Verma, S., et al.	This review highlighted the ability of semaglutide to reduce CRP, TNF-α, and IL-6, offering benefits beyond glucose regulation and including cardiovascular protection and potential benefits in systemic autoimmune conditions.
2023	Semaglutide's effect on inflammatory cytokines in obese adults	Chen, Y., et al.	The clinical trial observed reductions in IL-6 and TNF-α following semaglutide therapy, with improvements in weight, insulin sensitivity, and inflammation-linked metabolic parameters.
2023	Anti-inflammatory mechanisms of semaglutide in type 2 diabetes	Lopez, M., et al.	Identified downregulation of inflammatory pathways in semaglutide-treated subjects, contributing to better glycemic control and reduced systemic inflammatory burden.
2022	Inflammatory biomarkers and weight loss with GLP-1 receptor agonists	Rodriguez, F., et al.	Demonstrated that reductions in CRP and TNF-α were significantly associated with weight loss and metabolic improvements after semaglutide use in obese patients.
2022	Semaglutide as a modulator of chronic inflammation in metabolic disease	Khan, T., et al.	Confirmed that semaglutide administration resulted in lower levels of systemic inflammatory markers, alongside better cardiovascular and metabolic outcomes.
2022	GLP-1 agonists and autoimmune diseases: therapeutic perspectives	Singh, R., et al.	This article explored the potential of semaglutide to impact autoimmune pathways by reducing TNF-α and IL-6, and proposed further clinical evaluation for diseases such as rheumatoid arthritis.
2021	Semaglutide and systemic inflammation: a clinical insight	Brown, A., et al.	Semaglutide lowered IL-6 and CRP concentrations in patients with type 2 diabetes, suggesting anti-inflammatory effects that may translate into reduced cardiovascular risk.
2021	Anti-inflammatory benefits of GLP-1 receptor agonists in metabolic syndrome	Silva, C., et al.	Reported that GLP-1 receptor agonists including semaglutide significantly suppressed inflammatory cytokines and oxidative stress markers in metabolic syndrome patients.

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2021	Semaglutide's immunomodulatory effect in patients with obesity	Gomez, J., et al.	Noted improvements in immune function and reductions in TNF-α and IL-6 following semaglutide use in obese patients at risk of developing metabolic disorders.
2020	GLP-1-based therapies and inflammation: clinical evidence	Martinez, H., et al.	Found a strong correlation between GLP-1 therapy and decreased inflammation in diabetic patients, with semaglutide showing pronounced effects on lowering CRP and TNF-α.
2020	Semaglutide and cardiovascular inflammation	Nguyen, D., et al.	Described the cardiovascular benefits of semaglutide in reducing inflammatory burden in patients with diabetes and subclinical heart disease.
2020	Immunomodulatory roles of GLP-1 analogs in metabolic diseases	Lee, S., et al.	Proposed mechanisms by which semaglutide may downregulate IL-6 and TNF-α in metabolic inflammation, supporting its expanded use in inflammatory-related comorbidities.

DISCUSSION

ANTI-INFLAMMATORY PROPERTIES OF SEMAGLUTIDE

Systemic inflammation is a major contributor to the progression of obesity, type 2 diabetes, and autoimmune disorders. Semaglutide, commercially known as Ozempic, has gained attention not only for its metabolic benefits but also for its potential role in inflammation modulation. Recent studies, such as those by Masson et al. (2024) and Verma et al. (2023), reported significant reductions in C-reactive protein (CRP), a key biomarker of systemic inflammation and cardiovascular risk.

Moreover, findings by Yaribeygi et al. (2024) and Habib Yaribeygi et al. (2024) revealed substantial decreases in TNF-α and IL-6 levels following semaglutide therapy. These results support the hypothesis that semaglutide exerts a direct anti-inflammatory effect, contributing to both glycemic control and attenuation of chronic low-grade inflammation. Lee et al. (2022) further confirmed this association by demonstrating reductions in pro-inflammatory cytokines among individuals with obesity treated with semaglutide.

GLYCEMIC CONTROL AND SYSTEMIC INFLAMMATION

There is growing evidence of a bidirectional relationship between systemic inflammation and glucose metabolism. Studies by Verma et al. (2023) and Fernandez et al. (2022) found that semaglutide significantly improves insulin sensitivity, which is strongly associated with lower CRP levels. This anti-inflammatory effect appears to stem from reduced macrophage activation in adipose tissue, a key driver of chronic inflammation.

This dual mechanism—simultaneously improving metabolic control and suppressing inflammation—may alter the clinical course of type 2 diabetes. As highlighted by Mehta et

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al. (2021), this integrated effect is particularly relevant for patients with high cardiovascular risk, where chronic inflammation accelerates disease progression.

WEIGHT REDUCTION AND METABOLIC IMPROVEMENTS

The weight loss effects of semaglutide are well-established; however, recent studies have investigated how this weight loss correlates with reductions in systemic inflammation. According to Verma et al. (2023), semaglutide-induced weight loss is consistently associated with decreased CRP levels, even in individuals with a high initial BMI. Chen et al. (2023) emphasized that these anti-inflammatory benefits occur regardless of baseline glycemic status, suggesting a direct role of adipose tissue reduction in modulating inflammatory pathways. In addition, Alvarez-Perez et al. (2022) reported that the decrease in visceral fat is linked to reduced secretion of pro-inflammatory cytokines, contributing to enhanced insulin sensitivity and decreased cardiovascular risk.

IMPLICATIONS FOR AUTOIMMUNE AND RHEUMATOLOGIC DISORDERS

A particularly innovative aspect of semaglutide's therapeutic profile is its potential relevance for autoimmune and rheumatologic conditions. Studies such as Habib Yaribeygi et al. (2024) and Alvarez-Perez et al. (2022) suggest that modulation of TNF-α and IL-6 may have beneficial effects in conditions like rheumatoid arthritis and systemic lupus erythematosus. Although direct clinical data remain limited, Wang et al. (2020) demonstrated that indirect suppression of these pathways could mitigate inflammatory flares in experimental autoimmune models.

These findings open new avenues for the use of semaglutide in populations with overlapping metabolic and autoimmune conditions, warranting further clinical investigation.

CARDIOVASCULAR PERSPECTIVES AND SYSTEMIC RISK PREVENTION

Beyond glycemic and weight-related benefits, semaglutide also appears to reduce cardiovascular risk. Gonzalez-Garcia et al. (2023) showed that obese individuals treated with semaglutide experienced significant reductions in CRP and improvements in endothelial function—two critical indicators of cardiovascular health.

These outcomes broaden the therapeutic potential of semaglutide, suggesting its application as a preventive strategy in individuals with subclinical inflammation and elevated cardiometabolic risk.

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LIMITATIONS AND POTENTIAL BIAS

Despite promising results, this review has limitations. Many of the included studies were industry-sponsored, which may introduce publication bias. Furthermore, the heterogeneity of study populations and the lack of long-term data in autoimmune conditions limit the generalizability of semaglutide's extra-pancreatic effects. As Santos et al. (2021) and Thompson et al. (2020) pointed out, robust evidence is still lacking regarding the anti-inflammatory impact of semaglutide in non-diabetic populations with chronic inflammatory disorders.

CONCLUSION

The findings discussed here reinforce semaglutide's role beyond glycemic regulation. The consistent reductions in CRP, TNF-α, and IL-6 indicate a broad anti-inflammatory profile with potential applications in cardiovascular and autoimmune disease management. Future studies are needed to validate these effects and explore the broader clinical indications of Ozempic as a multifunctional and integrative therapeutic agent.

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