ORIGINAL RESEARCH

35. Managing Hyperphagia, Obesity, and Hyperglycemia in Prader-Willi Syndrome: A Meta-Analysis of GLP-1 agonists and SGLT2 inhibitors

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https://www.youtube.com/watch?v=4rJ3DHWeKRs&list=PLhqNq3xJClbafO0Y5bvBcgMmXpgzJxd44&index=6&t=15611s

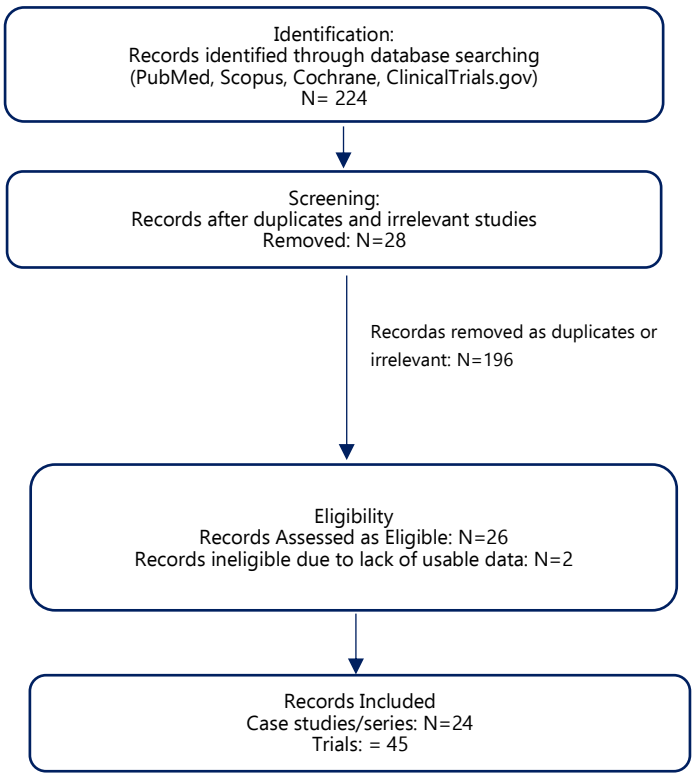
Background: Prader-Willi Syndrome (PWS) is a genetic disorder caused by a deletion, mutation, or imprinting error of the paternal 15q11-13 region or by maternal uniparental disomy of chromosome 15. One of the disorder's most noticeable characteristics is the development of a constant insatiable appetite, which often results in hyperphagia, hyperglycemia and severe obesity. Hyperphagia related incidents and obesity complications are the leading cause of death for individuals with PWS. Effective treatments for hyperphagia, obesity, and hyperglycemia are needed to improve the quality of life and life expectancy for patients with PWS.

Methods: This meta-analysis aims to assess changes in weight, HbA1c, and hyperphagia after the commencement of GLP-1 agonists and SGLT2 inhibitors in individuals with PWS. A review of the literature was conducted by searching Scopus, PubMed, clinicaltrials.gov, and Cochrane to identify relevant case studies, case series, retrospective studies, non-randomized clinical trials, and randomized clinical trials that involved treating PWS patients with any GLP-1 agonists or SGLT2 inhibitors. A total of 224 records were screened with 45 studies meeting inclusion criteria. Studies involving monotherapy and combination therapy regimens were included, and studies of all ages were included. Case and retrospective studies must have quantitative data on changes in weight, hyperphagia, BMI, or HbA1c to be included in the meta-analysis, and a meta-analysis of raw data extracted from these studies was conducted. For the studies involving trials, a fixed-effect meta-analytic model was used.

Results: Preliminary analysis of the studies showed promising results that indicated that GLP-1 agonists and SGLT2 inhibitors could help PWS patients with weight management, reduction of hyperphagia, and glycemic control. However, most of the studies were retrospective case reviews rather than trials, and the trials had less favorable results. The two clinical trials, which looked at the GLP-1 agonists exenatide and liraglutide, showed limited improvement in HbA1c and hyperphagia, but there were no clinically significant changes in weight in either trial.

Conclusions: Emerging evidence indicates that GLP-1 agonists and SGLT2 inhibitors may provide meaningful benefits for individuals with Prader-Willi Syndrome by reducing hyperphagia, improving glycemic control, and supporting weight management. Nonetheless, the current literature is limited primarily to case reports and small observational studies, and only two trials have been published. Future clinical trials are needed to assess the efficacy and safety of newer GLP-1 medications such as semaglutide and tirzepatide. In studies of the broader population, these newer drugs have demonstrated greater weight loss than older drugs in their class like liraglutide and exenatide. Additionally, further investigation into combination strategies, particularly pairing GLP-1 agonists or SGLT2 inhibitors with diazoxide choline, are needed. Diazoxide choline was recently approved for treating PWS-associated hyperphagia, but one adverse effect reported for this drug was hyperglycemia. Since GLP-1 agonists and SGLT2 inhibitors are effective glycemic control drugs, investigation into their interactions with diazoxide choline should be undertaken. These additional clinical trials are essential to improve the treatment options and ultimately improve both quality of life and long-term health outcomes in patients with PWS.

Figure 1. Overview of Search Strategy and Process



ISSN 2076-6327

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