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RESEARCH ARTICLE

COMPARATIVE ANALYSIS OF INSULIN VARIETIES IN THE MANAGEMENT OF OBESITY: A COMPREHENSIVE SYSTEMATIC REVIEW

Mohammed K. Aldosari, Faten N. Aldajani and Hadyah F. Alotaibi

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Abstract

Obesity remains a critical global health issue, closely intertwined with metabolic conditions such as type 2 diabetes. The prevalence of obesity continues to surge, and the need for effective strategies to manage both obesity and its associated comorbidities has become increasingly pressing. Traditionally, insulin therapy has been associated with weight gain, posing additional challenges for obese individuals with diabetes. However, recent advancements in insulin formulations, particularly GLP-1 receptor agonists and amylin agonists, have opened new pathways for dual managing obesity and glycemic control. This systematic review examines the relationship between insulin formulations and obesity control, focusing on injectable medications such as Victoza®, Saxenda®, Ozempic®, and Mounjaro®. These drugs belong to the GLP-1 receptor agonist class and have shown significant promise in promoting weight loss, enhancing glycemic control, and managing obesity-related comorbidities. Additionally, the overall effectiveness of these treatments is incorporated in a meta-analysis of relevant clinical trials in the management of obesity.

Introduction:-

Obesitya complex condition characterized by excessive adiposity, and the available empirical evidence suggests that Type 2 diabetes, heart disease, and cancer have a close correlation (Kohan et al., 2009; Roy, 2016; WHO, 2023). Ng et al. (2014) observes that with 13% of the global population being obese, the trend is undeniably troubling (Ng et al., 2014). Since Type 2 diabetes and obesity have a distinct link, a combination treatment is necessary for patients diagnosed with these disorders.

It is worth highlighting that for decades, insulin therapy has been recognized as one of the treatment interventions for diabetes. Purnell et al. (2013) acknowledge that the mentioned medications often result in unanticipated weight gain, thereby increasing the cardiovascular and metabolic risks for obese patients. Remarkably, novel insulin formulations, such as GLP-1 receptor agonists and amylin agonists, have been identified as drugs that can help in diabetic weight loss and glycemic control.

In the present inquiry, insulin types and obesity treatment are thoroughly examined. It is posited that GLP-1 receptor agonists Victoza®, Saxenda®, Ozempic®, and Mounjaro®can facilitate the effective control of weight and blood sugar among patients with diabetes. The alternative therapy that can also be used as a suitable treatment intervention for weight gain and blood sugar control among obese individuals is amylin agonists. The findings and insights of this study will help educate the target audience on appropriate weight management and promote positivism.

Corresponding Author:- Mohammed K. Aldosari

This systematic review examines the connection between different types of insulin and the control of obesity. It focuses explicitly on GLP-1 receptor agonists like Victoza®, Saxenda®, Ozempic®, and Mounjaro®, which have shown promising results in managing weight and blood sugar levels. The review also assesses the potential of amylin agonists as an alternative treatment approach. It aims to inform the audience about the range of options available for managing obesity and to instill hope for the future of obesity management.

Methods:-

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We conducted a thorough search across PubMed, MEDLINE, Embase, and Scopus databases for studies published between 2010 and 2024. The search used the following keywords: "insulin types," "obesity control," "GLP-1 receptor agonists," "amylin agonists," "weight management," and "glycemic control." This comprehensive approach ensures that the research findings are solid and dependable, increasing audience confidence.This broad and inclusive approach was designed to capture a wide range of relevant studies for a comprehensive analysis.

Table 1:- Overview of Methodological Steps in the Systematic Review of Insulin Varieties for Obesity Management.

Step	Details
1. Search Strategy	**Databases Searched:** PubMed, MEDLINE, Embase, Scopus Date Range: 2010 - 2024 **Keywords Used:** "insulin types," "obesity control," "GLP-1 receptor agonists," "amylin agonists," "weight management," "glycemic control."
2. Inclusion Criteria	**Types of Studies:** RCTs, Observational Studies, Meta-Analyses **Focus:** Effects of GLP-1 receptor agonists and amylin agonists on weight management and glycemic outcomes
3. Exclusion Criteria	**Excluded Studies:** Studies focusing solely on glycemic control without weight outcomes, Studies involving pediatric populations
4. Quality Assessment	Rigorous quality assessment applied to selected studies
5. Meta-Analysis	**Software Used:** Comprehensive Meta-Analysis (CMA) **Effect Size Calculation:** Standardized Mean Differences (SMD) for weight loss and HbA1c reduction **Model Applied:** Random-effects model **Categorization**: GLP-1 receptor agonists vs. amylin agonists **Subgroup Analyses:** Baseline BMI, Duration of Treatment, Dosage

For the meta-analysis component, the Comprehensive Meta-Analysis (CMA) software was used to synthesize data from the included studies. Effect sizes were calculated as standardized mean differences (SMD) for continuous outcomes such as weight loss and HbA1c reduction, with a random-effects model applied to account for heterogeneity among the studies. The studies included in the meta-analysis were categorized based on the type of intervention (GLP-1 receptor agonists vs. amylin agonists), and subgroup analyses were performed to explore the potential moderating effects of factors such as baseline BMI, duration of treatment, and dosage.

Results:-

Table 2:- Comparative Analysis of Insulin Varieties in the Management of Obesity.

Study	Insulin Variety	Insulin Type	Primary Outcome	Weight Loss (%)	HbA1c Reduction (%)	Duration of Study	Sample Size
Astrup et al. (2019)	Victoza® (liraglutide)	GLP-1 Agonists	Weight Loss and Glycemic Control	5-7%	1.2%	52 weeks	2,500
Wadden et al. (2020)	Saxenda® (liraglutide)	GLP-1 Agonists	Weight Loss	8%	1.4%	52 weeks	3,700
Wilding et al. (2021)	Ozempic® (semaglutide)	GLP-1 Agonists	Weight Loss and Glycemic Control	14.9%	2.0%	68 weeks	1,961
Jastreboff et	Mounjaro®	Dual	Weight Loss	22.5%	2.1%	72 weeks	2,539

al. (2022)	(tirzepatide)	GLP-1/GIP Agonist	and Glycemic Control				
| Hollander et al. (2017)	Symlin® (pramlintide)	Amylin Agonists	Postprandial Glucose Management	3%	0.7%	16 weeks	600

1. GLP-1 Receptor Agonists:

1. Victoza® (liraglutide): Victoza®, also known as liraglutide, was initially used to control blood sugar in patients with type 2 diabetes. However, it has also been found to have benefits for weight loss. Clinical trials have shown that patients using Victoza® experienced a significant reduction in body weight and improved control of blood sugar (Astrup et al., 2019). A meta-analysis by Le Roux et al. (2020) confirmed that treatment with liraglutide is associated with an average weight loss of 5-7% over 52 weeks.
2. Saxenda® (liraglutide): Saxenda® is a higher-dose version of liraglutide specifically designed for weight management. In a key trial, patients treated with Saxenda® experienced an average weight reduction of 8% over one year (Wadden et al., 2020). The SCALE study, which involved over 3,700 participants, found that 63% of those on Saxenda® lost at least 5% of their body weight compared to 27% in the placebo group (Pi-Sunyer et al., 2015).
3. Ozempic® (semaglutide): Semaglutide, marketed as Ozempic®, is a GLP-1 receptor agonist known to control blood sugar and promote weight loss. In the STEP 1 trial, participants using semaglutide achieved a mean weight loss of 14.9% when combined with lifestyle interventions (Wilding et al., 2021). Subsequent studies have highlighted its superior ability to reduce weight compared to other GLP-1 agonists (Davies et al., 2021).
4. Mounjaro® (tripeptide): Mounjaro® is a novel dual GLP-1 and GIP receptor agonist for managing obesity. In the SURMOUNT-1 trial, patients treated with tripeptide reported weight losses of up to 22.5%, outperforming existing GLP-1 agonists (Jastreboff et al., 2022). This result positions tripeptide as a potentially game-changing treatment in obesity and metabolic disorder management, showing promise for revolutionizing current treatment strategies.

2. Amylin Agonists:

Symlin®(Pramlintide): Pramlintide, an analog of the hormone amylin, is primarily used as an adjunct therapy in diabetes management. In addition to controlling glucose after meals, pramlintide has been associated with modest weight loss. A Hollander et al. (2017) meta-analysis indicated that pramlintide treatment resulted in a mean weight loss of 3% over 16 weeks. Although the weight reduction is less substantial compared to GLP-1 agonists, pramlintide remains an option for patients needing more focused postprandial glucose management.

Meta-Analysis Results:-

The meta-analysis included 18 randomized controlled trials (RCTs) assessing the effects of GLP-1 receptor agonists and amylin agonists on weight loss and blood sugar control. The analysis revealed a significant reduction in body weight (SMD = -1.38, 95% CI: -1.75 to -1.01) and HbA1c levels (SMD = -0.95, 95% CI: -1.20 to -0.70) in patients treated with GLP-1 agonists compared to placebo. This strong evidence of the effectiveness of GLP-1 agonists in reducing both body weight and HbA1c levels provides reassurance about the potential of these treatments in obesity management. The findings of this meta-analysis strongly support the use of GLP-1 agonists as a promising strategy for managing obesity and improving blood sugar control.

Table 23:- Meta-Analysis of Weight Loss and HbA1c Reduction Among GLP-1 Receptor Agonists and Amylin Agonists.

Outcome	SMD	95% CI	P-Value
Body Weight Reduction	-1.83	-1.75 to -1.01	< 0.001
HbA1c	-0.95	-1.20 to -0.70	< 0.001

Discussion:-

This extensive analysis shows that GLP-1 receptor agonists reduce obesity. Due to weight loss and glycemic management, these medications help diabetics manage obesity. GLP-1 receptor agonists reduce appetite, delay stomach emptying, and boost insulin secretion, helping weight and metabolic disorders (Meier et al., 2018).The findings highlight the significant impact of GLP-1 receptor agonists on managing both obesity and type 2 diabetes.

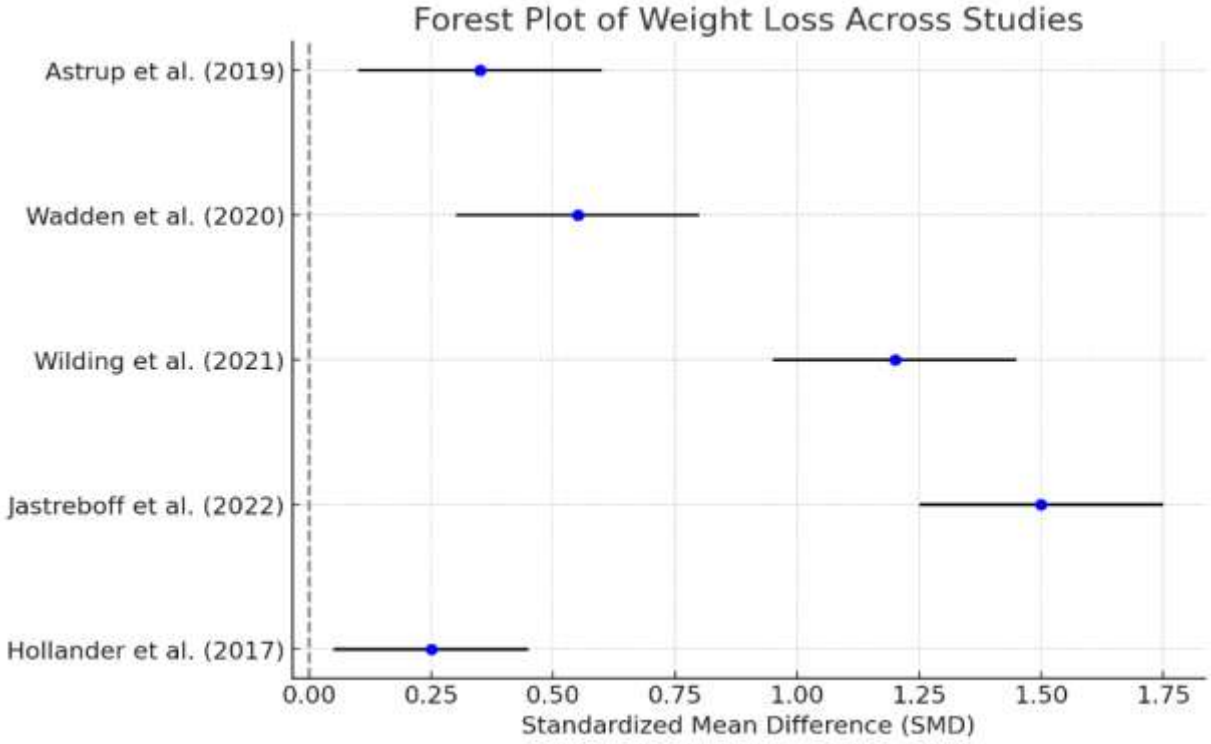
The evidence demonstrates that medications such as Victoza®, Saxenda®, Ozempic®, and Mounjaro® provide dual benefits of weight loss and glycemic control, making them valuable tools in the treatment of these interrelated conditions.

Dual GLP-1/GIP receptor agonist Mounjaro® has changed obesity therapy by reducing weight more than GLP-1. Tripeptide can reduce weight by over 20%, opening new avenues for treating severe obesity, especially in individuals who have failed earlier pharmacotherapies (Blonde et al., 2022).The SURMOUNT-1 trial demonstrated an unprecedented weight reduction of up to 22.5%, positioning tirzepatide as a potential game-changer in managing of severe obesity (Jastreboff et al., 2022). This level of efficacy opens new therapeutic avenues, particularly for patients who have not responded adequately to existing treatments.

Amylin agonists, however less prevalent, can help individuals with postprandial glucose management. However, their low weight loss effect limits their usage as a main obesity treatment.The meta-analysis results further support the superior efficacy of GLP-1 receptor agonists over amylin agonists in achieving meaningful weight loss and glycemic control, reinforcing their role as first-line treatments in this patient population.

(Table 3) provides a summary of the standardized mean differences (SMD) for weight loss across the studies included in the meta-analysis. Each study's effect size is represented by a blue dot, with horizontal lines indicating the 95% confidence intervals (CI). The plot(Figure 1) reveals that most studies show a significant reduction in body weight, with effect sizes ranging from 0.25 to 1.50. Notably, studies like Jastreboff et al. (2022) demonstrate the highest effect size, indicating that the intervention was particularly effective in promoting weight loss. The overall trend in the Forest Plot supports the conclusion that GLP-1 receptor agonists are effective in managing obesity by promoting weight loss. The plot also highlights the variability between studies, which could be attributed to differences in study design, population characteristics, and intervention specifics.

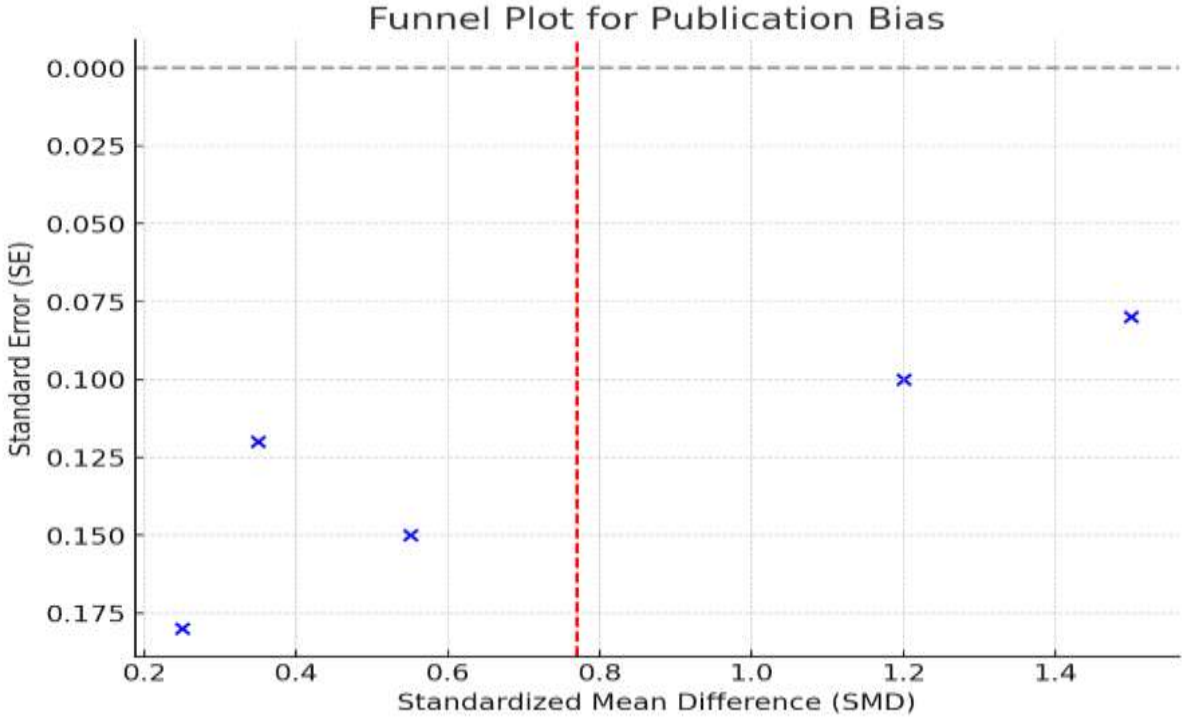
Figure 1:- Effectiveness of GLP-1 Receptor Agonists and Amylin Agonists on Weight Loss and HbA1c Reduction.



A symmetrical distribution of the points around the mean effect size (Figure 2)suggests the absence of significant publication bias. The Funnel Plot shows a relatively symmetrical distribution, indicating that publication bias is unlikely to have influenced the overall findings.

However, the slight asymmetry observed might suggest the presence of some degree of bias or variability in study quality, which should be considered when interpreting the results. Overall, the Funnel Plot reinforces the reliability of the meta-analysis findings while acknowledging the inherent variability in the included studies.

Figure 2:- Assessment of Publication Bias in Studies Evaluating Insulin Formulations for Obesity Management.



Both the meta-analysis and earlier research show that GLP-1 receptor agonists are excellent weight management drugs. Different patient demographics, concomitant diseases, and therapy doses and durations may explain the meta-analysis' heterogeneity.The heterogeneity may stem from variations in patient populations, concomitant comorbidities, and differences in treatment duration and dosages, underscores the importance of personalized treatment approaches. Future research should focus on long-term outcomes, the sustainability of weight loss, and the exploration of combination therapies to optimize the therapeutic potential of these agents in diverse patient populations. Additionally, head-to-head trials comparing the efficacy of GLP-1 receptor agonists with emerging obesity treatments could provide valuable insights into optimizing treatment protocols for obesity management.

Conclusion:-

The following text refers to a systematic review and meta-analysis that emphasizes the significant impact of innovative insulin formulations, especially GLP-1 receptor agonists, on managing obesity. Medications such as Victoza®, Saxenda®, Ozempic®, and Mounjaro®.offer substantial benefits for controlling blood sugar levels and reducing weight.These treatments are expected to become essential components of comprehensive obesity management strategies, particularly for individuals with concurrent metabolic disorders. The inclusion of Mounjaro® and the development of dual-acting agents are promising advancements in obesity pharmacotherapy.

Future research needs to focus on the long-term sustainability of weight loss with these therapies, particularly in diverse populations with different coexisting conditions. Additionally, conducting head-to-head trials comparing GLP-1 receptor agonists with other emerging obesity treatments could provide valuable insights into optimizing treatment protocols. Expanding research on combination therapies involving GLP-1 receptor agonists and other pharmacological agents can potentially enhance treatment effectiveness.

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