

Semaglutide for the Treatment of Type 2 Diabetes and Obesity

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ABSTRACT:-

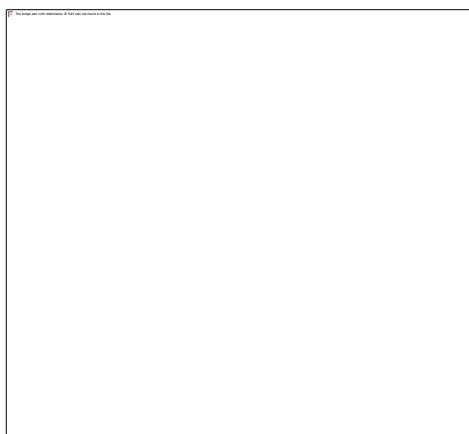
Semaglutide is a glucagon like peptide-1 receptor agonist that was recently approved by the US Food and Drug Administration for chronic weight management. Semaglutide has demonstrated the largest weight loss of any obesity medication to date with reductions of approximately 15% of initial weight at 68 weeks, the approval of this medication provides patients with a greater option for weight management. For Type 2 Diabetes 2.4mg of Semaglutide is for produce more insulin which reduce blood glucose (sugar). And also by using this drug there are less side effects and more beneficial when we use in lower dose. Semaglutide helps to reduce appetite, slow down digestion, and help people stick to a healthy diet, leading to gradual and safe weight loss.

KEY WORDS:- Semaglutide, Type 2 diabetes, Obesity, appetite and glucagon like peptide-1 receptor agonist.

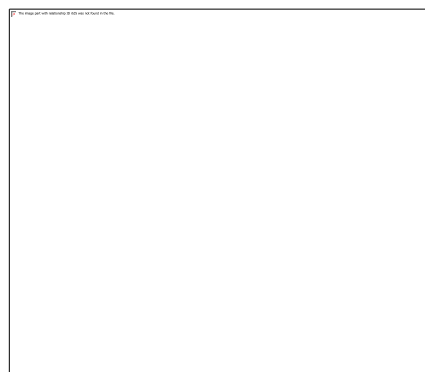
I. INTRODUCTION:

From 1999 to 2014, the prevalence of type 2 diabetes mellitus (T2DM) has increased from 8.8% to 11.7%. Most of T2DM patients are confined to abdominal obesity patients with ages over 45. [1] Obesity is a chronic relapsing, progressive disease [2] with a multi factorial origin, including genetic, metabolic, behavioral, sociocultural, and environmental factors [3,4]. Global prevalence estimates for obesity (at least 15% of adults) and type 2 diabetes (T2D) (>9% of adults) continue to rise, with especial concern for the very high prevalence of obesity (>25% of adults) and T2D (>13% of adults) in several regions of the Americas and Middle East and amongst Pacific island communities [5,6]. Obesity is a strong risk factor for

T2D and more than two thirds of patients are overweight or obese at the time of diagnosis. Both obesity and T2D are associated with high susceptibility for many co-morbidities, including non-alcoholic fatty liver, cardiovascular and renal diseases, which are major contributors to the premature mortality [7]. Its medical burden includes multiple co morbidities, such as T2D hypertension, dyslipidemia, stroke, coronary heart disease and various cancers [8]. As for the treatment of T2DM by first generation of GLP-1 RAs, once daily or twice daily administration is unavoidable. Recently, scientists make efforts on developing GLP-1 RAs for once weekly administration, which could improve patients' adherence, leading to a better effectiveness compared with the first generation of GLP-1 RAs. [9,10] Semaglutide (Novo Nordisk, Denmark) is a new GLP-1 RAs with 94% structural homology to native GLP-1, similar in structure with liraglutide, but less susceptible to degradation by enzyme protease dipeptidylpeptidase-4 (DPP-4) and more enzymatically stable [11]. Semaglutide, a glucagon-like peptide-1 receptor agonist, is approved to treat type 2 diabetes, [12] with subcutaneous injection doses of 0.25, 0.5, and 1 mg administered once weekly and oral doses of 3, 7, and 14 mg administered once daily. [13] In June 2021, the FDA approved subcutaneous semaglutide for long-term weight management, [14] with higher doses of 1.7 and 2.4 mg once weekly. [15] The Semaglutide Treatment Effect in People With Obesity (STEP) trials have shown the efficacy of semaglutide for the treatment of obesity. [16] In large RCTs, patients receiving semaglutide, 2.4 mg, lost a mean of 6% of their weight by week 12 and 12% of their weight by week 28 [16].



TYPE 2 DIABETES



OBESITY

SEMAGLUTIDE PHARMACOLOGY

Semaglutide is a long-acting GLP-1 analogue that mimics the effects of native GLP-1, which promotes WL by reducing energy intake, increasing satiety and satiation, and reducing hunger, as well as enhancing glycemic control [17]. Many GLP-1s have been approved for the treatment of T2D, but only liraglutide 3.0 mg daily has been approved for WM. Semaglutide is approved for treatment of diabetes at the dosage of ≤ 1.0 mg once weekly subcutaneously or in oral tablet form at a dosage of upto 14 mg [3,17,18]. Investigating semaglutide as a new GLP-1 analogue for the treatment of obesity because greater WL was observed with semaglutide than liraglutide [19]. The semaglutide in adults with obesity, a 0.4-mg dose daily was well tolerated, and patients experienced a mean WL at week 52 from baseline of -13.8% compared with -7.8% for liraglutide 3.0 mg and -2.3% for placebo [19]. The semaglutide daily resulted in dose-dependent, clinically relevant WL over 52 weeks and associated with an acceptable tolerability profile with respect to gastrointestinal symptoms [19]. However, based on comparisons with studies with weekly administration of semaglutide, it was reported that there was no difference in gastrointestinal adverse events with the daily versus weekly dosing regimen of semaglutide [20]. Average WL of 10% to 15% has been shown to significantly alleviate many complications associated with obesity, including diabetes, hypertension, osteoarthritis, and gastroesophageal reflux disease [21,22]. The benefits of WL have also been demonstrated in dyslipidemia, non-alcoholic fatty liver disease, sleep apnea, and stress incontinence [21,23,24,25].

DRUG INTERACTIONS:-

The therapeutic efficacy of Semaglutide can be decreased when used in combination with Drosiprenone. And a study has observed the effect of semaglutide on metformin and other weight loss drugs. It has been reported that semaglutide didn't pose significant effects on these drugs. **SIDE EFFECTS:-** Dizziness, Fatigue, Gastrointestinal issues (diarrhea, constipation and gasiness), Head ache, Nausea, Vomiting, pain or distension (bloat)

CONTRAINDICATION:-

In patients with a personal or family history of MTC or in patients with MEN. T1D, hypoglycemia, pancreatitis, cholelithiasis, gallbladder disease, Diabetic retinopathy, renal failure, renal impairment and also in pregnancy women.

II. DISCUSSION:-

Semaglutide is used for Type 2-diabetic and obesity patients. The effect of semaglutide 2.4 mg (given by oral administration and subcutaneously once weekly) on WM in adults with obesity or overweight and provide a comprehensive overview of the efficacy safety, and tolerability profile of semaglutide 2.4 mg. Semaglutide showed a significant improve in controlling glycemia and bodyweight as compared with other GLP-1 RAs. Recent head-to-head studies indicate that semaglutide is superior to other once weekly administered GLP-1 RAs (exenatide extended release and dulaglutide) with not just glycemia control but body weight control and other efficacy data [26,27]. The purpose of this review is to assess safety and uses of semaglutide doesn't show any adverse effect when used in lower dose for type 2 diabetes and obesity patients.

III. CONCLUSION:-

Semaglutide belongs to a class of medication known as glucagon-like peptide-1 (GLP-1)receptor agonists.Semaglutide drug is used for both Type2diabetic and Obesity patients.2.4mg amount of semaglutide is used for type2diabetic patients,for obesity patients we will take by considering patient weight.Semaglutide is used in weight loss for obesity patient. In Type2diabetic GLP-1 is used to prompt the body to produce more insulin, which reduce blood glucose(sugar).

REFERENCE:-

- [1]. Caspard H, Jabbour S, Hammar N, et al. Recent trends in the prevalence of type 2 diabetes and the association with abdominal obesity lead to growing health disparities in the USA: an analysis of the NHANES surveys from 1999 to 2014. *Diabetes ObesMetab* 2018;20:667–71
- [2]. Frühbeck G, Busetto L, Dicker D, et al. The ABCD of obesity: an EASO positionstatement on a diagnostic term with clinical and scientific implications. *Obes Facts* 2019;12:131-136.
- [3]. Bray GA, Frühbeck G, Ryan DH, Wilding JPH. Management of obesity. *Lancet* 2016;387:1947-1956.
- [4]. Ralston J, Brinsden H, Buse K, et al. Time for a new obesity narrative. *Lancet* 2018;392:1384-1386
- [5]. World Obesity Atlas 2022. Accessed 7 November 2022
- [6]. International Diabetes Federation Diabetes Atlas 2021. *IDF Atlas 10th Edition 2021.pdf* <https://diabetesatlas.org/> Accessed 7 November 2022.
- [7]. K. Iglay, H. Hannachi, P.J. Howie, J. Xu, X. Li, S.S. Engelet, et al., Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus, *Curr.Med. Res. Opin.*32 (2016) 1243–1252,.
- [8]. Pantalone KM, Hobbs TM, Chagin KM, et al. Prevalence and recognition of obesity and its associated comorbidities: cross-sectional analysis of electronic health record data from a large US integrated health system.*BMJ Open.* 2017;7(11):e017583. doi:10.1136/bmjopen-2017-017583
- [9]. Madsbad S, Kielgast U, Asmar M, et al. An overview of once-weekly glucagon-like peptide-1 receptor agonists—available efficacy and safety data and perspectives for the future. *Diabetes ObesMetab* 2011;13:394–407
- [10]. Polonsky WH, Fisher L, Hessler D, et al. Patient perspectives on once-weekly medications for diabetes. *Diabetes ObesMetab* 2011;13:144–9.
- [11]. Lau J, Bloch P, Schaffer L, et al. Discovery of the once-weekly glucagon-like Peptide-1 (GLP-1) analogue semaglutide. *J Med Chem* 2015;58:7370–80
- [12]. Miles KE, Kerr JL. Semaglutide for the treatment of type 2 diabetes mellitus. *J Pharm Technol.* 2018;34(6):281-289. doi:10.1177/8755122518790925
- [13]. Canadian Agency for Drugs and Technologies in Health. CADTH common drug review: pharmacoeconomic review report: semaglutide (Ozempic) (Novo Nordisk Canada Inc.). 2019. Accessed May 2, 2022.
- [14]. U.S. Food and Drug Administration. FDA approves new drug treatment for chronic weight management, first since 2014. June 4, 2021. Accessed May 2, 2022.
- [15]. Rubino DM, Greenway FL, Khalid U, et al; STEP 8 Investigators. Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: the STEP 8 randomized clinical trial. *JAMA.* 2022;327(2):138-150. doi:10.1001/jama.2021.23619
- [16]. Kushner RF, Calanna S, Davies M, et al. Semaglutide 2.4 mg for the treatment of obesity: key elements of the STEP trials 1 to 5. *Obesity (Silver Spring).* 2020;28(6):1050-1061. doi:10.1002/oby.22794
- [17]. Knudsen LB, Lau J. The discovery and development of liraglutide and semaglutide. *FrontEndocrinol (Lausanne)* 2019;10:155. doi:10.3389/fendo.2019.00155
- [18]. Novo Nordisk. VICTOZA (liraglutide 1.2/1.8 mg) injection, for subcutaneous use. Package insert. Novo Nordisk; 2017. Updated August 2017. Accessed October 8, 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022341s027lbl.pdf
- [19]. O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomized, double-blind,

- placebo and active controlled, dose-ranging, phase 2 trial. *Lancet* 2018;392:637-649
- [20]. Lingvay I, Desouza CV, Lalic KS, et al. A 26-week randomized controlled trial of semaglutide once daily versus liraglutide and placebo in patients with type 2 diabetes suboptimally controlled on diet and exercise with or without metformin. *Diabetes Care* 2018;41:1926-1937
- [21]. Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* 2013;310:2416-2425.
- [22]. Singh M, Lee J, Gupta N, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. *Obesity (Silver Spring)* 2013;21:284-290
- [23]. Garvey WT, Mechanick JI, Brett EM, et al.; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract* 2016;22(suppl 3):1-203.
- [24]. Foster GD, Borradaile KE, Sanders MH, et al.; Sleep AHEAD Research Group of LookAHEAD Research Group. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med* 2009;169:1619-1626
- [25]. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology* 2015;149:367-378.e5; quiz e14-e15
- [26]. Ahmann AJ, Capehorn M, Charpentier G, et al. Efficacy and safety of once-weekly semaglutide versus exenatide ER in subjects with Type 2 diabetes (SUSTAIN 3): a 56-week, open-label, randomized clinical trial. *Diabetes Care* 2018;41:258-66.
- [27]. Pratley RE, Aroda VR, Lingvay I, et al. Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. *Lancet Diabetes Endocrinol* 2018;6:275-86