

Awareness of Population Regarding GLP-1 (liraglutide and Semaglutide) Prescribing in PHCC in Abha City, KSA

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Received: Received: June 2023. Accepted: July 2023; Published: August 1, 2023.

Citation: Majed Al saleh et al. Awareness of Population Regarding GLP-1 (liraglutide and Semaglutide) Prescribing in PHCC in Abha City, KSA. World Family Medicine. August 2023; 21(7): 79-88

DOI: 10.5742/MEWFM.2023.95256163

Abstract

Background: GLP-1 is a peptide hormone related to the glucagon superfamily and shares a significant amino acid sequence with glucagon. The glucagon superfamily peptides are secreted from the small intestine, pancreas, brain, and peripheral nerves. Furthermore, GLP-1 controls intestinal motility and decreases gastric motility. It also has an effect of satiety, which may be attributed to its effect on the gut, but it also has a direct effect on the hypothalamic feeding centers.

Aim: This study aims to assess the population awareness level regarding GLP-1 prescribing in PHCC in Abha City.

Methods: A descriptive cross-sectional web-based study was used. An online questionnaire was developed by the study researchers based on a literature review and after consultation of the field experts. The questionnaire of this study included participants' demographic data, medical history, and GLP-1 use and satisfaction. Also, it covered participants' awareness regarding GLP-1 and its effects.

Results: A total of 160 participants who used GLP-1 completed the study survey. Participants' ages ranged from 18 to more than 50 years with a mean age of 34.8 ± 13.9 years old. Exactly 89 (55.6%) participants were females. The most used GLP-1 were Saxenda (39.4%), Ozempic (37.5%), and Trulicity (14.4%) while 8.8% used a combination of them. Exactly 127 (79.4%) participants had an overall poor awareness level regarding GLP-1 while only 33 (20.6%) had a good awareness level.

Conclusion: In conclusion, the current study revealed that a significant portion of diabetic and obese persons use GLP-1 for reducing weight and controlling blood glucose levels. On the other hand, their awareness level regarding the drugs was unsatisfactory.

Keywords: GLP-1, diabetes, obesity, awareness, use, population, knowledge, Saudi Arabia.

Introduction

Glucagon-like peptide-1 (GLP-1) agonists which are also termed GLP-1 receptor agonists or GLP-1 analogs are a category of medicines mostly used with type 2 diabetes in adults (1). This category includes lixisenatide, exenatide, liraglutide, albiglutide, dulaglutide, and semaglutide (2). Till now, metformin is still the recommended first-line therapy for type 2 diabetic patients, although, adding GLP-1 analog is preferred for patients with intolerance or contraindication to metformin, patients with poor glycemic control, or patients with elevated A1c for three months, especially patients with atherosclerosis, heart failure, or chronic kidney disease (3, 4).

Moreover, semaglutide and liraglutide are FDA approved as recommended management lines for obese and overweight patients with comorbidities (5). The use of GLP-1 analogs is an object of research with favorable hemoglobin A1c results and weight loss results in patients with type-1 diabetes mellitus. High costs, and tolerability are still the main barriers to prescribing these medications (6-8).

Many issues regarding the role of GLP-1 among different patients were discussed. For stroke and brain injury, Hyperglycemia is associated with poor clinical outcomes in stroke including hemorrhagic transformation, degree of neurological debility, and death (9, 10). For cardiac patients, GLP-1 has a role in glycemic control that makes them attractive for use in the immediate aftermath of AMI as they may act directly on the cardiac muscle to improve ventricular ejection fraction and cardiac index (11, 12).

Some patients may not prefer injectable medicines at first recommendation. The concept of the drug should be cleared and the patient should be informed about its possible benefits and hazards through improving their drug-related information and awareness. The current study aimed to assess the population awareness level regarding GLP-1 prescribing in PHCC in Abha City, the most prescribed GLP-1 medications, the main indications for prescribing GLP-1 medications, and determinants of population awareness level regarding GLP-1.

Methodology

A descriptive cross-sectional study was conducted to assess public awareness of GLP-1 and its related side effects in Aseer region, Southern Saudi Arabia. All residents aged 18 years or more and who live in Aseer region using GLP-1 medications who consented to participate in the study, were included in the study. Persons who declined to consent, those who were less than 18 years, or spoke a language other than Arabic and those who never used GLP-1 drugs were excluded from the study. An online questionnaire was developed by the study researchers after an intensive literature review and expert consultation. Questionnaire validity, clarity and applicability were assessed independently by a panel of 3 experts with all suggested changes applied until the final used version of the questionnaire was created. The

final questionnaire was published using social media platforms from 2022 to 2023 and participants were encouraged to participate in this study by clarifying the degree of confidentiality for their data and the significance of this research to the community. The questionnaire of this study included participants' demographic data (Age, Gender, medical history, employment, education, and work). Part 2 covered participants' awareness regarding GLP-1 use and related side effects in the form of general awareness, side effects, and source of their information. The third section covered participants use and pattern of using steroids. The last section covered the role of healthcare staff in providing information regarding GLP-1. All questions had one correct answer. The questionnaire was uploaded online by the researchers and their friends and relatives till no more new answers were obtained.

Data analysis

The data were collected, reviewed and then fed into Statistical Package for Social Sciences version 21 (SPSS: An IBM Company). All statistical methods used were two tailed with alpha level of 0.05 considering significance if P value was less than or equal to 0.05. Overall awareness level regarding GLP-1 was assessed through summing up discrete scores for different correct knowledge items. The overall awareness score was categorized to poor level if participants scored less than 60% of the overall score and good level of awareness was considered if the participants' score was 60% or more of the overall score. Descriptive analysis was done by describing frequency distribution and percentage for study variables including participants' personal data, awareness items, and use of GLP-1 while participants overall awareness level was graphed. Cross tabulation for showing distribution of participants' overall awareness level by their personal data and health care staff role in providing information was carried out with Pearson chi-square test for significance and Exact probability test if there were small frequency distributions.

Results

A total of 160 participants who used GLP-1 completed the study survey. Participants' ages ranged from 18 to more than 50 years with mean age of 34.8 ± 13.9 years old. Exactly 89 (55.6%) participants were females, 96 (60%) were married with 2-3 children among 49 (43%) and 21 (18.4%) had 1-2 children. Exactly 52 (32.5%) worked in the governmental sector, 55 (34.4%) in the private sector while 38 (23.8%) were not working. Monthly income less than 5000 SR was reported among 48 (30%), 5000-10000 SR among 64 (40%) while 37 (23.1%) had monthly income 10000-15000 SR. Exactly 82 (51.3%) were university graduates and 54 (33.8%) had secondary level of education. As for BMI, 54 (33.8%) had normal body weight, 51 (31.9%) had overweight and 55 (34.4%) were obese (Table 1).

Table 2. GLP-1 use with effects among study participants, Abha, Saudi Arabia. The most used GLP-1 were Saxenda (39.4%), Ozempic (37.5%), Trulicity (14.4%) while

8.8% used a combination of them. Obesity was the most reported reason for having these drugs (48.1%), followed by type 2 DM (30.6%), type 1 DM (13.8%), and gestational DM (7.5%). The most reported side effects among users were Nausea and vomiting (51.3%), Mood swings (40.6%), Indigestion (33.8%), Dizziness and low blood sugar (33.8%), and Diarrhea or constipation (25%). Exactly 61 (38.6%) reported losing 4-7 Kg after having the medications while 49 (31%) lost 1-3 Kg but 10 (6.3%) failed to lose weight. Also, 90 (56.3%) reported HbA1c less than 7.5%.

Table 3. Participants' awareness regarding GLP-1 in Abha, Saudi Arabia. Exactly 73 (45.6%) of the study participants reported that Cholecystitis is one of the most serious diseases that these drugs may cause, 71 (44.4%) told about pancreatitis and 39 (24.4%) about rare tumors of the endocrine glands. As for mechanism of actions, 59 (36.9%) told about reducing the movement of food from the stomach to the intestine, 55 (34.4%) told about reducing blood sugar, 42 (26.3%) know about appetite suppression while 43 (26.9%) mentioned all of these. The most reported sources of information about GLP-1 were physician (46.3%), social media (40.6%), pharmacists (30%) and calling MOH information centers (9.4%).

Figure 1. Overall participants' awareness regarding GLP-1, Abha, Saudi Arabia. Exactly 127 (79.4%) participants had an overall poor awareness level regarding GLP-1 while only 33 (20.6%) had good awareness level.

Table 4. Role of health care staff and participants' satisfaction in prescribing GLP-1. A total of 53.8% of the participants reported that doctor always / often explains how the treatment works, how to use it, and its side effects for the patients. As for pharmacists' role, 54 (33.8%) said that they explain how to use and times of use, 42 (26.3%) told said they write the instructions on the medication, 32 (20%) reported that pharmacists' role is only dispensing the drug. Exactly 69.4% of the study participants were satisfied with all the information provided to them at the physician clinic and 68.7% were satisfied with all the information provided to them when dispensing these medicines from pharmacy.

Table 5. Factors associated with participants' awareness regarding GLP-1, Abha, Saudi Arabia. Exactly 25.8% of females had good awareness about GLP-1 compared to 14.1% of males with recorded statistical significance ($P=.049$). Also, all participants with high income know about GLP-1 compared to 29.2% of others with low income level ($P=.009$). Good awareness about GLP-1 was detected among 31.6% of participants who usually had information from their doctor during visits versus 7.4% of others who sometimes had explanations ($P=.031$).

Table 1: Bio-demographic data of study participants using GLP-1, Abha, Saudi Arabia

Bio-demographic data`	No	%
Age in years		
18-25	21	13.1%
26-35	53	33.1%
36-45	58	36.3%
46-50	17	10.6%
> 50	11	6.9%
Gender		
Male	71	44.4%
Female	89	55.6%
Marital status		
Single	46	28.8%
Married	96	60.0%
Divorced / widow	18	11.3%
Number of children		
None	12	10.5%
1-2	21	18.4%
2-3	49	43.0%
4-5	18	15.8%
> 5	14	12.3%
Work		
Not working / retired	38	23.8%
Student	15	9.4%
Governmental sector	52	32.5%
Private sector	55	34.4%
Monthly income		
< 5000 SR	48	30.0%
5000-10000 SR	64	40.0%
>10000-15000 SR	37	23.1%
>15000-20000 SR	9	5.6%
> 20000 SR	2	1.3%
Educational level		
Below secondary	9	5.6%
Secondary	54	33.8%
University graduate	82	51.3%
Post-graduate	15	9.4%
Body mass index		
Normal weight	54	33.8%
Overweight	51	31.9%
Obese	55	34.4%

Table 2: GLP-1 use with effects among study participants, Abha, Saudi Arabia

GLP1 use	No	%
Type of used drugs		
<i>Saxenda</i>	63	39.4%
<i>Ozempic</i>	60	37.5%
<i>Trulicity</i>	23	14.4%
<i>Combined</i>	14	8.8%
Reason for having mentioned medication		
<i>Obesity</i>	77	48.1%
<i>T2DM</i>	49	30.6%
<i>T1DM</i>	22	13.8%
<i>GDM</i>	12	7.5%
Where was it dispensed to you		
<i>Diabetic center</i>	99	61.9%
<i>General hospital</i>	28	17.5%
<i>From the pharmacy without a prescription</i>	24	15.0%
<i>Health care center</i>	20	12.5%
Reported side effects of GLP1 medications		
<i>Nausea and vomiting</i>	82	51.3%
<i>Mood swings</i>	65	40.6%
<i>Indigestion</i>	54	33.8%
<i>Dizziness and low blood sugar</i>	54	33.8%
<i>Diarrhea or constipation</i>	40	25.0%
Weight loss after having GLP1 medications		
<i>No loss</i>	10	6.3%
<i>1-3 Kg</i>	49	31.0%
<i>4-7 Kg</i>	61	38.6%
<i>8+ Kg</i>	38	24.1%
HbA1c in the last 3 months after using drugs		
<i>< 7.5%</i>	90	56.3%
<i>7.5-8.5%</i>	47	29.4%
<i>8.6-10%</i>	23	14.4%

GDM: gestational DM

Table 3: Participants awareness regarding GLP-1 in Abha, Saudi Arabia

Awareness	No	%
The most serious diseases that these drugs may cause?		
<i>Pancreatitis</i>	71	44.4%
<i>Cholecystitis</i>	73	45.6%
<i>Rare tumors of the endocrine glands</i>	39	24.4%
Mechanism of these drugs action		
<i>Reducing the movement of food from the stomach to the intestine</i>	59	36.9%
<i>Reducing blood sugar</i>	55	34.4%
<i>Appetite suppression</i>	42	26.3%
<i>All of the above</i>	43	26.9%
Source of information about the drugs		
<i>Physician</i>	74	46.3%
<i>Social media</i>	65	40.6%
<i>Pharmacist</i>	48	30.0%
<i>MOH communication center</i>	15	9.4%

Figure 1. Overall participants awareness regarding GLP-1, Abha, Saudi Arabia

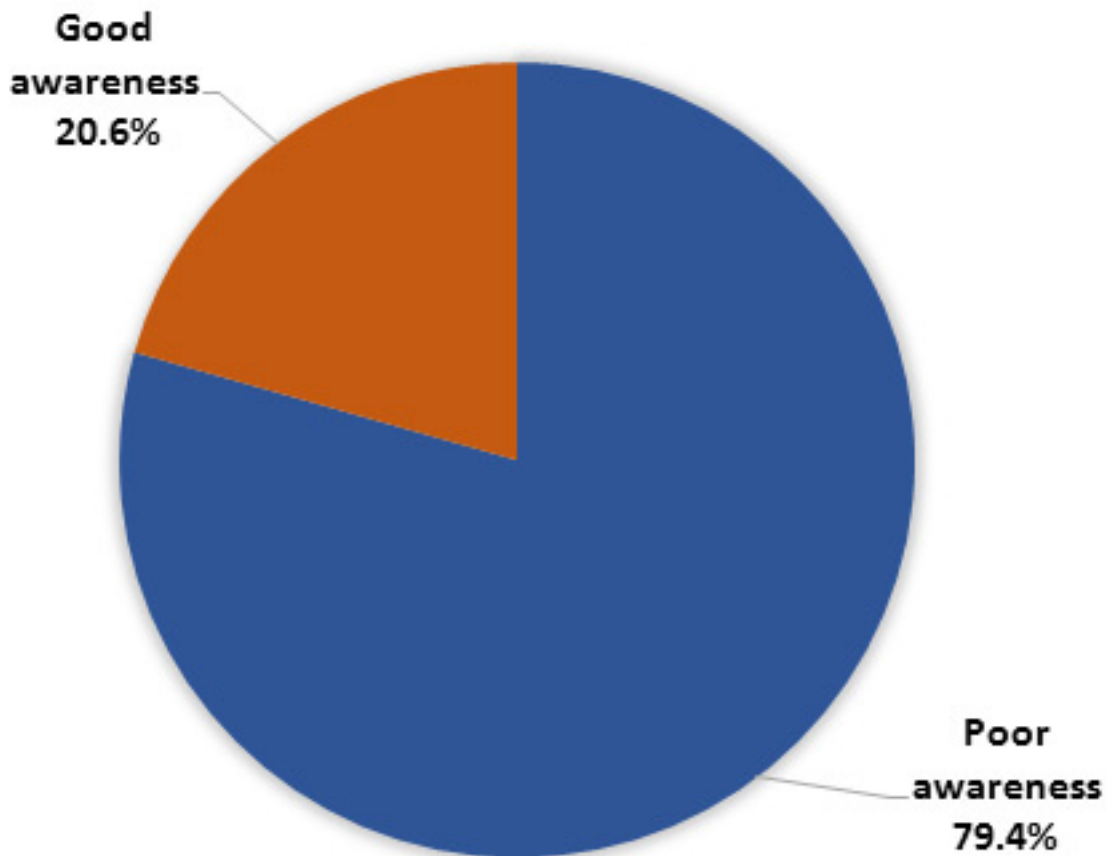


Table 4. Role of health care staff and participants' satisfaction in prescribing GLP-1

Health care staff role	No	%
When you go to the doctor in the clinic, does the doctor explain to you how the treatment works, how to use it, and its side effects?		
<i>Always</i>	38	23.8%
<i>Often</i>	48	30.0%
<i>Sometimes</i>	54	33.8%
<i>Rarely</i>	12	7.5%
<i>Never</i>	8	5.0%
When you go to the pharmacy to dispense these medicines, what is the pharmacist's role for you?		
<i>Explanation of how to use and times of use</i>	54	33.8%
<i>Try to see if you understood the given information well</i>	23	14.4%
<i>Write the instructions on the medication</i>	42	26.3%
<i>It gives you educational material about the medicine and how to use it</i>	9	5.6%
<i>Treatment dispensing only</i>	32	20.0%
How satisfied are you with all the information provided to you at the physician clinic?		
<i>Totally satisfied</i>	37	23.1%
<i>Somewhat satisfied</i>	74	46.3%
<i>Neutral</i>	30	18.8%
<i>Dissatisfied</i>	17	10.6%
<i>Totally dissatisfied</i>	2	1.3%
How satisfied are you with all the information provided to you when dispensing these medicines from pharmacy?		
<i>Totally satisfied</i>	49	30.6%
<i>Somewhat satisfied</i>	61	38.1%
<i>Neutral</i>	30	18.8%
<i>Dissatisfied</i>	16	10.0%
<i>Totally dissatisfied</i>	4	2.5%

Table 5. Factors associated with participants awareness regarding GLP-1, Abha, Saudi Arabia

Factors	Overall awareness level				p-value	
	Poor		Good			
	No	%	No	%		
Age in years	18-25	14	66.7%	7	33.3%	.223
	26-35	46	86.8%	7	13.2%	
	36-45	47	81.0%	11	19.0%	
	46-50	13	76.5%	4	23.5%	
	> 50	7	63.6%	4	36.4%	
Gender	Male	61	85.9%	10	14.1%	.049*
	Female	66	74.2%	23	25.8%	
Marital status	Single	35	76.1%	11	23.9%	.522
	Married	76	79.2%	20	20.8%	
	Divorced / widow	16	88.9%	2	11.1%	
Educational level	Below secondary	6	66.7%	3	33.3%	.507§
	Secondary	46	85.2%	8	14.8%	
	University graduate	63	76.8%	19	23.2%	
	Post-graduate	12	80.0%	3	20.0%	
Monthly income	< 5000 SR	34	70.8%	14	29.2%	.009*§
	5000-10000 SR	52	81.3%	12	18.8%	
	10000-15000 SR	34	91.9%	3	8.1%	
	15000-20000 SR	7	77.8%	2	22.2%	
	> 20000 SR	0	0.0%	2	100.0%	
Body mass index	Normal weight	46	85.2%	8	14.8%	.268
	Overweight	41	80.4%	10	19.6%	
	Obese	40	72.7%	15	27.3%	
Source of information about the drugs	Physician	54	73.0%	20	27.0%	.196
	Pharmacist	41	85.4%	7	14.6%	
	Social media	49	75.4%	16	24.6%	
	MOH communication center	12	80.0%	3	20.0%	
When you go to the doctor in the clinic, does the doctor explain to you how the treatment works, how to use it, and its side effects?	Always	26	68.4%	12	31.6%	.031*§
	Often	36	75.0%	12	25.0%	
	Sometimes	50	92.6%	4	7.4%	
	Rarely	10	83.3%	2	16.7%	
	Never	5	62.5%	3	37.5%	
When you go to the pharmacy to dispense these medicines, what is the pharmacist's role for you?	Explanation of how to use and times of use	41	75.9%	13	24.1%	.586
	Try to see if you understood the given information well	18	78.3%	5	21.7%	
	Write the instructions on the medication	33	78.6%	9	21.4%	
	Giving educational material	9	100.0%	0	0.0%	
	Treatment dispensing only	26	81.3%	6	18.8%	

P: Pearson X2 test

§: Exact probability test

* P < 0.05 (significant)

Discussion

Proper awareness assessments allow the evaluation and rating of the importance that patients place on specific treatment qualities of current therapies, besides assessing preferences for hypothetical products (13). Assessing patients' awareness regarding medications also helps in understanding their preferences which may affect patient's adherence and commitment.

The current study aimed to assess all related information regarding GLP-1 use, awareness, and related side effects among the population in Abha, Southern Saudi Arabia. The study showed that the most used GLP-1 were Saxenda, Ozempic, and Trulicity while a few percent used a combination of them. Obesity was the most reported reason for having these drugs (nearly half of the users) followed by type 2 DM (one-third of them), but a lesser percentage was used for type 1 DM and gestational DM. Alshaikh A et al. (14) in Saudi Arabia reported that 4.0% of GLP-1 users prefer the daily oral formula of GLP-1RA, while 16.0% prefer the once-weekly subcutaneous formula. About 40.2% of those who favor the injectable formula remark that the injectable formula is more effective, 30.3% reported that it is more suitable for them, and 28.6% said that they take too many oral medications. Also, many studies have documented that peripheral infusions of GLP-1 significantly and dose-dependently improve satiety and reduce food intake in normal subjects (15, 16). The consequence on food intake and satiety is well-maintained in obese persons (17) as well as in obese patients with type 2 diabetes (18, 19). This indicates that GLP-1 may not only be a biological controller of food intake but may also have a therapeutic likelihood. As for reported side effects, the most reported side effects among current study users were nausea and vomiting, mood swings, indigestion, dizziness and low blood sugar, and diarrhea or constipation.

With regard to the reported effects, about one-third of the current study participants reported losing 4-7 Kg after having the medications while 31% lost 1-3 Kg but 10 (6.3%) failed to lose weight. Also, more than half of the diabetics reported HbA1c less than 7.5% (glycemic control). These findings were consistent with Ajabnoor GM et al. (20) who found that the GLP-1RA effect on BMI was significantly decreased. Also, a significant effect was reported for HbA1c in study patients for six months of treatment duration with a conclusion that GLP-1RA treatments were associated with weight reduction and improved glycemic control for T2DM patients. Moreover, it is suggested that it has anti-inflammatory and hepatoprotective effects. This finding shows its role in handling glycemic parameters, consistent with previous studies (21-24). Therefore, it was found that GLP-1RAs improve beta cell functions, which improve insulin sensitivity and reduce glucagon secretion to the lowest basal level (21). Consequently, GLP-1RAs are efficiently exceptional in decreasing glycemic levels and reducing body weight. They also promote a decrease in glucosuria levels (25).

With regard to participants awareness about GLP-1, the current study showed that nearly one-fifth of the participants were knowledgeable about the drugs. Less than half of the study participants reported that cholecystitis is one of the most serious diseases that these drugs may cause, and also told about pancreatitis while only one-quarter reported rare tumors of the endocrine glands. As for mechanism of actions, one-third know about reducing the movement of food from the stomach to the intestine, and also told about reducing blood sugar, while one-quarter know about appetite suppression. The most reported sources of information about GLP-1 were physician, social media, and pharmacists. A study at Qassim University, Saudi Arabia found that about three-quarters of the participants gave correct answers for knowledge regarding GLP-1. Also, more than three-quarters reported positive attitude and practice (80.3%), although, poor knowledge was detected for some important issues such as the method of administration, precautions and possible risks associated with the therapy was lacking among the participants. Some of the demographic data such as profession, qualification and age of the participants were significantly affecting participants' knowledge level (26). The current study also showed that participants showed high satisfaction regarding the role of physician and pharmacists in explaining all aspects of GLP-1 and its use with availability of all relevant information.

Conclusion and Recommendations

In conclusion, the current study revealed that a significant portion of diabetic and obese persons use GLP-1 for reducing weight and controlling blood glucose level. On the other hand, their awareness level regarding the drugs was unsatisfactory. Participants' satisfaction regarding health care staff role in providing necessary information was high which means that other sources of information are required to improve their overall awareness regarding the medications. More effort should be paid to improve public awareness regarding this category of medications and its benefits and indications to avoid any unpleasant consequences and minimize economic and social burden.

References

1. Hunt B, Malkin SJP, Moes RGJ, Huisman EL, Vandebrouck T, Wolffenbuttel BHR. Once-weekly semaglutide for patients with type 2 diabetes: a cost-effectiveness analysis in the Netherlands. *BMJ Open Diabetes Res Care*. 2019;7 (1): e000705.
2. Burcelin R, Gourdy P. Harnessing glucagon-like peptide-1 receptor agonist for the pharmacological treatment of overweight and obesity. *Obes Rev*. 2017 Jan;18(1):86-98.
3. Gourgari E, Wilhelm EE, Hassanzadeh H, Aroda VR, Shoulson I. A comprehensive review of the FDA-approved labels of diabetes drugs: Indications, safety, and emerging cardiovascular safety data. *J Diabetes Complications*. 2017 Dec;31(12):1719-1727.
4. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2019. *Diabetes Care*. 2019 Jan;42(Suppl 1): S90-S102.
5. American Diabetes Association. 8. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2019. *Diabetes Care*. 2019 Jan;42(Suppl 1): S81-S89.
6. Janzen KM, Steuber TD, Nisly SA. GLP-1 Agonists in Type 1 Diabetes Mellitus. *Ann Pharmacother*. 2016 Aug;50(8):656-65. [PubMed]
7. Sanford M. Dulaglutide: first global approval. *Drugs*. 2014 Nov;74(17):2097-103.
8. Hinnen D. Glucagon-Like Peptide 1 Receptor Agonists for Type 2 Diabetes. *Diabetes Spectr*. 2017 Aug;30(3):202-210.
9. Baird TA, Parsons MW, Phan T, et al. Persistent poststroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. *Stroke*. 2003;34(9):2208-2214.
10. Lindsberg PJ, Roine RO. Hyperglycemia in acute stroke. *Stroke*. 2004;35(2):363-364.
11. Wroge J, Williams NT. Glucagon-like peptide-1 (GLP-1) receptor agonists in cardiac disorders. *Ann Pharmacother*. 2016;50(12):1041-1050.
12. Ban K, Noyan-Ashraf MH, Hoefer J, Bolz SS, Drucker DJ, Husain M. Cardioprotective and vasodilatory actions of glucagon-like peptide 1 receptor are mediated through both glucagon-like peptide 1 receptor-dependent and -independent pathways. *Circulation*. 2008;117(18):2340-2350.
13. Bridges JF, Onukwugha E, Johnson F, Hauber A. Patient preference methods – A patient centered evaluation paradigm. *ISPOR Connections*. 2007; 13(6):4-7.
14. Alshaikh A, Elbadawi H, Aleissa M, Alsabaan F, Alslail F, Almudaiheem H et al. Perceptions and Preferences Toward GLP-1 Receptor Agonists in Type 2 Diabetes Management in Saudi Arabia: A Cross-sectional, Two-arm Study. *Acta Scientific Medical Sciences*. 2022; 6 (11): 41-46.
15. Flint A, Raben A, Astrup A, Holst JJ. Glucagon-like peptide 1 promotes satiety and suppresses energy intake in humans. *The Journal of clinical investigation*. 1998 Feb 1;101(3):515-20.
16. Verdich C, Flint A, Gutzwiller JP, Naslund E, Beglinger C, Hellstrom PM, Long SJ, Morgan LM, Holst JJ, Astrup A. A meta-analysis of the effect of glucagon-like peptide-1 (7–36) amide on ad libitum energy intake in humans. *The Journal of Clinical Endocrinology & Metabolism*. 2001 Sep 1;86(9):4382-9.
17. Näslund E, Barkeling B, King N, Gutniak M, Blundell JE, Holst JJ, Rössner S, Hellström PM. Energy intake and appetite are suppressed by glucagon-like peptide-1 (GLP-1) in obese men. *International journal of obesity*. 1999 Mar;23(3):304-11.
18. Gutzwiller JP, Drewe J, Go-ke B, Schmidt H, Rohrer B, Lareida J, Beglinger C. Glucagon-like peptide-1 promotes satiety and reduces food intake in patients with diabetes mellitus type 2. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 1999 May 1;276(5): R1541-4.
19. Zander M, Madsbad S, Madsen JL, Holst JJ. Effect of 6-week course of glucagon-like peptide 1 on glycaemic control, insulin sensitivity, and β -cell function in type 2 diabetes: a parallel-group study. *The Lancet*. 2002 Mar 9;359(9309):824-30.
20. Ajabnoor GM, Hashim KT, Alzahrani MM, Alsuheili AZ, Alharbi AF, Alhozali AM, Enani S, Eldakhakhny B, Elsamanoudy A. The Possible Effect of the Long-Term Use of Glucagon-like Peptide-1 Receptor Agonists (GLP-1RA) on Hba1c and Lipid Profile in Type 2 Diabetes Mellitus: A Retrospective Study in KAUH, Jeddah, Saudi Arabia. *Diseases*. 2023 Mar 14;11(1):50.
21. Thomas M.K, Nikooienejad A, Bray R, Cui X, Wilson,J, Duffin K, Milicevic Z, Haupt A, Robins D.A. Dual GIP and GLP-1 Receptor Agonist Tirzepatide Improves Beta-cell Function and Insulin Sensitivity in Type 2 Diabetes. *J. Clin. Endocrinol. Metab*. 2020, 106, 388-396.
22. Bethel MA, Diaz R, Castellana N, Bhattacharya I, Gerstein HC, Lakshmanan MC. HbA1c change and diabetic retinopathy during GLP-1 receptor agonist cardiovascular outcome trials: a meta-analysis and meta-regression. *Diabetes Care*. 2021 Jan 1;44(1):290-6.
23. Ryan, D.H. Next Generation Antiobesity Medications: Setmelanotide, Semaglutide, Tirzepatide and Bimagrumb: What do They Mean for Clinical Practice? *J. Obes. Metab. Syndr*. 2021, 30, 196–208.
24. Karagiannis T, Avgerinos I, Liakos A, Del Prato S, Matthews DR, Tsapas A, Bekiari E. Management of type 2 diabetes with the dual GIP/GLP-1 receptor agonist tirzepatide: a systematic review and meta-analysis. *Diabetologia*. 2022 Aug;65(8):1251-61.
25. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes—state-of-the-art. *Molecular metabolism*. 2021 Apr 1; 46:101102.
26. AldhobaibAY, RabbaniSI, MobarkMA. Knowledge, Attitude and Practice about a Newer Class of Antidiabetic Drug (Glucagon-like peptide-1 receptor agonist) Among the Health Care Professionals of Qassim University, Saudi Arabia. *Journal of Pharmaceutical Research*. 2021 Oct;20(4):59.