Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 6 Issue 11 November 2022

Research Article

Perceptions and Preferences Toward GLP-1 Receptor Agonists in Type 2 Diabetes Management in Saudi Arabia: A Cross-sectional, Two-arm Study

Abdulrahman Alshaikh[1], Hussein Elbadawi[2], Mohammed Aleissa[3], Fahad Alsabaan[4], Fatima Alslail[5], Hajer Almudaiheem[5], Saud Alsifri[6] and Emad R Issak[7]*

1Dr. Soliman Fakeeh Hospital, Jeddah, KSA

2My Clinic Medical Center, Jeddah, KSA

3Prince Sultan Military Medical City, Riyadh, KSA

4Security Forces Hospital, Riyadh, KSA

5Ministry of Health, Riyadh, KSA

6Al Hada Armed Forces Hospital, Taif, KSA

7Medicine Department, Asalam Center, Cairo, Egypt

***Corresponding Author:** Emad R Issak, Specialist of Internal Medicine and Research Director, Asalam Center, Zahraa Al-Maadi, Cairo, Egypt.

ORCID: 0000-0003-4150-649X.

DOI: 10.31080/ASMS.2022.06.1388

Received: September 21, 2022

Published: October 17, 2022

Abstract

Backgrounds and Objectives: The preferences of patients for oral GLP-1 RA treatments, particularly in KSA, have not yet been sufficiently studied. In order to add to the body of knowledge already available in this field, the current study sought to determine the acceptance and preference of various GLP-1 RA formulations (weekly injectable vs. daily oral) among T2DM patients in KSA as well as to investigate how doctors who treat T2DM patients there felt about GLP-1RAs.

Methods: The current cross-sectional two-arm (patients-arm and physicians-arm) study was carried out all over KSA using an online survey. Two online surveys were used, one for each arm. The analyses were carried out on 700 T2DM cases and 400 physicians (150 diabetes specialists and 250 general practitioners) who completed the surveys. The primary outcome measure in the patients-arm was the preference for oral GLP-1RA or injectable GLP-1RA. For the physicians-arm, the primary outcome measure was the right time of GLP-1RA prescription or delay.

Results: Out of the 700 patient respondents, 588 (84.0%) prefer the daily oral formula of GLP-1RA, while 112 (16.0%) prefer the once-weekly subcutaneous formula. About 40.2% of those who prefer the injectable formula perceive that the injectable formula is more effective, 30.3% reported that it is more convenient for them, and 28.6% stated that they take too many oral medications. On the other hand, reasons for preference for oral formula were perception of injections as a 'last resort' treatment (23.0%), fear of injection (20.2%), fear of hypoglycemia (19.2%), convenience (19.0%), and poor communication with physicians (18.5%).

Out of the 400 physicians, 340 (85.0%) were delayed in the prescription of GLP-1RAs for their patients, and only 60 (15.0%) prescribed GLP-1RAs at the right time. Among different criteria of respondents, only specialty affects this delay (Table 2). Interestingly, the delay is only among the general physician group (73.%) of those who delay. Reasons behind hesitance differ among groups (p-value < 0.0001), among those who delay prescription of GLP-1RAs, were injectable (72.6%, followed by time constraints (20.3%), and unavailability (7.1%). However, in those who did not delay, they perceived that the reasons behind hesitance were time constraints (45.0%), followed by unavailability (33.3%), and being injectable (21.7%).

Conclusions: In conclusion, the preference for the oral form of GLP-1RAs is self-evident in this two-arm study among patients and physicians. That can help to tackle the problem of underutilization of this group when they are indicated.

Keywords: GLP-1RAs; Adminstration Form; Delay in Prescription; Control; Preference

Introduction

Diabetes mellitus (DM) is predicted to affect more than 600 million people worldwide by 2040, with a prevalence of over 9.5 percent [1]. Additionally, the prevalence of DM is rising quickly in the Kingdom of Saudi Arabia (KSA), leading to an overuse of the resources associated with the healthcare system [2].

The Saudi Food and Drug Authority (SFDA) approved many injectable treatments belonging to the glucagon-like peptide 1 receptor agonist (GLP-1RA) class, like liraglutide in 2014, followed by exenatide, dulaglutide, lixisenatide, and then semaglutide in 2020. In healthcare facilities like KSA, where sub-optimal control of T2DM is frequently observed, these GLP1RAs are advised [3].

When conventional oral anti-diabetic drugs (OADs), such as metformin, have failed to regulate a patient's condition, GLP-1 receptor agonists (GLP-1 RAs) are used to treat T2DM patients. These treatments provide effective glycemic control with minimal risk of hypoglycemia [4,5]. Despite a wealth of research confirming their efficacy, safety, and potential benefits for improving CV outcomes, GLP-1 RAs remain underutilized [6].

The first oral form of the semaglutide molecule was developed and approved by the US Food and Drug Administration in 2019, thanks to recent advancements in the field of GLP-1 Ras, which may pave the way for increased use of this class of drugs due to its demonstrated efficacy, safety, and patient preferences [7]. Additionally, the SFDA's medicine list now includes the new oral version of semaglutide, which was recently approved in KSA for T2DM patients [8].

In other regions of the World [9-13], numerous studies have been employed to gauge patient preferences among injectable GLP-1 RA treatments. The preferences of patients for oral GLP-1 RA treatments, particularly in KSA, have not yet been sufficiently studied. Therefore, in order to add to the body of knowledge already available in this field, the current study sought to determine the acceptance and preference of various GLP-1 RA formulations (weekly injectable vs. daily oral) among T2DM patients in KSA as well as to investigate how doctors who treat T2DM patients there felt about GLP-1RAs.

Patients and Methods

The current cross-sectional two-arm (patients-arm and physicians-arm) study was carried out all over KSA using an online survey. Two online surveys were used, one for each arm. The analyses were carried out on 700 T2DM cases and 400 physicians (150 diabetes specialists and 250 general practitioners) who completed the surveys.

The study conformed to the 2011 Declaration of Helsinki principles and the Good Pharmacoepidemiology Practices (GPP) guidelines. The study was approved by an accredited centralized institutional review board, and informed consent was part of the survey.

For patients-arm, T2DM patients followed in different hospitals, at least one-year diagnosis who are injection-naïve, male or female, aged more than 18 years and agree to answer the survey were included. For the physicians-arm, doctors male or female, DM specialist of primary care physician in one of preset ten hospitals all over KSA and agree to answer the survey were included.

Outcomes

The primary outcome measure in the patients-arm was the preference for oral GLP-1RA or injectable GLP-1RA. For the physicians-arm, the primary outcome measure was the right time of GLP-1RA prescription or delay.

Respondents

A sizable pre-existing panel of respondents with T2DM who were interested in taking the study was reached via the internet. Since respondents could opt out or be dropped midway through the survey, more people were added until there were 700 evaluable sets of results for the patient arm and 400 for the physician's arm.

All eligible respondents additionally attested to their readiness to participate and explicitly agreed to have their demographic and preference data collected, stored, and reported in an anonymous manner for research purposes.

Statistical analysis

All statistical tests were carried out using a significance level of 95%. A value of $P < 0.05$ was considered statistically significant. SPSS software (Statistical Package for the Social Sciences, version 25.0, SSPS Inc, Chicago, IL, USA) was used for the statistical analyses. Data was presented as (mean ± SD) for continuous variables, median (IQR) for ordinal and non-parametric data, and frequency and percentage for categorical variables. An Independent t-test was used to compare continuous variables between groups. The Chi-square test or Phi-Cramer test was used to compare categorical variables between groups.

Results

Patients-arm: characteristics of respondents

Of the total of 2445 respondents who initiated the survey, 1745 (71.37%) did not complete the survey. The majority of these excluded respondents did not meet the pre-defined inclusion/exclusion criteria set out in the patient screener; other reasons for exclusion included refusing to participate or providing invalid answers within the survey. Therefore, the final analysis sample included 700 respondents.

Patients-arm: demographic characteristics for the final analysis set

- Out of the 700 patients, 334 (47.7%) were females, and 366 (52.3%) were males. The mean age was 42.08 ± 13.30 years. Obese patients were 348 (49.7%) of them.
- 239 (34.1%) diagnosed as T2DM 1-3 years ago, 246 (35.1%) 4-10 years and 215 (30.7%) more than 10 years.
- The socioeconomic status of respondents was very high in 42 (6.0%) of them, middle to high in 282 (40.3%), low in 344 (49.1%), and very low in 32 (4.6%) of them. The educational level of respondents was illiterate in 27 (3.9%) of them, elementary in 39 (5.6%), a middle school in 39 (5.6%), high school or diploma in 264 (37.7%), and college degree or higher in 331 (47.3%).
- The respondents were distributed allover the KSA: North region 132 (18.9%), South region 147 (21.0%), East region 140 (20.0%), West region 147 (21.0%), and Central region 134 (19.1%).

Patients-arm: preference towards GLP-1RA formulas

- Out of the 700 respondents, 588 (84.0%) prefer the daily oral formula of GLP-1RA, while 112 (16.0%) prefer the once-weekly subcutaneous formula.
- The majority of those who preferred the injectable formula were male respondents 104/112 (92.9%) and only eight females (7.1%), p-value < 0.001). There was a significant difference between those who prefer the oral formula and those who prefer the injectable formula with regard to obesity (p-value = 0.046), as shown in Table 1, which demonstrated that 51.4% of those who prefer the oral formula and 41.1% of those who prefer the injectable formula were obese.
- The socioeconomic level has a great impact on patients' preferences, as shown in table 1 (p-value < 0.001). Very high levels prefer the oral formula to the injectable. Also, the educational level did affect the patients' preferences, as shown in table 1 (p-value = 0.023).

		Prefer daily oral formula		Prefer weekly injectable formula		p-value
		Mean	SD	Mean	SD	
Age		41.69	13.29	44.13	13.32	0.078
		N	%	N	%	
Cohort size		588	84.0%	112	16.0%	
Gender	Female	326	55.4%	8	7.1%	0.000
	Male	262	44.6%	104	92.9%	
Duration	Less than 3 years	202	34.4%	37	33.0%	0.426
	4-10 years	211	35.9%	35	31.3%	
	More than 10 years	175	29.8%	40	35.7%	
Obese	Non obese	286	48.6%	66	58.9%	0.046
	Obese	302	51.4%	46	41.1%	
Socioeconomic status	Very high	42	7.1%	0	0.0%	0.000
	Middle to high	233	39.6%	49	43.8%	
	Low	293	49.8%	51	45.5%	
	Very low	20	3.4%	12	10.7%	

Educational level	Illiterate	17	2.9%	10	8.9%	0.023
	Elementary	33	5.6%	6	5.4%	
	Middle school	35	6.0%	4	3.6%	
	High school or diploma	218	37.1%	46	41.1%	
	College degree or higher	285	48.5%	46	41.1%	
Region	North region	109	18.5%	23	20.5%	0.222
	South region	123	20.9%	24	21.4%	
	East region	117	19.9%	23	20.5%	
	West region	118	20.1%	29	25.9%	
	Central region	121	20.6%	13	11.6%	

Table 1: Patients-arm: factors related to preference.

- Neither the age nor the region of respondents had an impact on their preference (p-values > 0.05), as shown in table 1.

Patients-arm: reasons behind preference towards GLP-1RA formulas

Table 2 demonstrated that 40.2% of those who prefer the injectable formula perceive that the injectable formula is more effective, 30.3% reported that it is more convenient for them, and 28.6% stated that they take too many oral medications. On the other hand, reasons for preference for oral formula were perception of injections as a 'last resort' treatment (23.0%), fear of injection (20.2%), fear of hypoglycemia (19.2%), convenience (19.0%), and poor communication with physicians (18.5%).

	N	%
Prefer daily oral formula		
Fear of injection	119	20.2%
Perception of injections as 'last resort' treatment	135	23.0%
Fear of hypoglycemia	113	19.2%
Poor communication with physicians	109	18.5%
Convenience	112	19.0%
Prefer weekly injectable formula		
Perception of more efficacy	45	40.2%
More convenient for me	35	31.3%
I take too many oral medications	32	28.6%

Table 2: Patients-arm: reasons behind preference.

Physicians-arm: characteristics of respondents

Of the total of 915 respondents who initiated the survey, 515 (56.3%) did not complete the survey. The majority of these excluded respondents did not meet the pre-defined inclusion/exclusion criteria set out in the screener; other reasons for exclusion included refusing to participate or providing invalid answers within the survey. Therefore, the final analysis sample included 400 respondents.

Physicians-arm: demographic characteristics for the final analysis set

Out of the 400 physicians, 196 (49.0%) were females, and 204 (51.0%) were males. Diabetes specialists were 150 (37.5%) of them, and general physicians were 250 (62.5%). The mean age was 44.78 ± 8.66 years.

Physicians-arm: GLP-1RA delay on prescriptions

Out of the 400 physicians, 340 (85.0%) were delayed in the prescription of GLP-1RAs for their patients, and only 60 (15.0%) prescribed GLP-1RAs at the right time. Among different criteria of respondents, only specialty affects this delay (Table 2). Interestingly, the delay is only among the general physician group (73.%) of those who delay.

Reasons behind hesitance differ among groups (p-value < 0.0001), among those who delayed prescription of GLP-1RA were injectable (72.6%, followed by time constraints (20.3%), and un-availability (7.1%). However, in those who did not delay, they perceived that the reasons behind hesitance were time constraints (45.0%), followed by un-availability (33.3%), and being injectable (21.7%) (Table 2).

		Right time		Delayed		
Total		60		340		
		Mean	SD	Mean	SD	P-value
Age		42.9	8.5	45.1	8.7	0.064
		N	%	N	%	
Gender	Male	33	55.0%	171	50.3%	0.501
	Female	27	45.0%	169	49.7%	
Specialty	Diabetes specialist	60	100.0%	90	26.5%	0.000
	General physician	0	0.0%	250	73.5%	
Hospital	Ministry of health hospital	12	20.0%	65	19.1%	0.997
	Military hospital	12	20.0%	73	21.5%	
	National guard hospital	7	11.7%	37	10.9%	
	University hospital	10	16.7%	61	17.9%	
	Private hospital	19	31.7%	104	30.6%	
Reason for hesitance	Un-availability	20	33.3%	24	7.1%	0.000
	Time constraints in clinic	27	45.0%	69	20.3%	
	Injectable administration	13	21.7%	247	72.6%	

Table 3: Physician attitude towards GLP-1Ras.

Discussion and Conclusion

In this survey, the majority of those Saudi patients with T2DM preferred once orally administered GLP-1RA (84%) over once weekly SC GLP-1RA (16%). Reasons for preference of the oral formula were perception of injections as a 'last resort treatment, fear of injection, fear of hypoglycemia, convenience, and poor communication with physicians. This preference is very clear among the very high socioeconomic level.

On the other hand, the majority of physicians (85%) delay the prescription of GLP-Ras for their patients when they need it according to guidelines. Interestingly, this delay is only among the general physician group (73.%) of those who delay.

Reasons behind physicians' hesitance among those who delay prescription of GLP-1RAs were being injectable (72.6%) was the most reported reason, followed by time constraints (20.3%), and un-availability (7.1%). However, those who did not delay perceived that the reasons behind hesitance were time constraints (45.0%), followed by unavailability (33.3%), and being injectable (21.7%).

The administration form was the most important factor for patients' preference and for physicians' delay in the prescription of GLP-1RA. Therefore, the availability of oral GLP-1RA is one of the significant factors in increasing their utilization when recommended according to guidelines recommendations.

The current study has the advantage that it is a two-arm study of patients, and physicians, which highlighted the different aspects of the utilization and preference for GLP-1RAs formulations. Also, it has enough sample size; of 700 patients and 400 physicians all over the regions and hospitals of KSA.

In conclusion, the preference for the oral form of GLP-1RAs is self-evident in this two-arm study among patients and physicians. That can help to tackle the problem of underutilization of this group when they are indicated.

Bibliography

1. International Diabetes Federation, IDF Diabetes Atlas, International Diabetes Federation, Brussels, Belgium, 8th edition, (2017).

2. Al Dawish MA., *et al*. "Diabetes Mellitus in Saudi Arabia: A Review of the Recent Literature". *Current Diabetes Reviews* 12.4 (2016): 359-368.

3. Alkhatib N., *et al*. "Economic Analysis of glucagon like peptide-1 receptor agonists from the Saudi Arabia Payer Perspective". *Saudi Pharmaceutical Journal* (2020): 30.

4. DeFronzo RA. "Combination therapy with GLP-1 receptor agonist and SGLT2 inhibitor". *Diabetes, Obesity and Metabolism* 19.10 (2017): 1353-1362.

5. DeFronzo RA., *et al*. "Type 2 diabetes mellitus". *Nature Reviews Disease Primers* 1 (2015): 15019.

6. Mardetko N., *et al*. "Uptake of new antidiabetic medicines in 11 European countries". *BMC Endocrine Disorders* 21.1 (2021): 127.

7. FDA. "FDA Approves First Oral GLP-1 Treatment for Type 2 Diabetes". FDA. FDA (2019).

8. Drugs List | Saudi Food and Drug Authority (sfda.gov.sa) (2022).

9. Brooks A., *et al*. "Patient preferences for GLP-1 receptor agonist treatment of type 2 diabetes mellitus in Japan: a discrete choice experiment". *Diabetes Therapy* 10.2 (2019): 735-749.

10. Gelhorn HL., *et al*. "Evaluating preferences for profiles of glucagon-like peptide-1 receptor agonists among injection-naive type 2 diabetes patients in Japan". *Patient Prefer Adherence* 10 (2016): 1337-1348.

11. Gelhorn HL., *et al*. "Evaluating preferences for profiles of GLP-1 receptor agonists among injectionnaive type 2 diabetes patients in the UK". *Patient Prefer Adherence* 9 (2015): 1611-1622.

12. Hauber AB., *et al*. "A discrete-choice experiment to quantify patient preferences for frequency of glucagon-like peptide-1 receptor agonist injections in the treatment of type 2 diabetes". *Current Medical Research and Opinion* 32.2 (2016): 251-262.

13. Polster M., *et al*. "A comparison of preferences for two GLP-1 products—liraglutide and exenatide—for the treatment of type 2 diabetes". *Journal of Medical Economics* 13.4 (2010): 655-661.

14. Qin L., *et al*. "Glucagon-like peptide-1 receptor agonist treatment attributes important to injection-naive patients with type 2 diabetes mellitus: a multinational preference study". *Diabetes Therapy* 8.2 (2017a): 321-334.

15. Qin L., *et al*. "Glucagon-like peptide-1 receptor agonist treatment attributes important to injection-experienced patients with type 2 diabetes mellitus: a preference study in Germany and the United Kingdom". *Diabetes Therapy* 8.2 (2017b): 335-353.