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Original Research Article

Glucagon-like peptide-1 receptor agonist versus basal insulin in type-2 diabetic patients: An efficacy and safety analysis

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Abstract

Purpose: *To compare the effectiveness of glucagon-like peptide 1 receptor agonist with that of basal insulin in type 2 diabetes patients.*
Methods: *Type-2 diabetes patients who were insensitive to metformin were treated with glucagon-like peptide 1 receptor agonist (GP cohort, n = 115) or basal insulin (BI cohort, n = 152) with metformin. Hemoglobin A1c (HbA1c) level and body weight were determined, and adverse effects also recorded.*
Results: *After 16 weeks of treatment, glucagon-like peptide 1 receptor agonist did not significantly reduce HbA1c levels (7.45 ± 2.11 % vs. 7.01 ± 2.01, p = 0.107). In contrast, basal insulin significantly reduced the levels of HbA1c (7.91 ± 2.98 % vs. 7.13 ± 2.22 %, p = 0.010, q = 3.852). Glucagon-like peptide 1 receptor agonist reduced the body weight of patients (65.25 ± 7.55 kg vs. 62.16 ± 6.15 kg, p = 0.0008, q = 5.121), unlike basal insulin (63.71 ± 6.15 vs. 62.65 ± 6.76 kg, p = 0.154).*
Conclusion: *Glucagon-like peptide 1 receptor agonist and basal insulin + metformin produce identical effectiveness in the treatment of type-2 diabetic patients.*

Keywords: *Glucagon-like peptide-1 receptor agonist, Glycemic control, Insulin, Metformin, Type-2 diabetes*

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INTRODUCTION

It has been estimated that type-2 diabetes is prevalent in 11.6 % of the population of China, with 3000 new patients per day [1]. Diabetic patients have higher chances of developing complications, comorbidity, morbidity, and mortality than non-diabetic persons [2]. Many diabetic patients are unable to achieve glycemic control due to the failure of oral hypoglycemic agents [3]. Studies on several hypoglycemic agents e.g. sulfonylureas, insulin, glucagon-like peptide 1 receptor agonists, dipeptidyl peptidase 4 inhibitors, and their combinations have revealed consistent ineffectiveness in glycemic control [4]. Usually, the first drug of choice for type 2 diabetes patients is metformin. When metformin is not effective, other hypoglycemic agents are added for management of hyperglycemia [5]. Glucagon-like peptide 1 receptor agonists improve glucose homeostasis

in type 2 diabetes patients by mimicking the action of glucagon-like peptide 1 [6]. Basal insulin has a constant duration of action, and it acts for long periods without much fluctuation [7]. Basal insulin or glucagon-like peptide 1 receptor agonist is often used in combination with metformin. However, it is not clear whether this combination is able to control hyperglycemia without the risk of hypoglycemia [3,6]. Therefore, for the purpose of proper selection of hypoglycemic agents to be combined with metformin in cases where metformin is not effective for management of diabetes, there is a need for retrospective analysis to compare effectiveness and safety of insulin and glucagon-like peptide 1 receptor agonist among type 2 diabetes patients. The objective of this retrospective analysis was to compare glucagon-like peptide 1 receptor agonist and basal insulin with respect to their effectiveness and safety profiles in the treatment of type 2 diabetes.

EXPERIMENTAL

Ethical approval and consent to participate

Ethical approval for the study was obtained from Fujian Provincial Hospital Ethics cum Review Board (approval number of XMU/CL/14/19 dated 15 August 2019). The study adhered to the STROBE guidelines (strengthening the reporting of observational studies in epidemiology), as well as Helsinki guidelines as contained in 2008 Declarations of [8]. Patient's data were collected with approval from the parent hospital and the referring hospital.

Study population

The total sample size was comprised of 267 diabetic patients who were treated with metformin from January 15, 2018 to January 1, 2019. Metformin had no significant effect on the blood glucose levels of the selected patients. The GP cohort (115 patients) were treated with 1.2 mg subcutaneous glucagon-like peptide 1 receptor agonist ((Liraglutide, Novo Nordisk China, Tianjin, China) and 850 mg metformin (Sino-American Shanghai Squibb Pharmaceutical Ltd, Shanghai, China) every 12 h. The remaining 152 patients (BI cohort) were placed on 0.2 units/kg basal insulin (Lantus, Sanofi China, Shanghai, China) and 850 mg metformin. The flow chart for the study is shown in Figure 1.

Measurement of HbA1c

Levels of HbA1c were measured in all patients 16 weeks (4 months) and 32 weeks (8 months) after treatment. Data on bodyweights of patients and treatment-emergent adverse effects were collected and analyzed.

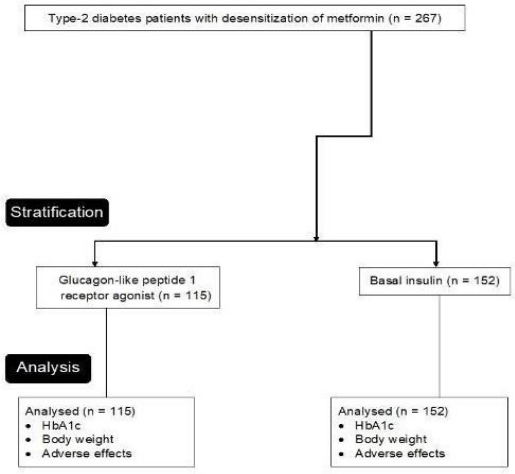

Figure 1: Flow chart of the study

Statistical analysis

Numerical data are expressed as mean ± SD, while ordinal data are presented as frequency (percentage). Statistical analysis was done with InStat 3.01, GraphPad, San Diego, CA, USA. The Fischer exact test was used for ordinal data, while Mann-Whitney U-test was applied for numerical data. Tukey test (considering critical value [q] > 3.323 as significant) was performed for post hoc analysis. All results were significant at 95 % level of confidence.

RESULTS

Demographical and clinical characteristics of patients

At the start of the treatment, there were no differences in the demographical and clinical characteristics of the patients ($p > 0.05$; Table 1).

HbA1C levels

After 4 months of treatment with glucagon-like peptide 1 receptor agonist, there were no decreases in HbA1c levels (7.45 ± 2.11 % *vs*. 7.01 ± 2.01, $p = 0.107$), but basal insulin treatment reduced HbA1c levels (7.91 ± 2.98 % *vs*. 7.13 ± 2.22 %, $p = 0.010$, $q = 3.852$). However, there were significant reductions in HbA1c level after 8 months of treatment with glucagon-like peptide 1 receptor agonist (7.45 ± 2.11 % *vs*.6.75 ± 1.81 %, $p < 0.0001$, $q = 3.792$) and basal insulin (7.91 ± 2.98 % *vs*. 6.56 ± 1.54 %, $p < 0.0001$, $q = 4.141$). These results are shown in Figure 2.

Changes in body weight

After 16-weeks of treatment with glucagon-like peptide 1 receptor agonist, there was reduction in mean body weight of patients (65.25 ± 7.55 kg *vs*. 62.16 ± 6.15 kg, $p = 0.0008$, $q = 5.121$) but basal insulin did not significantly affect the body weight of patients (63.71 ± 6.15 *vs*. 62.65 ± 6.76 kg, $p = 0.154$) after 16 weeks of treatment. After 32 weeks of treatment with glucagon-like peptide 1 receptor agonist, there were further significant decreases in the body weight of patients ($p < 0.0001$, $q = 10.11$). Basal insulin also significantly decreased the mean body weight of patients after 32 weeks of treatment ($p < 0.0001$, $q = 6.984$, Figure 3).

Treatment-emergent adverse effects

Patients in the two cohorts experienced irritation at the injection site. However, nausea, vomiting, diarrhea, constipation, and headache were reported only in patients in GP cohort. These results are presented in Table 2.

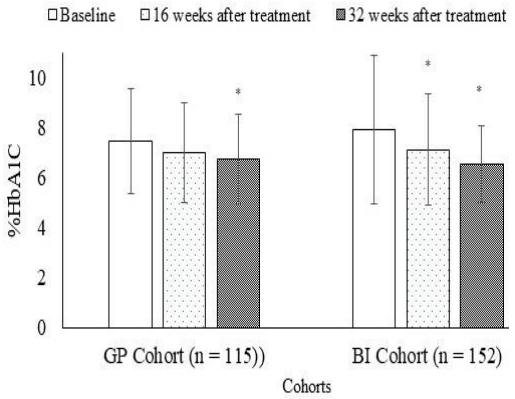

Figure 2: HbA1c levels of patients. Data are expressed as mean ± SD. *$p < 0.05$, compared to baseline

Table 1: Demographical, anthropological, and clinical characteristics of the enrolled patients HbA1c

Characteristic	Cohort			Comparison between cohorts (p)
		GP	BI	
Number of patients		115	152	
Age (years)	Minimum	35	35	0.392
	Maximum	72	72	
	Mean ± SD	55.45±8.91	56.42±9.45	
Gender	Male	67(58)	81(53)	0.457
	Female	48(42)	71(47)	
Ethnicity	Han Chinese	115(100)	152(100)	0.989
	Tibetan	9(8)	12(8)	
	Mongolian	2(2)	3(2)	
Duration of diabetes (years)	Minimum Maximum	3	3	0.204
		15	15	
	Mean ± SD	7.15±4.01	6.56±3.59	
Body weight (kg)		65.25±7.55	63.71±6.15	0.068
Body mass index (kg/m^2)	Minimum Maximum	23	23	0.119
		33	33	
	Mean ± SD	28.58±2.57	29.12±2.98	
HbA1c (%)	Minimum	7	7	0.156
	Maximum	13	13	
	Mean ± SD	7.45±2.11	7.91±2.98	

Numerical data are shown as mean ± SD, while ordinal data are shown as frequency (percentage). $P < 0.05$ and $q > 3.323$ were considered significant.

Table 2: Treatment-emergent adverse effects

Characteristic	Cohort		Comparison between cohorts (p)
	GP	*BI*	
Effects	115	152	
Irritation at the injection site	9(8)	15(10)	0.669
Nausea	17(15)*	1(1)	<0.0001
Vomiting	15(13)*	1(1)	<0.0001
Diarrhea	7(6)*	1(1)	0.023
Headache	9(8)*	1(1)	0.003
Constipation	11(10)*	1(1)	0.0005
Back pain	5(4)	1(1)	0.088

Data are shown as frequency (percentage). *$p < 0.05$ (significant treatment-emergent adverse effect for GP cohort)

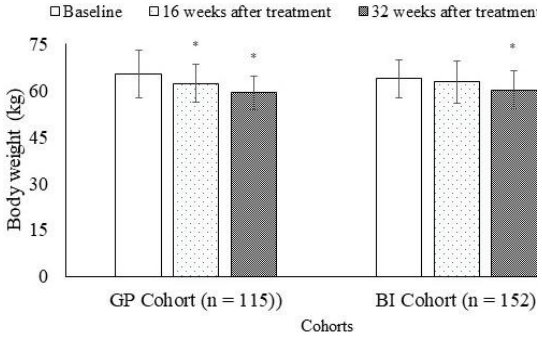

Figure 3: Bodyweight of patients. Data are expressed as mean ± SD. *P < 0.05, compared to baseline.

DISCUSSION

Treatment with glucagon-like peptide 1 receptor agonist or basal insulin for 32 weeks resulted in significant reduction in % Hb1Ac. The results of the study are consistent with those obtained in an open-label, randomized, parallel trial [6]. Treatment with only basal insulin for 16 weeks also produced marked reduction in % Hb1Ac, which is not in agreement with previous findings in open-label, randomized, parallel trials [6, 8, 10]. The sample size used in these studies were small, leading to αerror (type-I) error which caused significant differences [11]. The current study showed that the effect of combination of glucagon-like peptide 1 receptor agonist or basal insulin with metformin when glycemic control was not achieved in type-2 diabetes patients. After 32 weeks of treatment with glucagon-like peptide 1 receptor agonist or basal insulin, the body weight of patients was reduced. However, at 16 weeks of treatment with glucagon-like peptide 1 receptor agonist, body weight was reduced, but treatment with basal insulin for 16 weeks did not reduce body weight. These results are in agreement with results previously obtained in open-label, randomized, parallel trials [6,9,10,12]. Glucagon-like peptide 1 receptor agonist reduces appetite. Therefore, body weight can be reduced in patients who are on GLP 1 treatment [12]. However, basal insulin has not been associated with significant reduction in bodyweight [6]. Therefore, glucagon-like peptide 1 receptor agonist should be recommended for obese patients, while basal insulin should be recommended for non-obese patients.

Limitations of the study

First of all, this study was carried out as a retrospective analysis without any control group. Secondly, the effects of demographic and clinical conditions on HbA1c and body weight were not investigated.

CONCLUSION

The results obtained in this study have demonstrated that glucagon-like peptide 1 receptor agonist and basal insulin reduce HbA1c and body weight of type-2 diabetic patients after 32 weeks of combined treatment with metformin, with manageable treatment-emergent adverse effects. Thus, it is beneficial to use glucagon-like peptide 1 receptor agonist or basal insulin, in combination with metformin for type-2 diabetes patients when glycemic control is not achieved.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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