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Contrasting Three Non-hypoglycemic Antidiabetic Drug Effects on Glycemic Control in Newly Diagnosed Type II Diabetes Mellitus: An Experimental Study

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Abstract

BACKGROUND: Diabetes mellitus (DM) type 2 is the most public chronic, metabolic illness whose prevalence is quickly becoming high international. Insulin resistance, the essential metabolic problem leads to the development of DM type 2, is seen in about 90% of patients.

AIM: The study's aim was to compare the efficacy of three antidiabetic drugs on glycated hemoglobin.

METHOD: A cross-sectional comparative study for newly diagnosed type II diabetic patients were assigned randomly into one of three conditions: Group I: Metformin consuming patients, Group II: Pioglitazone consuming patients, and Group III: Vildagliptin consuming patients. All patients were newly diagnosed. For all of them, baseline glycated hemoglobin was requested. After that, random assignment was carried out. After 3 months, glycated hemoglobin was checked and compared.

RESULTS: Participants were distributed randomly into 27.9% metformin taking participants, 31.1% pioglitazone taking, and 41% vildagliptin taking patient. Findings suggested significant difference between Groups I and III (p =). Likewise, significant difference was seen between Groups II and III (p =). However, Groups I and II have comparable effects (p =). Indeed, all groups had shown significant efficacy on HbA1c.

CONCLUSION: Metformin, pioglitazone, and vildagliptin had shown significant impact on HbA1c with variable degree: Metformin and pioglitazone had shown comparably similar efficacy that was exerted more significant impact on HbA1c than vildagliptin does.

Introduction

Diabetes mellitus (DM) type 2 is the most public chronic, metabolic illness whose prevalence quickly becomes high international. Insulin resistance, the essential metabolic problem leads to the development of DM type 2, is seen in about 90% of patients [1]. In insulin resistance disorder, body cells mostly the marginal adipose, muscle, and liver cells fail to react correctly to insulin indicating, lead to reduce in uptake of outlying cells glucose and high yielding in hepatic glucose [2]. Moreover, insulin resistance disorder leads to deficiency of insulin excretion from pancreatic β-cells. Therefore, repair sensitivity of insulin is a chief action approach for the management of DM type 2 [1]. Metformin broadly suggested as treatment of hyperglycemia in patients with DM type 2 [3]. Metformin is low cost, infrequently has hypoglycemia when taken as monotherapy, has useful advantage on weight and lipid, and looks to decrease the danger of cardiovascular disease [4]. Utmost people tolerate metformin; gastrointestinal symptoms may need a change to long-acting preparations, low dose, or cessation [5]. Pioglitazone is a diabetes drug (thiazolidinedione-type, also called "glitazones"), the side effect of it is weight gain, peripheral edema, congestive cardiac failure, and high risk of bladder cancer, it used along with a good regime and exercise to control increase blood glucose in DM type 2. It helping to reestablish body good reaction to insulin, by dropping blood glucose. Pioglitazone acts to avoid kidney injury, blindness, nerve difficulties, loss of extremities, and sexual desire problems [6]. Vildagliptin is a solid inhibitor of dipeptidyl peptidase-4 that recuperates glycemic control by high competence of both A and B cells of pancreas to intellect and reply correctly to glucose [7], [8]. GLP-1 and GIP level become high after use vildagliptin by lowering glucose levels during the day [9] and lead to decrease HbA1c [10]. The aim of the study was to compare the efficacy of metformin, vildagliptin, and pioglitazone on glycated hemoglobin.

Method

A cross-sectional comparative study for newly diagnosed type II diabetic patients who were

assigned randomly into one of the three conditions: Group I (metformin consuming patients), Group II (pioglitazone consuming patients), and Group III (vildagliptin consuming patients). The present study extended from June 2020 to December 2020. During clinic visit, diabetic patients accepted to be enrolled in the study. All patients were newly diagnosed. For all of them, baseline glycated hemoglobin was requested. After that, random assignment was carried out. After 3 months, new glycated hemoglobin was checked and compared with baseline one. Exclusion criteria included all of the following conditions:

1. Volume overload states such as heart failure, renal failure, or liver failure.
2. Current infection.
3. Carcinoma of the bladder.
4. Pregnancy.
5. Type 1 DM

Statistical analysis was done by SPSS 22, frequency and percentage used for categorical data, mean, median, and SD for continuous data. ANOVA test used for evaluation differences between mean of continues variables. $p \leq 0.05$ is considered statistically significant.

Results

A cross-sectional study involving 61 patients with DM type 2; 27.9% of them were taking metformin, 31.1% were taking pioglitazone, and 41% were taking vildagliptin (Table 1).

Table 1: Distribution of patients according to the types of drug received

Variables	Frequency	Percentage
Metformin	17	27.9
Types of drug		
Pioglitazone	19	31.1
Vildagliptin	25	41.0

Figure 1 shows the distribution of gender according to types of drugs: 19.67% of females were taking vildagliptin, 18% taking metformin, and 9.84% were taking pioglitazone. For male counterpart, 21.31% of them were taking vildagliptin, 18% taking metformin, and 13.11% were consuming pioglitazone.

Table 2: Different between mean of age, Hb, HBA1c (before) drug giving, and types of drugs

Variables	Metformin	Pioglitazone	Vildagliptin	p-value
Age	42 ± 12	36.7 ± 5.7	39.8 ± 5.7	0.14
Hb	13.1 ± 1.6	12.3 ± 1.6	12.3 ± 1.6	0.24
HbA1c before	8.2 ± 0.6	8.6 ± 0.6	8.3 ± 0.7	0.08

$p \leq 0.05$ (significant).

The distribution of drugs effects according to the types of drugs giving. About 6.56% and 3.28% of patients take vildagliptin and metformin, respectively, affected by hydrochlorothiazide, while 8.2% and 6.56% of patients take vildagliptin and metformin, respectively, affected by thyroxine, as shown in Figure 2.

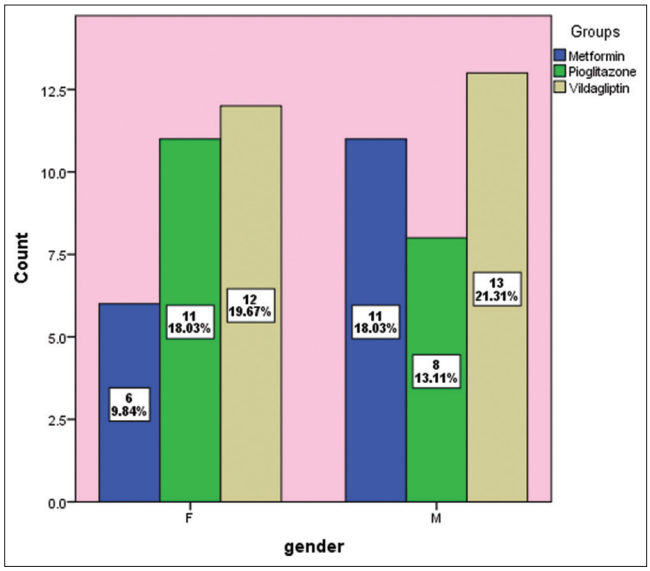

Figure 1: Distribution of gender according to the types of drugs giving

According to Table 2, there is no different between mean of age, Hb, HBA1c (before), and types of drugs.

According to Table 3, there is a significant different between mean of HbA1c (after) in patients take metformin and vildagliptin, metformin decreases HbA1c (after) more than vildagliptin. In addition, there is a significant different between mean of HbA1c (after) in patients take pioglitazone and vildagliptin, pioglitazone decreases HbA1c (after) more than vildagliptin. No significant different between mean of HbA1c (after) in patients takes metformin and pioglitazone.

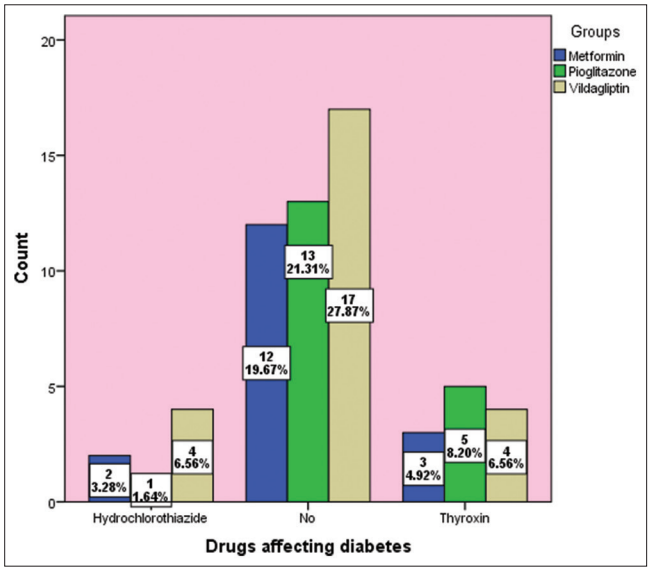

Figure 2: Distribution of drugs effects according to the types of drugs giving

Table 3: Different between mean of HBA1c (after) and types of drugs

Drugs	HBA1c after treatment		
	Mean	SD	p-value
Metformin	7.1	0.6	0.29
Pioglitazone	6.8	0.5	
Metformin	7.1	0.6	0.004
Vildagliptin	7.6	0.6	
Pioglitazone	6.8	0.5	0.0001
Vildagliptin	7.6	0.6	

$p \leq 0.05$ (significant).

In Table 4, there is a significant difference between mean of HbA1c (before and after) according to drugs taken. All types of drug decrease the mean of HbA1c after take it.

Table 4: Different between mean of HBA1C before and after drug giving, according to drugs

Variables	Mean	n	Std. deviation	p-value
Metformin	8.2	17	0.6	0.0001
HbA1C after	7.1	17	0.6	
Pioglitazone				
HbA1C before	8.6	19	0.6	0.0001
HbA1C after	6.8	19	0.5	
Vildagliptin				
HbA1C before	8.3	25	0.7	0.0001
HbA1C after	7.7	25	0.6	

$p \leq 0.05$ (significant).

Discussion

The present study aimed at contrasting the effects of three common antidiabetic drugs, namely, metformin, vildagliptin, and pioglitazone. The present study had hypothesized that pioglitazone would positively affect glycemic control as evidenced by glycated hemoglobin at a greater degree than the remaining drugs would do. After data analysis, study's findings suggested comparable effects for both pioglitazone and metformin on glycemic control. Indeed, both drugs' effects were superior to vildagliptin influence. These findings are, therefore, partially consistent with the study's hypotheses. Knowing that no known study had come up with similar findings; the present study's results can be considered as novel result.

Many mechanisms and action sites lead to differences in glucose-lowering efficacy. Pioglitazone as single therapy has efficacy to decrease HbA1c and has greater effect on FBS decreasing. In the present study, metformin, pioglitazone, and vildagliptin have significant effect as monotherapy to decrease HbA1c and FBS. Fahmida *et al.* have the same opinion pioglitazone to be better choice in decrease HbA1c and not less than metformin [1]. Many studies show that pioglitazone monotherapy maintained the continued antihyperglycemic effect [11], [12]. The efficacy of fixed dose of pioglitazone is better than multiple doses in improving glycemic control [13], [14]. Recommendation of the American Diabetes Association is that the metformin is the first line of treatment DM type 2 and decrease HbA1c [15].. Metformin reduces the risks of death and stroke more than insulin when comparing [16]. Metformin as a monotherapy leads to delay the glycemic control [17]. Vildagliptin, bettering A-cell and B-cell function and by decreasing insulin resistance, recovers insulin sensitivity in patients with Type 2 DM [18]. In the present study, there is a significant difference between metformin and vildagliptin in glycemic control and decrease HbA1c, metformin more preferable. Studies not agree with this results and state that the benefit of metformin over vildagliptin in lowering HbA1c was no longer clear in patients with baseline HbA1c levels < 8.0% and vildagliptin was newly revealed to have comparable efficacy with baseline HbA1c ≈ 8.7% [19]. In the present study, also there is a significant difference between pioglitazone and vildagliptin in glycemic control and decrease HbA1c, pioglitazone more preferable, other studies disagree with the current results that compared to pioglitazone, vildagliptin has a useful effect on HbA1c levels. Vildagliptin is more active than pioglitazone in patients with type 2 diabetes [20]. Type 2 diabetes patients whose had been ineffectually controlled with metformin were allocated to pioglitazone (15 mg/day), if the HbA1c levels of the subjects at 16 weeks overdid 6.5%, then up to 100 or 30 mg/day, correspondingly increased the dose of pioglitazone [21]. In the present study, also, there is no significant difference between metformin and pioglitazone in glycemic control and decrease HbA1c, this is similar to another study stated that metformin-pioglitazone had an excessive influence on the decrease of HbA1c, there was no significant difference between two groups ($p = 0.132$). Sung-Chen Liu stated that there is no statistically significant difference between them [22]. Old age can decrease the reaction to management. Older patients commonly have a longer duration of diabetes and insulin resistance when linked to younger patients [23]. All of these causes can decrease the reaction to management. Chawla *et al.* also could not find any statistically significant difference in HbA1c decrease between these two management groups [24]. However, despite the fact that the present study was conducted under strict conditions and standardized environments, confounding factors could not be perfectly eliminated which might interfered with results. Examples may include non-compliance of patients with the diet, drug's type (generic vs. brand), or dose [25], [26].

Conclusion

Metformin, pioglitazone, and vildagliptin act to decrease HbA1c significantly when used as monotherapy. Metformin and pioglitazone decrease HbA1c more significantly than vildagliptin. Indeed, both metformin and pioglitazone were comparable in decreasing HbA1c.

Weakness of Study

The present study involved collecting patients from a single portal. Upcoming studies should address this flaw and variegate the sample. The sample size, although sufficient and within the accepted limits of effect size, has to increase in future studies positively affect the study's findings. The study designed to be a single-blinded experiment. Upcoming experiment should adopt double-blinded approach for better outcomes.

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