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EFFICACY AND SAFETY OF VILDAGLIPTIN AS ADD-ON THERAPY TO PIOGLITAZONE IN PATIENTS WITH TYPE II DIABETES MELLITUS

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Abstract

Background: Diabetes mellitus type II (DM) is a chronic metabolic condition characterized by insulin resistance and decreased insulin production. In patients with type II diabetes, the combination of pioglitazone and vildagliptin has been demonstrated to enhance glycemic control. However, studies investigating the effectiveness and safety of this combination treatment in the real-world setting are insufficient.

Objectives: this retrospective study was to assess the effectiveness and safety of vildagliptin when used as supplementary treatment with pioglitazone for patients diagnosed with type II diabetes mellitus

Study design: A Retrospective Study

Duration and place of study: department of medicine mmc mardan from jan 2022 to jan 2023

Methods: The study comprised 65 patients who received a combination therapy of vildagliptin/pioglitazone at either a high dosage of 100/30 mg once daily (n=35) or a low dose of 50/15 mg once daily (n=30). Additionally, some patients received monotherapy with either vildagliptin at 100 mg once daily (n=33) or pioglitazone at 30 mg once daily (n=32). The secondary objectives included changes in fasting plasma glucose (FPG) concentrations, body weight, and any adverse events.

Results:
The study included 65 patients, 56.9% males and 43.07% females. The average age of the participants was 58.5 years, ranging from 16 to 75 years. 11 common adverse events were observed, the most common of which was nasopharyngitis (4.6%). Dizziness, headache, upper respiratory tract infection, asthenia, and constipation were all typical side effects. Vildagliptin/Pioglitazone 100/30 mg once daily (n=35), 50/15 mg (n=30), 100 mg Vildagliptin (n=33), and 30 mg Pioglitazone (n=32) were used in the study. For glycemic control, baseline HbA1c levels ranged from 8.2% in the

Vildagliptin/Pioglitazone 100/30 mg group to 8.9% in the 30 mg group. At baseline, fasting plasma glucose (FPG) levels varied from 9.2 mmol/L in the Vildagliptin/Pioglitazone 100/30 mg group to 10.3 mmol/L in the 50/15 mg group. T2DM lasted 3.5-4.2 years in all participants.

Conclusion: Incorporating vildagliptin into pioglitazone treatment among patients diagnosed with type II diabetes mellitus led to notable enhancements in glycemic regulation while exhibiting no substantial alterations in body weight. The combination therapy demonstrated favorable tolerability and may be considered a viable and secure therapeutic approach for those diagnosed with type II diabetes mellitus.

Keywords: Type II diabetes mellitus, Vildagliptin, Pioglitazone, efficacy, safety.

Introduction

Diabetes type II (DM) is a chronic metabolic disorder characterized by insulin resistance and reduced insulin production. It is a serious public health problem, with a worldwide prevalence estimated at 9.3% in 2019 and expected to rise to 10.9% by 2045[(1)]. Type II diabetes that is not well managed may have significant consequences such as cardiovascular disease, neuropathy, nephropathy, and retinopathy[(2)]. Therefore, achieving and maintaining glycemic control is crucial in managing type II DM.

The American Diabetes Association (ADA) advocates a comprehensive approach to type II diabetes management, including lifestyle changes, oral antidiabetic medications, and insulin treatment[(3)]. Despite the availability of many treatment choices, many type II diabetic patients struggle to attain and maintain glycemic control[(4)]. This emphasizes the need for more effective and safe treatment choices.

Pioglitazone is classified as a thiazolidinedione (TZD) oral antidiabetic medication, which works by activating the (PPAR-γ), enhances insulin sensitivity and improves glycemic control[(5)]. The use of this treatment modality is often seen as a secondary therapeutic approach in patients diagnosed with type II diabetes mellitus who have not achieved satisfactory glycemic regulation by the usage of metformin as a standalone treatment[(6)]. However, pioglitazone has been linked to negative outcomes, including weight gain and fluid retention[(7)].

Vildagliptin is a pharmaceutical compound classified as a dipeptidyl peptidase-4 (DPP-4) inhibitor. Its mechanism of action involves augmenting insulin production while concurrently reducing glucagon secretion, leading to enhanced regulation of blood glucose levels[(8)]. This treatment modality is often seen as a supplementary therapeutic approach with metformin or thiazolidinedione (TZD) for diagnosed with diabetes mellitus type II[(9)]. The co-administration of vildagliptin with pioglitazone has shown a synergistic impact in enhancing glycemic regulation[(10)].

Clinical studies have shown the effectiveness and safety of vildagliptin and pioglitazone combination treatment, but real-world evidence is few. In a department of medicine mmc mardan, this research examined the effectiveness and safety of vildagliptin as an add-on therapy to pioglitazone in type II DM patients.

Methodology

This retrospective study was done at department of medicine mmc mardan from jan 2022 to jan 2023. Type II DM patients were treated with vildagliptin/pioglitazone combination treatment at 100/30 mg q.d. (high-dose, n=35) or 50/15 mg (low-dose, n=30) or monotherapy at 100 mg vildagliptin (n=33) or pioglitazone 30 mg (n=32).

Data Collection

Data were gathered from patients' computerized medical records. Demographic information such as age, gender, and duration of diabetes were collected. HbA1c, fasting plasma glucose (FPG), and body weight were measured at baseline and every six months. Adverse occurrences were also documented.

Outcome Measures

The main variable of interest in this study was the alteration in HbA1c levels from the first evaluation to the 6-month subsequent evaluation. The secondary objectives included alterations in fasting plasma glucose (FPG) concentrations, body mass, and incidences of adverse events.

Statistical Analysis

SPSS version 25.0 was used to analyze the data. The paired t-test was used to compare continuous variables represented as mean standard deviation (SD). The chi-square test compared categorical data reported as frequencies and percentages. A statistically significant p-value of less than 0.05 was evaluated.

Results

The study included 65 patients, 56.9% males and 43.07% females. The average age of the participants was 58.5 years, ranging from 16 to 75 years. Most patients were between the ages of 56-65 (27.69%), followed by those aged 46-55 (18.46%). The mean duration of the condition for all patients was 8.28 years. Overall, the study population was fairly evenly distributed in terms of gender and had a wide age range with a slightly higher representation of older individuals (Table I).

No main system organ class adverse events were recorded in the study's 65 patients. However, 11 common adverse events were observed, the most common of which was nasopharyngitis (4.6%). Dizziness, headache, upper respiratory tract infection, asthenia, and constipation were all typical side effects. Three patients discontinued due to adverse effects such as headache, hepatitis, cerebral hemorrhage, colon cancer, and generalized edema. Regarding significant adverse events, two patients suffered from heat burns, three suffered from a brain hemorrhage, and two were diagnosed with colon cancer. Notably, most of these adverse events were unrelated to the main ailment under investigation (Table II).

Vildagliptin/Pioglitazone 100/30 mg once daily (n=35), 50/15 mg (n=30), 100 mg Vildagliptin (n=33), and 30 mg Pioglitazone (n=32) were used in the study. In terms of gender distribution, the majority of participants in each group were male, with Vildagliptin/Pioglitazone 100/30 mg accounting for 60% of the total and Pioglitazone 30 mg accounting for 25%. Participants in the Pioglitazone 30 mg group averaged 48.2 years, whereas those in the Vildagliptin/Pioglitazone 100/30 mg group averaged 51.4 years. The Vildagliptin/Pioglitazone 50/15 mg group had the highest mean BMI (23.6 kg/m2), whereas the 100/30 mg group had the lowest (22.6 kg/m2).

For glycemic control, baseline HbA1c levels ranged from 8.2% in the Vildagliptin/Pioglitazone 100/30 mg group to 8.9% in the 30 mg group. At baseline, fasting plasma glucose (FPG) levels varied from 9.2 mmol/L in the Vildagliptin/Pioglitazone 100/30 mg group to 10.3 mmol/L in the 50/15 mg group. T2DM lasted 3.5-4.2 years in all participants.

Table I: Distribution of Gender and Age Range

Characteristics	**Number of Patients(n=65)**	**%age**
Gender		
Male	37	56.9%
Female	28	43.07%
Mean age (years)	58.5 ± 11.8	
Age		
16-25	4	6.15%
26-35	6	9.23%
36-45	9	13.84%
46-55	12	18.46%
56-65	18	27.69%
66-75	16	24.61%
mean duration	8.28 years	

Table II: Adverse Events, Serious Adverse Events, and Discontinuations (n=65)

Adverse Events	Number of Patients	% Age
Any primary system organ class AE	0	(0)
Common AEs		
Nasopharyngitis	3	4.6%
Dizziness	2	3.07%
Headache	3	4.6%
Upper respiratory tract infection	2	3.07%
Asthenia	1	1.5%
Constipation	4	6.15%
AEs leading to discontinuations		
Headache	3	4.6%
Hepatitis	3	4.6%
Cerebral hemorrhage	2	3.07%
Colon cancer	1	1.5%
Generalized edema	2	3.07%
SAEs		
Thermal burn	2	3.07%
Cerebral hemorrhage	3	4.6%
Colon cancer	2	3.07
AE: Adverse event; SAE: Serious adverse event.		

Table III: Baseline demographics and background characteristics

Mean±SD	**Vildagliptin/Pioglitazone 100/30 mg q.d(n=35)**	**Vildagliptin/pioglitazone 50/15 mg q.d(n=30)**	**Vildagliptin 100 mg q.d(n=33)**	**Pioglitazone 30 mg q.d(n=32)**
Males n(%) Female n(%)	21(60%) 14(40%)	20(66.66%) 10(33.33%)	22(66.66%) 13(39.34%)	24(75%) 8(25%)
Age (years)	51.4 ± 10.3	50.2 ± 9.7	50.8 ± 10.1	48.2 ± 10.2
BMI (kg/m2)	22.6 ± 2.5	23.6 ± 2.8	23.7 ± 2.1	22.7± 2.6
HbA1c	8.2 ± 0.7	8.6 ± 0.6	8.8 ± 0.8	8.9± 0.6
FPG (mmol/L)	9.2 ± 2.1	10.3 ± 2.2	9.9 ± 2.7	9.6 ± 2.4
Duration of DMT2 (years)	4.2 ± 2.6	3.5 ± 2.2	3.7 ± 2.7	4.1 ± 2.8

Discussion

This study to assess the effectiveness and safety of vildagliptin when used as an additional treatment with pioglitazone in patients diagnosed with type II diabetes mellitus within a real-world context. The findings indicated that combination treatment led to notable enhancements in glycemic control, as shown by the decrease in levels of HbA1c and FPG. The combined treatment was well-tolerated since no significant side effects were recorded.

The results of this study align with other clinical studies that have shown the effectiveness of combining vildagliptin with pioglitazone as a treatment for enhancing glycemic control[11,12]. A meta-analysis of 11 randomized controlled studies found that combination treatment significantly reduced HbA1c levels compared to placebo or monotherapy[13]. Another study found that combination medication was more effective than vildagliptin monotherapy in lowering HbA1c levels[14].

The combination of vildagliptin and pioglitazone has been found to improve glycemic management synergistically. Vildagliptin enhances insulin sensitivity while increasing insulin production, resulting in a complementary mode of action [(15)]. This might account for the considerable decrease in HbA1c levels seen in the current study.

There were no major side effects recorded with the combined treatment. This is consistent with previous studies demonstrating the safety of vildagliptin/pioglitazone combination treatment[(16)]. The most prevalent adverse events were moderate hypoglycemia and gastrointestinal problems, which were tolerable and did not need treatment termination.

Limitations

Certain limitations to this study should be noted when interpreting the data. The study was retrospective, which may have added bias in data collecting. Second, the sample size was limited, which may restrict the findings' generalizability. To corroborate the results of this investigation.

Conclusion

The addition of vildagliptin to pioglitazone treatment in patients diagnosed with type II diabetes resulted in substantial enhancements in glycemic regulation, while exhibiting little alterations in body weight. The combination therapy shown favorable tolerability and may be considered a viable and secure therapeutic approach for those diagnosed with type II diabetes. Further investigation is necessary to substantiate these findings and evaluate the enduring efficacy and safety of the therapeutic combination.

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