AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 63, Issue 02, February, 2023

The Effect of Insulin, Glimepiride, and Metformin on weight and Glycemic state in Type 2 Diabetes mellitus

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Keywords:
Type 2 diabetes mellitus –Insulin –Glimepiride –Metformin –BMI

ABSTRACT

Insulin, glimepiride, and metformin prescribe as monotherapy or in combination to control glycemic state. A comparative retrospective case-control study followed by a follow-up study of added metformin and or glimepiride to establish the effect on weight and glycemic state. There are no significant differences in BMI, FPG, and HbA1c among comparative monotherapy groups, follow-up study show a highly significant reduction of glycemic parameters with varying effect on weight among antidiabetic agents. Insulin and its secretagogues glimepiride provide hypoglycemia with the incidence of increased weight while metformin is associated with weight loss. Adding metformin with insulin or glimepiride counterbalances the weight gain with improving glycemia.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a complex long-lasting illness with long-term metabolic and endocrine disturbances affect 9% of all individuals worldwide, demanding endless medical maintenance with multifactorial risk-drop policies besides glycemic control, according to “The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)” the primary objective of antidiabetic are maintaining good glycemic control with HbA1c level, not more than 7 %, we obtain with monotherapy or combine two or more antidiabetic, unfortunately, no radical cure has been established, all strategies of management involve treating diabetic symptoms, glycemic controller, with not free from adverse effects [1- 3]. Overweight and high dietary lipids may disrupt glucose homeostasis leading to glucotoxicity as well as lipotoxicity, and cellular and systemic dysfunction, elicit βeta-cells to release more insulin to recompense, with elicits hyperglycemia, which may be developed into T2DM [4].

2. Subjects, Materials, and Methods

The present study designed as a comparative retrospective case-control study involving equally distributed genders one hundred forty-four individuals were classed into five groups, forty-eight newly diagnosed patients termed as a group I, seventy-two diabetic patients divided into 3 groups of 24 patients treated with (insulin, glimepiride, or metformin) monotherapy termed as group II, III, and IV. Twenty-four healthy

individuals kept as control group termed as group V. Followed by follow-up study for 4 months involved hundred patients, newly diagnosed patients were divided into two subgroups treated with metformin alone, metformin plus glimepiride termed as group IA, IB respectively. add metformin to insulin, and glimepiride groups termed as group II and III, add glimepiride to metformin monotherapy in termed as group IV. Metformin's daily dose began at 500 mg and then increased to 1000 mg and reach 1850mg, and glimepiride beginning dose of 2 mg increased to 4mg. To show the effect of insulin, glimepiride, and metformin on BMI. FPG and HbA1c, measuring at baseline from comparative study and after the end of follow-up study. Age recorded. measured weight and height, BMI as mentioned by [5]. Two milliliters of blood drawn in the morning after an overnight fast, enough amount used for rapid examination of glycated hemoglobin utilizing an A1C EZ 2.0 analyzer system [6]. The remaining blood was centrifuged, aspirated supernatant for immediate glucose estimation by colorimetric enzymatic spectrometric methods using the Randox glucose kit [7].

3. Results and Statistics

Table (1) Show the results of a comparative study of BMI and glycemic parameters. No significant differences between Age, and BMI among all groups, FPG, and HbA1c of the three monotherapy groups show no significant differences, while these groups have a highly significant differences when compare with both groups I newly diagnosed and V control group at (P-value* 0.001).

Table (1): Comparison between glycemic parameters of five studied groups

Parameter	Group I M ± SD	Group II M ±SD	Group III M ± SD	Group IV M ± SD	Group V M ± SD
Age (years)	**51.2±6.08 A**	**51.9±3.23 A**	**50.0±4.7 A**	**51.6±5.88 A**	**51.8±6.02 A**
BMI (Kg/m^2)	**27.73±1.8 A**	**27.77±1.61 A**	**27.13±2.14 A**	**28.07±1.63 A**	**27.42±1.36 A**
FPG (mmol/l)	**11.8±1.75 A**	**9.3±0.68 B**	**9.0±0.85 B**	**9.4±0.98 B**	**4.9±0.39 C**
HbA1c %	**9.0±0.71 A**	**8.0±0.44 B**	**7.9±0.42 B**	**8.1±0.50 B**	**4.8±0.33 C**

* ANOVA-test (one-way) with applied " Turkey's Pairwise comparisons". "Means do not share a letter are significantly different".

Table (2): Show the results of BMI of the follow-up studied groups. There are significant differences in BMI in groups IA, II, and III, while no significant differences in groups I B, and IV.

Table (2): The changes in BMI among follow-up studied groups (20 patients each group)

Groups	Pre Mean ±SD	Post 4 Mon Mean ±SD	Improvement Rate %	P-value*
IA	28.7 ± 1.00	27.96 ± 1.31	2.5	**0.023**
IB	26.8 ± 1.81	26.5 ± 1.47	0.9	0.381
II	27.8 ± 1.61	27.4 ± 1.21	1.7	**0.035**
III	27.0 ± 2.23	26.5 ± 1.76	1.8	**0.016**
IV	27.9 ± 1.56	27.7 ± 1.58	1.0	0.153

ISSN: 0005-2523
Volume 63, Issue 02, February, 2023

* Paired T-test for two means was used. % Improvement rate = [(before – after) / Before] × 100

Table (3) Show the results of FPG of the follow-up studied groups. There are highly significant improvement rates in groups IA, I B, and IV, while groups II and III show significant improvement rates when comparing the baseline value.

Table (3): The changes in FPG among follow-up studied groups (20 patients each group)

Groups	Pre Mean ±SD	Post 4 Mon Mean ±SD	Improvement Rate %	P-value*
IA	11.1 ± 0.81	9.79 ± 0.49	11.4	**0.001***
IB	12.5 ± 0.72	9.96 ± 0.70	20.0	**0.001***
II	9.3 ± 0.67	8.9 ± 0.95	3.7	**0.028**
III	9.1 ± 0.86	8.83 ± 1.05	2.7	**0.016**
IV	9.3 ± 0.98	9.1 ± 0.87	2.4	**0.002**

* Paired T-test for two means was used. % Improvement rate = [(before – after) / Before] × 100.

Table (4): Show the results of HbA1c of the follow-up studied groups. There are highly significant improvement rates in groups IA, I B, and IV, while groups II and III show significant improvement rates when comparing the baseline value

Table (4): The changes in HbA1c among follow-up studied groups (20 patients each group)

Groups	Pre Mean ±SD	Post 4 Mon Mean ±SD	Improvement Rate %	P-value*
IA	**8.5 ± 0.45**	**8.2 ± 0.48**	**3.5**	**0.001***
IB	**9.4 ± 0.47**	**8.7 ± 0.68**	**7.3**	**0.001***
II	**7.9 ± 0.40**	**7.8 ± 0.37**	**2.4**	**0.022**
III	**7.9 ± 0.42**	**7.7 ± 0.40**	**2.3**	**0.034**
IV	**8.1 ± 0.51**	**7.7 ± 0.45**	**5.0**	**0.009**

* Paired T-test for two means was used. % Improvement rate = [(before – after) / Before] × 100.

4. Discussion

Results of the comparative study that show in Table (1). there are no significant differences in Age, BMI as well as equally distributed gender that a good match to eradicate the influence of these parameters on the results obtained. There are no significant differences in FPG and HbA1c among the monotherapy-treated groups. That in agreement with previous studies that show no significant differences in glycemic parameters between metformin, glimepiride, and insulin [8], [9]. The disagreement study shows significant differences among glycemic parameters with different antidiabetic monotherapy [10]. The results of the three monotherapy groups studied parameters FPG and HbA1c are higher significant differences when compared with group I the newly diagnosed at (P-value* 0.001). But still higher and remain above the glycemic target when compared with group V control group. These results are arguable with previous results that referee as a quarter of diabetic patients achieved the glycemic target at HbA1c less than7% with monotherapy, while three-quarters of diabetic patients require a combination of two or more, metformin has lower associated

failure than others, so adjustments every 6 months according to ADA recommended [11], [12].

Table (2) show BMI changes among follow-up studied groups, a highly significant reduction of BMI with group IA, II, and III of Adding metformin as monotherapy for the newly diagnosed and ad on insulin, glimepiride treated patients, carried a high improvement rate that in agreement with previous studies t concluded that metformin reduces the fat mass of a body, undergo loss of weight of 3%frombase line preliminary weight [13], [14]. Monotherapy with metformin shows significant loss of weight when compared with a combination of metformin and glimepiride [15]. The disagreement results that considered metformin statistically has no significant differences in weight [16]. T2DM patients who start insulin therapy to improve glycemic control may suffer from weight gain particularly individuals already overweight, with significant reduction of BMI in adding metformin while no significant when adding glimepiride. that in agreement with previous studies [17], [18]. These results disagreement with previous studies that showed glimepiride had a weight-neutral or reducing effect, due to extrapancreatic action reducing hyperinsulinemia [19], [20]. Metformin through its action reduces gluconeogenesis, regulates the oxidation of fat, increases insulin and leptin sensitivity, modulates the appetite-regulatory center of the hypothalamic, and locally enhanced increased secretion that improves satiety [21].

Tables (3 and 4): Show the results of the follow-up study of FPG and HbA1c of all studied groups. Group IA, the newly diagnosed patient treated with metformin alone. There are highly significant differences between FPG and HbA1c at (P-value* 0.001) but still over the glycemic target. These results are in agreement with previous results of studies show metformin monotherapies reduce FPG and HbA1c with a low incidence of hypoglycemia [22], [23].

The results of group IB the newly diagnosed patient treated with metformin and glimepiride are highly significant differences between FPG and HbA1c at (P-value*.001), These findings are in agreement with the results of previous studies that show early treatment with a combination of glimepiride and metformin have superiority for reducing glycemia more than both when used as a monotherapy that reaching the glycemic target and decrease the incidence of complication associated with elevated blood sugar [15], [24], [25]. The results of group II that add metformin to insulin therapy. There are significant differences in both FPG and HbA1c that are in agreement with previous studies that show insulin can be initiated as monotherapy for T2D at beginning of diagnoses with severe hyperglycemia, decompensating catabolic state, acute major surgery, later when the glycemic target still uncontrolled addition of metformin to improve glycemic control, reduce daily requirements of insulin, reduce hypoglycemic episodes associated [26], [27].

The results of a follow-up study of glycemic parameters of group III patients of adding metformin to glimepiride therapy. Glimepiride has been used as initial therapy or as an alternative when a failure of metformin monotherapy moved to sulphonylurea monotherapy might have been instructed by their doctors to switch from metformin monotherapy to Glimepiride monotherapy, rather than to add to metformin. later the fact that SUs have higher failure rates switching to re-add metformin or other OAD or even insulin [28], [29]. Locality patients with glimepiride monotherapy that prescribe glimepiride alone due to availability, cheapest, high ability to reduce glycemia, or not tolerate metformin from starting diagnosis or some bad idea that considered metformin as a regulator rather than a drug so the addition of metformin as obligatory for this patients to correct therapeutic strategies and achieved glycemic target if not contraindicated.

The results of a follow-up study of glycemic parameters of group IV patients that add glimepiride to metformin therapy. These results are in agreement with previous studies that show when metformin mono-

ISSN: 0005-2523
Volume 63, Issue 02, February, 2023

therapy fails to control the hyperglycemic status, glimepiride can be prescribed as add-on therapy that fasting glucose level and HbA1c, highly significantly improved after 12 weeks of glimepiride add on metformin monotherapy compared with baseline [30], [31]. Other studies show a statistically significant reduction of FPG and HbA1c with a more rapid decline in HgbA1C levels to less than 7% in 80 – 90 days on adding glimepiride to metformin. as metformin improves hepatic and peripheral tissue insulin resistance while glimepiride enhances insulin secretion [32], [33]. The disagreement studies show that the majority of patients who received a second-line regimen recommended received the newer drugs or directly move to a triple regimen or some harm related to SU therapy even though glimepiride seems to be the safest option over others SU. Nevertheless, glimepiride remains prescribed even though newer drugs are available but declined markedly, it is obligatory to take into account the hypoglycemia effect [15], [34], [35]. There are high improvement rates of FPG and HbA1c in groups IB and IA, then others. These results are in agreement with previous studies that show metformin as monotherapy improves the glycemic state properly but improvement of the glycemic state is better and faster achieve with the initial combination of metformin with glimepiride below 7% more than the combination of metformin with insulin [8], [15], [20], [25], [36]. These results are in disagreement with the study that shows no significant differences among HbA1C levels between metformin and its combination that effectively adds to metformin and the ADA recommendation of selection of initial and additional therapy according to consideration that specific to patients himself [37].

5. Conclusion

Insulin and insulin secretagogues lower blood glucose by increasing the uptake of glucose into fat and muscle cells, correcting glycosuria, and reducing energy loss, which may be associated with weight gain. Glimepiride provides glycemic control and promotes the release of insulin from beta cells with additional effects that enhanced peripheral tissues' sensitization to insulin. Metformin effectively improves the glycemic state and improves hepatic and peripheral tissue insulin resistance associated with weight loss, when combined with insulin or Glimepiride, metformin counterbalances the associated weight gain with an improving glycemic state.

Conflict of interest: Authors have no known rival monetary attention or private dealings that could affect the work of this manuscript

Funding No funding available.

Adherence to Ethical Standards: The present study had approval from the medical research ethics committee of Nineveh health directorate) and medical research ethics committee college of medicine, Mosul University, Nineveh, Iraq. Ethical approval reference number: UOM/COM/MREC/20-21(35).

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