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Efficacy of Oral Anti-Diabetic Agents for Glycaemic Control in Type-2 Diabetic Patients with Obesity

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Abstract: To evaluate "Efficacy of oral anti-diabetic agents for glycaemic control in type-2 diabetic patients with Obesity". A total of 80 patients were assigned in to two groups i.e., Diabetic only group and Diabetic with Hypertension group. Their Weights were measured by Standard weighing machine, Systolic blood pressure and Diastolic blood pressure measured by Sphygmomanometer, Hb measured by Cyanmethemoglobin Method, Serum creatinine by Modified Jaffe's reaction, Fasting blood sugar and Post lunch blood sugar was estimated by Glucose oxidase-Peroxidase method, Serum Cholesterol by Modified Roeschlau's Method, and other parameters like Body mass index, Haemoglobin A_1c, High density lipoprotein, Low density lipoprotein, Very low density lipoprotein, CHOL/HDL ratio, LDL/HDL ratio, Triglycerides were measured to investigate and to compare the efficacy of three treatment regimens i.e. monotherapy with Metformin, combination therapy (Metformin and Glimepiride). Results of the present study showed that in Diabetic only group the two regimens decreases FBS and PLBS levels where as in Diabetic + Obesity group, Metformin and Glimepiride combination therapy was proved to be effective in achieving glycaemic control.

Key words: Blood Sugar Levels · Diabetes · Glimeprimide · Obesity · Metformin

INTRODUCTION

Diabetes mellitus often simply diabetes is a syndrome characterized by disordered metabolism and inappropriately high blood sugar (hyperglycemia) resulting from either low-level of the hormone insulin or from abnormal resistance to insulin's effects coupled with inadequate insulin secretion [1]. Diabetes Mellitus is a worldwide health problem afflicting millions in both developed and developing countries. It is the prime cause of chronic kidney failure, blindness, high blood pressure and premature coronary artery diseases [2].

The disease affects more than 50 million Indians-7.1% of the nation's adults and kills about 1 million Indians a year. Currently, India is the diabetes capital of the world. It is estimated that over 40 million of those with diabetes are currently in India [3].

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases [4]. Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is however, expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented [5].

MATERIALS AND METHODS

A number of 80 patients, aged 30-65 years were assigned into four groups according to their complications based on medical history. Of these 18 patients were withdrawn from study. All the patients are

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diabetic (type 2 diabetes). Among these 40 patients are obese. Of these some patients received monotherapy with Metformin, rest of them received combination therapy i.e. Metformin and Glimepiride.

Inclusion Criteria:

- Either sex and age group between 30-65years.
- The study patients who were diagnosed with type2 diabetes.
- The patients who were diagnosed with obesity as other complications along with type 2 diabetes.
- Patients who were on treatment with Metformin monotherapy and combination therapy with Glimepiride.

Exclusion Criteria:

- Patients who were receiving only insulin.
- Patients were excluded if they had a history of type1 diabetes and secondary forms of diabetes.
- Pregnancy and lactation
- Pediatrics
- Patients who were very weak and severe disability
- Patients with other diseases like tuberculosis, asthma or any other diseases under polymorphism.

Parameters Assessed

Parameters	Methods	Units
Body Weight	Standard Weighing Machine	Kg
Blood Pressure	Sphygmomanometer	mm of Hg
BMI	BMI calculator	Kg/m^2
Hemoglobin [6]	Cyanmethemoglobin method	gm%
Serum Creatinine [7-9]	Modified Jaffe's reaction	mg/dl
Glucose [10-12]	GOD-POD method	mg/dl
Cholesterol [13,14]	Modified Roeschlau's method	mg/dl
HDL [15]	Precipitation method	mg/dl
LDL [15]	William Friedewald's equation	mg/dl
Triglycerides[16-18]	Method of Wako	mg/dl

RESULTS

In this study, diabetic patients with obesity aged between 30 to 60 years were enrolled.

Effect of Drugs on Various Parameters: There was no significant change in body weight, BMI SBP and DBP in all three visits in patients with Metformin alone and in combination with Glimepiride. Hb levels were increased from 10.95±1.69 to 11.79±1.48g% and 11.38±1.52 to 12.27±1.22g % in their third visit in patients treated with Metformin and in combination with Glimepiride respectively.

Table 1: Parameters (Mean±SD) during Visits1, 2, and 3 after a treatment with Metformin in Diabetic and Obese patients.

Treatment	Metformin		
Parameter	Visit 1	Visit 2	Visit 3
Weight	78.14±12.17	77.12^{ns}±11.66	77.38^{ns}±12.0
BMI	32.64±1.43	32.50^{ns}±1.41	32.50^{ns}±1.34
SBP	124.68±9.14	127.55^{ns}±8.39	123.96^{ns}±7.21
DBP	77.45±7.99	77.05^{ns}±7.18	79.64^{ns}±5.14
Hb	10.95±1.69	11.29^{ns}±1.69	11.79^{ns}±1.48
Serum creatinine	1.21±0.33	1.07^{ns}±0.16	0.93^{***}±0.11
FBS	122.68±29.48	121.27^{ns}±28.65	103.73^{*}±11.67
PBS	182.64±40.87	177.64^{ns}±45.22	141.55^{**}±26.43
HbA_1c	8.46±1.13	7.98^{ns}±0.94	7.29^{***}±0.53
Serum Cholesterol	198.96±55.56	197.09^{ns}±50.22	179.86^{ns}±40.94
HDL	39.06±18.33	39.43^{ns}±10.26	42.75^{ns}±9.31
LDL	118.54±57.66	119.93^{ns}±52.29	105.05^{ns}±41.13
VLDL	40.63±12.76	36.62^{ns}±8.99	30.68^{**}±7.79
CHO/HDL	5.59±1.55	5.07^{ns}±1.34	4.36^{**}±0.98
LDL/HDL	3.44±1.29	3.19^{ns}±1.24	2.49^{*}±0.92
TG	203.18±63.79	183.09^{ns}±44.95	153.41^{**}±38.95

*- Significant at $P<0.05$, **- Significant at $P<0.01$, ***- Significant at $P<0.001$ compared to parameters at Visit1.

Table 2: Parameters (Mean±SD) during Visits1, 2, and 3 after a treatment with Metformin and Glimepiride in Diabetic and Obese patients.

Treatment	Metformin and Glimepiride		
Parameter	Visit 1	Visit 2	Visit 3
Weight	78.56±12.04	77.73^{ns}±12.35	77.76^{ns}±12.24
BMI	32.33±1.14	32.22^{ns}±0.94	32.06^{ns}±0.99
SBP	125.78±10.87	126.78^{ns}±4.36	124.17^{ns}±6.69
DBP	75.61±9.99	76.56^{ns}±6.49	77.72^{ns}±2.54
Hb	11.38±1.52	11.84^{ns}±1.29	12.27^{ns}±1.22
Serum creatinine	1.23±0.25	1.00^{***}±0.18	0.95^{***}±0.09
FBS	151.78±54.39	132.39^{ns}±48.39	118.78^{ns}±35.55
PBS	234.78±65.86	219.28^{ns}±68.92	168.67^{**}±39.09
HbA_1c	9.80±1.83	8.96^{ns}±1.56	7.79^{***}±0.94
Serum Cholesterol	212.89±52.19	198.44^{ns}±54.21	179.89^{ns}±41.19
HDL	32.94±5.08	35.83^{ns}±4.69	38.94^{**}±4.76
LDL	137.26±50.01	124.53^{ns}±51.8	109.12^{ns}±39.58
VLDL	43.19±6.69	38.19^{*}±5.67	31.27^{***}±5.23
CHO/HDL	6.28±1.80	5.39^{ns}±1.62	4.49^{**}±1.15
LDL/HDL	4.19±1.53	3.48^{ns}±1.43	2.81^{**}±1.01
TG	215.94±33.47	190.94^{*}±28.34	156.33^{***}±26.17

* $P<0.05$, ** $P<0.01$, *** $P<0.001$ compared to parameters at Visit1.

There was no significant change in serum creatinine levels in all three visits in patients treated with Metformin alone and in combination with Glimepiride.

FBS was decreased from 122.68±29.48 to 103.73±11.67mg/dl in patients treated with Metformin. Significant decrease ($P<0.01$) was observed in FBS in patients treated with Metformin and Glimepiride combination.

Table 3: Comparison of various parameters (Mean+SD) during visits 1, 2 and 3 after treatment with Metformin, Metformin and Glimepiride in diabetic and Obese patients.

Disease	Metformin			Metformin + Glimepiride		
Parameter	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3
Weight	78.14±12.17	77.13±11.66	77.38±12.0	78.56ns±12.04	77.73ns±12.35	77.76ns±12.22
BMI	32.65±1.43	32.5±1.41	32.5±1.34	32.33ns±1.14	32.22ns±0.94	32.06ns±0.99
SBP	124.68±9.14	127.55±8.39	123.95±7.21	125.78ns±10.87	126.78**±4.36	124.17ns±6.69
DBP	77.45±7.99	77.05±7.18	79.64±5.14	75.61ns±9.99	76.56ns±6.49	77.72**±2.54
Hb	10.95±1.69	11.29±1.69	11.79±1.48	11.38ns±1.52	11.84ns±1.29	12.27ns±1.22
Serum creatinine	1.21±0.33	1.07±0.16	0.93±0.11	1.23ns±0.25	1.0ns±0.18	0.95ns±0.09
FBS	122.68±29.48	121.27±28.65	103.73±11.67	151.78**±54.4	132.39***±48.39	118.78*±35.55
PBS	182.64±40.87	177.64±45.22	141.55±26.43	234.78*±65.86	219.28ns±68.92	168.67ns±39.09
HbA1c	8.46±1.13	7.98±0.943	7.29±0.53	9.80*±1.83	8.96*±1.56	7.79*±0.94
Serum Cholesterol	198.95±55.56	197.09±50.22	179.86±40.94	212.89ns±52.19	198.44ns±54.21	179.89ns±41.185
HDL	39.06±18.33	39.43±10.258	42.75±9.31	32.94***±5.08	35.83**±4.69	38.94**±4.76
LDL	118.54±57.56	119.93±52.29	105.03±41.13	137.26ns±50.01	124.53ns±51.81	109.12ns±39.58
VLDL	40.63±12.75	36.62±8.99	30.68±7.79	43.19**±6.69	38.19ns±5.67	31.27ns±5.23
CHO/HDL	5.59±1.55	5.07±1.34	4.35±0.98	6.28ns±1.89	5.39ns±1.62	4.49ns±1.15
LDL/HDL	3.44±1.29	3.19±1.24	2.49±0.92	4.19ns±1.53	3.48ns±1.43	2.81ns±1.01
TG	203.18±63.79	183.09±44.95	153.41±38.94	215.94**±33.47	190.94ns±28.34	156.33ns±26.15

*- Significant at P<0.05, **- Significant at P<0.01, ***- Significant at P<0.001 compared to parameters at Visit1, Visit2, Visit 3 of Metformin treated groups.

PBS levels were decreased from 182.64±40.87 to 141.55±26.43mg/dl and 234.78±65.86 to 168.67±39.09mg/dl in their third visit in patients treated with Metformin and in combination with Glimepiride respectively.

There was no significant change in HbA1c in all three visits in patients treated with Metformin alone. In patients treated with combination of Metformin and Glimepiride HbA1c levels decreased in slightly significant levels.

Serum cholesterol levels were not significantly changed all three visits.

HDL levels were not significantly changed in Metformin alone treated patients but in patients treated with Metformin in combination with Glimepiride there was no significant increase (P<0.01) in third visit.

LDL levels were decreased from 198.95±55.56 to 179.86±40.94mg/dl and 212.89±52.19 to 179.89±41.18mg/dl in their third visit in patients treated with Metformin alone and in combination with Glimepiride respectively.

VLDL levels were decreased from 40.63 to 30.68±7.79mg/dl and 43.19±6.69 to 31.27±5.23mg/dl in their third visit in patients treated with metformin alone and in combination with Glimepiride respectively.

There was no significant change observed in CHO/HDL and LDL/HDL ratio in all three visits in both patient groups.

TG levels were decreased from 203.18±63.79 to 153.41±38.94mg/dl and 215.94±33.47 to 156.33±26.15mg/dl in their third visit in patients treated with Metformin alone and in combination with Glimepiride respectively.

By treatment with Metformin there was significant difference (P<0.05) in fasting blood sugar, LDL/HDL ratio during visit3, significant difference (P<0.01) in post lunch blood sugar, VLDL, cholesterol/HDL ratio and TG during visit3 significant difference (P<0.001) in HbA_1c and serum creatinine during visit 3 when compared to visit1.

By treatment with Metformin and Glimepiride there was a significant difference (P<0.05) in VLDL and TG during visit2, significant difference (P<0.01) in post lunch blood sugar, HDL, cholesterol/HDL ratio during visit3 and significant difference (P<0.001) in serum creatinine during visit2 and 3, HbA1c, VLDL, TG during visit3 when compared to visit1.

DISCUSSION

Metformin monotherapy is one of the main therapeutic options for type 2 Diabetes with overweight or obesity. Metformin produces strong beneficial changes in glycaemic control and moderated in weight, lipids, insulinaemia and diastolic blood pressure.

Glycaemic response to Metformin alone in obese patients gradually decreased from an elevated levels, the earlier studies also shown glycaemic response to obese and non obese is similar suggesting that an individual's BMI should not influence the choice of oral agent [19]. The conditions of the patients who are on Metformin monotherapy and other lipid lowering agents like atorvastatin shown to have an elevated LDL levels in all their three visits maintaining all other parameters at an optimal range.

For Obese diabetics and people at risk of diabetes, Metformin remains a treatment able to moderately reduce body weight (5% on average). This is believed to be an additional benefit in treating diabetes and suggested to be caused by reducing of insulin resistance and hyperinsulinaemia rather than anoerexic or other effect [20].

HbA_1c level significantly decreased compared with those at the baseline time. The course of HbA_1c was similar between non obese and obese group, while the dose of Metformin required to control blood glucose was significantly lower in the non-obese group than in the obese group. Similar studies were also reported earlier on long-term effect of Metformin on blood glucose control in non-obese patient [21].

The combination therapy selected in patients with type 2 diabetes and is obese in nature, the administration of Metformin and Glimepiride also fails to normalize the HbA_1c levels, but there is a significant reduction from the baseline value. The previous studies describe that the combination Metformin and Glimepiride reduced the gycosylated hemoglobin, FBS, PBLS levels significantly as observed in the present study. LDL level was not decreased in combination therapy and HDL level was significantly increased as reported in the previous studies.

CONCLUSION

In this work various parameters Weight, BMI, SBP, DBP, Hb, Serum creatinine, FBS, PLBS, HbA1c, Serum Cholesterol, HDL, LDL, VLDL, CHOL/HDL ratio, LDL/HDL ratio, TG were measured to investigate and to compare the efficacy of three treatment regimens i.e.,Metformin monotherapy and Metformin with Glimepiride in Diabetic patients, Diabetic patients with Obesity.

In diabetic patients with obesity, combination therapy of Metformin with Glimepiride was effective in glycaemic control.

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