Asian Journal of Pharmaceutical Research and Health Care, *Vol 12(4), 223-233, 2020*

ISSN (Online) : 2250-1460
DOI: 10.18311/ajprhc/2020/25567

Comparative Efficacy of Metformin and Sulfonylurea in Monotherapy or Combination for Type 2 Diabetes

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Abstract

Despite the extensive efforts of physicians to achieve better control and management for blood glucose level in type 2 diabetics, maintaining near normal blood glucose level in these patients remain unsatisfactory. The objective of the study was to compare the effectiveness of sulfonylureas, metformin and combination of metformin plus sulfonylureas in controlling blood glucose in type 2 diabetics. Retrospective cohort research design conducted during the period of two months from 1st November 2019 to 1st March 2020 at Northern Area Armed Forces Hospital in Hafr Al Batin- Saudi Arabia on sample of 217 diabetic patients' files, all data coded with serial number and analyzed by SPSS program through and inferential and descriptive statistics. Mean decrease in HbA1c for metformin therapy was 1.5(%), for sulfonylurea was 1.4(%), for combination therapy was 1.9(%). Mean decrease in HbA1c fasting blood glucose for metformin therapy was 1.8(mmol/l), for sulfonylurea was 1.6(mmol/l), for combination therapy was 3(mmol/l). Mean decrease in postprandial blood glucose for metformin therapy was 3.2(mmol/l), for sulfonylurea therapy was 3(mmol/l), for combination therapy was 3.7(mmol/l). There was a significant difference between levels of HbA1c between metformin group and combination group (metformin and sulfonylurea) ($p = 0.002$) and also there was a significant difference between sulfonylurea group and combination group (metformin and sulfonylurea) in relation to HbA1c levels ($p = 0.001$). However, there was no significant difference between metformin and sulfonylurea in decreasing HbA1c ($p = 0.09$). In conclusion, metformin or sulfonylurea as a single therapy is similar in efficacy in reducing glycosylated hemoglobin level, fasting and post-prandial plasma glucose levels to equal degree. However, combination of both therapies resulted in significant greater control of blood glucose level.

Keywords: Combination Type 2 Diabetes, Efficacy, Metformin, Monotherapy, Sulfonylureal

1. Introduction

Diabetes Mellitus (DM) is one of the major fast growing Non-Communicable Disease (NCD) threats to global public health. Trends in the incidence of diabetes indicate a disproportionate increase due to current rapid demographic transitions from traditional to more westernized and urbanized lifestyles[1].

The epidemiologic transition in the Kingdom of Saudi Arabia (KSA) has been fast and complete. Rapid economic growth during the last 4 decades led to a remarkable increase in living standards and adoption of a 'Westernized' lifestyle, characterized by unhealthy dietary patterns, and decreased physical activity[2]. An increase in the prevalence of T2DM is also observed during the same period, which is attributed to the

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dramatic changes in lifestyle, in addition to genetic predisposition of Saudi people to diabetes, and a high prevalence of consanguineous marriages[3]. A national survey in 2004 estimated that 23.7% of Saudi adults (age 30-70 years) suffered from T2DM, and another 14.1% had impaired fasting glucose[4]. Prevalence of diabetes was significantly higher in urban areas (25.5% versus 19.5% in the rural areas). The burden of diabetes in KSA is likely to increase to disastrous levels, unless a comprehensive epidemic control program is implemented rigorously promoting healthy diet, exercise and active lifestyles, and curbingobesity[5,6].

Type 2 diabetes is defined as a syndrome characterized by insulin deficiency, insulin resistance and increased hepatic glucose output[7] leading to hyperglycemia which subsequently result in irreversible damage in a wide range of tissues e.g. in retine (retinopathy), in kidney (diabetic nephropathy), in nervous tissue (diabetic neuropathy)[8]. T2DM present with many symptoms such as polyuria, polydipsia, polyphagia. In severe cases, hyperglycemia leads to diabetic ketoacidosis or non ketotic hyperosmolar state which may develop to coma and death if not treated properly[9].

Medications used to treat type 2 diabetes are designed to correct one or more of these metabolic abnormalities. Currently, there are five distinct classes of hypoglycemic agents available, each class displaying unique pharma cologic properties. These classes are the sulfonylureas, meglitinides, biguanides, thiazolidinediones and alpha-glucosidase inhibitors[10]. In patients for whom diet and exercise do not provide adequate glucose control, therapy with a single oral agent can be tried. When choosing an agent, it is prudent to consider both patient- and drug-specific characteristics. If adequate blood glucose control is not attained using a single oral agent, a combination of agents with different mechanisms of action may have additive therapeutic effects and result in better glycemic control[11].

1.1 Rationale

Despite the extensive efforts of physicians to achieve better control and management for blood glucose level in type 2 diabetics, maintaining near normal blood glucose level in these patients remain unsatisfactory. This continues to pose a real challenge to physicians as the prevalence of this disease in the Saudi Arabia continues to rise. However, no sufficient studies investigating the effect of oral ant diabetics on blood glucose of type 2 diabetic patients in Saudi Arabia.

1.2 Objective of the Study

- To compare the effectiveness of sulfonylureas, metformin and combination of metformin plus sulfonylureas in controlling blood glucose in type 2 diabetics.
- To investigate which is the best and effective oral hypoglycemic agent in controlling of blood glucose level in type 2 Diabetes Mellitus patients.

2. Literature Review

Saudi Arabia is now considered among the countries with highest prevalence of DM in the world with incidence reaching as high as 23.7%[12] and diabetes is the most challenging health problem facing this country[13]. According to a report by the Saudi Arabian Ministry of Health, approximately 0.9 million people were diagnosed with diabetes in 1992, but this figure increased to 2.5 million people in 2010, representing a 2.7 times increase in the incidence rates in less than two decades. In 2015, 4660 patients with diabetes attended the family and medical clinics across Saudi Arabia[14]. This increasing burden of diabetes is due to various factors, including a rising obesity rate and an aging population[15]. Prevalence rates of T2DM were reported in six studies, three of which were nationwide[16-18]. One study was conducted in Riyadh[19], one in Jeddah[20] and one in the Eastern province[21]. The studies demonstrated varying prevalence rates in different geographical regions in the country, ranging from 18.2% (in 2004–2005) in the study conducted in the Eastern province[21] to 31.6% in 2011 in the study conducted in Riyadh[19] nationwide prevalence rate increased from 23.7% between 1995 and 2000 to 25.4% between 2007 and 2009[17,18].

A traditional approach to diabetes therapy is to use single oral agent titrated to maximum dosage. If good glycemic control not achieved, addition of another agent is required, in which each of the two agents targets a single pathological defect of type 2 diabetes as its primary mechanism of action[22].

Treatment of type 2 diabetes is based on interplay of patient characteristics, severity of hyperglycemia and available therapeutic options. Metformin, sulfonylureas (SU) and thiazolidinediones (TZD) are the most studied of the oral medications used worldwide. They play a

prominent initial role in the type 2 diabetes treatment algorithm recommended by the American Diabetes Association (ADA) and the European Diabetes Association for the Study of Diabetes (EASD)[23].

Metformin is considered first-line therapy unless not tolerated or contraindicated. Second-line therapy then includes SUs, TZDs, dipeptidyl peptidase-IV (DPP-4) inhibitors, glucagon-like polypeptide-1 (GLP-1) agonists or insulin. The expected improvement in HbA1c with the use of metformin, SUs and TZDs is approximately 1-1.5%[24].

The majority of type 2 diabetes mellitus do not primarily need insulin therapy. The frequency of type 2 diabetes mellitus occurrence in adults is more than in children. The incidence of the disease is increased with age, particularly after 40 years old[25]. Several different mechanisms are included in the reduction of serum glucose level by metformin without increasing insulin secretion, predominately through non pancreatic pathways. Metformin is often called insulin sensitizer as it increases the effects of insulin in the body[26].

Metformin also suppress the endogenous glucose production in the liver by reducing the rate of gluconeogenesis with little effect on level of ATP in the cell. Metformin achieve beneficial metabolic effects through targeting AMP-activated protein kinase (AMPK). The AMPK is a multi subunit enzyme that is recognized as a major regulator of lipid biosynthesis mechanisms due to its role in the phosphorylation and subsequent inactivation of pivotal enzymes (such as acetyl-CoA carboxylase)[26]. Recent researches strongly suggest that AMPK has a wider role in metabolic regulation, which include many effects including muscle glucose uptake, fatty acid oxidation. So, it is an ideal therapeutic target of type 2 diabetes mellitus. Activation of AMPK on chronic basis may also induce the expression of muscle hexokinase and glucose transporters, mimicking the effects of extensive exercise training. Metformin also showed protective properties against diabetic complications, especially by reducing the diabetes-related deathrate[26].

The common reported side effects of metformin include abdominal pai, constipation, distension, flatu lence, heartburn, dizziness, headache, upper respiratory infection, taste disturbance and liver function abnormalities which resolve upon discontinuation of metformin[27].

Sulfonylurea group including {glyburide, glipizide, glimepiride and glibenclamide} which act by binding to and inhibiting the ATP-sensitive potassium channels inhibit regulatory subunit sulfonylurea receptor 1 (SUR1) in pancreatic beta cells. This inhibition causes cell membrane depolarization, opening of voltage dependant calcium channels resulting in an increase in intracellular calcium in beta cell and subsequent stimulation of insulin release[28].

Side effects of sulfonylurea include hypoglycemia, weight gain mainly as a result of their effect to increase insulin levels and thus utilization of glucose and other metabolic fuels. Other side effects include gastrointestinal upset, headache and hypersensitivity reactions[28].

Metformin and sulfonylurea can be used in combi nation with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes[28].

3. Methodology

3.1 Study Design and Setting

Retrospective cohort research design conducted during the period of two months from 1st November 2019 to 1st March 2020 at Northern Area Armed Forces Hospital in Hafr Al Batin- Saudi Arabia.

3.2 Study Population, Data Collection and Sampling

217 diabetic patients' files extracted from hospital database according to inclusion criteria.

3.3 Inclusion Criteria

- Type 2 Diabetes Mellitus patients
- Newly prescribed single or combination oral hypog lycemic agents for at least three months within the preceding 12 months of study enrollment
- Have recorded baseline and follow up measurement of HbA1c, fasting and postprandial blood glucose
- Age range more than 30 years.

3.4 Exclusion Criteria

- Type 1 Diabetes Mellitus patients on insulin
- Type 2 Diabetes Mellitus patients on oral hypoglycemic agents who changed their therapy
- Type 2 Diabetes Mellitus patients on oral hypoglycemic agents plus insulin

- Haven't recorded baseline and follow up measurement of HbA1c
- Age below 30 old years or with co-morbidity that might affect diabetes treatment.

3.5 Data Collection and Data Collection Tool

A data collection sheet specially designed for the study purpose was used to collect relevant information about patient demographics (age and gender), HbA1c value, and fasting and postprandial blood glucose prior initiation of oral antidiabetic treatment and after at least three months of treatment. The study sample divided into three groups (first group on Metformin, second group on Sulfonylurea and last group both of them), selection flow represented in (Figure 1).

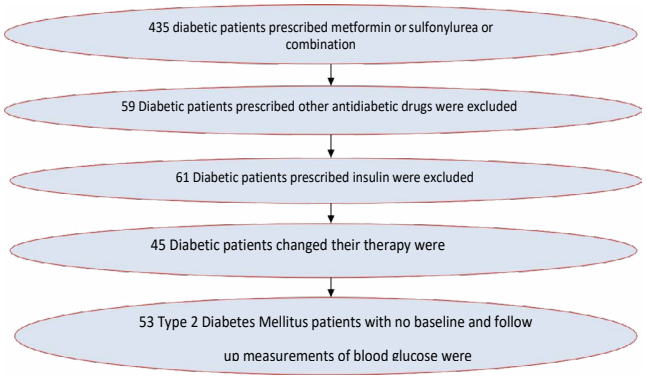

Figure 1. Selection flow of study subjects.

3.6 Statistical Analysis

All data coded with serial number and analyzed by SPSS program through descriptive and inferential statistics. Mean and standard deviation calculated for age of diabetic patients, HbA1c, fasting and postprandial blood glucose before and during oral antidiabetic's therapy, t-test used to compare between HbA1c between different study groups of treatment. (P-value>0.05) was considered statistically significant.

4. Results

4.1 Demographics of Study Subjects

From the total sample included in the study, males re present (63%) and females represent (37%). The youngest age among the collected data of the patients was 31 years and the oldest was 86 with mean ± (SD) 50.3± (10.5) (Table 1a).

Among the study sample, there were 70 (32%) patients on Metformin, 70 (27%) on Sulfonylureas and 77 (41%) on combination of these two drugs (Table 1b).

Table 1a. Distribution of the study sample according to their demographic characters (n=217)

Variable	Categories	Frequency	Percentage (%)
Sex	Male	137	63%
	Female	80	37%
Age (years)	31-45 years	80	37%
	46-60 years	101	46%
	61-86 years	36	17%
	Maximum= 86 yrs Minimum=31 yrs Mean ± SD = 50.3± (10.5).		

Table 1b. Type of oral antidiabetic used (n=217)

Oral antidiabetic	Frequency	%
Metformin	70	32%
Sulfonylurea	**70**	**23%**
Combination Therapy	77	36%

4.2 Change in HbA1c in Diabetic Patients with Metformin Therapy

Maximum level of HbA1c before therapy with metformin therapy was 13.9, after therapy the level became 11.2, minimum level of HbA1c before therapy with metformin was 7.3, after therapy the level became 5.1 and the mean level of HbA1c was 8.9 ± 1.7 and after treatment it was 7.4 ± 1.3 with difference equal to 1.5 (%) (Table 2).

Table 2. Difference in HbA1c level caused by metformin therapy (n=70)

Variable		Before therapy with metformin (%)	After therapy with metformin (%)	Difference
Metformin therapy	Maximum (HbA1c)	13.9 ± 1.9	11.2 ± 1.4	2.7
	Minimum (HbA1c)	7.3 ± 0.8	5.1 ± 1.2	2.2
	Mean ± SD (HbA1c)	8.9 ± 1.7	7.4 ± 1.3	1.5

All data is represented as mean ± standard deviation

4.3 Change in HbA1c in Diabetic Patients with Sulfonylurea Therapy

Maximum level of HbA1c before therapy with sulfonyl urea therapy was 14, after therapy the level became 12, minimum level of HbA1c before therapy with combination of oral antidiabetics was 8.2, after therapy the level became 5.6 and the mean level of HbA1c was 9.3 ± 2.8 and after treatment it became 7.9 ± 1.7 with difference equal to 1.4 (%) (Table 3).

4.4 Change in HbA1c in Diabetic Patients with Combination Therapy

Maximum level of HbA1c before therapy with combination therapy was 14, after therapy the level became 11.3, minimum level of HbA1c before therapy with sulfonylurea was 6.9, after therapy the level became 6.1 and the mean level of HbA1c was 9.6 ± 1.7 and after treatment it became 7.7 ± 1.3 with difference equal to 1.9 (%) (Table 4).

4.5 Change in Fasting Blood Glucose in Diabetic Patients with Metformin Therapy

Maximum level of fasting blood glucose before therapy with metformin therapy was 19.3, after therapy the level became 17.1, minimum level of fasting blood glucose before therapy with metformin was 7.4, after therapy the level became 5.1 and the mean level of fasting blood glucose was 10.2 ± 3.0 and after treatment it became 8.4 ± 2.7 with difference equal to 1.8(mmol/l) (Table 5).

4.6 Change in Fasting Blood Glucose in Diabetic Patients with Sulfonylurea Therapy

Maximum level of fasting blood glucose before therapy with metformin therapy was 18.7, after therapy the level became 16.3, minimum level of fasting blood glucose before therapy with metformin was 7.1, after therapy

Table 3. Difference in HbA1c level caused by sulfonyl urea therapy (n=70)

Variable		Before therapy with sulfonylurea (%)	After therapy with sulfonylurea (%)	Difference (%)
sulfonylurea therapy	Maximum (HbA1c)	14 ± 1.1	12 ± 1.4	2
	Minimum (HbA1c)	8.2 ± 1.5	5.6 ± 1.9	2.6
	Mean ± SD (HbA1c)	9.3 ± 2.8	7.9 ± 1.7	1.4

All data is represented as mean ± standard deviation

Table 4. Difference in HbA1c level caused by combination therapy (n=77)

Variable		Before therapy with (metformin, sulfonylurea) (%)	After therapy with (metformin, sulfonylurea) (%)	Difference (%)
Combination therapy (metformin, sulfonylurea)	Maximum (HbA1c)	14± 1.9	11.3 ± 1.5	2.7
	Minimum (HbA1c)	6.9 ± 1.8	6.1 ± 1.2	0.8
	Mean ± SD (HbA1c)	9.6 ± 1.7	7.7 ± 1.3	1.9

All data is represented as mean ± standard deviation

Table 5. Difference in fasting blood glucose caused by metformin therapy (n=70)

Variable		Before therapy with metformin (mmol/l)	After therapy with metformin (mmol/l)	Difference
Metformin therapy	Maximum (fasting blood glucose)	19.3 ± 3.6	17.1 ± 3.4	2.2
	Minimum (fasting blood glucose)	7.4± 2.9	5.1 ± 3.2	2.3
	Mean ± SD (fasting blood glucose)	10.2 ± 3.0	8.4 ± 2.7	1.8

All data is represented as mean ± standard deviation

the level became 5.3 and the mean level of fasting blood glucose was 11.7 ± 3.1 and after treatment it was 10.1 ± 2.4 With difference equal to 1.6(mmol/l) (Table 6).

4.7 Change in Fasting Blood Glucose in Diabetic Patients with Combination Therapy

Maximum level of fasting blood glucose before therapy with metformin therapy was 23, after therapy the level became 17.8, minimum level of fasting blood glucose before therapy with metformin was 7.8, after therapy the level became 5.1 and the mean level of fasting blood glucose was 13.4 ± 4.3 and after treatment it was 10.4 ± 3.7 With difference equal to 3(mmol/l) (Table 7).

4.8 Change in Postprandial Blood Glucose in Diabetic Patients with Metformin Therapy

Maximum level of postprandial blood glucose before therapy with metformin therapy was 23, after therapy the level became 20.8, minimum level of postprandial blood glucose before therapy with metformin was 7.1, after therapy the level became 5.2 and the mean level of postprandial blood glucose was 15.6 ± 4.8 and after

Table 6. Difference in fasting blood glucose caused by sulfonylurea therapy (n=70)

Variable		Before therapy with sulfonylurea (mmol/l)	After therapy with sulfonylurea (mmol/l)	Difference
Sulfonylurea therapy	Maximum (fasting blood glucose)	18.7 ± 3.1	16.3 ± 2.4	2.4
	Minimum (fasting blood glucose)	7.1 ± 2.9	5.3 ± 2.2	1.8
	Mean ± SD (fasting blood glucose)	11.7 ± 3.1	10.1 ± 2.4	1.6

All data is represented as mean ± standard deviation

Table 7. Difference in fasting blood glucose caused by combination therapy (n=77)

Variable		Before therapy with (metformin, sulfonylurea) (mmol/l)	After therapy with (metformin, sulfonylurea) (mmol/l)	Difference
Combination Therapy (metformin, sulfonylurea)	Maximum (fasting blood glucose)	23 ± 4.3	17.8 ± 3.4	5.2
	Minimum (fasting blood glucose)	7.8 ± 3.6	5.1 ± 2.8	2.7
	Mean ± SD (fasting blood glucose)	13.4 ± 4.3	10.4 ± 3.7	3

All data is represented as mean ± standard deviation

treatment it was 12.4 ± 4.2 with difference equal to 3.2(mmol/l) (Table 8).

4.9 Change in Postprandial Blood Glucose in Diabetic Patients with Sulfonylurea Therapy

Maximum level of postprandial blood glucose before therapy with metformin therapy was 30.7, after therapy the level became 27.7, minimum level of postprandial blood glucose before therapy with metformin was 8.3, after therapy the level became 5.1 and the mean level of postprandial blood glucose was 13.4 ± 4.3 and after treatment it was 10.4 ± 3.7 with difference equal to 3(mmol/l) (Table 9).

4.10 Change in Postprandial Blood Glucose in Diabetic Patients with Combination Therapy

Maximum level of postprandial blood glucose before therapy with metformin therapy was 27.2, after therapy the level became 23.8, minimum level of postprandial blood glucose before therapy with metformin was 7.8, after therapy the level became 4.2 and the mean level of postprandial blood glucose was 14.8 ± 4.3 and after treatment it was 11.1 ± 3.7 with difference equal to 3.7(mmol/l) (Table 10).

4.11 Comparison between the Effect of the Three Modalities of Treatment on HbA1c Level

There was a significant difference between levels of HbA1c between metformin group and combination group (metformin and sulfonylurea) ($p = 0.002$) and also there was a significant difference between sulfonylurea group and combination group (metformin and sulfonylurea) in relation to HbA1c levels ($p = 0.001$). However, there was no significant difference between metformin and sulfonylurea in decreasing HbA1c ($p = 0.09$).

Table 8. Difference in postprandial blood glucose caused by metformin therapy (n=70)

Variable		Before therapy with metformin (mmol/l)	After therapy with metformin (mmol/l)	Difference
Metformin therapy	Maximum(post prandial blood glucose)	23± 4.3	20.8 ± 3.5	2.2
	Minimum (post prandial blood glucose)	7.1 ± 3.3	5.2 ± 2.6	1.9
	Mean ± SD (post prandial blood glucose)	15.6 ± 4.8	12.4 ± 4.2	3.2

All data is represented as mean ± standard deviation

Table 9. Difference in postprandial blood glucose caused by sulfonylurea therapy (n=70)

Variable		Before therapy with metformin (mmol/l)	After therapy with metformin (mmol/l)	Difference
Metformin therapy	Maximum (post prandial bloodglucose)	30.7± 4.3	27.7 ± 3.2	3
	Minimum (post prandial blood glucose)	8.3 ± 3.3	5.1 ± 2.6	3.2
	Mean ± SD (post prandial blood glucose)	13.4 ± 4.3	10.4 ± 3.7	3

Table 10. Difference in post prandial blood glucose caused by combination therapy (n=77)

Variable		Before therapy with (metformin, sulfonylurea) (mmol/l)	After therapy with (metformin, sulfonylurea) (mmol/l)	Difference
Combination therapy (metformin, sulfonylurea)	Maximum (post prandial blood glucose)	27.2 ± 4.0	23.8 ± 4.2	3.4
	Minimum (post prandial blood glucose)	7.8 ± 3.8	4.2 ± 3.2	3.6
	Mean ± SD (post prandial blood glucose)	14.8 ± 4.3	11.1 ± 3.7	3.7

5. Discussion

The aim of the present study was to compare efficacy of metformin and sulfonylurea in mono therapy or combination for type 2 diabetes. The study included (63%) males and (37%) female diabetic patients, mean age of study subjects was 50.3 years.

Treatment with metformin and sulfonylurea primarily targets insulin resistance and insulin deficiency of type 2 diabetes which may account for greater effects on glycemic control. The results indicated that monotherapy with metformin or sulfonylurea caused comparable decrease in the level of HbA1c and fasting blood glucose in type 2 diabetic patients but metformin cause higher decrease in the level of HbA1c, fasting and post prandial blood glucose (HbA1c:1.5% for metformin, 1.4% for sulfonylurea, fasting blood glucose:1.8(mmol/l) for metformin, 1.6(mmol/l) for sulfonylurea and post prandial blood glucose:3.2(mmol/l) for metformin, 3(mmol/l) for sulfonylurea and 3.7(mmol/l) for combination therapy) and also, the combination therapy cause decrease in HbA1c and fasting blood glucose with much higher level which is similar to what is reported in previous study which indicated that most oral hypoglycemic work with the same efficacy in lowering blood glucose when used as monotherapy as measured by hemoglobin A1c (HbA1c). They lower HbA1c about 1 percentage point on average (i.e., HbA1c can go from 8 percent to 7 percent after a medication is started). An exception was metformin, which reduced HbA1c levels more than other antidiabetics used as monotherapy. Combination therapy (including the combination of metformin and sulfonylurea) decreased HbA1c levels more than monotherapy did, by about 1 absolute percentagepoint[29].

A previous systemic review analyzing the results of 15 controlled studies on treatment with metformin versus control reported a weighted mean absolute difference in HbA1c levels of 1.14%[30] which is similar to the present study results. Also, many reports refer to a reduction of HbA1c by 1-2%[31].

Sulphonylureas are effective antihyperglycaemic agents that reduce HbA1c by greater than 1% in monotherapy regimens[31]. Analysis of 11 controlled studies of monotherapy with sulfnylurea against control

found that the weighted mean decrease in HbA1c was 1.52[30] which is higher than the present study results.

Some companies produce formulae that contain MET in addition to another medication. These drugs have been oral antihyperglycaemic agents suggested to encourage patient compliance as a result of reduced pill burden. The bioavailability, tolerability and efficacy of these combinations were similar to the individual components in dual therapy[32]. Patients who switched from dual therapy to fixed combination had a 12.4% increase in adherence to medication[33]. One of their major limitations involves the lack of flexibility of the dose. In some combinations, metformin is available in an extended release formula. In other combination, it is available as an immediate release formula, which may not be tolerated by some patients[34]. The results supported by another evidence indicated that combinations of metformin and a sulfonylurea reduces HbA1c more than using metformin or a sulfonylurea alone.

Sulfonylureas cause hypoglycemia than metformin. It occurs in about 14 percent of people taking a sulfonylurea and 12 percent of people taking repaglinide but the current results didn't show any evidence of hypoglycemia with sulfonylurea[29].

The risk of hypoglycemia increases with combination therapy. People taking a combination of oral hypoglycemics have about an 11-percent higher risk than people on monotherapy which is obvious in this present study results from the difference in HbA1c level between before and after therapy[29].

5.1 Limitations of the Study

First, not all types of sulfonylurea included in the study because only the types present at the hospital where the study conducted were included.

Second, the results can't be generalized as we used the data from a single district general hospital.

Third, the small sample size according to inclusion criteria of the study as the proportion of patients with laboratory test results, such as HbA1c, for both baseline and after oral antidiabetic treatment for at least three months was low as this observational study was conducted in a real-world setting.

Fourthly, the study didn't put into consideration other co morbid conditions or other medication taken by the patients of the study sample.

6. Conclusion and Recommendation

In conclusion, metformin or sulfonylurea as a single therapy are similar in efficacy in reducing glycosylated hemoglobin level, fasting and post-prandial plasma glucose levels to equal degree. However, combination of both therapies resulted in significant greater control of blood glucose level.

Further research with experimental studies as well as large scale RCTs with good study design, long-term follow up are needed on this topic.

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