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Metformin v/s glibenclamide : for intial therapy of type 2 diabetes mellitus in a tertiary care hospital, a comparative study, for efficacy and tolerability

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ABSTRACT

Background

One of the commonest non-communicable disease in nearly all age groups and particularly in old age is diabetes mellitus. For most of the newly diagnosed cases of type 2 diabetes mellitus and for initial treatment, many drugs are used as single drug therapy. Due to not much availability of information for the choice of initial single drug therapy for type 2 diabetes mellitus, the present study is undertaken.

Objectives

To find any differences in the efficacy and tolerability of metformin and glibenclamide for initial therapy of type 2 diabetes mellitus.

Materials and methods

In this study, 100 pateints are taken with type 2 diabetes mellitus. Fifty patients were given metformin and fifty were given glibenclamide, once daily or twice daily accordingly, after the meals. Random blood glucose level is recorded daily for one month using standard techniques. The data collected was analyzed statistically using descriptive statistics. And patients are followed for any adverse effects and compliance.

Results

At the end of the study, 90% subjects in metformin group showed normal blood glucose level as compared 76% in glibenclamide. Metformin seems to be better than glibenclamide in controlling blood glucose level. More side effects are seen in metformin group. Patient compliance was good with all study groups.

Interpretation and conclusion

It appears that metformin is better than glibenclamide for initial therapy of type 2 diabetes mellitus as it decreases the blood glucose level more effectively than glibenclamide in single drug therapy.

Keywords: Diabetes mellitus, Metformin, Glibenclamide.

INTRODUCTION

One of the commonest non-communicable disease in nearly all age groups and particularly in old age is diabetes mellitus. For most of the newly diagnosed cases of type 2 diabetes mellitus and for initial treatment, many drugs are used as single drug therapy. Due to not much availability of information for the choice of initial single drug therapy for type 2 diabetes mellitus, the present study is undertaken.

REVIEW OF LITERATURE

Diabetes mellitus is a metabolic disorder that shows a common feature, hyperglycemia. Etiological factors for diabetes mellitus are many like genetic factors, immune-mediated factors, idiopathic, pancreatic cancer, endocrinopathies, drugs, infections etc. In diabetes mellitus there may be reduced insulin secretion, decreased glucose utilization or increased glucose production that's leads to hyperglycemia. [4]

Diabetes mellitus is classified into types. Type 1 diabetes mellitus - results from severe decrease or loss of insulin production. Type 2 diabetes mellitus – results from insulin resistance, impaired insulin secretion or increased glucose production. [4]

Clinical features of type 2 diabetes mellitus

A person with type 2 diabetes mellitus suffers from polyuria, polyphagia, increased thirst, weight loss, nocturnal enuresis, weakness and fatigue. Many a times diabetes mellitus presents along with its complications as loss of vision, infections, improper wound healing etc [20]

Complications of type 2 diabetes mellitus

Early detection of diabetes mellitus is essential to prevent complications of type 2 diabetes mellitus [19, 38] that may be acute like Hyperglycemic Hyperosmolar State or chronic like retinopathy, neuropathy, nephropathy, peripheral arterial disease, cerebrovascular disease. Complications are mainly due to changes in blood vessel wall. [4]

Diagnosis

Diabetes mellitus is diagnosed based on clinical features, blood glucose level at different periods of time, Hb A1C etc. Diagnosis of diabetes mellitus is done as per National Diabetes Data Group and World Health Organization. [4, 7]

Management of type 2 Diabetes mellitus

Type 2 diabetes mellitus is treated according to the level of hyperglycemia, severity of clinical features and complications of diabetes mellitus. Initially, only lifestyle interventions are enough like high fibrous and low-fat diet and exercise. If this is not sufficient to control hyperglycemia, than monotherapy of any oral hypoglycemic drug is tried. If again the blood glucose level doesn't comes to normal, than the combination therapy is tired. If still the blood glucose level doesn't becomes normoglycemic, than insulin is added along with oral hypoglycemic drugs in type 2 diabetes mellitus. [4, 1, 33, 10, 12, 40] In this study, two oral hypoglycemic drugs are used:

Criteria for the Diagnosis of Diabetes Mellitus : 4 options			
	Normal glucose level (normoglycemic)	Chance of impaired glucose tolerance (prediabetics)	Diabetics
1.Symptoms of diabetes plus random blood glucose	Less than 140 mg/dL	140 to 199 mg/dL	More than 200 mg/dL
2.Fasting plasma glucose	Less than 100 mg/dL	110 to 125 mg/Dl	More than 126 mg/dL
3. Two-hour plasma glucose during an oral glucose tolerance test	Less than 140 mg/dL	140 to 199 mg/dL	More than 200 mg/dL
4. Hb A1C	Below 6% (42mmol/mol)	6.0% to 6.4% (42 to 47 mmol/mol)	6.5% or over (48 mmol/mol or over)

Management of type 2 Diabetes mellitus

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Metformin

Metformin, one of the preferred drug as monotherapy in initial treatment of type 2 diabetes mellitus because it is well tolerated. It acts by many ways and decreases the blood glucose level. It also reduces HbA1c in combination with other drugs. Metformin shows pharmacogenetic variations. Lactic acidosis is less common with metformin. Metformin is far better than placebo in newly diagnosed type 2

diabetes mellitus. Metformin is associated with fewer cardiovascular side effects in type 2 diabetes mellitus. Metformin is used PCOD (polycystic ovarian disease) and in cancer also. [22, 34, 35, 25, 24, 11, 13, 15, 17, 26, 30, 28]

Glibenclamide

Glibenclamide is less preferred for initial therapy of type 2 diabetes mellitus because it is less effective than metformin and causes serious cardiovascular side effects. Glibenclamide is associated with neonatal hypoglycemia when used in gestational diabetes. [33, 35, 25, 11, 26, 41]

MATERIALS AND METHODS

In this study, 100 patients are taken with type 2 diabetes mellitus. Fifty patients were given metformin and fifty were given glibenclamide, once daily or twice daily accordingly, after the meals. Random blood glucose level is recorded daily for one month using standard techniques. The data collected was analyzed statistically using descriptive statistics. And patients are followed for any adverse effects and compliance.

RESULTS

Table 1 showing age distribution

Age group	Total number of patients	Number of patients with glibenclamide treatment	Number of patients with metformin therapy
0-18	0	0	0
19-60	80	35	45
>60	20	15	5
Total	100	50	50

Table 2 showing blood glucose level of the patients on different days of the study

Visits	Glibenclamide treatment			Metformin therapy			Total
	Normoglycemic	Prediabetic	Diabetic	Normoglycemic	Prediabetic	Diabetic	
Day 1	0	22	28	0	18	32	100
Day 5	0	29	21	0	22	28	100
Day 10	2	26	22	4	22	24	100
Day 15	8	26	16	12	20	18	100
Day 20	15	20	15	28	18	4	100
Day 25	20	19	11	41	9	0	100
Day 30	38	10	2	45	5	0	100

Graded as per ADA, Criteria for the Diagnosis of Diabetes Mellitus: Symptoms of diabetes plus random blood glucose (all the subjects had symptoms of diabetes mellitus)

DISCUSSION

In this study, a simple observation is made on metformin v/s glibenclamide: for initial therapy of type 2 diabetes mellitus in a tertiary care hospital, a comparative study, for efficacy and tolerability. Half of study patients are given metformin 500mg tablet twice a day and other half are given glibenclamide 5mg (instead of 2.5mg) [21] tablet single dose after meals on daily basis to respective study groups.

Table 1 shows age distribution of the study subjects. Maximum subjects (80%) are in 19 to 60 years age group. In that, 45% subjects were in metformin therapy.

Random blood glucose level is recorded daily of all subjects for one month as per American Diabetic Association, ADA [7]. Random blood glucose is graded as per ADA, as normoglycemic (less than 140 mg/dL), prediabetics (140 to 199 mg/dL) or diabetics (more than 200 mg/dL). Any signs and symptoms of diabetes mellitus or any side effects to the medicine in the follow-up are also noted.

Table 2 shows blood glucose level of the patients on different days of the study. At the start of the study i.e on baseline day 1, 60% were diabetic (28 persons in glibenclamide and 32 persons in metformin) and 40% were prediabetics (22 persons in glibenclamide and 18 persons in metformin) and no normoglycemic persons.

At day 5, 49 subjects showed diabetic blood sugar level (21 in glibenclamide and 28 in metformin group). At day 10, 6 subjects shown normoglycemia (2 in glibenclamide and 4 in metformin group). At day 15, 20 subjects shown normoglycemia (8 in glibenclamide and 12 in metformin group). At day 20, 43 subjects shown normoglycemia (15 in glibenclamide and 28 in metformin group). At day 25, 61 subjects shown normoglycemia (20 in glibenclamide and 41 in metformin group). At the end of the study i.e on day 30, 83% subjects showed

normoglycemia (76% in glibenclamide and 90% in metformin group).

Metformin, the only biguanide now in use (phenformin is removed due to severe lactic acidosis) acts by enhancing AMP-dependent protein kinase (AMPK) enzyme activity. Metformin causes less hypoglycemic attacks and has high safety profile due to few drug interactions on single therapy use that's why it is commonly used for initial therapy in type 2 diabetes mellitus and also for prediabetics patients, even in PCOD (polycystic ovarian disease). But it is not effective in the treatment of type 1 diabetes. Adverse effects of metformin are gastrointestinal (commonest), lactic acidosis (rare) and weight loss. In renal failure, metformin should be avoided. [35, 36, 37, 9, 13, 15, 43, 8, 27, 3, 1, 2, 5, 31, 23, 29, 42, 16]

Glibenclamide, second generation Sulfonylurea, acts by increase release of insulin from pancreas. Hypoglycaemia (commonest) and weight gain are the adverse effects of it. In healthy subjects, Glibenclamide causes hypoglycemic attacks through various mechanism. It is potent but slow acting, that's why very less used as single therapy. [1, 3, 2, 5, 39]

In this study, subjects showed steady decrease in their random blood glucose levels as the study progressed, more decline in blood sugar level is seen in metformin as compared to glibenclamide (the same is also seen in different studies). [32, 6, 18]. Also, incidence of hyperglycemic episodes were less in metformin therapy. Adverse effects were some what more in patients with metformin therapy. Compliance was good.

CONCLUSION

It appears that metformin is better than glibenclamide for initial therapy of type 2 diabetes mellitus as it decreases the blood glucose level more effectively than glibenclamide in single drug therapy.

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