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A prospective study of effectiveness and comparison of anti-diabetic agents in their glycemic control in type 2 diabetes mellitus in Department of Surgery at RMMCH

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Abstract

Diabetes mellitus is a serious, complex and lifelong condition that affects almost all the vital organs in the body. This study is done to compare the effectiveness of anti-diabetic agents in department of general surgery at Rajah Muthiah Medical College Hospital, Chidambaram, Tamilnadu. A total of 39 patients were enrolled in the study. The objective of the study is to establish effective anti-diabetic agents in the therapy. All the patients enrolled in the study were prescribed with anti-diabetic agents. Among these metformin and sitagliptin phosphate was the commonly prescribed effective anti-diabetic combination in this study.

Aim of the study

- To observe the commonly prescribed anti diabetic agents.
- To observe the glycemic interpretations of the patients.
- To compare the effectiveness of prescribed anti diabetic agents.

Keywords: Anti-diabetic, Diabetes mellitus

Introduction

Diabetes mellitus is primarily a disorder of carbohydrate metabolism yet the metabolic problems in properly treated diabetes are not usually troublesome and are relatively easy to control. It is the long-term complications of diabetes that are the main causes of morbidity and mortality. People with diabetes suffer far more from cardiovascular and renal disease than other people, and diabetes is the principal cause of acquired blindness in the West. Most people with diabetes do not die from metabolic crises such as ketoacidosis but from stroke, MI or chronic renal failure. Diabetes is associated with obesity and lack of exercise, and the steady increase in prevalence in the West is being reproduced in large parts of the developing world as they adopt that lifestyle. Diabetes is in danger of becoming almost pandemic. Particularly worrying is the rise in the incidence of diabetes of both types in every younger patients. This threatens to put an intolerable strain on health services, particularly in developing countries.

Physiological principles of glucose and insulin metabolism

Insulin action

Insulin is the body's principal anabolic hormone. It expands energy stores during times of adequate nutrition against times of foodshortage. Opposing this action are several catabolic 'counter regulatory' or 'stress' hormonesthat mobilize glucose for use when increasedenergy expenditure is necessary. The mostimportant of these are adrenaline (epinephrine), corticosteroids, glucagon, growth hormone and Growth factors. These two opposing systems work in harmony to maintain glucose homeostasis. Insulin also enhances amino acid utilization and protein synthesis, the latter action being shared with growth hormone. Insulin action has three main components

Rapid: in certain tissues (e.g. muscle), insulin facilitates the active transport of glucose and amino acids across cell membranes, enhancing uptake from the blood.

Intermediate: within all cells, insulin promotes the action of enzymes that convert glucose, fatty acids and amino acids into more complex, more stable storage forms.

Long-term: because of increased protein synthesis, growth is promoted. One important consequence is the prompt (though not complete) clearance of glucose from the blood after meals. Glucose would otherwise be lost in the urine because of the kidney's limited capacity for reabsorbing glucose filtered at the glomerulus.

Partial deficiency (type 2)

Even small amounts of insulin will prevent severe metabolic disruption, especially accelerated fat metabolism, i.e. ketosis. Thus, although fasting blood glucose levels may be raised, the main problems only arise after meals; these arise from impaired glucose transport and cellular uptake resulting in impaired clearance from the blood. Adipose and muscle tissue cannot take upglucose efficiently, causing it to remain in the blood, and glucose deficiency in muscle maycause weakness. Because other tissues cannotcompensate sufficiently to assimilate theentire postprandial glucose load, the blood[3]

Type 2 diabetes

These patients have one or more of the following fundamental abnormalities, and in established disease all three commonly coexist:

• Absolute insulin deficiency, i.e. reduced insulin secretion.
• Relative insulin deficiency: not enough insulin is secreted for metabolic increased needs (e.g. in obesity).
• Insulin resistance and hyperinsulinaemia a peripheral insulin utilization defect.

In most cases type 2 diabetes is associated with obesity (particularly abdominal obesity) on first presentation, and in a quarter of all people with diabetes simple weight reduction reverses the hyperglycaemia. This is commonly associated with peripheral insulin resistance owing to receptor-binding or post-receptor defects. Obesity and reduced exercise also contribute to insulin resistance and are modifiable risk factors for type 2 diabetes. The resultant hyperglycaemia induces insulin hyper secretion, hyperinsulinaemia and insulin receptor down regulation, i.e. further insulin resistance. Hyperglycaemia itself is known to damage beta-cells owing to the direct toxic effect of excessive intracellular Glucose metabolism, which produces an excess of oxidative by-products; these cannot be destroyed by natural scavengers such as catalase and superoxide dismutase. The vicious cycle eventually depletes ('exhausts') the beta-cells, intrinsic insulin levels fall and some patients may eventually come to require exogenous insulin therapy.

Thus, type 2 diabetes is usually a progressive disease, although the late onset usually means that some patients die before requiring insulin.

There is still debate as to the primary defect of type 2 diabetes. It has also been proposed that the amyloid deposits (insoluble protein) long known to be found in the pancreas of type 2 patients are related to abnormalities in amylin secretion and contribute to the pancreatic defect. There is an association between abdominal obesity, hyperinsulinaemia, insulin resistance, hyperlipidaemia, type 2 diabetes and hypertension, and this combination of risk factors is termed metabolic syndrome. However, despite much research, as yet it is not known which of these factors (if any) is the prime cause, or if there is another underlying reason.

Genetics

The genetic component in type 2 diabetes is much greater than in type 1. A family history is very common, often involving several relatives. Identical twins almost always both develop the disease and offspring with both parents having diabetes have a 50% chance of developing the disease. The 'thrifty gene' hypothesis proposes that the ability to store fat efficiently - and hence develop obesity – conferred a survival advantage in more primitive societies where famine was a regular phenomenon, hence its persistence in the genome. This may explain why some pre-industrial groups (e.g. Pacific Islanders) readily develop diabetes when exposed to the industrialized lifestyle.[4]

Secondary diabetes

Most diabetes results from primary defects of the pancreatic islet cells. However, there are occasionally other causes of ineffective insulin action, impaired glucose tolerance and hyperglycaemia.

Natural history

Onset

About 80–90% of diabetic patients have type 2diabetes, which tends to occur late in life, hence the obsolete description 'maturity onset'. Onset is usually insidious and gradual, patients tolerating mild polyuric symptoms perhaps for many years.

The other 10-20% has type 1 diabetes and requires insulin at the outset. Almost invariably they become ill at an early age: the peak onset of type 1 is around puberty, starting most commonly in the winter months. Although the disease may be present sub clinically for some considerable time (months, or possibly years), clinical onset is invariably abrupt.[2]

Diagnosis of diabetes

The diagnosis of diabetes requires the identification of a glycemic cut point, which discriminates normal persons from diabetic patients. The present cut points reflect the level of glucose above which micro vascular complications have been shown to increase. Cross-sectional studies from Egypt, in Pima Indians, and in a representative sample from the United States have shown a consistent increase in the risk of developing retinopathy at a fasting glucose level above 99 to 116 mg/dL (5.5 to 6.4 mmol/L), at a 2-hour postprandial level above 125 to 185 mg/dL (6.9 to 10.3 mmol/L), and a hemoglobin A1c (HbA1c) above 5.9 to 6.0% The ADA recommends using the fasting glucose test as the principal tool for the diagnosis of DM in non-pregnant adults. In addition, as show, they defined a new category of glycemia, impaired fasting glucose (IFG). IFG is plasma glucose of at least 100 mg/dL (5.6 mmol/L) but less than 126 mg/d.

Impaired Insulin Secretion

The pancreas in people with a normal-functioning β cell is able to adjust its

secretion of insulin to maintain normal glucose tolerance. Thus in non-diabetic individuals, insulin is increased in proportion to the severity of the insulin resistance, and glucose tolerance remains normal. Impaired insulin secretion is a uniform finding in type 2 diabetic patients and the evolution of β-cell dysfunction has been well characterized in diverse ethnic populations.[1]

Materials and methods

This study was done in RMMCH, tertiary care teaching hospital, Chidambaram.39 patients who had regular visits for the treatment from period of Jul 2016 to Aug 2016 were taken for the study in the department. The background details like age, sex, occupations, habits, family history, concurrent illness, and present medical and laboratory interpretations were collected.

Study Type: prospective observational study

Study Recruitment Procedure:

The recruitment of subjects was carried out with the help of physician who has the knowledge of the patient's medical history.

Inclusion Criteria:

Patients admitted in surgery wards for various surgeries at the age group of above 30 years.

Exclusion Criteria:

Patients above 70 years of age. Patients who are not willing to participate.

Results and discussion

A total of 39 patients were enrolled in this study, of these 28 (72%) were males and 11 (28%) were females.

Table 1: Distribution of sex.

S. No	Sex	No. of patients
1.	Male	28
2.	Female	11

The age distribution of the study showed majority of patients with diabetes belongs to 60-70 years, whereas the patients below 40 years occupy the least.

Table 2: Distribution of age.

S. No	Age	No. of patients
1.	30 – 40	05
2.	40 – 50	09
3.	50 – 60	19
4.	60 – 70	13

Among 39 patients, METFORMIN + GILIMIPRIDE (18 patients) was the most commonly prescribed oral hypoglycemic agent.

Table 3: distribution of oral-hypoglycemic agents.

S. No	Drugs	No. of patients
1.	METFORMIN + GILIMIPRIDE	18
2.	METFORMIN + GLIBENCLAMIDE	06
3.	METFORMIN + VOGLIBOSE	04
4.	METFORMIN + PIOGLITAZONE	05
5.	METFORMIN + SITAGLIPTIN PHOSPHATE	06

Table 4: Laboratory interpretations (fasting blood glucose) of METFORMIN+ GILIMIPRIDE.

Drugs	S. No	Day 1	Day 7	Blood glucose level
METFORMIN + GILIMIPRIDE	1.	147	139	↓
	2.	190	186	↓
	3.	181	200	↑
	4.	176	137	↓
	5.	200	213	↑
	6.	198	164	↓
	7.	184	178	↓
	8.	220	242	↑
	9.	156	130	↓
	10.	160	172	↑
	11.	178	230	↑
	12.	191	170	↓
	13.	186	152	↓
	14.	206	190	↓

[↓]- 09 patients (controlled blood glucose) , [↑]-09 patients (uncontrolled blood glucose).
Among 18 patients who were prescribed with METFORMIN + GILIMIPRIDE, percentage ranges 50% in glycemic control

Table 5: Laboratory interpretations of (fasting blood glucose) METFORMIN + GLIBENCLAMIDE.

Drugs	S. No	Day 1	Day 7	Blood glucose level
METFORMIN + GLIBENCLAMIDE	1.	160	142	↓
	2.	178	156	↓
	3.	165	150	↓
	4.	180	178	↓
	5.	202	216	↑
	6.	19	216	↑

[↓]- 04 patients (controlled blood glucose), [↑]-02 patients (uncontrolled blood glucose).
Among these 06 patients, who were prescribed with METFORMIN +GLIBENCLAMIDE percentage ranges 66% in glycemic control.

Table 6: Laboratory interpretations of (fasting blood glucose) METFORMIN + VOGLIBOSE.

Drugs	S. No	Day 1	Day 7	Blood glucose level
METFORMIN + VOGLIBOSE	1.	158	162	↑
	2.	190	216	↑
	3.	174	160	↓
	4.	188	194	↑

[↓]- 01 patients (controlled blood glucose),[↑]-03 patients (uncontrolled blood glucose).
Among these 04 patients, who were prescribed with METFORMIN +VOGLIBOSE percentage ranges 50% in glycemic control.

Table 7: Laboratory interpretations of (fasting blood glucose) METFORMIN + PIOGLITAZONE.

Drugs	S. No	Day 1	Day 7	Blood glucose level
METFORMIN + PIOGLITAZONE	1.	186	170	↓
	2.	188	196	↑
	3.	228	242	↑
	4.	240	220	↓
	5.	199	216	↓

[↓]- 02 patients (controlled blood glucose), [↑]-03 patients (uncontrolled blood glucose).
Among these 05 patients, who were prescribed with METFORMIN +PIOGLITAZONE percentage ranges 40% in glycemic control.

Table 8: Laboratory interpretations of (fasting blood glucose) METFORMIN + SITAGLIPTIN PHOSPHATE.

Drugs	S. No	Day 1	Day 7	Blood glucose level
METFORMIN + SITAGLIPTIN PHOSPHATE	1.	256	212	↓
	2.	198	160	↓
	3.	230	190	↓
	4.	276	210	↓
	5.	243	199	↓
	6.	21	188	↓

[↓]- 06 patients (controlled blood glucose), [↑]-0 patients (uncontrolled blood glucose).
Among these 06 patients, who were prescribed with METFORMIN +SITAGLIPTIN PHOSPHATE percentage ranges 100% in glycemic control.

Table 9: Comparison of glycemic percentages of anti-diabetic agents.

S. No	Combinations	Percentage
1.	METFORMIN + GILIMIPRIDE	50%
2.	METFORMIN + GLIBENCLAMIDE	66%
3.	METFORMIN + VOGLIBOSE	50%
4.	METFORMIN + PIOGLITAZONE	40%
5.	METFORMIN + SITAGLIPTIN PHOSPHATE	100%

Conclusion

Our study shows that male patients in the age group of 60-70 years affected mostly by diabetes. The commonly prescribed anti-diabetic agents are METFORMIN, GILIMIPRIDE, GLIBENCLAMIDE, VOGLIBOSE, PIOGLITAZONE, and SITAGLIPTIN PHOSPHATE, in which certain combinations are effective and some are less effective in diabetes treatment. Effectiveness comparison is based on first and seventh day fasting blood glucose levels of the patients who are admitted for various complications.

The present study reveals that METFORMIN + SITAGLIPTIN PHOSPHATE combination was very effective (ranges 100%) in diabetic patients in order to control blood glucose level compared to other combinations.

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