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A Comparative Clinical and Hematological Study to Assess the Efficacy of “Glitazones” and “Alpha Glucosidase Inhibitors” as Second Line of Therapy in Patients Having Type II Diabetes Mellitus

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Abstract

This study dealt with determining the Clinical and Hematological. Efficacy of Glitazones and Alpha glucosidase inhibitors as a second line of therapy in patients having Type II Diabetes Mellitus on Sulphonyl urea and Metformin therapy since 2 years prior to the conduction of the study. It involved a population size of a total number of 10 male and female patients suffering from Type II Diabetes Mellitus who were on Sulphonyl urea therapy since a period of 3 months with the primary test products involved were PIOMED and ELITOX. Both the test drugs showed almost similar efficacy for the disease. As this Study was of short duration (3 months), it was difficult to assess which drug would have been better as a third agent for treatment of type 2 Diabetes Mellitus as both showed almost similar efficacy and were able to maintain the blood glucose level within optimal range. In order to observe a substantial and noticeable change in the population a prolonged time span is required.

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Keywords

Diabetes Mellitus; TIIDM; Efficacy; PIOMED; ELITOX; Inhibitors.

Introduction

Today there are 73 million people with diabetes in India. Nearly one in five of all patients with diabetes are expected to develop at least one complication of diabetes. Indeed, diabetes has already emerged as one of the leading causes of blindness, kidney failure, amputations and heart attack in India. Unfortunately, many people do not even discover they have diabetes until complications set in. This is where proper management becomes very important.

Increasing physical activity reduces cardiovascular risk by lowering serum cholesterol and increasing insulin sensitivity. Besides, these exercises have significant effects on mental health as it releases Endorphins and thus having antidepressant effects and reduce anxiety levels. Individuals who exercise regularly, reports improved sense of well-being and self-esteem. Indian phenotype and life-style changes associated with urbanization and lethargic life-style are reported to add up to the rise of diabetes in India. It is known that early insulin therapy is required for tight glycemic control and delay in the onset of complications. Even though a large number of Indians with diabetes fail to achieve glycemic targets. Fear of hypoglycemic event, weight gain, and cardiovascular complications among patients has delayed the initiation of insulin. Insulin and insulin analogues were also reported to be associated with raised concerns over their mitogenic potential. Regular monitoring of blood glucose through self-monitoring devices is insufficiently practiced by diabetic patients. Pain, inconvenience and financial limitation along with low knowledge of diabetes influence the use of self-monitoring devices by patients. Injecting at a specific time in a day especially in public places might lead to inconvenience and embarrassment which along with busy life-styles lead to poor compliance. Pain caused due to insulin injection also adds up for non-adherence to treatment among people with diabetes. Similarly, some patients also reported self-monitoring their blood glucose levels as inconvenient and painful and do not effectively adhere to the monitoring. Thiazolidinediones (piomed 15 mg) and alpha glucosidase inhibitor (elitox 25mg) are selected for the study because they are cost effective, show less side effects in comparison to the other class of drugs, are easily available on Prescription and has better patient compliance in comparison to other drugs [1-4].

Methodology

Aim and objectives

To determine the Clinical and Hematological Efficacy of Glitazones and Alpha glucosidase inhibitors as a second line of therapy in patients having Type II Diabetes Mellitus on Sulphonyl urea and Metformin therapy since 2 years.

Design of the study

Randomized, Open Label, Comparative, and Prospective Study to compare the clinical and hematological efficacy of Glitazones and Alpha glucosidase inhibitors as a second line of therapy inpatients having Type II Diabetes Mellitus on Sulphonyl urea and Metformin therapy since 2 years.

Subject selection

The Study involved a total number of 10 male and female patients suffering from Type II Diabetes Mellitus who were on Sulphonyl urea therapy since a period of 3 months. Firstly, patients were screened and then selected depending upon the criteria of the study and were assessed for the period of 3 months [5,6].

Selection and Withdrawal of subjects

Inclusion Criteria

- Both Male and Female Patients.
- Age Group-30 to 60years
- Patients having Type II Diabetes Mellitus and on Sulphonyl urea and Metformin therapy since 2 years.
- HbA1c values not under normal range (4- 7%)
- All participants of child bearing potential who are sexually active and agree to routinely use adequate contraception from randomization throughout the duration of study.
- Patients who are willing to sign Informed Consent.

Exclusion criteria

- Patients having any other Systemic disease.
- Patients with recently diagnosed type 2Diabetes Mellitus.
- Patients with Type 1 Diabetes Mellitus.
- Medical history of arrhythmia as atrial fibrillation, atrial flutter, atria-ventricular dissociation disorders or ventricular arrhythmias.
- Severe hypoglycemic event requiring third party help in the last 6months.
- Clinically significant abnormal hematology, biochemistry, lipids, hormones, coagulation or urinalysis
- Patients who underwent any surgery within 3 months of participating in the study.
- Patients having history of drug abuse and alcohol.
- Patients who have participated in any other study within the period of 3months.
- Any mental disorders or psychiatric conditions which may interfere with understanding or conduction of study related procedures.

Withdrawal criteria

- In any case of withdrawal, it is necessary to record it appropriately. Subjects may be withdrawn or may be discontinued from the study for any of the following reasons, such as:
- The Subject voluntarily withdraws the consent.

- Occurrence of any intolerable adverse event.
- Pregnancy or intention of being pregnant during the study time period

Test products

1. **PIOMED (15mg)**- Belongs to Glitazones group of anti-diabetic drugs used to lower down glucose level in the blood.

Mechanism of Action- It reduces free fatty acid accumulation, decreases inflammatory cytokines, increases adiponectin levels and causes preservation of β cell structure and function, all leading to improvement in insulin resistance and β cell failure.

2. **ELITOX (25mg)**- belongs to alpha glucosidase inhibitor group of anti-diabetic drugs used to lower down the blood sugar levels in diabetic patients.

Mechanism of Action- It delays the absorption of carbohydrates from the small intestine and thus has a lowering effect on postprandial blood glucose and insulin levels. They delay the absorption of carbohydrates by the gut, by inhibiting alpha-Glucosidase in the small intestine, and thus have an effect on lowering postprandial blood glucose and insulin levels.

Study procedure

Study subjects were randomized into two groups by using computer generated randomization method. Subjects continued to take their usual prescribed, stable regimen of Sulphonyl urea and Metformin medications. They were then prescribed with the treatment drug Piomed 15mg and Elitox 25 mg tablet orally once daily for 3 months. Subjects were screened for all the necessary laboratory tests in the beginning of the study and after 3 months (completion of study) for assessment of the results [7-9].

Screening laboratory tests

The laboratory investigations were performed in the following categories: -

- Biochemistry
- Hematology
- Urine
- Serology
- Others

Biochemistry

- Fasting blood sugar
- Post Prandial (PP) Blood sugar
- Glycated hemoglobin (HbA1c)
- Total cholesterol
- LDL
- SGOT
- SGPT
- ACR

- Micro Albumin

Hematology

- Total RBC count
- Total WBC count
- Differential leukocyte count
- Hemoglobin
- Hematocrit (PCV)
- Platelet's count

Urine

- Turbidity
- Color
- RBCs
- Bilirubin
- Ketone
- Protein
- Glucose
- pH
- Specific Gravity

Serology

- HIV-1 & HIV-2
- Hepatitis B surface antigen
- Hepatitis C antigen
- Syphilis

Others

- ECG

Handling and reporting of AE and SAE

It had been planned to monitor, record and report the adverse drug reactions or adverse events if any had occurred during the study period and the followup process. However, no adverse event was observed during the study time period.

Clinical laboratory evaluations

During the evaluation of screening laboratory results, if any abnormal borderline deviations were observed, the investigator had correlated with the other related lab parameters, clinical findings and examination to decide whether the out-of-range values were clinically significant or not [10-14].

Handling of emergencies

Pioglitazone and Elitox were safely used in the clinical practice and hence no life-threatening adverse event were expected to happen. However, to handle the unexpected adverse events, the intensive care unit was kept ready during the study with all the necessary instruments and the emergency medicines.

Results

The Study was performed on 10 individuals who were suffering from type 2 Diabetes Mellitus and were on Sulphonyl urea and Metformin medication since 2 years. Patients were screened for all necessary laboratory tests and to the selected patients both the test drugs were given. It was a Randomized, Open Label, Comparative, and Prospective Study. No adverse events were observed till the completion of the study (12 weeks). Certain hematological parameters were taken under consideration to analyze the efficacy of the test drugs, namely the Piomed 15mg and Elitox 25mg. Patients bloods samples were screened once at the beginning of the study and once after 12 weeks at the end of the study. The study results were then tabulated and were analyzed for their efficacy parameters.

After calculating the mean changes for the values of HbA1c in the 1st visit and the follow up, it turned out as-

Average mean reduction in the value of HbA1c for Piomed= 1.17

Average mean reduction in the value of HbA1c for Elitox= 1.29

As seen from the above values, the mean results are almost similar to each other, thus it can be inferred that both the drugs show similar efficacy in the treatment of type 2 diabetes mellitus. There were no such major differences seen in comparison in both of the drugs as the study was of short duration. To assess the proper difference as which group of drugs is more efficacious as the second line agent in treatment of diabetes mellitus, a longer duration study of probably 1 year duration has to be carried out (Table 1).

		Diagnostic criteria						
		HbA1c (%)	T.Chol (mg/dL)	LDL (mg/dL)	SGOT (U/L)	SPGT (U/L)	ACR	Micro Albumin
Patient-1	1st Visit	7.5	198	136	71	87	14.3	13.5
	Follow up	7.1	178	104.2	66	107	13.83	6.92
	Mean reduction	0.4	20	31.8	5	20	0.53	6.58
Patient-2	1st Visit	8.4	202	142	39	46	54	50
	Follow up	6.8	180	100	29	32	36.74	41.9
	Mean reduction	1.6	22	42	10	14	17.26	8.1
Patient-3	1st Visit	8.6	159	100	36	45	48	33
	Follow up	7.1	138	83.8	16	18	30	26.3
	Mean reduction	1.5	21	16.2	20	27	18	6.7
	1st Visit	9	174	95	51	55	65	59
	Follow up	6.84	118	89	40	30	56.8	44.3

Patient-4	Mean reduction	2.16	56	6	11	25	8.2	14.7
Patient-5	1st Visit	7.3	205	115	62	50	63	58
	Follow up	7.5	196	100	39	39	61.5	51.7
	Mean reduction	-0.2	9	15	23	11	1.5	6.3

Table 1: Patients on Piomed.

		Diagnostic criterias						
		HbA1c (%)	T.Chol (mg/dL)	LDL (mg/dL)	SGOT (U/L)	SPGT (U/L)	ACR	Micro Albumin
Patient-1	1st Visit	10.4	265	136	50	55	56.9	52
	Follow up	10.04	282	123	45	40	49.2	47.3
	Mean reduction	0.36	17	13	5	15	7.7	4.7
Patient-2	1st Visit	7.1	124	61.1	39.9	32.5	71	70.6
	Follow up	5.98	112	43.7	38.8	30.8	67.4	65
	Mean reduction	1.12	12	17.4	1	1.7	3.6	5.6
Patient-3	1st Visit	7.9	198	107	39	27.4	83	81.3
	Follow up	6.7	157	86	34	21.6	77.2	78.6
	Mean reduction	1.2	41	21	5	5.8	5.8	2.7
Patient-4	1st Visit	8.1	187	86	40.4	52	63.7	60
	Follow up	6.5	134	80	36.2	49.3	58	55.3
	Mean reduction	1.6	53	6	4.2	2.7	5.7	4.7
Patient-5	1st Visit	8	200	103	42.1	54	35.9	33
	Follow up	5.8	176	62.7	35.4	49.1	32	31.7

Mean reduction	2.2	24	40.3	6.7	4.9	3.9	1.3
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Table 2: Patients with Elitox.

Discussion

Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damages many of the body's systems, particularly the blood vessels and nerves. People with diabetes who have higher blood glucose levels tend to develop more complications than those with lower blood glucose levels. Blood glucose management has an important role in preventing the development and progression of complications in diabetes mellitus.

Clinical practice guidelines recommend Sulphonyl urea as the first-line oral antihyperglycemic drug beside Metformin in most patients with T2DM when glycemic control cannot be achieved by lifestyle interventions & Metformin. Clinical practice guidelines recommend Sulphonyl urea as the first-line oral antihyperglycemic drug beside Metformin in most patients with T2DM when glycemic control cannot be achieved by lifestyle interventions & Metformin. Hence, there is a need to determine whether newer agents offer significant advantages over older therapies. The question of optimal third-line pharmacotherapy is particularly relevant given the large number of treatment options available. Among the various options available as second line of drugs for the treatment of Type 2 diabetes mellitus, this study focused primarily on the use of THIAZOLIDINEDIONES (Piomed-15mg) and ALPHA GLUCOSIDASE INHIBITORS (Elitox-25mg).

These two groups of drugs were selected for the study depending on the following criteria-

- Cost effective
- Show less side effects in comparison with other class of drugs
- Are easily available
- And has better patient compliance in comparison to other drugs.

The aim of the Study was to determine the Clinical and Hematological Efficacy of Glitazones and alpha glucosidase inhibitors as a second line of therapy in patients having Type II Diabetes Mellitus on Sulphonyl urea and Metformin therapy since 2 years. The Study had involved a total number of 10 Male and Female patients belonging to Urban and Semi urban areas suffering from Type II Diabetes Mellitus who were on Sulphonylurea and Metformin therapy since a period of 2 years. Patients selected were all Out Patients. They were screened and selected depending upon the criteria of the study and were assessed for the period of 3 months. All the required biochemical tests were performed at the beginning and end of the study to assess the effectiveness of the test drugs.

Patients were screened and who came under the diagnostic criteria for the Study were selected. Study

subject were randomized into two groups by using computer generated randomization method. Subjects continued to take their usual prescribed, stable regimen of Sulphonylurea and Metformin medications. They were then prescribed with the treatment drug Piomed 15mg and Elitox 25 mg tablet orally once daily for 12 weeks. The Patients were summoned at the end of the study duration for another round of the biochemical tests to assess the efficacy of the test drugs. As seen from the results obtained, both the test drugs showed almost similar efficacy for the disease and they were able to control glucose level in optimal levels in patients with type 2 Diabetes Mellitus with insignificant adverse reactions. There were no major differences seen in comparison in both of the drugs as the study was of short duration. To assess the proper difference as which group of drugs is more efficacious as the third agent in treatment of diabetes mellitus, a longer duration study of probably 1 year duration has to be carried out.

Conclusion

The Current Study on Piomed (15mg) and Elitox (25mg) was done to analyze the efficacy of these two drugs as a second line of treatment in patients having Type 2 Diabetes Mellitus and on the medication of Sulphonylurea and Metformin since the period of 2 years. The study results were assessed on the basis of Clinical and Hematological Criteria. The Patients selected were all Out-Patients and were called for regular follow up. As seen from the results obtained, both the test drugs showed almost similar efficacy for the disease. As this Study was of short duration (3 months), it was difficult to assess which drug would have been better as a third agent for treatment of type 2 Diabetes Mellitus as both showed almost similar efficacy and were able to maintain the blood glucose level within optimal range. Thus, to obtain the long-term effect of the test drugs and to find which drug would be more efficacious a long duration study is required.

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