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Original Research Article

A Cross Sectional Study to Determine the Therapeutic Response of Anti-Diabetic Agents Used in Type 2 Diabetic Patients at Tertiary Care Centre in Western Rajasthan

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Abstract:

Introduction: This study aimed to determine the optimum therapeutic response of Antidiabetic drugs by measuring the Glycated Hemoglobin (HbA1c) and Fasting Blood Sugar (FBS) levels in Type 2 Diabetes Mellitus (T2DM) patients above 40 years of age taking monotherapy and combination therapy.

Methods and Materials: This is a prospective observational study. The study participants were recruited from among patients with a confirmed diagnosis of Type 2 Diabetes Mellitus, with a medical history of more than three months, and who had been consistently using the same anti-diabetic agents for the same duration. Prescribed anti-diabetic agents and therapeutic response in the form of FBS and HbA1c were recorded.

Results: This study included 245 patients out of which, 143 Patients (58%) had uncontrolled diabetes mellitus which showed poor glycemic control after treatment. Glimepiride with Metformin was the most common antidiabetic drug prescribed but only 38% of patients had controlled FBS levels and 30% of patients had controlled HbA1c levels among the group. Biguanide was the most commonly prescribed group of antidiabetic agents. Prescribed Insulin preparations were Human Insulin and Glargine Insulin and newer oral antidiabetic agents like Glucagon-like peptide-1 (GLP-1) receptor agonists and Dipeptidyl Peptidase-4 (DPP-4) inhibitors are also prescribed.

Discussion: In our study polytherapy was predominant over monotherapy, although the aim of the therapy should be to achieve optimum glycaemic control by monitoring FBS and HbA1c levels in patients.

Keywords: Type 2 diabetes mellitus**,** Anti-diabetic drugs, HbA1c, Fasting blood glucose, Polytherapy, Monotherapy.

Introduction

Diabetes Mellitus is the leading non-communicable disease in India and worldwide accounting for the ninth leading cause of death in the world [1]. It is critical to address the issue because Type 2 diabetes mellitus accounts for 90% of all cases of Diabetes Mellitus (DM). The impaired insulin response in Type 2 Diabetes Mellitus (T2DM) is referred to as Insulin resistance. In order to maintain glucose homeostasis in this scenario, the body, therefore, produces more insulin at first, but with time, these decreases, which results in T2DM. Those over 45 are most usually diagnosed with T2DM yet, due to rising rates of obesity, inactivity, and calorie-dense meals, it is becoming increasingly prevalent in children, teenagers, and young adults [2].

Although T2DM is associated with obesity and lifestyle modification has great value in management, most of the patients require pharmacological management in the form of oral hypoglycemic agents like biguanides, insulin sensitizers, alpha-glucosidase inhibitors, incretin mimetics, amylin antagonists, and sodium-glucose co-transporter-2 (SGLT2) inhibitors or Insulin preparations. Patients who are unable to achieve treatment goals with first-line oral hypoglycemic medicines as monotherapy frequently receive recommendations for dual medication regimens [3].

HbA1c ≥ 6.5 % or Random plasma glucose ≥ 200 mg/dl or Fasting blood glucose (FBS) ≥ 126 mg/dl or Oral glucose tolerance test- 2-hour glucose in venous plasma ≥ 200 mg/dl suggests diabetes mellitus4 which can be used to assess therapeutic response after treatment. Oral hypoglycaemic medications and different injectable insulin analogues

are both used in the pharmacological therapy of diabetes mellitus. Due to improvements in the medical field, a variety of innovative pharmaceuticals are being introduced on the market, providing doctors with more options but also potentially varying results. We wish to see the effect of various hypoglycaemic agents on HbA1c and fasting blood sugar levels.

Patients and Methods

This study was a cross-sectional observational study conducted at our institute to investigate and analyze various aspects of Type 2 Diabetes Mellitus (T2DM) in patients above 40 years of age. Prior to commencing the study, the required approval was obtained from our Institutional Ethical Committee, ensuring adherence to ethical guidelines. The study aimed to gain valuable insights into the management and characteristics of T2DM patients attending the outpatient department of our institute.

Patient Inclusion and Exclusion Criteria: The study participants were recruited from among patients with a confirmed diagnosis of Type 2 Diabetes Mellitus, with a medical history of more than three months, and who had been consistently using the same anti-diabetic agents for the same duration. Patients were carefully selected to ensure a homogeneous study population. However, certain groups were excluded to maintain the study's focus and minimize confounding factors. Pregnant women, gestational diabetic patients, individuals with Type 1 Diabetes Mellitus, and those with known comorbidities were excluded from the study.

Data Collection and Consent Process: Ethical guidelines were strictly followed during the study, and informed consent was obtained from each participant before their inclusion. Personal information, including name, age, gender, address, and relevant medical and family history, was collected through direct conversations with the patients or their prescription records. Anthropometric data, such as height and weight, were measured, and the body mass index (BMI) was derived to assess the participant's overall health status.

Recording Drug Treatment Details: Detailed information regarding the drugs used to treat Type 2 Diabetes Mellitus was meticulously recorded in the Case Record Form. This included the type of medication, dose duration, dosage, and form used for each patient. Such comprehensive data allowed for a thorough analysis of the effectiveness and adherence to prescribed treatment regimens.

Investigations and Outcome Measures: Fasting blood sugar levels and HbA1c levels were recorded as essential outcome measures for each participant. Fasting blood sugar levels were categorized into three groups: values below 100 mg/dl were considered normal, levels between 101 and 125 mg/dl were classified as prediabetic, and values exceeding 126 mg/dl were marked as diabetic. Regarding HbA1c values, patients with HbA1c levels below 5.7% were classified as normal, those with values ranging from 5.7% to 6.5% were considered prediabetic, and participants with HbA1c levels above 6.5% were labeled as diabetic.

Results

A total of 245 patients who fulfilled the inclusion criteria of T2DM were recruited after taking written informed consent. Out of 245 patients, 135 (53%) were male and 110 (47%) were female. Male to female ratio was 1.23:1. We recruited Patients with 40 years and above age group. The major contribution of patients was between the age of 60-69 years (34%) followed by 50-59 years, 40-49 years, and 70 years and above at last.

We measured the height and weight of patients in the Outpatient department and derived body mass index (BMI). Out of 245 patients, 4 patients had BMI < 18.5 kg/m^2, whereas 112 patients had a normal BMI (18.5- 25 kg/m^2) while 129 were overweight or obese (>25 kg/m^2).

The average FBS of all the patients was 152 mg/dl. Out of 245, 143 Patients (58.4%) had uncontrolled fasting blood sugar levels (>126 mg/dl) while 23% of patients had FBS levels between 101-125 mg/dl, and only 18% had normal FBS values less than 100 mg/dl. HbA1c values were noted along with FBS values. The average HbA1c of all the patients was 7.57 %. Out of 245 patients, only 76 Patients had HbA1c value of less than 6.5 % while 169 patients had uncontrolled diabetes mellitus.

A total of 370 Antidiabetic agents which includes monotherapy as well as multidrug therapy in the form of fixed dose combination (FDC) and/or single agent were prescribed in 245 patients. Glimepiride + Metformin was the most common antidiabetic drug prescribed (37.03%) followed by Teneligliptin (20 mg) in 16% of patients. Though Glimepiride+ Metformin was the most frequently prescribed Fixed dose combination in our study population, only 38% of patients had controlled FBS levels and 30% had controlled HbA1c levels.

Out of all the patients taking Teneligliptin, only 38% had controlled FBS levels whereas 43% of patients taking Voglibose had controlled FBS levels. Sulfonylurea with Biguanide was the most common fixed dose combination given to the 138 patients where 53 patients had controlled FBS values whereas 41 patients had HbA1c values below 6.5% (Table 1). Monotherapy was prescribed in only 28 patients while 217 patients were prescribed polytherapy (Table 2)

Table 1: Study population according to antidiabetic agent and glycemic control

Antidiabetic Group Prescribed	Total number Patients	Patients with FBS < 126 mg/dl	Patients with HbA1c < 6.5%
Biguanide	14	7	6
Biguanide, Sulfonylurea	86	34	22
Biguanide, Sulfonylurea, DPP4 Inhibitor	29	10	8
Biguanide, Sulfonylurea, DPP4 Inhibitor, Glitazone	14	6	4
Biguanide, Sulfonylurea, DPP4 Inhibitor, Glitazone, Insulin	1	0	1
Biguanide, Sulfonylurea, DPP4 Inhibitor, Glitazone, SGLT2 Inhibitor	1	1	1
Biguanide, Sulfonylurea, DPP4 Inhibitor, SGLT2 Inhibitor	4	2	2
Biguanide, Sulfonylurea, DPP4 Inhibitor, α glucosidase Inhibitor	17	8	6
Biguanide, Sulfonylurea, DPP4 Inhibitor, α glucosidase Inhibitor, Glitazone	2	1	2
Biguanide, Sulfonylurea, DPP4 Inhibitor, α glucosidase Inhibitor, SGLT2 Inhibitor	6	4	3
Biguanide, Sulfonylurea, α glucosidase Inhibitor	13	4	5
Biguanide, Sulfonylurea, α glucosidase Inhibitor, Insulin	1	1	0
Biguanide, Sulfonylurea, α glucosidase Inhibitor, SGLT2 Inhibitor	3	0	0
Biguanide, Sulfonylurea, Glitazone	5	3	1
Biguanide, Sulfonylurea, Glitazone, Insulin	1	0	0
Biguanide, Sulfonylurea, Insulin	4	1	1
Biguanide, Sulfonylurea, SGLT2 Inhibitor	3	0	0
Biguanide, α glucosidase Inhibitor	1	1	1
Biguanide, DPP4 Inhibitor	14	7	7
Biguanide, DPP4 Inhibitor, Insulin	1	0	0
Biguanide, DPP4 Inhibitor, SGLT2 Inhibitor	1	0	0
Biguanide, DPP4 Inhibitor, α glucosidase Inhibitor	1	1	1
Biguanide, Insulin	3	2	0
DPP4 Inhibitor	3	1	1
Glitazone	1	1	0
Insulin	11	4	2
Insulin, DPP4 Inhibitor	1	0	0
Sulfonylurea	3	2	1
Sulfonylurea, DPP4 Inhibitor	1	1	1
Total	245		

Abbreviations: DPP4- Dipeptidyl Peptidase 4; SGLT2- Sodium Glucose Cotransporter 2.

Table 2: Study population according to monotherapy and polytherapy and their glycemic control

	Total	Controlled FBS (Number)	Controlled FBS (Percentage)	Controlled HbA1c (Number)	Controlled HbA1c (Percentage)
Monotherapy	28	14	50	10	36
Polytherapy	217	89	41	67	31

Abbreviations: FBS- Fasting Blood Sugar, HbA1c- Glycated Hemoglobin

Discussion

In the present study, we recruited 245 diabetic patients out of which 53% were male while 47% were female patients which give Male to Female ratio of 1.13: 1 which shows that both gender represented equally in diabetes. Males in Eastern, Middle, and Southern Africa were found to have a similar overall prevalence of diabetes mellitus compared to women, according to research by Hilawe EH et al.[5]. Most of the Patients in our study were overweight or obese which was similar to the results of Daousi C et confirming that obese people are at the highest risk of developing T2DM [6,7].

In the present study, the majority of patients belong to FBS group >125 mg/dl (58.4%) and 41.6% of patients belong to <126 mg/dl FBS group which

shows poor glycemic control after treatment main reason behind this can be lack of follow up, poor dietary control, lack of awareness, poor patients' compliance, poor socioeconomic status, ignorance, illiteracy but most importantly advancing age (most patients were above 60 years of age) and long-standing diabetes.

Metformin (Biguanide) was the most commonly prescribed drug followed by Glimepiride in the present study whereas, in FDC, the most frequently prescribed combination was Metformin + Glimepiride (500mg+2mg) (23.8%). Tablet Teneligliptin was the most frequently prescribed drug as a monotherapy which was given to 60 patients out of 245 patients. Metformin 500 mg was the most frequently given anti-diabetic medicine and Metformin 500 mg + Glimepiride 2 mg most frequently prescribed combination drug according to Afroz Abidi et al [8]. Similarly, Alex SM et al [9] recorded in their study that Metformin was the most commonly used drug. In the present study, all Insulin preparations used were Human Insulin and Glargine insulin, unlike our study, the Cross-sectional study of Dashputra A et al found that all Insulin preparations used were human insulins in their study.

Similar to our study, Patel Bet al study showed, Metformin (biguanide) was the most utilized (87.7%) antidiabetic drug for type-2 diabetes. Glimepiride + Metformin combination was the most commonly prescribed antidiabetic combination10. Similarly, Ahmed Z et al recorded in their study that oral anti-diabetic drugs were advised in the majority of patients and they found an underutilization of sulphonylureas and metformin-sulphonylurea combination [11].

In the present study, Overall polypharmacy was found to be predominant over monotherapy and there was a significant increase in the prescribing of newer oral antidiabetic agents like GLP-1 receptor agonist and DPP-4 inhibitors. In their investigation, Lozano OG et al. found that SGLT2 inhibitors are at least as effective at lowering HbA1c levels as other antidiabetic drugs. Similar results were seen with GLP-1 analogues [12].

A study done by Agarwal M et al in their study concluded that a total of 140 anti-diabetic agents contained 79 Oral hypoglycaemic agents (OHA) and 61 Insulin derivatives. In comparison, in our study out of 370 antidiabetic agents, only 27 were insulin derivatives and 343 were oral hypoglycaemic agents. They found that Sulfonylurea was the most prescribed OHA while Metformin was the most common monotherapy. In their study, out of 100 patients 41 had controlled glycemic control while 59 had inadequately controlled glycemic control [13]. Similar results were obtained in the study done by Shrestha et al [14].

Kosachunhanun N et al reported that only 26.3% of type 2 DM patients in their study had an HbA1c value of less than 7% while in our study 35% of all the Patients had an HbA1c value of less than 6.5%. Metformin with sulfonylurea was the most common combination prescribed in their study [15].

A study done by Wu D et al in their metanalysis on the efficacy of DPP-4 inhibitors and metformin as initial combination therapy and as monotherapy in patients with type 2 DM found that DPP-4 inhibitors monotherapy was associated with a lower reduction in HbA1c level and FBS level. Compared with metformin monotherapy, DPP-4 inhibitors plus metformin as initial combination therapy was associated with a higher reduction in HbA1c and FBS levels [16].

The study has its own limitations since the follow-up of the patients was not possible and hence the effectiveness of the anti-diabetic agents over a long time could not be assessed. The study was a hospital-based study and may not truly reflect findings in the rural areas and the entire state.

Conclusion

Our scholarly investigation has led us to deduce that Polytherapy has demonstrated predominance over monotherapy in the context of pharmacological treatment for diabetes. Among the prescribed agents, Metformin, a Biguanide medication, emerged as the most frequently administered drug. Additionally, the combination of Metformin and Glimepiride constituted a commonly prescribed Fixed-Dose Combination (FDC). A substantial majority of patients (58%) fell within the Fasting Blood Sugar (FBS) category of >126 mg/dl, while an even larger proportion (69%) belonged to the Glycated Hemoglobin (HbA1c) group exceeding 6.5%, indicative of inadequate glycemic control among the patient population. Consequently, we recommend the implementation of patient education programs to enhance diabetes awareness and foster greater adherence to therapeutic regimens

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