A COMPARATIVE ANALYSIS OF ADVERSE DRUG REACTIONS IN T2DM: METFORMIN, GLIMEPIRIDE AND ALPHA-GLUCOSIDASE INHIBITORS.

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Abstract

Objectives: This study aimed to investigate the frequency of adverse drug reactions (ADRs) in patients with type 2 diabetes mellitus (T2DM) undergoing treatment with different combinations of antidiabetic medications, focusing on regimens containing alpha-glucosidase inhibitors.

Methods: This prospective, non-randomized, open-label study was conducted at Varun Arjun Medical College & Rohilkhand Hospital, Uttar Pradesh, with a sample size of 240 patients in six treatment groups. The occurrence of ADRs was recorded, and the severity was classified according to the Hartwig and Siegel scale.

Results: The total number of ADRs reported was 47 by 24 study subjects accounting for 10% of the sample population. Flatulence was the most common ADR reported (25.53%), followed by hypoglycemia (23.4%). No severe ADRs were reported across the groups, with most reactions being mild (95.74%). The highest number of ADRs was observed in Group-II (Metformin).

Conclusion: Despite no severe ADRs, gastrointestinal symptoms and hypoglycemia were common, particularly in patients on combined regimens. This highlights the need to balance optimal glycemic control with the potential for ADRs. Further research is warranted to confirm these findings and explore strategies to manage these reactions, thus improving patient outcomes.

Keywords: Type 2 diabetes mellitus, Adverse drug reactions, Acarbose, Voglibose, Patient safety.

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic condition affecting millions worldwide.[1] Prolonged uncontrolled blood glucose levels necessitate long-term medication use, often involving a combination of antidiabetic agents. [2] This polypharmacy is due to the progressive nature of T2DM and the multifactorial intervention required to control hyperglycemia and manage associated risk factors.[3]

However, the individual patient's physiological responses to medication and polypharmacy's effects make T2DM management challenging. An increased regimen complexity often leads to adverse drug reactions (ADRs),[4] undermining patient adherence to medication.[5] Understanding the occurrence and characteristics of ADRs is crucial to improve therapeutic outcomes and patient compliance and reduce morbidity and healthcare costs.[6]

A prospective, open-label, non-randomized study aims to evaluate the frequency and severity of ADRs in different T2DM treatment groups over six months at Varun Arjun Medical College & Rohilkhand Hospital, Uttar Pradesh. The outcomes of this research can contribute to patient safety, enhance the quality of T2DM manage-ment, and guide healthcare providers in making informed decisions regarding medication regimens for T2DM patients.

Materials and Methods

A prospective, open-label, non-randomized study was conducted over six months at Varun Arjun Medical College & Rohilkhand Hospital, Uttar Pradesh, India. Ethical approval (VAMC/ IEC/ 2020/I) was obtained from the Institutional Ethics Committee before the study's commencement.

Patient Selection

The study included 240 T2DM patients attending the Department of General Medicine Outpatient Clinic aged between 30 and 65. They were divided into six treatment groups (I to VI), each comprising 40 patients. Participants were included if they had a confirmed diagnosis of T2DM, were taking antidiabetic therapy for at least three months, and had given informed consent to participate. Patients were excluded if they had other severe systemic diseases, were pregnant or lactating, or were allergic to the drugs under study.

Treatment Groups

The six treatment groups were defined as follows: Group-I received Glimepiride, Group-II received Metformin, Group-III received Glimepiride plus Acarbose, Group-IV received Glimepiride plus Voglibose, Group-V received Metformin plus Acarbose, and Group-VI received Metformin plus Voglibose.

Adverse Drug Reaction Monitoring

At every visit, patients were interviewed, and their medical records were reviewed to identify any ADRs. An ADR was defined as any noxious, unintended, and undesired effect of a drug that occurs at doses used in humans for prophylaxis, diagnosis, or therapy.[7] All the ADRs were documented and reported per the Pharma-covigilance Programme of India (PvPI) guide-lines.[8]

Severity Assessment

The severity of the ADRs was classified according to the Hartwig and Siegel scale into mild, moderate, and severe.[9] A team of physicians with extensive clinical experience assessed the severity.

Data Analysis

Data collected were analyzed using SPSS Statistics software version 22. Descriptive statistics were used for data summarization, and the results were reported as frequencies and percentages.

Results

The distribution of patients and the frequency of adverse drug reactions (ADRs) in each of the six treatment groups is summarized in Table 1. A total of 240 patients, with 40 patients per group, were included in the study. A total of 24 patients, accounting for 10% of all participants, reported experiencing ADRs. Group III showed the highest percentage of patients experiencing ADRs at 20.83%, while the total number of ADRs reported was highest in Group II at 21.27%.

TABLE. 1: PATIENT DISTRIBUTION AND ADR RATES IN DIFFERENT T2DM TREATMENT GROUPS

Group	No. of Patients with ADRs (%)	Total ADRs reported (%)
I	4 (16.66%)	6 (12.77%)
II	4 (16.66%)	10 (21.27%)
III	5 (20.83%)	7 (14.89%)
IV	4 (16.66%)	8 (17.02%)
V	3 (12.50%)	7 (14.89%)
VI	4 (16.66%)	9 (19.14%)
TOTAL	24 (10%)	47 (100%)

The specific ADRs experienced in each treatment group are detailed in Table 2. The most commonly reported ADRs across all groups were flatulence (25.53%), hypoglycemia (23.4%), and nausea

(21.28%). Group I demonstrated the most balanced distribution of ADRs, with an equal frequency of nausea, diarrhoea, abdominal pain and flatulence. Group V displayed the highest occurrence of hypoglycemia and diarrhoea, both at 28.57%.

TABLE. 2: ADVERSE DRUG REACTIONS (ADR) IN DIFFERENT TREATMENT GROUPS

Group	**Hypoglycemia**	**Nausea**	**Diarrhoea**	**Flatulence**	**Abdominal Pain**
Group I	2 (33.33%)	1 (16.67%)	1 (16.67%)	1 (16.67%)	1 (16.67%)
Group II	2 (20%)	3 (30%)	2 (20%)	3 (30%)	0 (0%)
Group III	1 (14.28%)	2 (28.57%)	1 (14.28%)	2 (28.57%)	1 (14.28%)
Group IV	2 (25%)	2 (25%)	1 (12.5%)	2 (25%)	1 (12.5%)
Group V	2 (28.57%)	1 (14.29%)	2 (28.57%)	2 (28.57%)	1 (14.29%)
Group VI	2 (22.22%)	2 (22.22%)	2 (22.22%)	2 (22.22%)	1 (11.11%)
Total	11 (23.4%)	10 (21.28%)	9 (19.14%)	12 (25.53%)	5 (10.64%)

The severity of the ADRs was classified as mild, moderate, or severe according to the Hartwig and Siegel scale. As per Table 3, most of the reactions were mild (95.74% of all ADRs), followed by moderate reactions (4.26% of all ADRs). Notably, no severe reactions were reported in any of the groups.

TABLE. 3: DISTRIBUTION OF ADVERSE DRUG REACTIONS BY SEVERITY AMONG DIFFERENT TREATMENT GROUPS

Group	Mild	Moderate	Severe
Group I	6 (13.33%)	0 (0%)	0 (0%)
Group II	10 (22.22%)	0 (0%)	0 (0%)
Group III	5 (11.11%)	2 (100%)	0 (0%)
Group IV	8 (17.77%)	0 (0%)	0 (0%)
Group V	7 (15.55%)	0 (0%)	0 (0%)
Group VI	9 (20%)	0 (0%)	0 (0%)
Total	45 (95.74%)	2 (4.26%)	0 (0%)

These findings suggest a predominantly mild ADR profile across all T2DM treatment groups in the study, with Metformin exhibiting the highest frequency of ADRs.

Discussion

Comparing our findings with those from previous studies, we found similarities and differences in ADR profiles across the treatment groups. The most common ADRs noted in our study were flatulence, hypoglycemia, and nausea. This observation aligns with findings from previous studies showing that gastrointestinal symptoms and hypoglycemia are common ADRs of alpha-glucosidase inhibitors and sulfonylureas, respectively. [10, 11]

Our findings also highlighted that the combination of Glimepiride and Acarbose (Group III) had the highest percentage of patients experiencing ADRs, while Metformin alone (Group II) resulted in the highest total number of ADRs reported. This suggests that careful consideration and patient monitoring are needed when prescribing these drug combinations, given the potential for increased ADRs. However, it is essential to balance the risk of ADRs against the potential benefits of improved glycemic control.[12]

Interestingly, our study found no severe ADRs in any treatment groups. This contrasts with other studies that reported severe ADRs with similar T2DM treatments.[13,14] Notably, the absence of severe ADRs in our study could be due to its short duration, small sample size, or careful selection and monitoring of patients. Moreover, our results emphasize robust post-marketing surveillance's importance in identifying and managing ADRs.[15]

Conclusion

In conclusion, this study demonstrated the presence of adverse drug reactions in patients treated with different combinations of antidiabetic medications, notably alpha-glucosidase inhibitors. Although no severe reactions were observed, gastrointestinal symptoms and hypoglycemia were common, particularly in patients on combined regimens. It is imperative to balance the benefits of achieving optimal glycemic control with the risk of adverse drug reactions. Further large-scale, multicenter studies are warranted to confirm these findings and explore strategies for managing these reactions to improve treatment tolerance and patient outcomes.

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Conflict of Interest

The research article ensured impartiality with no conflict of interest

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