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Original Research Article

To Investigate the Impact of Metformin, Voglibose as Individual Interventions, and their Combination on Body Mass Index (BMI) among Non-Diabetic Obese Individuals of Eastern Indian Region

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Abstract:

Background: Obesity has become a prevalent issue on a global scale and is linked to various chronic ailments such as osteoarthritis, obstructive sleep apnea, gallstones, fatty liver disease, reproductive and gastrointestinal cancers, dyslipidemia, hypertension, type 2 diabetes, heart failure, coronary artery disease, and stroke. Lifestyle modifications, including dietary and exercise interventions, play a crucial role in the prevention and management of obesity.

Aim: To investigate the impact of metformin, voglibose as individual interventions, and their combination on body mass index (BMI) among non-diabetic obese individuals of Indian descent.

Materials and methods: The present case-control study was conducted on 90 (Ninety) patients attending the OPD of General Medicine in collaboration with the Department of Physiology at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India, following the necessary approval from the institutional ethical review board. The participants were categorised into three distinct groups, labelled as Group 1, Group 2, and Group 3. Each group consisted of a total of 30 individuals who volunteered for the study. Group I was administered with Tab Metformin 500 mg, Group II was administered with Tab Voglibose 0.3 mg and Group III with Tab Metformin (500 mg) + Tab Voglibose (0.3 mg).

Results: The inter-group comparison between the Voglibose group (27.49±2.88) and the Metformin group (27.11±2.11) was conducted using an unpaired t-test. The results indicated that there was no statistically significant difference in BMI between the two groups ($p = 0.22$). There was a statistically significant difference in BMI between the Metformin group (27.11±2.11) and the combination group in the inter-group comparison. The combination of Voglibose and Metformin yielded a mean value of 21.99±2.39, as determined through the application of an unpaired t-test. This analysis revealed a statistically significant result, with a p-value of less than 0.0001. The inter-group comparison between the Voglibose group (mean BMI: 27.49±2.88) and the combination group (Voglibose + Metformin) (mean BMI: 21.99±2.39) revealed a significant statistical difference in BMI.

Conclusion: In conclusion, the current study suggests that Metformin should be considered as the preferred choice for managing BMI and type-2 Diabetes Mellitus due to its demonstrated efficacy and safety profile compared to other available anti-diabetic drugs.

Keywords: Voglibose, Metformin, BMI, Non-diabetic

Introduction

Obesity has become a prevalent issue on a global scale and is linked to various chronic ailments such as osteoarthritis, obstructive sleep apnea, gallstones, fatty liver disease, reproductive and gastrointestinal cancers, dyslipidemia, hypertension, type 2 diabetes, heart failure, coronary artery disease, and stroke. Lifestyle modifications, including dietary and exercise interventions, play a crucial role in the prevention and management of obesity. In cases where these interventions prove ineffective for individuals

with a body mass index (BMI) of 25 kg/m or higher, pharmacotherapy may be considered, particularly when co-morbidities such as hypertension or type 2 diabetes mellitus are present. Nevertheless, anti-obesity medications are commonly used as supplementary treatments due to the limited efficacy of these interventions in achieving sustainable weight loss over an extended period [1, 2]. Therapeutic interventions for non-diabetic individuals with obesity encompass several strategies. These include the promotion of weight loss through lifestyle modifications, such as adhering to a low-calorie diet and engaging in regular exercise. Additionally, the use of anti-obesity medications may be employed. Furthermore, it is crucial to address common associated risk factors, such as arterial hypertension and dyslipidemia, in order to enhance cardiovascular outcomes. A variety of treatment modalities are accessible for adults who are overweight or obese, including behavioral interventions, pharmacological interventions sanctioned by the US Food and Drug Administration (FDA), and bariatric surgery for individuals with the highest level of risk. The Food and Drug Administration (FDA) has granted approval to a number of anti-obesity medications, such as Sibutramine, Rimonabant, and Orlistat. Sibutramine has received approval for extended duration of administration. However, in October 2010, the withdrawal of Sibutramine from the market occurred due to its correlation with heightened occurrences of cardiovascular events and strokes [3]. Rimonabant, the initial selective CB1 receptor antagonist, was initially introduced as a pharmaceutical intervention for obesity in 56 nations. However, it was subsequently withdrawn from the market in 2006 due to an elevated susceptibility to psychiatric adverse events, such as depression, anxiety, and suicidal tendencies.

According to current regulations, Orlistat is the sole anti-obesity medication that has been approved for extended periods of use [4]. The inhibition of pancreatic lipase leads to a reduction in the absorption of fat in the intestines. Orlistat is well-known for its gastrointestinal adverse effects, notably including steatorrhea, characterized by the presence of oily and loose stools. However, while they are the most commonly reported adverse effect of the medication, they have a tendency to diminish over time. The approval of over-the-counter medications has been a subject of controversy in the United States, as it has faced opposition from consumer advocacy group Public Citizen due to concerns regarding safety and efficacy [5]. The co-administration of metformin and voglibose has been examined as a potential therapeutic approach for the treatment of diabetes and obesity. The concurrent administration of metformin and voglibose may potentially exhibit synergistic effects in terms of weight reduction and metabolic parameters. The observed effects can be ascribed to complementary mechanisms of action that specifically target glucose metabolism and appetite regulation [6].

Metformin is a frequently prescribed oral medication for the management of type 2 diabetes. Furthermore, it is occasionally recommended for off-label use in non-diabetic individuals as a means of weight management. Voglibose functions as an inhibitor of alpha-glucosidase, potentially exerts an influence on body weight and body mass index (BMI) by modulating carbohydrate metabolism. In addition, it is important to acknowledge that lifestyle modifications, including alterations in dietary patterns and engagement in physical activity, play a crucial role in the management of weight and should be taken into account in conjunction with the utilization of medications.

Aims and Objectives

The current study aims to conduct a comparative evaluation of the impact of Metformin and Voglibose on body mass index (BMI) among individuals without diabetes.

Materials and Methods

The present case-control study was conducted on 90 (Ninety) patients attending the OPD of General Medicine in collaboration with the Department of Physiology at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India, following the necessary approval from the institutional ethical review board. Prior to their participation, all subjects provided written consent. The duration of the study was seven months, from May 2022 to November 2022. Subsequently, comprehensive information pertaining to each patient, encompassing their demographic characteristics, prior medical records, and physical assessment (including vital signs), was meticulously documented within the Case Report Form (CRF). The participants were admitted to and accommodated in the clinical facility for a duration of one hour prior to the administration of the dosage. Participants who did not experience any adverse events were discharged at the conclusion of the study. The volunteers were subjected to observation in the event of any unfavourable occurrences.

The participants were categorised into three distinct groups, labelled as Group 1, Group 2, and Group 3. Each group consisted of a total of 30 individuals who volunteered for the study.

- Group I was administered with Tab Metformin 500 mg,
- Group II was administered with Tab Voglibose 0.3 mg and
- Group III with Tab Metformin (500 mg) + Tab Voglibose (0.3 mg).

The present study was conducted in accordance with the International Council for Harmonisation of

Technical Requirements for Pharmaceuticals for Human Use (ICH) Step 5, specifically the "Guidance for Good Clinical Practises (GCP)," as well as the principles outlined in the Declaration of Helsinki (Scotland, October 2000).

Inclusion Criteria

This study included individuals between the ages of 18 and 60, of any gender, who were classified as obese or overweight based on a body mass index (BMI) greater than 25 kg/m^2. Additionally, participants were required to provide written informed consent before any study-related procedures and to adhere to the study protocol.

Exclusion Criteria

This study excluded individuals who met the following criteria: patients diagnosed with Diabetes Mellitus and pre-diabetes with a HbA1c level of 5.7%, pregnant and lactating women, individuals with a known drug allergy or sensitivity, and patients currently taking other medications known to affect obesity.

A comprehensive physical examination, laboratory investigations, and assessment of body mass index (BMI) were conducted for all patients. The participants underwent baseline assessment of HbA1c levels for the purpose of screening. The study recruited a group of non-diabetic individuals who were in good health, and their Body Mass Index (BMI) was measured at the beginning and end of the study period.

Statistical Analysis

The statistical evaluation was done by ANOVA with the help of SPSS (Statistical Package for Social Service) value less than $p < 0.05$ was taken as significant.

Results

The majority of the participants consisted of females, accounting for 61.11% of the total, while males constituted 38.89% of the sample. The average age of the participants was found to be 47.85±3.67 years. In the current investigation, a total of 90 individuals without diabetes were recruited and successfully participated in the study. A comparative assessment was conducted to evaluate the efficacy of Voglibose and Metformin, both individually and in combination, with respect to body mass index (BMI). All the groups were carefully selected to ensure that they had similar baseline characteristics, including age, sex, and weight. The body mass index (BMI) exhibited a significant decrease when compared to the initial baseline measurement across all three groups.

Table 1: Gender and age distribution of the participants

Parameters	Number	Percentage
Gender		
Male	35	38.89
Female	55	61.11
Age		
below 30	12	13.33
30-40	39	43.33
40-50	19	21.11
Above 50	20	22.22

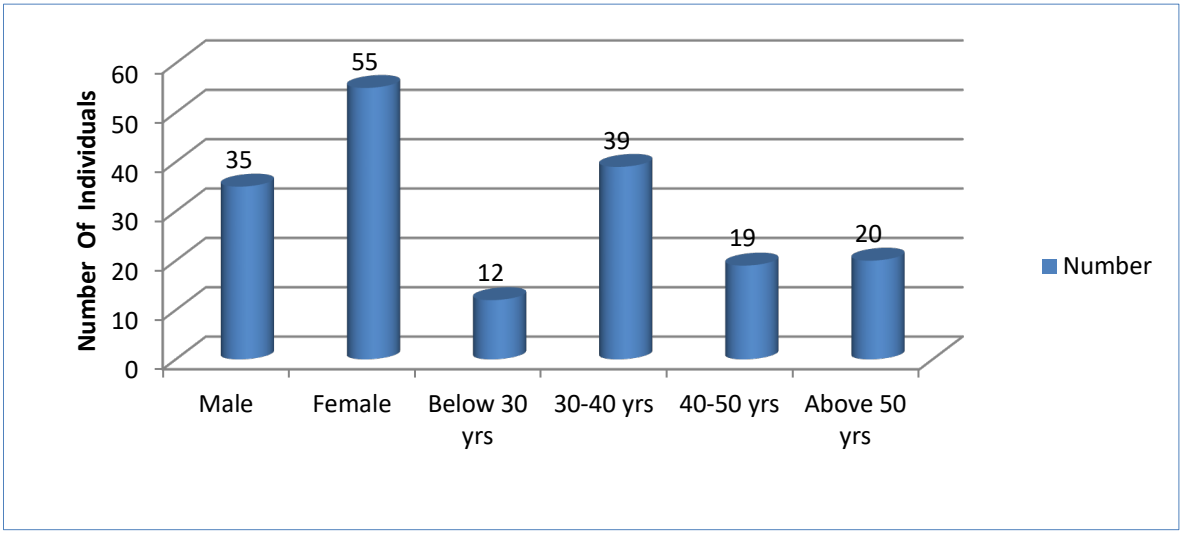

Figure 1: Gender and age distribution of the participants

Table 1 & Fig 1 presents the gender and age distribution of the participants

Table 2: Effect of Voglibose Metformin alone and in combination on BMI in non- diabetic

Groups	BMI		P value
	Before treatment	After treatment	
I	28.55±2.58	27.49±2.88	0.001
II	29.44±2.47	27.11±2.11	0.001
III	27.69±2.19	21.99±2.39	0.001

Intergroup Comparison

Group I and Group II

The inter-group comparison between the Metformin group (27.49±2.88) and the Voglibose group (27.11±2.11) was conducted using an unpaired t-test. The results indicated that there was no statistically significant difference in BMI between the two groups (p = 0.22).

Group I and Group III

The inter-group comparison between the Metformin group (mean BMI: 27.49±2.88) and the combination group (Voglibose + Metformin) (mean BMI: 21.99±2.39) revealed a significant statistical difference in BMI. This was determined using an unpaired t-test, and the difference was found to be statistically significant with a p-value of less than 0.0001.

Group II and Group III

There was a statistically significant difference in BMI between the Voglibose group (27.11±2.11) and the combination group in the inter-group comparison. The combination of Voglibose and Metformin yielded a mean value of 21.99±2.39, as determined through the application of an unpaired t-test. This analysis revealed a statistically significant result, with a p-value of less than 0.0001.

Table 3: Side effect of drugs

Parameters	Group I	Group II	Group III
Nausea	2	4	2
Flatulence	2	0	4
Diarrhoea	2	0	2
Abdominal pain	1	0	1
Total	7	4	9

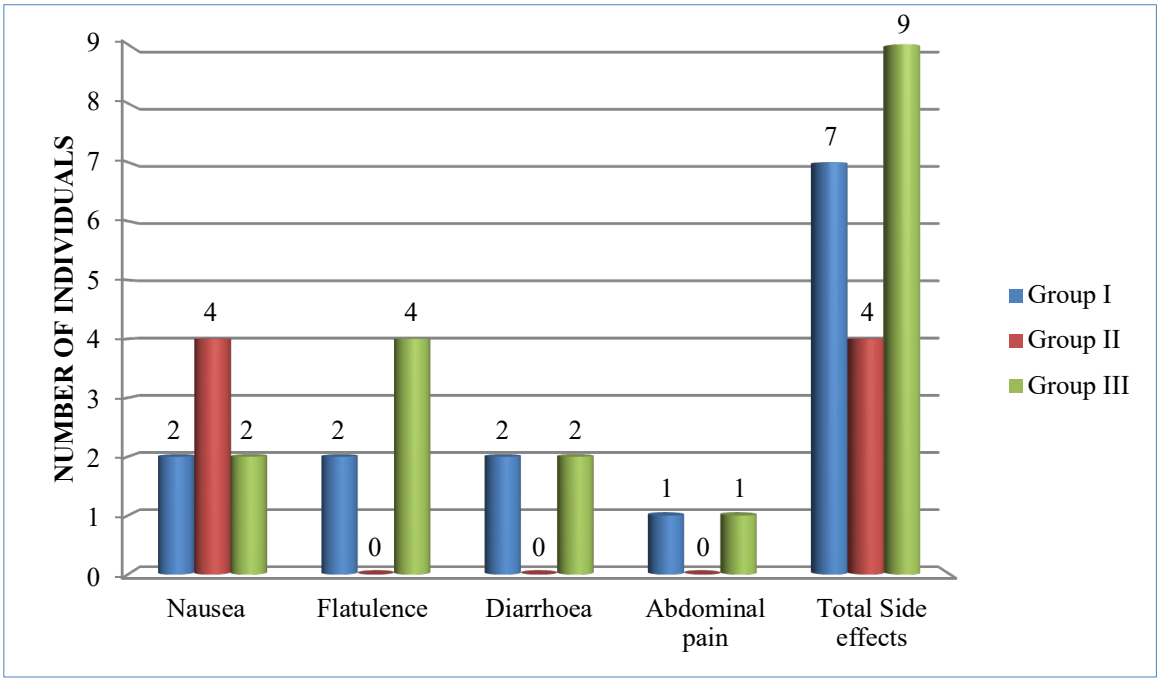

Figure 2: Side effect of drugs

Table 3 & Fig 2 shows the gastrointestinal system was found to be the primary site of adverse drug reactions in all three groups. In the Voglibose group, a total of 7 patients (23.33%) experienced adverse

drug reactions. In the Combination group, 9 patients (30%) exhibited adverse drug reactions. Similarly, in the Metformin group, 4 patients (13.33%) displayed adverse drug reactions. In the Voglibose group, observed gastrointestinal adverse drug reactions included nausea in 2 patients (6.67%), flatulence in 2 patients (6.67%), diarrhoea in 2 patients (6.67%), and abdominal pain in 1 patient (3.33%). In the Combination group, the observed adverse drug reactions included nausea in 2 patients (6.67%), flatulence in 4 patients (13.33%), diarrhoea in 2 patients (10%), and abdominal pain in 1 patient (3.33%). In the Metformin group, a total of four patients (13.33%) experienced the adverse drug reaction of nausea.

Discussion

Metformin, classified as a biguanide, functions as an agent that mitigates hyperglycaemia. Metformin is considered the primary pharmacological intervention for the management of type 2 diabetes, particularly in individuals who are overweight or obese. The primary application of this treatment is in the management of non-diabetic obesity, as it has demonstrated efficacy in facilitating weight reduction.6-8Additionally, it is employed in individuals who do not exhibit diabetes or polycystic ovary syndrome (PCOS). It has been observed to enhance the condition of hyperglycemia. The observed effects of weight loss have been ascribed to the suppression of glucose production by the liver, as well as the anorectic and lipolytic effects of metformin [9]. When administered in a suitable manner, it elicits minimal negative consequences (with gastrointestinal discomfort being the most prevalent) and is linked to a low likelihood of hypoglycemia. Voglibose is a novel alpha glucosidase inhibitor that belongs to the class of N-substituted derivatives of valiolamine. Valiolamine is a cyclitol or pseudo amino sugar with a branched chain structure. The N-substituted moiety of voglibose is derived from glycerol. Voglibose is a pseudo-oligosaccharide that functions as an a-glucosidase inhibitor. It exhibits comparable effectiveness to acarbose, even at lower therapeutic dosages. Additionally, voglibose offers the benefit of being non-hepatotoxic [10]. The compound has demonstrated robust anti-obesity and anti-diabetic properties due to its potent inhibition of glucosidase, making it a promising therapeutic agent for non-insulin dependent diabetes mellitus (NIDDM) in Japan, China, and Korea. Research has demonstrated a notable decrease in postprandial blood glucose levels in certain animal models and individuals without underlying health conditions [11,12]. This substance retards the process of carbohydrate digestion and absorption, consequently impeding the occurrence of postprandial hyperglycemia and hyperinsulinemia. As a result, it can be utilised as a therapeutic agent in the management of diabetes. In clinical trials, it was observed that a significantly higher proportion of subjects (58%) reported experiencing gastrointestinal symptoms when administered Acarbose, as compared to Voglibose, which exhibited a lower incidence of adverse symptoms. Moreover, a notable trend was observed wherein the incidence of these adverse reactions exhibited a gradual decrease during the duration of Voglibose therapy [13]. Hence, it can be concluded that Voglibose exhibits greater efficacy and a reduced incidence of adverse effects compared to Acarbose.

In contemporary times, there has been a steady rise in the prevalence of Diabetes Mellitus patients, primarily attributed to various factors such as sedentary lifestyle and genetic predisposition. The body mass index (BMI) is widely recognised as a significant contributing factor to the development of both macrovascular and microvascular complications.

The current study demonstrated that the administration of Voglibose 0.3 mg and Metformin 500 mg twice daily to the participants over a period of seven months resulted in a decrease in body mass index (BMI). However, a more notable decrease in body mass index (BMI) was observed when Voglibose and Metformin were administered concurrently [13].

The intergroup comparison conducted between Voglibose and Metformin did not yield any statistically significant differences. However, the comparison between the Voglibose and Metformin groups, as well as the combination group (Voglibose + Metformin), revealed a statistically significant difference. As anticipated, the predominant adverse effect observed across all three cohorts was gastrointestinal manifestations, including diarrhoea, flatulence, nausea, and abdominal pain. However, the incidence of adverse drug reactions (ADR) in the Metformin group was significantly lower (13.33%) compared to the Voglibose group (30%) and the Combination group (25%).

Limitation of study

Small sample size and short duration of follow up

Conclusion

In the current study, it has been demonstrated that all three treatment groups, namely Voglibose, Metformin, and the combination of both, exhibit effectiveness in reducing body mass index (BMI). Both Metformin and Voglibose demonstrate comparable effectiveness in reducing body mass index (BMI). One notable advantage of Metformin over Voglibose is its superior safety profile in clinical settings. In conclusion, the current study suggests that Metformin should be considered as the preferred choice for managing BMI and type-2 Diabetes Mellitus due to its demonstrated efficacy

and safety profile compared to other available anti-diabetic drugs.

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