

Cost-Effective Analysis of Generic versus Branded Oral Hypoglycaemic Agents in Patients with Type 2 Diabetes Mellitus- A Prospective Observational Study

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Abstract: Diabetes is a disproportionately expensive disease which requires a lifelong medical treatment. Many patients cut back on medication use because of cost pressures. It is claimed that the cost of generic medicines having the same quality as that of branded medicines is much cheaper than their branded equivalent. The present study was conducted to compare hypoglycemic effect and cost of generic oral hypoglycemic agents or oral antidiabetic agents (OADs) with their branded counterparts in this part of country. Patients, who fulfilled the selection criteria, were divided into 3(three) categories with two subgroups in each category as follows: Category 1: Patients received generic or branded metformin-500mg/day. Category 2: Patients received generic or branded metformin-1000mg/day. Category 3: Patients received generic or branded (Glimeperide 1mg + metformin 500mg)/day. Body weight, blood pressure, fasting and postprandial glucose level were recorded at initial visit and at the end of 30 days. The cost of 30days therapy of branded OADs and their generic versions were recorded. Patients were monitored continuously throughout the study for any adverse event. In this study 162 patients were enrolled, out of all patients 99 were male and 63 were female. The reduction of fasting and postprandial glucose level by generic metformin 500mg/day, generic metformin 1000mg/day and generic (glimepiride 1mg+metformin 500mg)/day was comparable with their branded counterparts. There was no statistical difference between generic drug and branded counterparts in relation to weight and blood pressure change. The cost of generic OADs in this study was much cheaper (3.79 to 11 times) than their branded counterparts. There was no significant difference of AEs among the groups. The generic metformin and generic glimepiride-metformin combination are equally effective and safe as compared to their branded counterparts.

Keywords: Type 2 diabetes, oral antidiabetic agents, generic medicine, and branded medicine.

INTRODUCTION

Diabetes Mellitus is a common metabolic disorder characterized by hyperglycemia, glucosuria, hyperlipidaemia, negative nitrogen balance and sometimes ketonemia[1]. The number of individuals with diabetes is rising rapidly throughout the world [2]. The International Diabetes Federation predicts that the number of people living with diabetes will rise from 366 million in 2011 to 552 million by 2030[3]. India has the largest population living with diabetes after China [4]. Over 90% cases of diabetes are type 2 diabetes mellitus [1]. It is a disproportionately expensive disease. Type 2 Diabetes Mellitus requires a lifelong medical attention to limit the development of its devastating complications and to manage them when

they occur [5,6]. In India only 6.4% of urban low-income group receives reimbursement, whereas this was 21.3% in high-income group [7]. Data based on studies as well as surveys demonstrate that some patients cut back on medication use because of cost pressures, and cost related medications adherence problems have been linked to serious adverse health events including diabetes[8-13].

World health organization (WHO) defines generic drug as “a pharmaceutical product, usually intended to be interchangeable with an innovator product, that is manufactured without a license from the innovator company and marketed after the expiry date of the patent or other exclusive rights”[14]. By

definition generic drugs are equivalent to branded drugs in all respects including efficacy, safety, strength and quality. Shrank WH et al, in their study observed that many physicians are reluctant to prescribe these drugs because they are usually thought to be inferior to branded drugs [15]. It is claimed that the cost of generic medicines having the same quality as that of branded medicines is much cheaper than their branded equivalent [16].

Very few studies were conducted in India on the cost-effectiveness of generic versus branded OADs. No such study was conducted in North Eastern region of India. Hence, this study was undertaken to compare the hypoglycaemic effect and cost of therapy of generic OADs with their branded counterparts in patients with Type 2 Diabetes.

MATERIALS AND METHODS

- Type of study: Prospective observational study.
- Study design: Longitudinal study.
- Study site: Medicine Out Patient Department (OPD) of Tripura Medical College and DR. BRAM Teaching Hospital, Hapania, Agartala.
- Study period: 02(Two) months w.e.f 1st June 2018 to 31st July 2018.
- Sample size: All patients who fulfilled the selection criteria and willing to give consent during the study period were included in the study. Total 162 patients were enrolled in the study.
- Study population: Newly diagnosed Type 2 Diabetic patients.

Inclusion criteria

- Adults of either gender aged between 18-60 years

Exclusion criteria

- Patients with any complications of Diabetes Mellitus like retinopathy, neuropathy etc.
- Patients taking medications that could affect blood glucose level i.e. patients on non-selective beta blockers, diuretics, corticosteroids etc.
- Patients who required insulin therapy.

Study tools and technique

Patients, who fulfilled the selection criteria, were divided into 3(three) categories with two subgroups in each category as follows:

Category 1

Patients received metformin-500mg/day. Total 48 patients were included in this category. Out of which 21 patients received generic Metformin & 27 patients received branded metformin.

Category 2

Patients received metformin-1000mg/day. Total 60 patients were included in this category. Out of which 36 patients received generic Metformin & 24 patients received branded metformin.

Category 3

Patients received (Glimeperide 1mg + metformin 500mg)/day. Total 54 patients were included in this category. Out of which 27 patients received generic Glimepiride-Metformin combination & 27 patients received branded Glimepiride-Metformin combination.

The choice of drugs was decided by the treating physician accordingly to his/her routine medical practice. The different variables were recorded at initial visit and at the end of 30 days. The cost of 30days therapy of branded OADs were taken from the maximum retail price (MRP) printed on the medicine strips. The prices of the generic versions of these OADs were obtained from the official price list of generic medicines published by the Department of Pharmaceuticals, Government of India[17].

Study variables

- Body weight,
- Blood pressure,
- Fasting blood glucose
- Postprandial blood glucose

The data were collected in the case record form. Reduction of blood glucose level and cost of therapy between the groups after 30 days were compared. Patients were monitored continuously throughout the study for any adverse event (AE). Adverse drug reaction form of Pharmacovigilance Programme of India (PvPI) were filled up in case of any AE and World Health Organization- Uppsala Monitoring Centre (WHO-UMC) criteria [18] were used for causality assessment of AE.

Ethical approval

Prior approval of Institutional Ethics committee was obtained.

Confidentiality

The confidentiality of study population was strictly maintained.

Statistical analysis

The 't'-Test were used to analyse intra and inter group comparison

RESULTS

In this study 162 patients were enrolled, out of all patients 99 were male and 63 were female. Mean age of male and female patients was 54.24 years and 54.23 years respectively (Table-1).

Table-1: Demographic profile of the patients

Gender	No of the patients	Age in years [Mean± Standard deviation (SD)]
Male	99	54.24±3.61
Female	63	54.23±4.36

Effects on glycaemic control of Generic vs Branded oral anti-diabetic agents

After 1 month of therapy generic metformin and branded metformin 500mg/day reduced fasting plasma glucose level by 42mg/dl and 40mg/dl respectively. The reduction of postprandial glucose level was 46 mg/dl and 55.44mg/dl in generic and branded groups respectively. The fasting and postprandial glucose level after 1 month was similar ($p>0.05$) in both generic and branded metformin 500mg/day groups.

The reduction of fasting plasma glucose with generic and branded metformin 1000mg/day was 46.33mg/dl and 49.88mg/dl respectively. The reduction of postprandial glucose level was 72mg/dl and 78mg/dl in generic and branded group respectively. There was no significant difference in fasting ($p=0.7572$) and postprandial ($p=0.0544$) glucose level after 1 month of therapy in both the groups.

The reduction of fasting and postprandial glucose level by generic (glimepiride 1mg+metformin 500mg)/day was comparable with branded counterpart ($p>0.05$) (Table-2).

Table-2: Effects on glycaemic control of Generic vs Branded oral anti-diabetic agents

Group	At initial visit		After 30 days		Reduction of plasma glucose in mg/dl (% of reduction)	
	Plasma glucose in mg/dl		Plasma glucose in mg/dl		mg/dl (% of reduction)	
	Fasting	Postprandial	Fasting	Postprandial	Fasting	Postprandial
Generic metformin 500mg/day (n=21)	162±9.68	240±22.34	120±7.34	194±12.38	42(25.92)	46(19.16)
Branded metformin 500mg/day (n=27)	158±7.15	245±8.78	118±7.21	189.56±25.19	40(25.31)	55.44(22.63)
<i>P value</i>	0.1063	0.2926	0.3491	0.4631		
Generic metformin 1000mg/day (n=36)	171.5±13.27	265.33±18	125.17±16.85	193.33±25.07	46.33(27.01)	72(27.16)
Branded metformin 1000mg/day (n=24)	176.26±6.71	259.5±6.57	126.38±10.9	181.5±19.03	49.88(28.29)	78(30.11)
<i>P value</i>	0.1104	0.1347	0.7572	0.0544		
Generic (Glimeperide 1mg + metformin 500mg)/day (n=27)	167.78±24.5	359.56±32.12	137.78±10.17	208±24.17	30(17.96)	151.56(42.15)
Branded (Glimeperide 1mg + metformin 500mg)/day (n=27)	169.11±15.69	343.78±56.09	133.22±8.74	202.33±12.10	37.89(22.40)	141.45(41.15)
<i>P value</i>	0.8132	0.2102	0.0831	0.254		

Values are expressed in (Mean ± SD). P values from unpaired t test. Generic OADs are compared with corresponding branded OADs.

Effects on blood pressure and body weight

There was no change in body weight in Generic metformin 500 mg/day group after one month of therapy. But Branded metformin 500mg/day caused mild decrease (0.18kg) in body weight. Generic and

branded metformin 1000mg/day caused 0.28kg and 0.25kg reduction in body weight respectively. But generic and branded (glimeperide 1mg + metformin 500mg combination)/day caused 0.45kg & 0.21kg increased in body weight respectively. There was no statistical difference between generic drug and branded counterparts in relation to weight and blood pressure change (Table-3).

Table-3: Effects of generic vs branded oral antidiabetic agents on blood pressure and body weight

Group	At initial visit		After 30 days		Change	
	Blood pressure (Systolic /diastolic mmHg)	Body weight (Kg)	Blood pressure (Systolic/diastolic mmHg)	Body weight (Kg)	Blood pressure (Systolic/diastolic mmHg)	Body weight(Kg)
Generic metformin 500mg/day	128.85±9.37 /78±5.88	60.85 ±3.72	128.29±8.97 /75.71±5.35	60.85 ±3.72	-0.56/-2.29	0
Branded metformin 500mg/day	126.22±9.92/ 78.66±6.48	64.4 ±5.29	123.11±7.42 /77.33±7.68	64.22 ±4.99	-3.11/-1.33	-0.18
Generic metformin 1000mg/day	134.18±9.14 /81.45±6.20	66.66 ±4.96	131.83±8.96 /81.83±6.06	66.38 ±4.49	-2.35/+0.38	-0.28
Branded metformin 1000mg/day	132±11.71 /81.75±5.70	65.63 ±7.93	129.75±12.49 /79.25±6.50	65.38 ±7.73	-2.25/-2.5	-0.25
Generic (glimeperide 1mg + metformin 500mg)/day	132.44±7.67 /79.11±5.40	68.11 ±4.28	130.22±7.64 /76.66±5.09	68.56 ±4.48	-2.22/-2.45	+0.45
Branded (glimeperide 1mg + metformin 500mg)/day	130.66±7.07 /81.33±3.61	67.56 ±4.00	131.33±8.37 /78.44±5.17	67.77 ±4.63	+0.67/-2.89	+0.21

Values are expressed in (Mean ±SD)

Cost of therapy of generic vs branded oral antidiabetic agents

The cost of therapy per month of generic metformin 500mg/day, generic metformin 1000mg/day

and generic (glimepiride 1mg + metformin 500 mg)/day groups were much cheaper than their branded counterparts (Table-4).

Table-4: Cost of therapy of generic vs branded oral antidiabetic agents

Group	Cost of therapy (Rs) per month
Generic metformin 500mg/day	15.3
Branded metformin 500mg/day	59.2
Generic metformin 1000mg/day	30.6
Branded metformin 1000mg/day	115.95
Generic (Glimeperide 1mg + metformin 500mg)/day	20.1
Branded (Glimeperide 1mg + metformin 500mg)/day	221.2

Safety Analysis of Drug Therapy

Safety analysis of both generic and branded metformin & glimepiride-metformin combination was carried out. All patients who were receiving treatments were considered for safety analysis. Total 34 patients developed AEs. The reported AEs were nausea, vomiting, abdominal bloating, epigastric pain, diarrhoea, anorexia & dizziness. There was no significant difference of AEs among the groups (p=0.407). These AEs were mild in nature. Causality assessment showed that they were in the “possible” category.

DISCUSSION

In this study we enrolled 162 newly diagnosed diabetic patients and compared the effect of generic [metformin 500mg/day, metformin 1000mg/day and (glimepiride 1mg + metformin 500mg)/day] with their branded counterparts. We observed that the generic OADs equally reduce fasting and postprandial plasma glucose level as compared to branded OADs. The effect on blood pressure and body weight was similar in generic and branded OADs groups. In an earlier study,

Dunne S et al found that generic medicines function equivalently to their innovator counterparts [19].

The cost of generic OADs in this study was much cheaper (3.79 to 11 times) than their branded counterparts. In another study, Lopes Gde L found that the cost of generic medicines was up to 91% less than that of the innovator medicine in India [20]. So, Generic OADs are very cheap and equally effective in comparison with branded OADs.

Many patients cannot continue antidiabetic agents because of their high cost. This study may encourage the physicians to prescribe generic drugs. Further long term prospective studies also will guide us in this aspect.

CONCLUSION

This study shows that the generic metformin and generic glimepiride-metformin combination are equally effective and safe as compared to their branded counterparts.

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