RESEARCH ARTICLE

An open randomized cross over study to compare the clinical effectiveness and safety of economical generic with branded generic telmisartan in essential hypertension

Kamayani Gupta1, Poonam Patel1, Krishna Kaushal Bhardwaj2, Prem Nyati1, Suraj Tripathi1

1Department of Pharmacology, Index Medical College, Hospital and Research Center, Indore, Madhya Pradesh, India, 2Department of Pharmacology, MGM Medical College, Indore, Madhya Pradesh, India

Correspondence to: Poonam Patel, E-mail: dr.pp84@gmail.com

Received: August 12, 2021; Accepted: September 09, 2021

ABSTRACT

Background: Hypertension is a chronic disease and is a major risk factor for chronic heart disease, stroke, coronary heart disease, and its complications include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment. Antihypertensive drugs are important to avoid such complications but compliance of patient is needed which may depend on the cost of therapy. Aim and Objective: This study aimed to assess the efficacy and safety of a branded generic with an economical generic. Materials and Methods: Out of 110 patients, 105 patients (53 patients in group A and 52 patients in group B) completed the study with follow-up over a period of 6 months. Group A patients received generic Telmisartan 40 mg in the beginning (0th day) which was continued for 12 weeks, cross-over was done with branded generic Telmisartan (Telma 40) which was given for further 3 months. Group B patients received the branded generic followed by generic Telmisartan in that sequence for 3 months each. Blood pressure (BP) was recorded at the baseline visit and at the end of 4, 8, 12, 16, 20, and 24 weeks. The adverse events were assessed throughout the study period. Results: Intra-group comparison show significant reduction in systolic (SBP) and diastolic BP (DBP) in each groups (P < 0.001) but when we compare the reduction of SBP and DBP in between the two groups the difference was not significant. Common adverse events were headache, dizziness, light-headedness, and vertigo. Conclusion: There was a huge difference between the prices of branded generic and unbranded generic. This study showed that both branded generic and unbranded generic are comparable in terms of efficacy, safety except the cost of therapy. Thus substitution of a Pharmacological generic (unbranded generic) drug could save lot of expenses.

KEY WORDS: Branded Generic; Unbranded Generic; Telmisartan; Hypertension

INTRODUCTION

Hypertension is a major public health problem in India and all around the world. Hypertension can be stated as abnormally high arterial blood pressure (BP) and is a major risk factor for coronary heart disease and stroke. It can result in various complications like heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment.

Worldwide, an estimated 26% of the population (972 million people) has hypertension, and the prevalence is expected to increase to 29% by 2025.[1] Nearly 1.13 billion people worldwide suffer from hypertension, with (two-thirds) in low- and middle-income. Elevated level of BP has been a cause of 7.5 million deaths, about 12.8% of the total of all
deaths in the entire world which causes 57 million disability adjusted life years (DALYS) or else 3.7% of total DALYS. The prevalence of hypertension is rising in India and causes significant burden on the health system. Global Burden of Disease (GBD) study of 2016 showed that hypertension led to 1.63 million deaths in India in the year 2016 alone. GBD data also showed that over half of the deaths due to ischemic heart disease (54.2%), stroke (56.2%), and chronic kidney disease (54.5%) were attributable to high systolic BP (SBP). Hypertension prevalence was common even among younger age groups, with approximately one out of every 10 individuals aged 18–25 year suffering from it.[3]

The use of antihypertensive drugs is an effective approach to decrease the morbidity and mortality. A huge number of antihypertensive drugs are available for clinical use; the first-line treatment is limited to four major categories of medications, viz. Thiazide-type diuretics, Calcium channel blockers, Angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers (ARBs).

ARBs are widely used in the treatment of essential hypertension. In ARBs telmisartan is more commonly used. In addition to blocking the RAS, telmisartan acts as a selective modulator of peroxisome proliferator-activated receptor-gamma, a central regulator of insulin and glucose metabolism. Its dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease.[4]

The cost of medicine has been raising worldwide leading to a greater strain on the national budgets. A huge proportion of people get deprived of the essential medications. Common method of reducing the cost of pharmaceuticals is the use of generic substitution. The role of generic medicines in reducing the healthcare expenditure has been recognized for a long time. However, the actual benefits of generic medicines are not being transferred to the ordinary people. This is in part due to the rise of branded generics, which are marketed at a price quite close to the innovator brands. Pharmacological generic medicines are not finding their way into prescriptions due to fear of quality control.[31]

Hence, this study was planned with aim to compare the clinical effectiveness and safety of economical generic with branded generic Telmisartan in essential hypertension.

Objectives of this study were
- To evaluate the clinical effectiveness of generic versus branded generic Telmisartan in hypertension with respect to SBP and diastolic BP (DBP) reduction
- To evaluate the safety of generic versus branded generic Telmisartan in hypertension by assessing the frequency and quality of reported adverse effects.

MATERIALS AND METHODS

Study was hospital-based, Prospective, open labeled, crossover, comparative single centered to compare generic and branded generic Telmisartan in newly diagnosed patients of Essential Hypertension Stage I spanning a period of 1 year (2019 to 2020) and including a total of 110 patients. The study was conducted in the Department of Pharmacology and Department of Medicine at Index Medical College, Hospital, and research center, Indore.

Inclusion Criteria
1. All newly diagnosed patients of essential hypertension Stage I
2. Age between 18 and 70 years of either gender
3. The patients willing to give written informed consent.

Exclusion Criteria
1. Already on antihypertensive treatment
2. Patients with BP more than 160/99
3. Female patient planning pregnancy, pregnant and lactating female
4. Patient with bilateral Renal artery stenosis and single Kidney
5. Patient with concomitant disease and on other medication
6. Patient with secondary hypertension.

Procedure of Study
After recruiting the patients according to inclusion and exclusion criteria, informed consent was taken. Random allocation of the patients into groups A and B was done on odd and even basis respectively. Dropout cases were excluded.

Group A patients received generic Telmisartan in the beginning (0th day) which was continued for 12 weeks, crossover was done with branded generic Telmisartan which was given for further 3 months. Group B patients received the branded generic followed by generic Telmisartan in that sequence for 3 months each.

The dose of Telmisartan was 40 mg once daily orally in morning either generic or branded generic in a crossover manner as per the allotment. Brand used in our study was “Telma 40” from any pharmacy (other branded generics telmisartan available are Adcom, Angitel, Arbitel, Astel, Axiten, Cortel, Cesar, Hytel, Macsart, Oditel, Telmisart, Telmikind, T, T-Press, Telecard and so on)[6] and “Telmisartan 40 mg” from Jan Aushadhi Kendra.

- Patient was educated for recognition of adverse effects, and reporting of any adverse event if occurred during therapy in addition to the monitoring for adverse effects on each visit.
• Assessment was done for a period of 24 weeks (6 months) for each subject with regard to reduction in BP and appearance of adverse events if any.

Data Collection and Method
At first visit, basic epidemiological data was collected.

• BP was recorded using digital manometer with a standard cuff size at the baseline visit and at the end of 4, 8, 12, 16, 20, and 24 weeks each. BP was recorded in sitting position for consecutive 3 times at an interval of 5 min each and in different arms and average of the readings was taken
• Fasting blood sugar, Serum Potassium, Creatinine, at baseline visit and at the end of 12 weeks and further at the end of 24 weeks was done.

Parameters to Evaluate Efficacy
• Mean SBP and DBP value at different follow-up visits
• Reduction in SBP and DBP at 12 and 24 weeks.

Parameter to Evaluate Safety
• All adverse events reported or observed by the patients
• Investigations like Fetal Bovine Serum, Serum Creatinine, Serum Potassium level at 12 and 24 weeks.

Statistical Analysis
The collected data were subjected to statistical analysis using Statistical Package for Social Sciences version 20.

• Reduction in mean SBP and DBP per visit in the two groups was compared by “Student’s t-test”, while the intra-group comparison was done by “Repeated measure ANOVA”
• The adverse events in the two groups were compared by “Chi-square test”. All means were expressed as mean ± Standard error of mean (SEM)
• The critical level of significance of the results was considered at 0.05 i.e. \( P < 0.05 \) was considered significant.

Prior approval of the synopsis was taken from Institutional Ethics Committee of Index Medical College. Certificate No. IMCHRC/IEC/2019/51, Dated-March 9, 2019.

RESULTS
A total of 110 patients were selected, 105 patients (53 patients in group A and 52 patients in group B) completed the study with follow-up over a period of 6 months. Remaining 05 patients dropped out and were excluded from the study.

Both groups were comparable, and there were no statistically significant differences between the two groups at baseline [Table 1].

Out of 105 patients, most of the patients were employed 68 (64.76%), housewives were 16 (15.2%), 03 (2.8%) were found unemployed, 14 (13.3%) were farmers, and 04(3.8%) were students.

Both the group are comparable for substance abuse, with 49 patients are using either alcohol or tobacco and its product or both. [Table 2].

Figures 1 and 2 shows that after 12 weeks of regular follow-up the Mean ± SEM value of SBP/DBP was reduced to 132.79 ± 0.629/80.15 ± 0.437 mm of Hg. After the cross over has been done from generic to branded generic, the mean SBP/DBP at 24 completed weeks was 124.43 ± 0.478/73.68 ± 0.488 mm of Hg.

Figures 3 and 4 show that after 12 weeks of regular follow-up the Mean ± SEM value of SBP/DBP was reduced to 133.19 ± 0.627/79.96 ± 0.416 mm of Hg. After cross-over has been done from branded generic to generic in group B patients, the value of mean SBP/DBP at the end of 24 weeks treatment was 124.34 ± 0.576/73.04 ± 0.477 mm of Hg.

Statistical analysis revealed a similar and non-significant difference in reduction of mean SBP/DBP at 12th week and 24 weeks between the group A and B.

Mild adverse effects were reported in 9.43% of patients after 12-week treatment among the generic drug users. Furthermore, among the branded generic Telmisartan users it was found that 5.76% of patients reported adverse events at 12th week.

After 24 weeks, 5.76% of patients with generic Telmisartan and 5.66% of patients on branded generic Telmisartan reported adverse events. Overall 5.71% of study subjects

<table>
<thead>
<tr>
<th>Table 1: Patients characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Mean age±SD (year)</td>
</tr>
<tr>
<td>Male: Female (%)</td>
</tr>
<tr>
<td>Mean weight±SD (kg)</td>
</tr>
<tr>
<td>SBP (Mean±SEM) at visit</td>
</tr>
<tr>
<td>DBP (Mean±SEM) at visit</td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure, DBP: Diastolic blood pressure
reported adverse events, which were headache, dizziness, light-headedness, and vertigo.

There was a non-significant difference in the adverse events reported among the study subjects on generic and branded generic Telmisartan at 12th week ($P = 0.479$) as well as at the end of the study ($P = 0.981$).

Table 3 shows the expense of treatment per month with generic Telmisartan 40 mg from Jan-Aushadhi Kendra and branded generic Telmisartan 40 mg (Telma 40) from any medical store. Cost per month for generic Telmisartan is 28.8 Rs per month and that for branded generic Telmisartan is 216.69 Rs and expense per year with generic Telmisartan is 350.4 Rs and it is almost 2636 with branded generic. It is clear that there is a huge difference in cost of treatment between generic and branded generic Telmisartan.

### DISCUSSION

The prevalence of hypertension is continuously increasing and Antihypertensive drugs are the major burden in our country and world-wide. It puts pressure on both the payers and providers and created a need to implement cost-effective approaches that can reduce the expenditure. Looking generic drug as effective alternative to branded drug we carried this study with the aim to compare the clinical effectiveness and safety of economical generic with branded generic Telmisartan in essential hypertension. Study results clearly show that there is no significant difference in terms of effectiveness and

![Figure 1: Systolic blood pressure value of Group A Patients $P < 0.001$](image)

![Figure 2: Diastolic blood pressure value of Group A Patients $P < 0.001$](image)

![Figure 3: Systolic blood pressure value of Group B Patients $P < 0.001$](image)

![Figure 4: Diastolic blood pressure value of Group B Patients $P = 0.01$](image)
safety between branded generic and generic Telmisartan but branded drugs are nearly 8 times more costlier than generic Telmisartan.

110 patients were selected in our study out of which 105 patients (53 patients in group A and 52 patients in group B) completed the study with follow up over a period of 6 months. Most common age group of patient involved were 51–60 years indicating advancing age is an important risk factor which might due to the Lack of endogenous estrogens, that modulate vascular endothelial function. A well-known fact that hypertension is more prevalent in overweight and obese subjects compared with normal-weight subjects and this is evident in our results with mean weight study subjects was 64.92 ± 5.95 kg. We find the prevalence of hypertension is more in employed persons which were evident by other studies.

Effects of job strain enhance the BP through sympathetic pathways and pituitary–adrenocortical hormones. Substance abuse is important risk factor for hypertension. In our study, 46.7% of patients are involved in substance abuse either of alcohol, tobacco, and its product or both. There is a positive association between alcohol and tobacco consumption and hypertension. Tobacco contains nicotine that stimulates the body to produce adrenaline, making the heartbeat faster as well as enhancing the BP.

Alcohol may enhance the BP by producing an imbalance in the nervous activity, stimulation of the renin-angiotensin-aldosterone system, increased cortisol levels, increased intracellular calcium levels, and induction of vascular endothelial oxidative stress.

Our results show a significant reduction in SBP/DBP from baseline to 24 weeks which is consistent with other studies but here we were interested to know whether generic or branded generic Telmisartan is more clinically effective and safe since there is no study which directly compare generic or branded generic Telmisartan in term of efficacy and safety. The study results show reduction in mean SBP/DBP of group A and B at 12 weeks which further maintained after crossover in both groups. Statistical analysis reveals a non-significant difference in the values of mean SBP/DBP at 0th week, 12th week, and 24 weeks [Tables 4 and 5].

We used a Cross-over design in view of the advantages that a small number of patients could be good enough to give the significant comparative status, since here the subject himself or herself acts as his or her own control. Although there’s a disadvantage of the enhancement in duration of study it is affordable in sake of the authenticity of the data. Thus, it could be concluded that generic telmisartan is not inferior to branded generic in its efficacy as proven by other studies.

Few patients only reported adverse drug reaction (ADR) with nonsignificant P-value as evident in Figures 5 and 6. The commonly observed ADR were headache, dizziness, light-headedness, vertigo. None of them was significant enough to change the medicine.

Our study shows a huge difference in the price of the generic and a branded generic, i.e., branded generic is nearly 8 times more expensive than the generic one [Table 5]. Common method to reduce the cost of pharmaceuticals is the use of generic substitution. Generic drugs are copies of brand-name drugs that have exactly the same dosage, intended use, effects, side effects, route of administration, risks, safety, and strength as the original drug. Though Generic substitution of brand prescriptions is well accepted in many parts of the world but in India generic substitution is not a universally

---

**Table 3:** Comparison of cost of therapy between generic and branded generic Telmisartan

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Cost of one tablet</th>
<th>Total cost per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic Telmisartan</td>
<td>40 mg once a day</td>
<td>0.96 Rs.</td>
<td>350.4 Rs.</td>
</tr>
<tr>
<td>Branded generic Telmisartan</td>
<td>40 mg once a day</td>
<td>7.23 Rs.</td>
<td>2636.3 Rs.</td>
</tr>
</tbody>
</table>

**Table 4:** Comparison of SBP value per visit

<table>
<thead>
<tr>
<th>Group</th>
<th>0 week</th>
<th>12th week</th>
<th>24 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n=53)</td>
<td>149.26 ± 0.640 (Generic)</td>
<td>132.79 ± 0.629 (Generic)</td>
<td>124.43 ± 0.478 (Branded Generic)</td>
</tr>
<tr>
<td>Group B (n=52)</td>
<td>148.83 ± 0.613 (Branded-genic)</td>
<td>133.19 ± 0.627 (Branded-genic)</td>
<td>124.34 ± 0.576 (Generic)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.623</td>
<td>0.654</td>
<td>0.947</td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure

**Table 5:** Comparison of DBP value per visit

<table>
<thead>
<tr>
<th>Group</th>
<th>0 week</th>
<th>12th week</th>
<th>24 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n=53)</td>
<td>95.47±0.425 (Generic)</td>
<td>80.15±0.437 (Generic)</td>
<td>73.68±0.488 (Branded Generic)</td>
</tr>
<tr>
<td>Group B (n=52)</td>
<td>95.46±0.385 (Branded-genic)</td>
<td>79.96±0.416 (Branded-genic)</td>
<td>73.04±0.477 (Generic)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.986</td>
<td>0.755</td>
<td>0.350</td>
</tr>
</tbody>
</table>

DBP: Diastolic blood pressure
accepted which may be due to disbelief on generic medicines by practitioners often due to perceived inferior quality, and counterfeiting of drugs. However, it should be kept in mind that generic drugs are actually identical and bioequivalent to an innovator brand. Our study results also reveal that there is no significant difference in efficacy and ADR of generic and branded generic drug but only there is huge difference in cost of treatment that can affect compliance of patient on long term.

CONCLUSION

Our study entitled “An open randomized cross-over study to compare the clinical effectiveness and safety of economical generic with branded generic Telmisartan in essential hypertension” reveals that Telmisartan produces significant reduction of both systolic as well DBPs over a period of time with no difference in the efficacy of generic as well as branded generic Telmisartan as for as the efficacy is concerned. Both generic as well as branded generic Telmisartan are well tolerated with no difference in the reported adverse effects. Generic Telmisartan is more cost-effective than the branded generic counter-part and could reduce the economic burden in a chronic disease like hypertension which requires long-term treatment. Thus, our study concludes that substitution to economical generic formulation of Telmisartan could be promoted to reduce the financial burden of the patients and the nation in view of the lifelong need of the drug. Such studies should be promoted to compare other generic medicines with their branded generics in hypertension as well as other chronic disorders so that the prescribing habits of the prescribers could be directed to a fearless and fruitful prescription of the generics.

ACKNOWLEDGMENT

The authors would like to thank the faculty and postgraduate students from the Department of Medicine, Index Medical College and Research Institute, Indore for their support in conducting the project work.

REFERENCES


