Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20184318

Original Research Article

Evaluation of antihypertensive efficacy of Losartan + Hydrochlorthiazide versus Telmisartan + Hydrochlorthiazide in patients with stage 1 or stage 2 hypertension: a randomized controlled trial

Manreet Singh Sekhon[1], Anjleen Kaur[1]*, Vijay K. Bajaj[2], Harcharan Singh[1], Anita Gupta[1]

[1]Department of Pharmacology, [2]Department of Cardiology, Government Medical College, Patiala, Punjab, India

Received: 19 August 2018
Accepted: 26 September 2018

***Correspondence to:**
Dr. Anjleen Kaur,
Email: anjleen9@gmail.com

ABSTRACT

Background: Cardiovascular disease (CVD) is the most common contributor of morbidity and mortality in underdeveloped and developing countries including the South Asian countries (including India and Pakistan). Amongst the cluster group of CVDs, Hypertension (HTN) represents the most common cardiovascular risk factor. The aim of this trial was to evaluate of antihypertensive efficacy and effect on biochemical parameters of Losartan + Hydrochlorthiazide versus Telmisartan + Hydrochlorthiazide in patients with stage 1 or stage 2 hypertension with a randomized controlled trial.
Methods: This was a prospective, randomized controlled trial of Losartan + Hydrochlorthiazide versus Telmisartan + Hydrochlorthiazide in patients with stage 1 or stage 2 hypertension. The primary endpoint on treatment was analysis of antihypertensive efficacy of these drug combinations. The variables were compared at different time points- baseline, 3 and 6 months.
Results: In the present study, 76 patients were enrolled with 38 patients each allocated to each treatment groups. The effect of Losartan 50mg + Hydrochlorthiazide 12.5mg OD was found to be significant on SBP and DBP in both supine as well as sitting position than Telmisartan 80mg + Hydrochlorthiazide 12.5mg OD group at 3 and 6 months.
Conclusions: The results on anti- hypertensive efficacy was far better in Losartan 50mg + Hydrochlorthiazide 12.5mg OD group than Telmisartan 80mg + Hydrochlorthiazide 12.5mg OD group.

Keywords: Cardiovascular disease, Hypertension, Hydrochlorthiazide, Losartan, Uric acid, Telmisartan

INTRODUCTION

Cardiovascular disease (CVD) is the most common contributor of morbidity and mortality in underdeveloped and developing countries including the South Asian countries (including India and Pakistan). It has been estimated that 78% of all deaths and 86.3% of all loss of disability adjusted life years are attributable to this cause.[1] Amongst the cluster group of CVDs, Hypertension (HTN) represents the most common cardiovascular risk factor. Several previous studies have clearly shown longitudinal associations between HTN and coronary artery disease, myocardial infarction, stroke, congestive heart failure, and peripheral vascular disease and lowering blood pressure (BP) significantly reduces the cardiovascular morbidity and mortality.[2]

Hypertension is defined as systemic blood pressure of 140/90mmHg.[3] The prevalence of HTN increases with advancing age; for example, about 50% of people between

the ages of 60 and 69 years have HTN and the prevalence is further increased beyond age 70.[4]

Meta-analyses of titration-to-response studies have proved Telmisartan to be superior to Losartan as monotherapy in controlling DBP and SBP.[5] According to various standardized protocols like the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and European Society of Hypertension (ESH) guidelines, combination antihypertensive therapy is warranted particularly patients with systolic blood pressure (SBP) more than 20mm Hg or DBP more than 10mm Hg above goal and among patients at high cardiovascular risk.[6,7] One of the commonly used drug combination is of an ARB and diuretic. The pharmacological rationale of combining an ARB and diuretic lies in the fact that ARBS cause the antagonism of angiotensin II at the vascular and myocardial level by direct AT-1 receptor blockade while diuretics blocks sodium chloride reabsorption at the distal convoluted tubule.[8] The aim of this trial was to evaluate of antihypertensive efficacy of Losartan + Hydrochlorthiazide versus Telmisartan + Hydrochlorthiazide in patients with stage 1 or stage 2 hypertension with a randomized controlled trial.

METHODS

This prospective, randomized controlled trial was conducted at Rajindra Hospital, Government Medical College, Patiala, Punjab. Recruitment occurred between April 2014 and March 2015. Approval for the study was obtained from the Institutional Ethics Committee. Informed consent was obtained from the patient or from a substitute decision maker prior to study enrollment.

Selection criteria

Inclusion criteria

- Patients with Stage 1 or stage 2 hypertension willing to give written and informed consent.
- Adult male/ female aged 21 years or older and non pregnant females not planning for conception.
- Patient not on any other antihypertensive medication.

Exclusion criteria

- Patients with type 1 or type 2 Diabetes Mellitus
- Patient with history of hypersensitivity to Losartan or Telmisartan or Hydrochlorthiazide.
- Pregnant / lactating/ women planning to conceive.
- Patient with history of refractory, secondary or malignant hypertension.
- Patient with history of renal and hepatic disease.
- Patient unwilling or unable to comply with the study proceedings to give informed written consent.
- Patient with history of stroke, myocardial infarction, cerebral Haemorrhage and hypertensive encephalopathy.
- Patient with history of use of the drugs under investigation in last 30 days.
- Patient with history of any uricosuric drug or Allopurinol or Febuxostat or any drug affecting uric acid levels.

Intervention

A total of 76 patients were recruited and randomly allocated into two groups of 38 each, Group I and Group II. Every patient recruited into the study was followed up for a period of 6 months. Group I patients were started on Losartan 50mg + Hydrochlorthiazide 12.5mg OD and subsequent titration was carried up to maximum recommended dose of Losartan 100mg + Hydrochlorthiazide 12.5mg OD depending on clinical response. Group II patients were put on Telmisartan 40mg + Hydrochlorthiazide 12.5mg OD and subsequent titration was carried up to maximum dose Telmisartan 80mg + Hydrochlorthiazide 12.5mg OD depending on clinical response.

Responders and Non responders were identified. Those patients whose blood pressure reached to normotensive range with treatment were categorized as responders while those patients whose blood pressures did not fall to normotensive range with maximum dose were categorized as non responders. The end point of this study was attainment of BP<140/90mmHg for all patients and then maintain it. Patient were discontinued from the study at any stage if it was found that the patient has developed life threatening symptoms like hypersensitive encephalopathy, decompensated heart failure, and cardiogenic shock or if it was observed that continuation in the study was not in the interest of the patient.

Study parameters/ outcomes and measurements

Blood pressure, both systolic and diastolic were recorded by LED sphygmomanometer. Subsequent visits were done for BP monitoring at 3 months and 6 months. At every visit patient were asked about any adverse effects and overall well being.

Sample size

A sample of 76 patients was calculated to achieve a power of 80% at a significance level of 5%.

Randomization

Randomization was stratified by institution with 1:1 allocation to treatment arm.

Statistical analysis

The results of observations of individual patients were pooled for each group. Statistical analysis was performed using SPSS software version 20. All the analyses were performed on an intention to treat basis. For analysis of

efficacy of each treatment, paired t test was used. For categorical variables chi-square test was used for analysis.

A difference between two groups which would have arisen by chance is 'p' value. If it is less than 0.05, it is considered significant, 'p' value less than 0.001 is considered highly significant. If it is more than 0.05, it is considered non-significant.

RESULTS

Recruitment and baseline characteristics

After taking a thorough history, clinical examination and biochemical investigations (as per the proforma attached), patients were randomly allocated to two age and sex matched groups of 38 cases each. However, 3 patients left out from each group (drop outs) so that finally 35 patients completed the study procedure. Every patient recruited into the study was followed up for a period of 6 months. Group I patients were started on Losartan 50mg + Hydrochlorthiazide 12.5mg OD and subsequent titration was carried up to maximum recommended dose of Losartan 100mg + Hydrochlorthiazide 12.5mg OD depending on clinical response. Group II patients were put on Telmisartan 40mg + Hydrochlorthiazide 12.5mg OD and subsequent titration was carried up to maximum dose Telmisartan 80mg + Hydrochlorthiazide 12.5mg OD depending on clinical response. On subsequent visits BP was monitored and effect on Biochemical parameters i.e. Serum Uric Acid was seen at 3 months and 6 months as per study protocol (Table 1). The results of observations of individual patients were pooled for each group.

Efficacy end-point

Systolic blood pressure in supine position

The mean systolic blood pressure in Group I at baseline in supine position was 153.95±12.76mm of Hg which was significantly reduced to 147.06±9.83mm of Hg after 3 months and 138.29±9.76mm of Hg after 6 months of study (Table 2). Mean systolic blood pressure in the Group II at baseline in supine position was 153.05±11.71mm of Hg which was significantly reduced to 141.67±8.62mm of Hg after 3 months and 134.17±6.85 mm of Hg after 6 months of study (Table 2). There was a significant difference between the means of two groups ($p<0.05$) at 3 months and 6 months (Table 2).

In Group II the reduction in systolic blood pressure in supine position from baseline to 6 months was higher i.e. 12.34% than the reduction in Group I i.e. 10.17% ($p<0.05$).

Diastolic blood pressure in supine position

The mean diastolic blood pressure in supine position in Group I at baseline period was 100.42±6.41mm of Hg which was significantly reduced to 93.61±4.70mm of Hg after 3 months and by end of the study it was 89.54±4.06mm of Hg (Table 3). The mean diastolic blood pressure in supine position in the Group II at baseline period was 99.37±7.92mm of Hg and was significantly reduced to 91.33±4.85mm of Hg after 3 months and 86.69±3.56mm of Hg after 6 months of study (Table 3). There was a significant difference between the means of two groups ($p<0.05$) at 3 months and 6 months (Table 3).

In Group II the overall reduction in diastolic blood pressure in supine position was more from baseline to 6 months i.e. 12.76% than the reduction in the diastolic blood pressure in Group I i.e. 10.83% ($p<0.05$).

Systolic blood pressure in sitting position

In the present study, mean systolic blood pressure in the Group I at baseline in sitting position was 146.95±14.30mm of Hg which was significantly reduced to 142.39±8.33mm of Hg after 3 months andto 136.51±9.71mm of Hg after 6 months of study (Table 4). Mean systolic blood pressure in the Group II at baseline in sitting position was 146.08±10.92mm of Hg which was significantly reduced to 137.67±7.07mm of Hg after 3 months and to 129.60±8.29mm of Hg after 6 months of study (Table 4). There was a significant difference between the means of two groups ($p<0.01$) at 3 months and 6 months (Table 4).

In Group II the reduction in systolic blood pressure in sitting position from baseline to 6 months was higher i.e. 11.28% than the reduction in Group I i.e. 7.10% ($p<0.01$).

Table 1: Baseline characteristics.

Parameters		Group I		Group II		p-value
		No. (Mean±SD)	%age	No. (Mean±SD)	%age	
Age Range (in Years)		54.58±12.14		56.74±12.32		6.25 (>0.05)
Sex	Female	18	47.37%	18	47.37%	>0.05
	Male	20	52.63%	20	52.63%	>0.05
SBP (SUPINE)		153.95±12.76		153.05±11.71		>0.05
DBP (SUPINE)		100.42±6.41		99.37±7.92		>0.05
SBP (SITTING)		146.95±14.30		146.08±10.92		>0.05
DBP (SITTING)		93.53±6.09		93.05±7.68		>0.05

Table 2: Comparison of SBP (supine) at baseline, 3 and 6 months in Group I and Group II.

Time interval	Group I		Group II		p-value
	Mean±SD	p-value	Mean±SD	p-value	
Baseline	153.95±12.76	--	153.05±11.71	--	>0.05 (NS)
After 3 Month	147.06±9.83	<0.001 (HS)	141.67±8.62	<0.001 (HS)	<0.05 (S)
After 6 Month	138.29±9.76	<0.001 (HS)	134.17±6.85	<0.001 (HS)	<0.05 (S)
% Change	-10.17		-12.34		

Table 3: Comparison of DBP (supine) at baseline, 3 and 6 months in Group I and Group II.

Time interval	Group I		Group II		p-value
	Mean±SD	p-value	Mean±SD	p-value	
Baseline	100.42±6.41	--	99.37±7.92	--	>0.05 (NS)
After 3 Month	93.61±4.70	<0.001 (HS)	91.33±4.85	<0.001 (HS)	<0.05 (S)
After 6 Month	89.54±4.06	<0.001 (HS)	86.69±3.56	<0.001 (HS)	<0.05 (S)
% Change	-10.83		-12.76		

Table 4: Comparison of SBP (sitting) at baseline, 3 and 6 months in Group I and Group II.

Time interval	Group I		Group II		p-value
	Mean±SD	p-value	Mean±SD	p-value	
Baseline	146.95±14.30	--	146.08±10.92	--	>0.05 (NS)
After 3 month	142.39±8.33	<0.01 (S)	137.67±7.07	<0.001 (HS)	<0.01 (S)
After 6 month	136.51±9.71	<0.001 (HS)	129.60±8.29	<0.001 (HS)	<0.01 (S)
% Change	-7.10		-11.28		

Table 5: Comparison of DBP (sitting) at baseline, 3 and 6 months in Group I and Group II.

Time interval	Group I		Group II		p-value
	Mean±SD	p-value	Mean±SD	p-value	
Baseline	93.53±6.09	--	93.05±7.68	--	>0.05 (NS)
After 3 Month	90.17±5.37	<0.001 (HS)	86.94±6.44	<0.001 (HS)	<0.05 (S)
After 6 Month	87.09±4.61	<0.001 (HS)	83.14±5.25	<0.001 (HS)	<0.001 (HS)
% Change	-6.88		-10.65		

Diastolic blood pressure in sitting position

In the present study, mean diastolic blood pressure in sitting position in Group I at baseline period was 93.53±6.09mm of Hg which was significantly reduced to 90.17±5.37mm of Hg after 3 months and by end of the study it was 87.09±4.61mm of Hg (Table 5). The mean diastolic blood pressure in sitting position in the Group II at baseline period was 93.05±7.68mm of Hg and was significantly reduced to 86.94±6.44mm of Hg after 3 months and 83.14±5.25mm of Hg after 6 months of study (Table 5). There was a significant difference between the means of two groups ($p<0.05$) at 3 months which became highly significant ($p<0.001$) at 6 months (Table 5).

In Group II the overall reduction in diastolic blood pressure in sitting position was more from baseline to 6 months i.e.10.65% than the reduction in the diastolic blood pressure in the Group I i.e. 6.88% ($p<0.001$).

Adverse events

No adverse events occurred as a result of study participation.

DISCUSSION

Demographic distribution

Mean age in group I was 54.58±12.14 years and in group II was 56.74±12.32 years. Maximum number of individuals were in age group of 61-70 years in both the groups.

In group I, there were 20 males and 18 females. In group II, there were 20 males and 18 females. Distribution of patients in two groups according to gender and age distribution was statistically comparable.

Antihypertensive efficacy

Systolic blood pressure in supine position

The mean systolic blood pressure in Group I at baseline in supine position was 153.95±12.76mm of Hg which was significantly reduced to 147.06±9.83mm of Hg after 3 months and 138.29±9.76 mm of Hg after 6 months of study. The mean systolic blood pressure in the Group II at baseline in supine position was 153.05±11.71mm of Hg which was significantly reduced to 141.67±8.62mm of Hg after 3 months and 134.17±6.85mm of Hg after 6 months of study. There was a significant difference between the means of two groups ($p<0.05$) at 3 months and 6 months. In Group II the reduction in systolic blood pressure in supine position from baseline to 6 months was higher i.e.12.34% than the reduction in Group I i.e.10.17% ($p<0.05$).

Diastolic blood pressure in supine position

The mean diastolic blood pressure in supine position in Group I at baseline period was 100.42±6.41mm of Hg which was significantly reduced to 93.61±4.70mm of Hg after 3 months and by end of the study it was 89.54±4.06mm of Hg. The mean diastolic blood pressure in supine position in the Group II at baseline period was 99.37±7.92mm of Hg and was significantly reduced to 91.33±4.85mm of Hg after 3 months and 86.69±3.56mm of Hg after 6 months of study. There was a significant difference between the means of two groups ($p<0.05$) at 3 months and 6 months. In Group II the overall reduction in diastolic blood pressure in supine position was more from baseline to 6 months i.e. 12.76% than the reduction in the diastolic blood pressure in Group I i.e. 10.83% ($p<0.05$).

Systolic blood pressure in sitting position

In the present study, mean systolic blood pressure in the Group I at baseline in sitting position was 146.95±14.30mm of Hg which was significantly reduced to 142.39±8.33mm of Hg after 3 months and to 136.51±9.71mm of Hg after 6 months of study. Mean systolic blood pressure in the Group II at baseline in sitting position was 146.08±10.92mm of Hg which was significantly reduced to 137.67±7.07mm of Hg after 3 months and to 129.60±8.29mm of Hg after 6 months of study. There was a significant difference between the means of two groups ($p<0.01$) at 3 months and 6 months. In Group II the reduction in systolic blood pressure in sitting position from baseline to 6 months was higher i.e. 11.28% than the reduction in Group I i.e. 7.10% ($p<0.01$).

Diastolic blood pressure in sitting position

In the present study, mean diastolic blood pressure in sitting position in Group I at baseline period was 93.53±6.09mm of Hg which was significantly reduced to 90.17±5.37mm of Hg after 3 months and by end of the study it was 87.09±4.61mm of Hg. The mean diastolic blood pressure in sitting position in the Group II at baseline period was 93.05±7.68mm of Hg and was significantly reduced to 86.94±6.44mm of Hg after 3 months and 83.14±5.25mm of Hg after 6 months of study. There was a significant difference between the means of two groups ($p<0.05$) at 3 months which became highly significant ($p<0.001$) at 6 months. In Group II the overall reduction in diastolic blood pressure in sitting position was more from baseline to 6 months i.e.10.65% than the reduction in the diastolic blood pressure in the Group I i.e. 6.88% ($p<0.001$).

A similar study conducted by Lacourcière et al, evaluated the efficacy of two fixed-dose telmisartan/HCTZ combinations (40/12.5mg and 80/12.5mg) versus a fixed-dose combination of losartan/ HCTZ (50/12.5mg) for 6 weeks found that losartan/ HCTZ reduced last 6 hours mean SBP/DBP by 15.0/ 9.7mm Hg whereas lower-dose telmisartan/ HCTZ combination reduced last 6hours mean SBP/DBP by a further 2.5/1.8mmHg ($p<0.05$ for both). For the higher-dose telmisartan/HCTZ combination, there was an additional reduction in last 6hours mean SBP/DBP of 3.4/ 2.5mm Hg ($p<0.01$ for both) compared with the losartan/ HCTZ combination.[9]

Another study conducted by Neutel et al, reported that the mean reductions in the last 6 hour mean diastolic blood pressure for the telmisartan 40mg/HCTZ 12.5mg and telmisartan 80mg/ HCTZ 12.5mg groups were significantly greater: -2.0 mmHg ($P = 0.0031$) and -2.8mmHg ($P = 0.0003$), respectively, than the losartan 50mg/ HCTZ 12.5mg group thus supporting the superiority of telmisartan/HCTZ regimens over losartan/ HCTZ with respect to their blood pressure-lowering effects.[10]

However, Minami J et al, conducted a study on 22 Japanese outpatients with mild to moderate hypertension. The study reported that sitting blood pressure with Telmisartan/ HCTZ and Losartan/ HCTZ were 129.2±16.1/ 77.1±9.6mm Hg and 127.7±12.9/ 74.9±11.9mm Hg respectively. The difference was not statistically significant ($p= 0.663$ systolic and $p= 0. 371$ diastolic).[11]

In a study done by Shiga et al in 2012 on 44 hypertensive patients (22 males, age 71±14 years) who showed uncontrolled BP despite the use of high-dose ARBs or medium-dose of losartan (50mg/day)/hydrochlorothiazide (HCTZ) (12.5mg/day) were switched from high-dose ARBs or losartan (50mg/day)/hydrochlorothiazide (HCTZ) (12.5mg/day) to high-dose telmisartan (80mg/day)/HCTZ (12.5mg/day) for 3 months. Systolic BP and diastolic BP significantly decreased (125±15/69±11mmHg) and 85% of the patients achieved their target BP at 3 months after changeover. There were no significant changes in HR during the study period. High-dose telmisartan/HCTZ therapy was thus associated with a significant reduction in BP and helped patients achieve their target BP.[12]

Hamada T et al, did a study on fifty-nine hypertensive patients with allocations into a combination therapy with either Losartan (50mg/day)/ HCTZ (12.5mg/day) or Telmisartan (40mg/day)/ HCTZ (12.5mg/day) respectively. The study reported both systolic and diastolic blood pressures significantly decreased in Telmisartan/ HCTZ and Losartan/ HCTZ groups, without any statistical differences among them.[13]

Effect on pulse rate

The average pulse rate in group I at baseline period was 78.21±15.60 beats per minute which was significantly reduced to 70.86±5.80 beats per minute by the end of the study. Among the group II, pulse rate measured at baseline period was 77.58±11.52 beats per minute which was significantly reduced to 73.77±5.20 beats per minute by the end of the study.

There was a significant difference between the means of two groups ($p<0.05$) at 3 months and 6 months. In Group I the overall reduction in pulse rate was more among the subjects (9.39 %) as compared to the reduction in pulse rate for the subjects under group II (4.91%) ($p<0.05$).

The present study can be compared to a combination therapy with losartan (25-50mg/day) and HCTZ (12.5mg/day) conducted by Eto et al, in elderly patients of hypertension for 4 weeks. It was found that heart rate tended to decrease by 3.8±1.7 beats per minute with the combination therapy.[14]

In a study conducted by Shiga et al in 2012 evaluated the effect of telmisartan/HCTZ combination therapy on heart rate found insignificant reduction in heart rate from 73 beats per minute to 71 beats per minute.[12]

CONCLUSION

The present study concluded that both Losartan + Hydrochlorthiazide (Group I) and Telmisartan + Hydrochlorthiazide (Group II) combination were effective antihypertensives and caused smooth reduction in both systolic and diastolic blood pressure in supine and sitting position and heart rate.

However, Telmisartan + Hydrochlorthiazide (Group II) had a slight edge over Losartan + Hydrochlorthiazide (Group I) as it produced greater reduction in blood pressure that too diastolic blood pressure in sitting position. Here, it is pertinent to suggest that more clinical studies need to be done on a larger population to confirm these results.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ismail J, Jafar TH, Jafary FH, White F, Faruqui AM, Chaturvedi N. Risk factors for non-fatal myocardial infarction in young South Asian adults. Heart. 2004;90:259-63.
2. Stafylas PC, Sarafidis PA. Carvedilol in hypertension treatment. Vase Health Risk Manag. 2008 February;4(1):23-30.
3. Bell K, Twiggs J, Olin BR. Hypertension: The Silent Killer: Updated JNC- 8 Guideline Recommendations. Alabama Pharmacy Association; 2015.
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC report. JAMA. 2003;289(19):2560-72.
5. Smith DH, Cramer MJ, Neutel JM, Hettiarachchi R, Koval S. Comparison of telmisartan versus losartan: meta-analysis of titration-to-response studies. Blood Press Monit. 2003 Jun;8(3):111-7.
6. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206-52.
7. European Society of Hypertension-European Society of Cardiology Guidelines Committee. 2003 European Society of Hypertension European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens. 2003;21:1011-53.
8. Kalra S, Kalra B, Agrawal N. Review Combination therapy in hypertension: An update. Diabetology and Metabolic Syndrome. 2010;2:44.
9. Lacourcière Y, Gil-Extremera B, Mueller O. Efficacy and tolerability of fixed-dose combinations of telmisartan plus HCTZ compared with losartan plus HCTZ in patients with essential hypertension. Int J Clin Pract. 2003;57:273-9.
10. Neutel JM, Littlejohn TW, Chrysant SG, Singh A. Telmisartan Study Group. Telmisartan/ Hydrochlorothiazide in comparison with losartan/ hydrochlorothiazide in managing patients with mild-to- moderate hypertension. Hypertens Res. 2005;28:555-63.
11. Minami J, Furukata S, Ishimitsu T, Matsuoka H. Comparison of therapies between fixed-dose Telmisartan/ Hydrochlorthiazide and Losartan/ Hydrochlorothiazide in Patients with Mild to Moderate Hypertension. Int Heart J. 2009;50(1):85-93.
12. Shiga Y, Miura S, Mitsutake R, Norimatsu K, Nagata I, Arimura T, et al. Efficacy and safety of a single-pill fixed-dose combination of high-dose telmisartan/hydrochlorothiazide in patients with uncontrolled hypertension. Journal of the Renin-Angiotensin- Aldosterone System. 2012;13(3):394-400.
13. Hamada T, Kuwabara M, Watanabe A, Mizuta E, Ohtahara A, Omodani H, et al. A comparative study on the effectiveness of losartan/ hydrochlorothiazide

and telmisartan/ hydrochlorothiazide in patients with hypertension. Clin Exp Hypertens. 2014;36(4):251-7.
14. Eto K, Tsuchihashi T, Abe I, Iida M. Efficacy and safety of combination therapy with losartan and hydrochlorothiazide in elderly hypertension. Nihon Ronen Igakkai Zasshi. [Article in Japanese] Mar 2002;39(2):181 PMID:11974942.

Cite this article as: Sekhon MS, Kaur A, Bajaj VK, Singh H, Gupta A. Evaluation of antihypertensive efficacy of Losartan + Hydrochlorthiazide versus Telmisartan + Hydrochlorthiazide in patients with stage 1 or stage 2 hypertension: a randomized controlled trial. Int J Basic Clin Pharmacol 2018;7:2144-50.