ORIGINAL ARTICLE

A Randomized, Double-blinded, Controlled, Multicentre Phase III Study to Evaluate the Efficacy and Safety of Telmisartan/ Amlodipine/Hydrochlorothiazide Compared to Telmisartan/ Hydrochlorothiazide in Patients with Essential Hypertension

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Abstract

Objective: Triple drug combination has shown to be effective in controlling blood pressure (BP) with low rates of drug-related side effects. The present study was conducted to compare the efficacy and safety of a triple pill of telmisartan/ amlodipine/hydrochlorothiazide (HCTZ) with a dual combination of telmisartan/ HCTZ in treating hypertensive patients who did not respond to monotherapies.

Methods: A total of 512 patients were randomized to receive either low-dose triple pill or the dual combination therapy. The primary endpoint was BP normalization after 8 weeks. The secondary endpoints were BP normalization at 4 weeks, changes in BP from baseline to Week 8, comparison of BP normalization between treatment groups, and difference in BP responder rates. The analysis was conducted on the intent-to-treat (ITT), modified intent-to-treat (mITT) and per protocol (PP) population.

Results: Statistically significant difference was noted between triple pill and telmi+HCTZ in the normalization of BP at Week 8 in the mITT (p=0.041) and PP (p=0. 038) populations. Also, a statistically significant improvement was observed in BP normalization in triple pill group compared with telmi+HCTZ group in ITT (p=0.022) and mITT (p=0.015) populations after 4 weeks. At Week 8, a significant reduction in BP was seen compared to the baseline in both the treatment groups. There was no statistically significant difference between the two treatment groups in BP normalization. Diastolic BP responder rates were significantly better for triple pill group in PP population (p=0.046).

Conclusions: The triple pill was found to be effective in achieving early normalization of BP in hypertensive patients who did not respond to monotherapies.

Introduction

Hypertension is one of the major and growing public health burdens in India and globally which is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India.[1, 2] Stage I hypertension (systolic blood pressure [SBP] 140 to 159 and/or diastolic blood pressure [DBP] 90 to 99 mmHg) has a significant cardiovascular risk and requires prompt BP control.[3] Hypertension occurs more commonly in diabetics than in non-diabetics. More than 75% of adults with diabetes have BP levels ±130/80 mmHg.[4] Patients with both hypertension and diabetic conditions are at a higher risk for micro and macrovascular complications.[5]

Early control of BP immediately after the onset of hypertension helps in reduction of subsequent comorbidities like cardiovascular, diabetes and kidney diseases and can easily achieve the target goal.[6] In hypertension management, compared to SBP, DBP has more grounds of significance as it is more closely related to end-organ damage and hence the value of DBP needs to be considered.[7] According to the Joint National Committee (JNC) 8, importance has been given to the reduction of DBP to <90 mmHg especially in younger patients to prevent end organ failures.[8] Also, optimal BP achievement is a major concern and in most cases one drug may not be adequate to control BP. As BP being a multifactorial condition requires early multiple drug treatment with complimentary mechanisms of action (MOA). Various clinical study results and hypertension management guidelines recommend the use of a combination of two or more drugs to achieve the goal of lowering the BP. When compared to other single agents with higher doses, combination of two or more drugs from different classes in low doses showed more efficacy and tolerability.[1, 9] For high risk patients whose BP is not under control requires multiple combination of agents with complementary MOA which act on different physiological pathways by blocking complementary pressor mechanisms.[10] One such combination that has been recognized to be rational and effective include renin-angiotensin-aldosterone system blocker (RAAS), calcium channel blocker (CCB), and diuretic as these are associated with low rates of drug-related side effects and discontinuations.[11] These single pill

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triple drug combination early treatment options enhance patient adherence in view of the ease in administration, optimizing long-term compliance and rapid BP control.[12] They can also reduce health care utilisation and medical costs as compared to multiple single-pill therapies.[13]

Our study compared the efficacy and safety of the study drug, a triple pill of telmisartan (20/40 mg), amlodipine (2.5/5 mg) and hydrochlorothiazide (HCTZ; 6.25/12.5 mg) and a dual combination of telmisartan (40/80 mg) with HCTZ 12.5 mg [telmi+HCTZ] in treating hypertensive patients who did not respond to monotherapies. The half dose of telmisartan in the triple drug combination as compared to the dual combination could also ascertain the starting efficacious and optimal dose of telmisartan.

Material and Methods

Patient Selection

The study included patients of either sex aged ≥18 to ≤65 years with uncontrolled hypertension (SBP 140-179 mmHg and DBP 90-109 mmHg) and without coronary artery disease. These patients had uncontrolled hypertension despite receiving treatment with either full dose of monotherapy or any combination therapy (at the specified doses equipotent or less potent than combination of telmi 40 mg + HCTZ 12.5 mg). The patients with Stage 2 hypertension (SBP ≥ 180 mmHg and DBP ≥ 110 mmHg), with uncontrolled hypertension (SBP ≥ 140 mmHg and DBP ≥ 90 mmHg) when treated with specified doses of monotherapy or combination therapy at doses more potent than combination of telmi 40 mg + HCTZ 12.5 mg, with uncontrolled diabetes (HbA1c ≥ 9%), or with significant cardiovascular, cerebrovascular, renal or hepatic disease, malignant retinopathy or electrolyte imbalances were excluded.

The protocol was approved by the regulatory authority and Institutional Ethics Committee at each site. The study was conducted in accordance with the Declaration of Helsinki, consistent with Good Clinical Practices and applicable regulatory requirements. Written informed consent was obtained from all patients before participation in the study.

Study Design

The randomized, double-blind, double-dummy, active control, parallel group study was conducted across 18 centres in India. The study evaluated the efficacy and safety of fixed dose combination (FDC) tablets of telmisartan 20/40mg+amlodipine 2.5/5mg+HCTZ 6.25/12.5mg and dual combination of telmi+HCTZ in the treatment of essential hypertension. The strengths of telmi+HCTZ used were 40/80 mg + 12.5/12.5 mg and of triple pill included 20/40 mg+2.5/5 mg+ 6.25/12.5 mg.

After screening, eligible patients were randomized into the study and stratified into four strata based on the screening BP (SBP < 160 mmHg and DBP < 100mmHg; SBP ≥ 160 mmHg and DBP < 100mmHg; SBP < 160 mmHg and DBP ≥ 100mmHg; SBP ≥ 160 mmHg and DBP ≥ 100mmHg). According to the stratum to which the patient's screening BP belongs, the patient was randomized to either low dose triple pill group (telmisartan 20 mg+amlodipine 2.5 mg+HCTZ 6.25 mg) or the dual combination of telmi 40 mg+HCTZ 12.5 mg. All the study drugs were administered as one tablet once daily in the morning for 4 weeks (Visit 2, Week 2 and Visit 3, Week 4) in both treatment groups. Patients were assessed at the end of four weeks for normalization of BP (seated SBP ≤139 and DBP ≤89 mmHg in non-diabetics and seated SBP ≤129 and DBP ≤79 mmHg in diabetics). Those patients who were normalized at Week 4 were continued with the low dose till Week 8. The nonresponders received an up-titrated dose of triple pill (telmisartan 40 mg+amlodipine 5 mg+HCTZ 12.5 mg) or telmi 80 mg+HCTZ 12.5 mg) for the remaining four weeks. The compliance was assessed by counting the pills returned at each visit.

Efficacy Evaluations

During all visits, three measurements of sitting BP and standing BP were taken at two minute intervals along with the sitting pulse rates. Mean of the three sitting BP measurements was considered for efficacy evaluation. The efficacy analysis was conducted on the intent-to-treat (ITT), modified intent-to-treat (mITT) and the per protocol (PP) population. The efficacy evaluation was compared between responders and non-responders (who required dose increment), and in diabetic and nondiabetic patients.

The primary efficacy parameter was normalization of BP (non-diabetic patients: SBP ≤139 and DBP ≤89 mmHg, diabetic patients: SBP ≤129 and DBP ≤79 mmHg) at the end of 8 weeks treatment period.

The secondary efficacy analysis included normalization of BP pattern at the end of 4 weeks, change from baseline in SBP and DBP values and comparison of the SBP or DBP normalization pattern between two treatment groups at the end of 8 weeks. The difference in BP responder rates (SBP <140 mmHg in non-diabetics and <130 mmHg in diabetics or change from baseline ≥15 mmHg; DBP <90 mmHg in nondiabetics and <80 mmHg in diabetics or change from baseline ≥10 mmHg) at the end of 8 weeks was assessed in both treatment groups.

Safety Assessments

Physical examination, collection and monitoring of adverse events (AEs), serious adverse events (SAEs) and their relationship to study drug was performed at each visit. The concomitant medications were also reviewed throughout the study. Hematological and biochemical laboratory evaluations were done at baseline and at Week 8. Vital characteristics and orthostatic hypotension was recorded at baseline and all other visits.

Statistical Analyses

The sample size was determined using a non-inferiority study of test versus control product with 1:1 patient ratio. Descriptive analyses were used to assess the physician's global evaluation efficacy, demographic, physical and lab parameters. The last observation carried forward approach was used for the ITT, mITT, and PP analysis.

Depending upon the type of distribution of variables, the Z test or analysis of variance or Wilcoxon Rank sum test was used to evaluate the BP, pulse rate and global evaluation of efficacy. Chi square test or non-parametric tests were used for the evaluation of association between different variables. All tests were one-tailed analysis, with a significance level of $p<0.025$. Safety was assessed by reporting of AEs coded according to Medical Dictionary for Regulatory Activities.

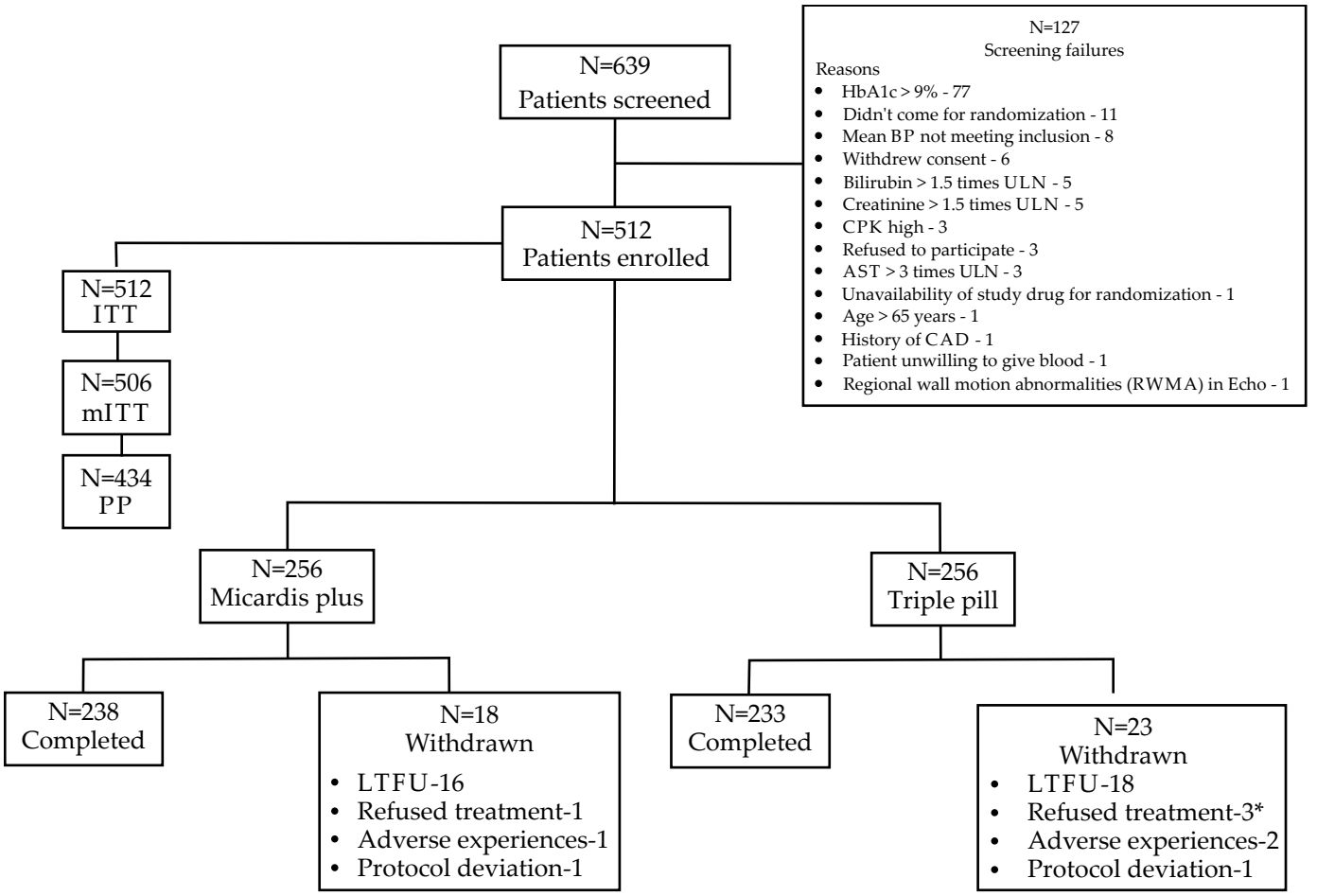

Fig. 1: Patient disposition. AST: aspartate aminotransferase; BP; blood pressure; CAD: coronary artery disease; CPK: creatinine phosphokinase; ITT: Intent-to-treat; mITT: modified intent-to-treat; N: number of patients; PP: per protocol; LTFU: loss to follow up; ULN: upper limit of normal. *One patient (472, Site 14) had adverse experiences and refused treatment as reasons for discontinuation; adverse events causing discontinuation were headache and dizziness. The patient dropped out after visit 2. †One patient (512, Site 5) had refused treatment and failure to return for follow-up as reasons for discontinuation; the patient dropped out after visit 2

Table 1: Baseline demographic characteristics of patients

Baseline characteristics	Telmi+HCTZ (N=256)	Triple pill (N=256)	Total (N=512)
Age (years), mean (SD)	49.46 (9.20)	47.79 (9.86)	48.63 (9.56)
Sex, n (%)			
Male	140 (54.69)	136 (53.13)	276 (53.91)
Female	116 (45.31)	120 (46.88)	236 (46.09)
Heart rate (per minute), mean (SD)	80.50 (10.67)	81.08 (11.05)	80.79 (10.86)
BMI (kg/m^2), mean (SD)	27.13 (4.46)	26.51 (4.14)	26.82 (4.31)
Hypertension duration (months), mean (SD)	51.25 (51.86)	44.15 (42.78)	47.70 (47.62)
Baseline pulse rate, mean (SD)	84.85 (13.17)	86.29 (12.99)	85.57 (13.09)
Diabetic, n (%)	96 (37.50)	96 (37.50)	192 (37.50)
Smoker, n (%)	35 (13.67)	33 (12.89)	68 (13.28)
CAD status, n (%)			
Non-CAD	252 (98.44)	255 (99.61)	507 (99.02)
Stable angina	4 (1.56)	1 (0.39)	5 (0.98)

BMI: body mass index; DBP: diastolic blood pressure; N: number of patients; SBP: systolic blood pressure; SD: standard deviation; CAD: coronary artery disease

Results

Patient Population

A total of 639 patients were screened and 512 patients were randomised to 8 weeks of double-blind treatment with either the triple pill (n=256) or telmi+HCTZ combination (n=256). The patient disposition is described in Figure 1. Patients in both the treatment groups showed good compliance (96.12% in triple pill treatment group versus 96.22% in telmi+HCTZ group).

No significant differences in the baseline characteristics were observed between the two treatment groups except for age which was higher in the telmi+HCTZ treatment group (Table 1). The most common co-existing illness was diabetes mellitus (DM) in the study population. Of 512 patients, in the telmi+HCTZ group, 35.16% (90/256) patients needed up-titrated doses compared with 27.34% (70/256) in the triple pill group. There were no statistically significant differences between the two treatment groups in the up-titration status.

Primary Efficacy Analysis

Attaining Normalization of BP at Week 8

At Week 8, in the ITT populations, the normalization of BP was observed in 346 subjects: (183 [71.48%] patients in the triple pill group *vs.* 163 [63.67%], though the difference was

Table 2: Normalization of blood pressure at week 4 and week 8 in intent-to-treat population

Normalization of BP	Telmi+HCTZ, N (%)	Triple pill, N (%)	p value
At week 4	149 (58.20)	174 (67.97)	0.022
At week 8	163 (63.67)	183 (71.48)	0.059
With no up-titration at week 4	148 (89.16)	170 (91.40)	0.477
With no up-titration at week 8	118 (71.08)	142 (76.34)	0.262
With up-titration at week 4	1 (1.11)	4 (5.71)	0.097
With up-titration at week 8	45 (50.00)	41 (58.57)	0.281
Diabetic patients at week 4	37 (38.54)	51 (53.13)	0.043
Diabetic patients at week 8	43 (44.79)	47 (48.96)	0.563
Non-diabetic patients at week 4	112 (70.00)	123 (76.88)	0.164
Non-diabetic patients at week 8	120 (75.00)	136 (85.00)	0.025

BP: blood pressure; N: number of patients

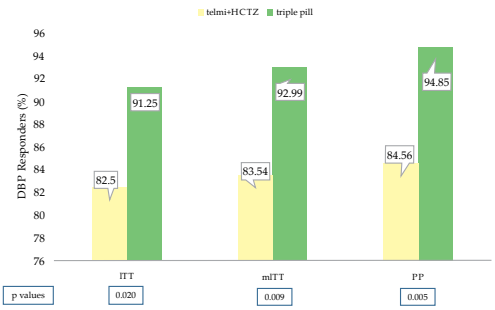

Fig. 2: Diastolic blood pressure responders in non-diabetics at week 8. DBP: diastolic blood pressure; Telmi: telmisartan; HCTZ: hydrochlorothiazide; ITT: intent-to-treat; mITT: modified intent-to-treat, PP: per protocol

Table 3: Normalization of diastolic blood pressure at week 4 and week 8

Arms and p value	ITT	mITT	PP
Normalization of DBP at week 4			
Telmi+HCTZ	70.70%	71.26%	74.43%
Triple pill	79.69%	80.95%	81.86%
p value	0.019	0.011	0.061
Normalization of DBP at week 8			
Telmi+HCTZ	70.70%	71.26%	72.60%
Triple pill	76.56%	77.78%	79.53%
p value	0.132	0.093	0.091
Normalization of DBP in non-diabetics at week 4			
Telmi+HCTZ	81.25%	82.28%	84.56%
Triple pill	89.38%	91.08%	91.91%
p value	0.040	0.022	0.060
Normalization of DBP in non-diabetics at week 8			
Telmi+HCTZ	80.00%	81.01%	82.35%
Triple pill	90.00%	91.72%	93.38%
p value	0.012	0.006	0.005

Telmi: telmisartan HCTZ: hydrochlorothiazide; ITT: intent-to-treat; mITT: modified intent-to-treat; PP: per protocol

not statistically significant. Statistically significant difference between triple pill and telmi+HCTZ in the normalization of the BP at Week 8 was observed in the mITT (p=0.041) and PP (p=0.038) populations. Among the non-diabetic patients, significantly better normalization of BP at Week 8 was observed in the triple pill group compared with the telmi+HCTZ group in the ITT (p=0.025), mITT (p=0.015) and PP (p=0.016) populations (Table 2).

Secondary Efficacy Analysis

Normalization of BP at Week 4

A statistically significant improvement in normalization of BP at Week 4 was observed in triple pill group compared with telmi+HCTZ group in ITT (p=0.022) and mITT (p=0.015) populations. In the diabetic subgroup of patients, a statistically significant normalization of BP at Week 4 was seen in patients treated with triple pill compared with telmi+HCTZ in all three populations (Table 2).

Normalization of Blood Pressure at Week 8

At Week 8, a significant reduction compared to the baseline in DBP and SBP was seen in both the treatment groups in all the three populations. The change in DBP between the triple pill and telmi+HCTZ treatment groups was insignificant in the ITT population (p=0.446), mITT population (p=0.344) and PP populations (p=0.175). Similarly, the change in SBP between the two treatment groups was not statistically significant in ITT population (p=0.759), mITT population (p=0.618) and PP populations (p=0.284).

Blood Pressure Normalization

SBP normalization at Week 4 and Week 8 differed insignificantly between the two treatment groups. This result was also consistent in the diabetic and nondiabetic subgroup populations, where insignificant changes occurred in SBP normalization between treatment groups was observed at Week 4 and Week 8 in ITT (p=0.841), mITT (p=0.677) and PP (p=0.639) populations, respectively.

Normalization of DBP achieved among patients in the non-diabetic subgroup was higher in the triple pill group (ITT: 89.38%; mITT: 91.08%; and PP: 91.91%) as compared with the telmi+HCTZ group (ITT: 81.25%; mITT: 81.01%; and PP: 84.56%) at Week 4. In addition, the difference between the two groups was statistically significant (p=0.04 [ITT]; p=0.022 [mITT]; and p=0.060 [PP]). A similar pattern was observed at Week 8 wherein, DBP normalization was higher in the triple pill group (ITT: 90%; mITT: 91.72%; and PP: 93.38%) as compared with the telmi+HCTZ group (ITT: 80%; mITT: 81.01%; and PP: 82.35%) and the difference between the two groups was statistically significant (p=0.012 [ITT]; p=0.006 [mITT]; and p=0.005 [PP]). Although normalization of DBP was observed to a considerable extent in patients with diabetes, the change did not achieve statistical significance at both Week 4 (p=0.019 [ITT]; p=0.011 [mITT]; and p=0.061 [PP]) and Week 8 (p=0.132 [ITT]; p=0.093 [mITT]; and p=0.091 [PP], Table 3).

Responder Rates

The DBP responder rates in non-diabetic patients demonstrated significant improvement (p=0.020 [ITT]; p=0.009 [mITT]; p=0.005 [PP]) in both telmi+HCTZ group and triple pill group however; the proportion of responders were higher in the triple pill group (ITT: 91.25%; mITT: 92.99%; and PP: 94.85%) as compared with the telmi+HCTZ group (ITT: 82.5%; mITT: 83.54%; and PP: 84.56%) at Week 8 (Figure 2). At Week 4 and Week 8, the SBP responder rates differed insignificantly between the test and control drug whereas the DBP responder rates were significantly better for triple pill group in PP population (p=0.046).

In the up-titrated patients, significantly (p=0.043) better DBP responder rates in triple pill group (telmisartan 40 mg/amlodipine 5 mg/HCTZ 12.5 mg) was observed at Week 8 in the PP population.

Physician's Global Evaluation of Efficacy

The overall treatment response was either 'Good' or 'Excellent' in 96.23% of patients in triple pill group and 93.45% of patients in the telmi+HCTZ group.

Safety

A total of 77 [telmi+HCTZ group:46); triple pill group:31)] AEs were observed which were mostly of mild to moderate in intensity (Table 4). Constipation (n=7) and headache (n=7) were the

Table 4: Occurrence of adverse events

	Telmi+HCTZ (N=256)	Triple pill (N=256)	All
Total no. of patients with AEs, N (%)	31 (12.11)	19 (7.42)	50 (9.77)
Total no. of AEs	46	31	77
Serious adverse events, N (%)	3 (1.17)	3 (1.17)	3 (1.17)
No. of patients with AEs according to maximum severity			
Mild, N (%)	28 (10.94)	14 (5.47)	42 (8.20)
Moderate, N (%)	2 (0.78)	4 (1.56)	6 (1.17)
Severe, N (%)	1 (0.39)	1 (0.39)	2 (0.39)
No. of AEs according to action taken			
None, N (%)	20 (43.48)	12 (38.71)	32 (41.56)
Symptomatic treatment, N (%)	26 (56.52)	16 (51.61)	42 (54.55)
Study medication stopped, N (%)	0 (0.00)	3 (9.68)	3 (3.90)
No. of AEs according to outcome			
Subsided, N (%)	36 (78.26)	24 (77.42)	60 (77.92)
Persists, N (%)	10 (21.74)	7 (22.58)	17 (22.08)
Disabled	-	-	-
Died	-	-	-
AEs reported by ≥1% of patients			
Constipation, N (%)	5 (1.95)	2 (0.78)	7 (1.37)
Blood creatinine phosphokinase increased, N (%)	3 (1.17)	1 (0.39)	4 (0.78)
Blood uric acid increased, N (%)	4 (1.56)	0 (0.00)	4 (0.78)
Headache, N (%)	4 (1.56)	3 (1.17)	7 (1.37)
Asthenia, N (%)	4 (1.56)	1 (0.39)	5 (0.98)

AE: adverse event; N: number of patients

most common adverse events. Serious adverse events (SAEs) were reported in 5 patients (3 in telmi+HCTZ group and 2 in triple pill group). Majority of AEs did not require any intervention except for three AEs which required stopping the study medication of triple pill. One death was reported in the triple pill group, which was unrelated to the study medication.

Clinically significant abnormalities were observed in four patients (3 in the telmi+HCTZ group and 1 in the triple pill group). No clinically significant differences were observed between the two treatment groups in the laboratory investigations (biochemical or hematological parameters). There was an enhanced compliance seen with the triple pill group.

Discussion

The study showed that triple pill in both the doses was non-inferior to the control group on telmi+HCTZ combination. The dose of telmisartan in the triple pill is half (which is 20 mg) that of telmi+HCTZ combination (which is 40 mg) and could be one of the advantages as most of the patients achieved the target with the combination. Combination therapies are the mainstay therapeutic options as mentioned in the seventh report of the JNC when the BP is not controlled by monotherapies.[14] The European society of hypertension and the European society of cardiology treatment guidelines also recommends combination therapy in patients whose SBP is >20 mmHg above and DBP is >10 mmHg above the desired BP goals.[9] The availability of these drugs as a FDC in a single pill may offer additional advantage in terms of acceptance and compliance to the therapy.

Our study showed effective results with a strength of telmisartan 20 mg/amlodipine 2.5 mg/HCTZ 6.25 mg and reduced cardiovascular events. Similar results were observed in previous studies which used a triple pill strength of telmisartan 40 mg/amlodipine 5 mg/HCTZ 12.5 mg.[1, 15]

Our study observed that the triple pill achieved the treatment goal of normalization of BP as early as Week 4 (71.48%). The study also showed normalization of BP at Week 8 but was statistically insignificant. Early restoration of BP could be one of the important determinants to improve the cardiovascular prognosis in patients with hypertension.[16] The use of single pill combinations as first-line treatment reduced the gap between antihypertensive use and achievement of BP target control. In addition to the usage of single pill combination, selection of suitable combinations based on the patients' preferences, treatment adherence, compliance also helps in achieving the early control of BP and reducing the long-term comorbidities. Renin-angiotensin system (RAS) inhibitors provide beneficial effects in patients with CVDs, renal disease, diabetes, hypertension *etc*. Among the angiotensin receptor blockers (ARBs), telmisartan provides better treatment adherence and tolerability. It is the only approved drug that offers CV risk reduction and reduce BP over 24 hours. RAS plus CCB combinations showed a more reduction than RAS alone in CV morbidity, renal diseases and in hypertension. RAS when combined with diuretic thiazide lowered the risk of CV.[17, 18] Similar study showed a 65% normalization of BP at 30th day of treatment.[19] Our study also showed a normalization of BP in diabetics at Week 4 on triple pill compared to telmi+HCTZ combination. Studies recommend usage of RAAS blocker-based combination therapy for the treatment of hypertension associated co-morbidities like diabetes.[9, 20]

The DBP control at Week 4 in both diabetics and non-diabetics in our study helps in quick identification and reduction of incidences of hypertension which in turn reduces cardiovascular events. Similar results were observed at 60th day of treatment with triple pill in another study. There was also a significant reduction of SBP and DBP at Week 8 compared to baseline with triple pill.[1] In Maladkar et al study, superior reduction in DBP and improved quality of life of patients were observed when treated with triple pill combination.[15] Similar results have been observed in triple drug combination in the management of hypertension with or without co-morbidities for 120 days reported change in SBP/DBP from baseline to 60th day of treatment ($p<0.0001$) as -19.0 ± 2.61 / -25.0 ± 4.07 mmHg, respectively.[1]

The global evaluation of efficacy done by physicians showed a superior efficacy response that was either 'Excellent' or 'Good' in triple pill. Similar efficacy results were observed in other studies on triple drug combination of telmisartan, amlodipine, and HCTZ and with other triple drug combination.[11, 21, 22]

The triple pill was found to have good compliance and tolerability in our study which can influence the continued therapy in the patients and maintaining

a near normal BP levels. The adverse effects encountered were few and mild to moderate in intensity which were managed accordingly and consistent with previous controlled studies.[1, 23] No clinically meaningful changes were observed in the laboratory parameters assessed in the current study. Overall, the most commonly reported adverse event was headache in the triple pill arm which was in conformance with the previous trials.[23, 24] One death and two SAEs were reported in the triple pill group but the death was unrelated to the study drug.

The main strength of the study is measurement of major parameters of the BP control in terms of normalization of BP at different intervals, responder rates of SBP and DBP and considering diabetic and non-diabetic patients separately. Hypertension is not an isolated disease but presents with co-morbidities in majority of cases. The most important of them is diabetes and the management is different when both the diseases co-exist.

One of the limitation of the study could be the two drugs (telmisartan and HCTZ) being same in the control drug which could be a cause of statistically insignificant results for some parameters. A larger trial could address this issue and the results could be extrapolated to the population in a better way.

Conclusion

The study has observed that the effect of triple pill comparable to the dual therapy of telmisartan and HCTZ. The triple pill is effective in achieving early normalization of BP at 4 weeks and also has a significant effect in reduction of DBP at Week 4. The triple pill due to its better BP control and against a higher dual combination dose, demonstrated synergy between the three components to achieve goal BP. To conclude, early reduction of BP can have a positive impact on patient outcome and the triple pill can be a good therapeutic option for managing hypertension in patients not responding to monotherapies and especially with DM.

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