Based Treatment Algorithm for Essenssial Hypertension with Olmesartan Medoxomil

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Summary

Background: The national and international guidelines emphasize the importance of the effective treatment of arterial hypertension. Nevertheless, low levels of control are observed, as well as low attainment of the recommended goals, indicating that it is important to plan and implement better treatment strategies.

Objective: To evaluate the efficacy of a based treatment algorithm with olmesartan medoxomil.

Methods: This is an open, national, multicentric and prospective study of 144 patients with primary arterial hypertension, stages 1 and 2, naïve to treatment or after a 2-to-3 week washout period for those in whom treatment was ineffective. The use of olmesartan medoxomil was assessed in a treatment algorithm divided into 4 phases: (i) monotherapy (20 mg), (ii-iii) associated to à hydrochlorothiazide (20/12.5 mg and 40/25 mg) and (iv) addition of amlodipine besylate (40/25 mg + 5 mg).

Results: At the end of the algorithm treatment, 86% of the study subjects attained the goal of BP < 130/85 mmHg. Maximum reductions in SBP and DBP were -44.4 mmHg and -20.0 mmHg, respectively. The rate of systolic responders (SBP ≥ 20 mmHg) and of diastolic responders (DBP ≥ 10 mmHg) was 87.5% and 92.4%, respectively.

Conclusion: The study was based on a treatment regimen that was similar to the therapeutic approach in daily clinical practice and showed that the use of olmesartan medoxomil in monotherapy or in association with hydrochlorothiazide and amlodipine was effective in the attainment of the recommended goals for stage 1 and 2 hypertensive individuals. (Arq Bras Cardiol 2008;91(3):168-176)

Key words: Hypertension; angiotensin II type 1 receptor blockers, olmesartan.

Introduction

The national and international guidelines and consensus point out the need for the optimized treatment of essential hypertension (EH); however, low rates of control and attainment of the recommended goals are observed. This fact indicates that better treatment strategies must be planned and implemented[1-3].

In general, the V Brazilian Guidelines of Arterial Hypertension (V DBHA) and the JNC 7 recommend that, for stage 1 hypertension*, the pharmacological treatment must be initiated with monotherapy, which can be a escale-dose regimen, in case of failure in attaining the blood pressure (BP) goal; it also recommends the use of associations when the SBP is 20 mmHg and DBP is 10 mmHg, respectively, above the goal. For patients with stage 2** EH, the use of drug associations can be considered in the beginning of the treatment, although the monotherapy is also indicated in some cases[2-5]. The goal for stage 1 and 2 EH with low and moderate cardiovascular risk is BP < 140/90 mmHg; for those with high cardiovascular risk, the goal is BP < 130/85 mmHg and for those with very high risk, the goal is BP < 130/80 mmHg. Patients with nephropathy and proteinuria > 1.0 g/L a BP < 120/75 mmHg is recommended. However, is possible, it is better to attain even lower BP levels (BP ≤ 120/80 mmHg)[1].

The continuous follow-up of the patient, providing

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information and emphasizing the importance of controlling the BP is fundamental for the therapeutic success. It also allows the monitoring of the clinical conditions and the assessment of the need to increase the dose or add other types of anti-hypertensive drugs.

Olmesartan medoxomil (OM) is the newest drug of the class of Angiotensin II (A-II) receptor (AT1 receptor) blockers (ARBs). In comparative studies, it showed higher anti-hypertensive efficacy when compared to other drugs from the same class and similar to amlodipine[6-10]. It can be associated with a thiazide diuretic [in general, hydrochlorothiazide (HCT)] and/or a calcium channel blocker to potentiate its effect in patients that are non-responsive to the monotehrapy[1,4,5].

Methods

Study design and population

This was an open, national, multicentric and prospective study. The study population was defined by the inclusion criteria listed in Table 1. The inclusion and exclusion criteria were based on the IV Brazilian Guideline of Hypertension - IV DBHA (applicable at the time of the study planning), on the safety aspects of the medications and the guidelines established by the regulatory authorities and by the International Conference on Harmonization (ICH)/Good Practices in Clinical Research (GPC).

This study was carried out in 14 research centers in Brazil with competitive inclusion 2 months after the inclusion of the first study subject, started in August 2006.

Treatment protocol and follow-up procedures

The study was carried out according to the ICH-GCP, Declaration of Helsinki and the Brazilian legislation, after being approved by the Committee of Ethics in Research (CEP) of each Institution, in addition to CONEP (the National Council of Ethics in Research) and ANVISA (the National Agency of Sanitary Vigilance).

After the sreening visit (SV), the patients that met all inclusion and none of the exclusion criteria were selected to participate in the study (Table 1). From visit 1 onward, the study subjects received the study medication, following a scale-dose regimen according to the defined treatment plan (Figure 1).

Treatment Plan

The study was based on a four-phase treatment approach, each one lasting 4 to 9 weeks (Figure 1A). The measurements of casual BP in the 4th, 8th and 9th weeks were the parameters for the changing of phase, determining the uptitration-dose regimen or not. If the study subject had BP≥ 140/90 mmHg, he/she was immediately assigned to the next phase (at any time); if the BP levels were ≥ 130/85 mmHg and/or < 140/90 mmHg, the medication was maintained for four more weeks (totaling 8 weeks) and, if necessary, for one more week (totaling 9 weeks). The home blood pressure monitoring (HBPM) was performed only in the 9th week of treatment, so it could be used as retrospective comparison with the main efficacy parameter of casual BP < 130/85 mmHg. When the study subject did not attain this goal, he or she was assigned to the next phase (Figure 1B).

Table 1 – Inclusion and exclusion criteria

Inclusion criteria
Age: 30 to 75 years
Male and female individuals of any ethnicity. Women must be post-menopausal or surgically sterilized.
Negative pregnancy test for reproductive-age women at the start of the study
Stage 1 and 2 EH (casual DBP ≥90 mmHg and <110 mmHg and casual SBP ≥140 mmHg and <180 mmHg)::
- no treatment for at least two weeks
- undergoing ineffective anti-hypertensive treatment, wash out period of 14 to 21 days
Sign the Informed Consent Form.
No previous history of mental disability.
Exclusion criteria
If the study participation results in risk to the health and safety of the study subject..
Cardiovascular diseases:
- Hypertension stage 3 (BP≥180/110 mmHg) or secondary hypertension.
- Hypotension (SBP<100 mmHg) throughout the study;
- Myocardial infarction with or without surgical interventions in the previous 6 months
- Congestive cardiac failure, pulmonary edema, valvular alterations or rheumatic cardiopathy
- Cerebrovascular events during the previous 6 months;
- Clinically relevant disorders in formation or conduction of the cardiac impulse or other clinically significant arrhythmias.
Comorbidities
- Uncontrolled Diabetes mellitus (through assessment and clinical history and/or fasting glycemia levels > 160 mg/dl)
- Angioedema, renal function alterations, clinically significant liver, gastrointestinal, neurological , hematologic or cardiovascular diseases;
- Gout, symptomatic hyperuricemia
- Hydroelectrolytic disorders;
- Severe and/or active autoimmune or endocrine diseases
- Neoplasic, psychiatric and infecto-contagious diseases.
Others
- Alcohol or medication abuse, illicit drug use
- Concomitant use of medications that are not allowed by the protocol
- Hypersensitivity to the components of any of the study medications
- Pregnant or nursing women, women who wish to get pregnant or those who presented a positive urinary pregnancy test throughout the study.

** Diastolic blood pressure (DBP) from 90 to 99 mmHg, and Sistolic blood pressure (SBP) from 140 to159 mmHg.*

*** (DBP) from 100 to 109 mmHg, and (SBP) from 160 to 179 mmHg.*

The objective of the HBPM in this study was to evaluate the percentage of individuals that presented the "white-coat effect", even after 8 weeks of treatment. This information would not result in any alteration of conduct and would be used only for a posterior analysis, providing a perspective on its use in new clinical studies, as it has been confirmed that it has a better prognostic value when compared to the casual BP measurement at the office. Stergiou et al[11] calculated the size of the sample necessary for a comparative study between medications, using different methods of BP measurement based on their reproducibility and with a significance level of 0.05. Comparing to the casual BP measurement at the office, the use of the HBPM can reduce the sample by 30%[12].

A BP level < 130/85 mmHg was considered as sign of therapeutic efficacy and, upon reaching it, the study subject concluded the study. Those who did not reach the primary BP goal at the end of the algorithm treatment regimen were considered as therapeutic failures (Figure 1).

Parameters of the study efficacy

The parameter of the study efficacy was the casual measurement of the blood pressure (BP) of the study subject, through the mean of three BP measurements, in the seated position, at each follow-up visit, even after the HBPM. The measurement was always carried out in the morning, in the same arm (chosen as the one with the highest pressure at the screening visit) and using the same device (OMRON HEM-705CP), according to the recommendations of the IV DBHA, applicable at the moment when the protocol was designed.

The analysis of the parameter of efficacy allowed us to determine the percentage of BP goal attainment of BP < 130/85 mmHg. This BP value encompasses most of the stage 1 and 2 hypertensive patients defined by the current guidelines; thus, a large part of the patients with more stringent BP levels is contemplated, considering that patients with stage-2 arterial hypertension (approximately 50% of the sample) are already considered as moderate risk and some can be considered high risk if they have other associated risk factors (as exclusion

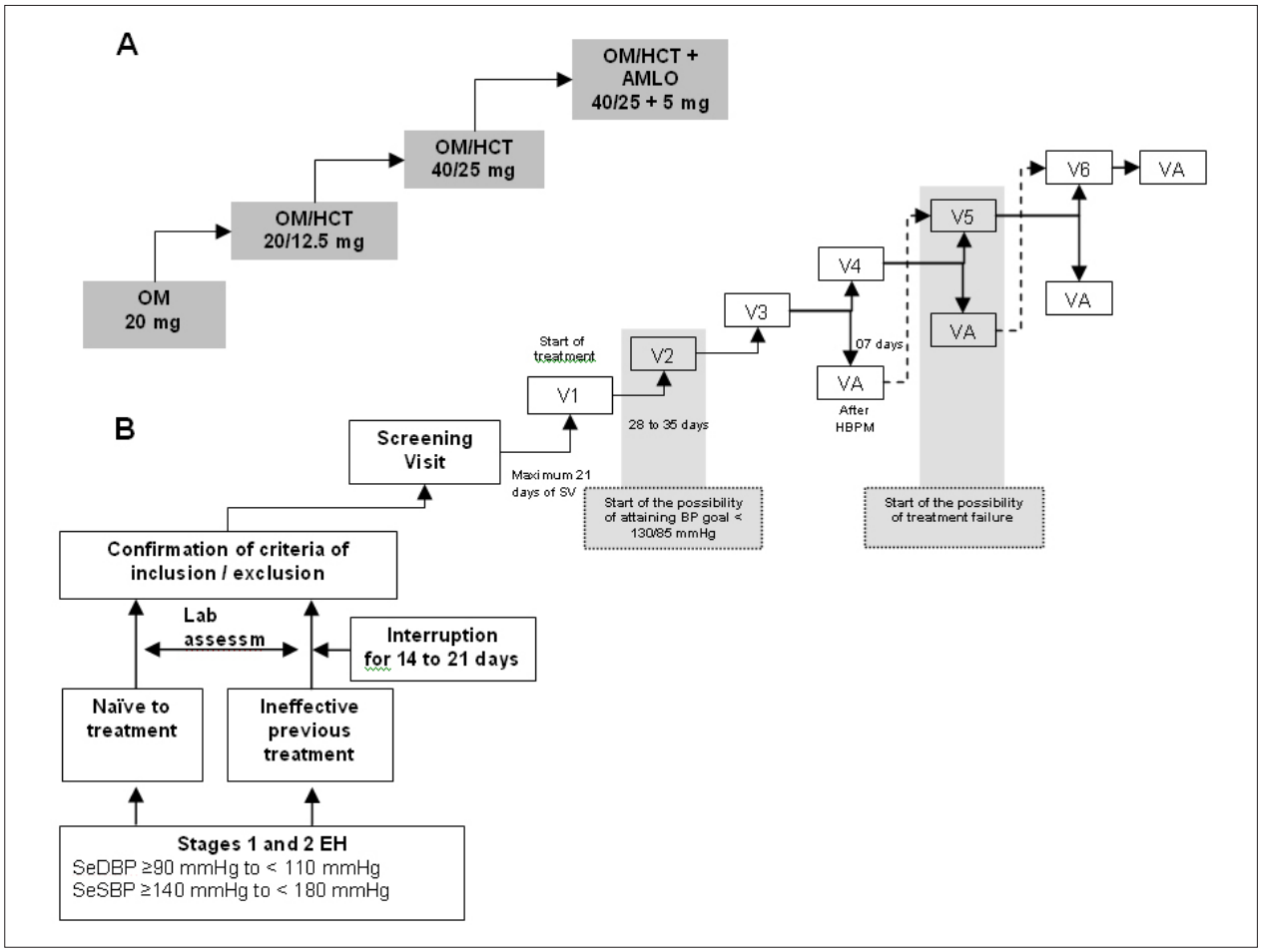

Figure 1 - Based treatment algorithm with olmesartan medoxomil (A) and follow-up procedures (visits) (B); SeDBP- seated diastolic blood pressure; SeSBP- seated systolic blood pressure; EH- essenssial hypertension; Lab assess.- laboratory assessment; OM- olmesartan medoxomil; HCT- hydrochlorothiazide; AMLO- Amlodipine Besylate; HBPM- home blood pressure monitoring; V- visit. VA- Visit A (after HBPM)..

criteria, we considered only patients with uncontrolled diabetes mellitus, defined through clinical assessment and/or glycemia levels > 160 mg/dl), who, in the present study were evaluated through the clinical examination of the cardiovascular system, electrocardiogram and laboratory assessment.

Additionally, the IV and V DBHA also suggest that, although the goals to be attained vary from individual to individual, whenever possible one must seek values that are lower than 120/80 mmHg. This information is based on the results published by Lewington et al[13], who demonstrated that the risk for the development to an encephalic vascular accident and myocardial acute infarction increases 2-fold when the BP increases from 115/75 mmHg to 135/85 mmHg.

The BP measurement [casual at the doctor's office or through Home Blood Pressure Monitoring (HBPM)] and the response and control rates of DBP and SBP in relation to the initial measurement allowed the attainment of the secondary objectives of the study, of evaluating the influence of the time of use (4 or 8 weeks) and the safety of OM, OM/HCT and OM/HCT+AMLO.

Statistics

The sample size was calculated considering an open study of 4 consecutive phases with different expected response proportions for each one, that is, for each phase of the algorithm-treatment, it is expected that the proportion of responses be increasingly higher, which makes it necessary to have 154 valid study subjects. The risk of a false-positive result was defined as 5% and of a false-negative result, 10%.

Results

Patient distribution and baseline characteristics

In total, 459 patients were selected; of these, 276 were not approved at the screening process, thus resulting in a sample of 183 study subjects that comprised the intent-to-treat population (who received at least one dose of olmesartan medoxomil 20 mg). Thirty-nine study subjects were excluded: 12 due to lack to treatment adherence or protocol violation; 7 abandoned the study protocol; 4 did not meet the inclusion criteria; 2 presented some exclusion criteria throughout the study; 9 presented some adverse event or use of proscribed medication and 5 due to error in medication dispensation. The elected cohort was then comprised of 144 study subjects, who were followed successfully up to the end of the study.

The initial study data (collected at V1), such as the main demographic data, previous anti-hypertensive treatment, body mass index (BMI), SBP, DBP and HR, are shown in Table 2. These data contemplate the main demographic characteristics of the 183 study subjects included in the study.

Efficacy

The BP mean at the start of the study for the intent-to-treat population (ITT=183 study subjects) was 158/97 mmHg, as shown in Table 2. The final BP of this group was not calculated, as it was not the population assessed for the analysis of efficacy. The BP mean at the start of the study of the subjects that comprised the elected cohort (n=144) was 158/97 mmHg and 125/78 mmHg at the end of the study.

The number of subjects assessed for each phase of the algorithm-treatment was, respectively, 144, 106, 73 and 32 (Figure 2).

With the use of olmesartan medoxomil 20 mg in monotherapy, 26% of the study subjects reached the main BP goal of BP < 130/85 mmHg. With the addition of HCT 12.5 mg, a further 23% of the study subjects reached the BP goal, totaling 49% and with OM/HCT 40/25 mg, 74% reached the BP goal. At the end of the algorithm treatment, 86% of the study subjects, of a total of 144 assessed subjects, reached the goal of BP < 130/85 mmHg (Figure 2). The decreases in SBP and DBP for each treatment phase were, respectively: -30.5 and -19.1mmHg; -34.8 and -21.6 mmHg; -27.1 and -15.5 mmHg and -28.6 and -15.3 mmHg. If we evaluate only the study subjects that attained the BP goal (n=124), the decreases in SBP and DBP for each treatment phase were, respectively: -30.5 and -19.1 mmHg; -34.8 and -21.6 mmHg; -34.2 and -9.8 mmHg and -44.4 and -20.0 mmHg (Figure 3).

Regarding the time of treatment, that is, the time assessment in the dose-response to the use of the medication during each phase that varied from 4 to 9 weeks, it was observed that 60.4% (n=87) of the study subjects attained the recommended BP goal (BP<130/85 mmHg) after 4 weeks of treatment, whereas 18.1% (n=26) did so after 8 weeks and 7.6% (n=11) after 9 weeks of treatment.

The number of study subjects in whom the HBPM would have prevented the algorithm-treatment was 80% (n=16) of the 20 study subjects that carried out the 9th week of treatment with the same dose of medication.

Among the 144 assessed study subjects, the rate of systolic responders (reduction in SBP ≥ 20 mmHg) was 87.5% with a mean reduction of -36 mmHg; regarding the diastolic responders (reduction in DBP ≥ 10 mmHg) it was 92.4%, with a mean reduction of –20 mmHg. As for the systolic and diastolic responders, (SBP ≥ 20 mmHg and DBP ≥ 10 mmHg) it was 86.8% with reductions of -36 mmHg and -20 mmHg, respectively.

For the study subjects that attained the recommended BP goal, and who, in the beginning of study presented stage-1 EH (n=56), the mean reductions in SBP and DBP observed for each phase of the algorithm-treatment were -28.8 and -17.6 mmHg; -31.1 and -17.6 mmHg; -31.0 and -17.4 mmHg and -30.8 and -14.7 mmHg, respectively.

Similarly, for the subjects that had been classified as stage-2 EH, the mean reductions in SBP and DBP observed were: -35.7 and -23.6 mmHg; -37.8 and -22.7 mmHg; -38.8 and -21.4 mmHg and -44.5 and -21.5 mmHg (Figure 4). The goal attainment outcome for this population is shown in Figure 5.

Safety

The general incidence of adverse events that appeared during treatment was 21.5% and the main ones were: 3.5% headaches; 1.4% anxiety; 1.4% lumbar pain; 1.4% dizziness (Table 3). No case of lower limb edema was reported, not even with the use of OM/HCT+AMLO 40/25+5 mg.

Table 2 - Demographic data and baseline characteristics of the patients (ITT sample) (n=183)

Variable	Value
Age in years	
30 to 39 yrs (%)	13.7
40 to 49 yrs (%)	26.8
50 to 59 yrs (%)	35.5
60 to 69 yrs (%)	18.6
≥70 yrs (%)	5.5
Mean age (yrs)	52
Sex	
Male (%)	47.0
Female (%)	53.0
Ethnicity	
Caucasian (%)	59.6
Black (%)	19.1
Asian (%)	3.8
Other (%)	17.5
Previous anti-hypertensive treatment	
Naïve patients (%)	53.6
Treated patients (%)	46.4
Monotherapy (%)	58.8
Combined therapy (%)	41.2
Main medications	
Hydrochlorothiazide (%)	19.6
Amlodipine besylate (%)	15.0
Captopril (%)	13.5
Enalapril maleate (%)	11.3
Atenolol (%)	8.3
BMI† (kg/m²)	28.71 ± 4.58*
SBP (mmHg)	157.91 ± 10.89*
DBP (mmHg)	96.84 ± 5.3*
HR (bpm)	74.92 ± 11.38*

** Values presented as means ± SD; †BMI (Body Mass Index) calculated with n=182; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate.*

Table 3 – More common adverse events occurring during treatment

Adverse Event	OM 20 mg (n=144)	OM/HCT 20/12.5 mg (n=106)	OM/HCT 40/25 mg (n=73)	OM/ HCT+AMLO 40/25+5 mg (n=32)
Miscellaneous	17 (11.8%)	11 (10.4%)	10 (13.7%)	5 (15.6%)
Anxiety	4 (2.7%)	2 (1.9%)	0 (0.0%)	0 (0.0%)
Headache	1 (0.7%)	1 (0.9%)	0 (0.0%)	0(0.0%)
Lumbar pain	1 (0.7%)	1 (0.9%)	0 (0.0%)	0(0.0%)
Dizziness	0 (0.0%)	2 (1.9%)	0 (0.0%)	1 (3.1%)

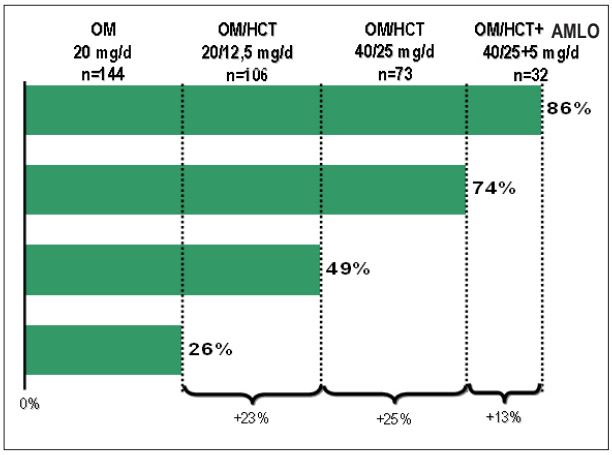

Figure 2 - Proportion of the study subjects that reached BP goal of BP<130/85 mmHg at each phase of the algorithm-treatment (n=144); Mean initial BP: 158/97 mmHg; OM- olmesartan medoxomil; HCT- hydrochlorothiazide; AMLO- amlodipine besylate.

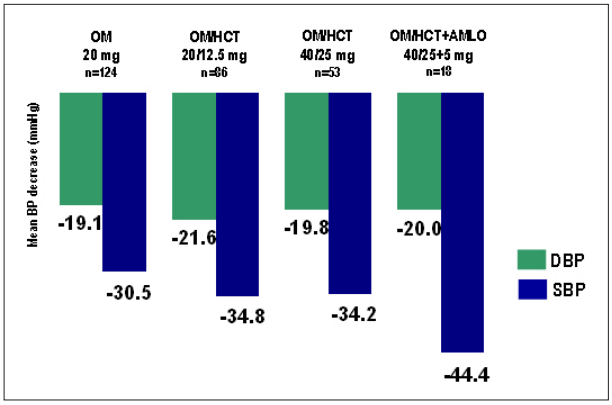

Figure 3 - Decreases in BP of the study subjects that reached the BP goal of BP<130/85 mmHg, by phase of the based treatment algorithm (n=124); SBP- systolic blood pressure; DBP- diastolic blood pressure; OM- olmesartan medoxomil; HCT- hydrochlorothiazide; AMLO- amlodipine besylate.

Discussion

The low rates of control and the stringent goals for patients with EH and additional cardiovascular risk factors clearly indicate the need for effective strategies in BP control, as it is well known that the percentage of hypertensive, non-controlled patients in the United States is high, being around 64.9%[14].

Although the design of the present study, when it was first designed, used the IV DBHA, we observed that it remained up-to-date, as it contemplates the requirements and recommendations of the most current guidelines, i.e., the V DBHA. The guidelines recommend, for stage-1 hypertension, initiating the pharmacological treatment with monotherapy, which can be uptitratesd in cases of failure in attaining the BP goal. For patients with stage-2 hypertension, the use of drug

associations must be considered, when there is no response to the monotherapy. Regarding the BP goal of BP<130/85 mmHg, used in the present study as an efficacy parameter, most of the assessed study subjects presented moderate or high cardiovascular risk; additionally, the presence of comorbidities, especially diabetes mellitus, was not considered an exclusion criteria, as long as the parameters defined in protocol were respected (Table 1). Therefore, with the BP goal established for hypertensive patients with high cardiovascular risk stratification (including those with diabetes mellitus), most of the study subjects were contemplated, in addition to favoring a better prognosis of arterial hypertension with lower rates of cardiovascular outcomes[1,14].

With the objective of reproducing the clinical practice, a titration treatment was established and evaluated every four weeks, which is the necessary period for the observation of the full action of olmesartan medoxomil, in a Brazilian population originated from several Brazilian cities (Recife, Maceio, Belo Horizonte, Rio de Janeiro, Sao Paulo, Sao Jose do Rio Preto, Campinas, Curitiba, Florianopolis and Porto Alegre).

The rationale of the study used three anti-hypertensive medications from different therapeutic classes for the algorithm treatment: an ARB (angiotensin II receptor blocker),

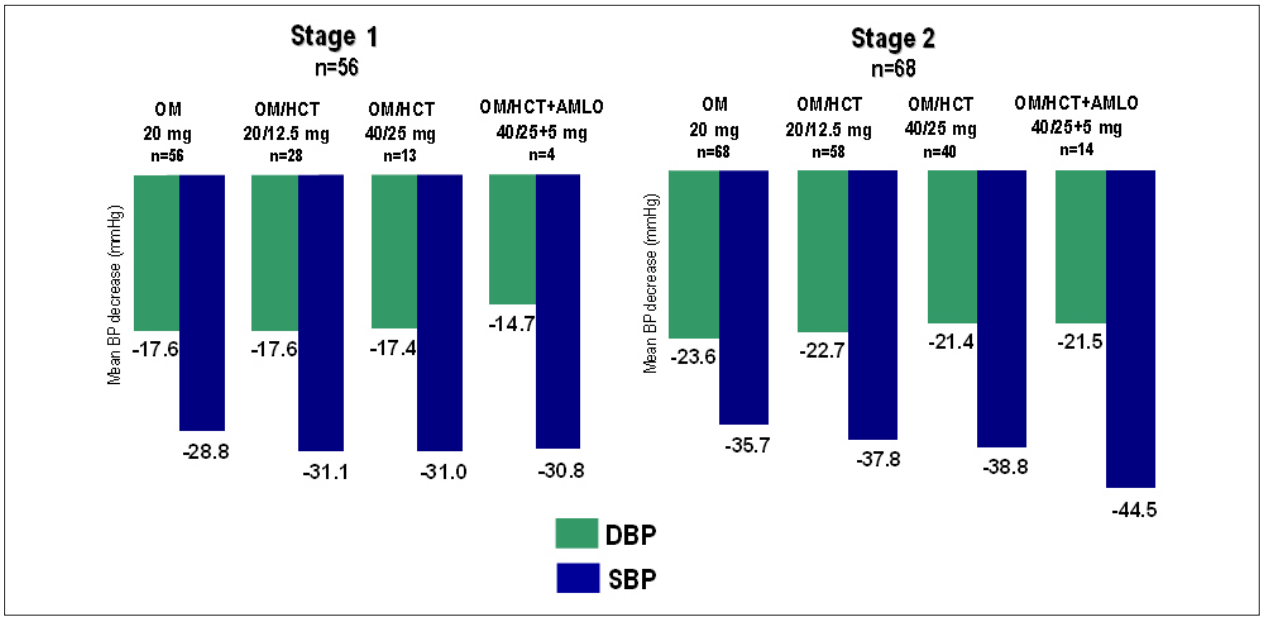

Figure 4 - Decreases in BP of the study subjects that reached the BP goal of BP<130/85 mmHg, by phase of the based treatment algorithm and by stage of hypertension; SBP- systolic blood pressure; DBP- diastolic blood pressure; OM- olmesartan medoxomil; HCT- hydrochlorothiazide; AMLO- amlodipine besylate.

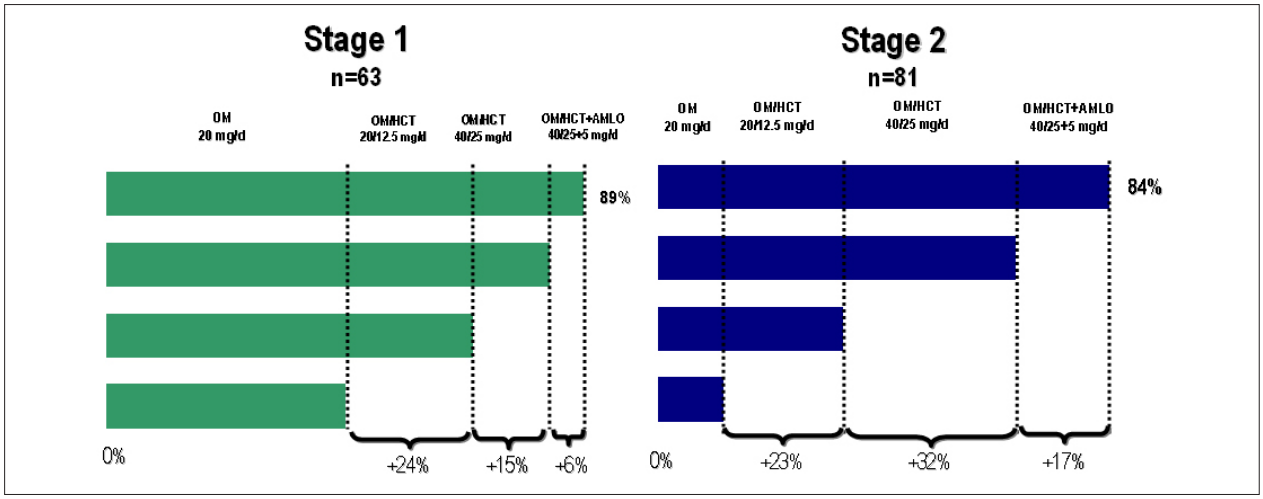

Figure 5 - Proportion of study subjects that reached the BP goal of BP<130/85 mmHg at each phase of the based treatment algorithm according to the classification of hypertension; Mean initial BP: 158/94 mmHg (stage 1) and Mean initial BP: 164/99 mmHg (stage 2); OM- olmesartan medoxomil; HCT- hydrochlorothiazide; AMLO- amlodipine besylate.

in this case, olmesartan medoxomil, a thiazide diuretic, hydrochlorothiazide, and a calcium-channel blocker, the amlodipine besylate. Olmesartan blocks the AT_1 receptors for longer periods and has a higher rate of fixation, resulting in higher anti-hypertensive efficacy in relation to other ARBs, as observed in several comparative clinical studies[6-10]. For patients that need the combined therapy to attain the BP goals, the most frequent association is a thiazide diuretic (in general, hydrochlorothiazide) and/or a calcium-channel blocker[1].

Hydrochlorothiazide is known to activate the renin-angiotensin-aldosterone system (RAAS), providing an effective combination with the angiotensin II-AT_1 receptor blockers. It is a thiazide diuretic that acts on the mechanisms of electrolyte resorption in the renal tubules, directly increasing sodium and chloride excretion in approximately equivalent amounts[15].

Amlodipine besylate is a calcium-channel blocker from the subgroup of dihydropyridines. It acts by preventing the entrance of calcium in the vascular smooth muscle cells, which decreases the peripheral vascular resistance[6]. As the associations of anti-hypertensive drugs must follow a logical decision of not combining two medications with similar actions, the addition of amlodipine to the ARB+HCT association is very convenient to promote the control in a larger number of patients[1,3,5].

As for the initial demographic characteristics of the present study, there was a higher percentage of hypertensive patients aged 50 to 59 years, with 35.5%, followed by 40 to 49 years, with 26.8%. Of the total number of patients, 53% were females, 59.6% were Caucasians and 53.6% were naïve to treatment.

Of those who had been previously treated and did not have controlled BP (< 140/90 mmHg), 58.8% used monotherapy and the most often employed medication was, in general, hydrochlorothiazide, in monotherapy as well as associated to other medication.

At the beginning of the study, the mean casual SBP was 158 mmHg and the mean casual DBP was 97 mmHg. The mean BMI of the study subjects was classified as overweight (24.9 to 29.9 Kg/m^2). According to the V DBHA, the excess body mass is a predisposing factor for hypertension and it can be responsible for 20% to 30% of the cases of EH[1].

According to Caro et al[16], the choice of the initial agent for long-term adherence to the anti-hypertensive therapy is very important. The results of the present study suggest that the use of an ARB, such as olmesartan medoxomil, followed by the addition of a thiazide diuretic, if necessary, and a calcium-channel blocker, represents an effective and safe algorithm-treatment regimen for hypertension. Considering that 81 study subjects (56.2%) presented stage-2 EH, it was necessary to attain significant reductions in SBP and DBP for the BP goal to be attained. As the study subjects were discontinued from the study as soon as they attained a BP goal of BP < 130/85 mmHg, the reductions in BP could be even higher. The regimen with more than one medication was well tolerated from the beginning to the end, without any increase in adverse events observed with the addition of HCT or amlodipine.

The absence of reports of lower-limb edema as an adverse event might be occurred due to the methodology of the study, which did not include a specific questionnaire for the reporting of this specific adverse event, but a general inquiry about possible alterations that occurred during treatment. Other factors that might have contributed to this fact were the short duration of the treatment and the small sample size submitted to the treatment with amlodipine.

The use of an ARB as a first-line agent for the treatment of hypertension is a known and frequently employed approach, due to its efficacy and safety profile, in addition to its capacity to promote the protection of target-organs[1].

In an algorithm study carried out by Neutel et al[17], it was demonstrated that the algorithm-treatment, based on olmesartan medoxomil and the addition of HCT and amlodipine, although with somewhat different times and doses, 87.7% of the patients attained the BP goal of BP ≤ 130/85 mmHg after 24 weeks of treatment, which was very similar to the outcome of the present study (86%).

Izzo et al[18] evaluated patients with isolated systolic hypertension (stage 2) in a algorithm-treatment study with OM and addition of HCT (20 mg, 40 mg, 40/12.5 mg and 40/25 mg), and they observed that 70.4% of the patients attained the BP goal of BP< 140/90 mmHg and 15.4%, the BP goal of BP < 120/80 mmHg, which shows that the results of the efficacy as well as those of safety obtained in the present study are compatible and consistent with the results of studies published in American literature.

The monotherapy with Olmesartan medoxomil 20 mg showed to be effective, as 26% of the study subjects attained the BP goal. Oparil et al[9,10] observed that after 8 weeks of treatment with the same dose, 12.5% of the assessed patients attained the same BP goal; in both cases, the evaluation occurred in stage-1 and 2 EH patients.

The data of 8 weeks of treatment with the same dose, in case of patients that presented a BP level at a range considered to be borderline, i.e., < 140/90 mmHg, but not within the normal range (< 130/85 mmHg), made it possible to evaluate the influence of time on medication response. Therefore, it was observed that in 25.7% of the study subjects, the increase in the dose would be unnecessary.

The study of the 9th week of treatment (study subjects who, after prolonged use of the same dose, 8 weeks of treatment, maintained BP levels that were "borderline" for the control i.e., <140/90 mmHg, but above the study goal of 130/85 mmHg), can determine the number of subjects in whom the HBPM would have prevented the uptitration or the association with another medication, that is, making it possible to demonstrate by HBPM that the BP was within the goal ranges in a percentage of these study subjects, evaluating the influence of the "white coat effect" on BP control. We observed that, in this situation, the HBPM would prevent the titration in 80% of the cases, demonstrating its importance in the follow-up of patients with EH (considering the normal values of HBPM BP<135/85 mmHg).

The BP reductions obtained in the present study for the study subjects that had stage-1 and 2 EH in the beginning of the study, were on average, a little higher than those obtained by Neutel et al[19]. Furthermore, it was observed that

the study subjects that had stage-2 EH needed an association of medications to attain the BP goal (Figure 4 e 5). Thus, as recommended by the V DBHA, to initiate the treatment with a combination of drugs can help the patients attain the recommended BP goal.

The present study was designed based on the physician's clinical practices when giving treatment directions and thus, there was no need to perform a randomized, double-blind study with placebo. The main parameter of efficacy, the casual BP measurement, was obtained according to strict criteria and methodology, as it was necessary to follow the recommendations of the V DBHA to measure BP, use a standard digital BP measurement device and consider the mean of three measurements recorded to proceed with the decision-making regarding the next step, i.e., goal attainment, uptitration or dose maintenance for a complementary period for four more weeks. Hence, all efforts were made in order to avoid a bias regarding the study subjects as well as the physicians, which reflects the data accuracy.

Conclusion

The assessments performed every four weeks and the use of medications from different therapeutic classes with an algorithm treatment showed that the treatment regimen proposed by the study can be a feasible and an effective therapeutic option.

The treatment with olmesartan medoxomil in monotherapy and associations showed to be very effective and safe. In patients with stage 1 and 2 hypertension (mean of 158/97 mmHg), 86% of the individuals reached the goal of BP < 130/85 mmHg. Additionally, there were significant decreases of up to 44 mmHg in SBP and up to 22 mmHg in DBP without a significant increase in adverse events. These data suggest that this approach is an effective option for the treatment for hypertension.

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Potential Conflict of Interest

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Study Association

This study is not associated with any graduation program.

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