CLINICAL SCIENCE

How to avoid discontinuation of antihypertensive treatment. The experience in São Paulo, Brazil

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OBJECTIVES: To evaluate the importance of providing guidelines to patients via active telephone calls for blood pressure control and for preventing the discontinuation of treatment among hypertensive patients.

INTRODUCTION: Many reasons exist for non-adherence to medical regimens, and one of the strategies employed to improve treatment compliance is the use of active telephone calls.

METHODS: Hypertensive patients (n = 354) who could receive telephone calls to remind them of their medical appointments and receive instruction about hypertension were distributed into two groups: a) ''uncomplicated'' – hypertensive patients with no other concurrent diseases and b) ''complicated'' - severe hypertensive patients (mean diastolic ≥110 mmHg with or without medication) or patients with comorbidities. All patients, except those excluded (n = 44), were open-block randomized to follow two treatment regimens (''traditional'' or ''current'') and to receive or not receive telephone calls (''phone calls'' and ''no phone calls'' groups, respectively).

RESULTS: Significantly fewer patients in the ''phone calls'' group discontinued treatment compared to those in the ''no phone calls'' group (4 vs. 30; p<0.0094). There was no difference in the percentage of patients with controlled blood pressure in the ''phone calls'' group and ''no phone calls'' group or in the ''traditional'' and ''current'' groups. The percentage of patients with controlled blood pressure (<140/90 mmHg) was increased at the end of the treatment (74%), reaching 80% in the ''uncomplicated'' group and 67% in the ''complicated'' group (p<0.000001).

CONCLUSION: Guidance to patients via active telephone calls is an efficient strategy for preventing the discontinuation of antihypertensive treatment.

KEYWORDS: Hypertension; Medication Compliance; Patient Adherence; Therapeutics; Antihypertensive Drugs.

INTRODUCTION

Most patients with hypertension do not benefit from treatment.[1] Data from NHANES/NCHS 1999–2004 showed that 71.8% of individuals were aware of their condition, 61.4% were under current treatment and 35.1% had it under control.[2] Although the percentage of individuals with controlled blood pressure in Brazil is unknown, we estimate it to be low because the percentage of patients with their high blood pressure under control is around 30-35% at outpatient clinics that specialize in hypertension, and these clinics do not represent the national reality.[3]

Many reasons exist for non-adherence to medical regimens, including adverse drug effects, poor instructions, poor provider-patient relationship, poor memory, a patient's disagreement with the need for treatment or inability to afford medication.[4,5] One of the strategies employed to improve treatment compliance is the use of active telephone calls[6] to patients through which they are given guidance and treatment questions are answered. Using this strategy, several studies have shown an increase in treatment compliance, a higher percentage of blood pressure control[6-8] and a decrease in mortality.[9-11]

Another strategy that aims at improving treatment compliance is the employment of two low-dose medications. Evidence suggests that the combination of two antihypertensive agents provides a higher percentage of blood pressure control due to complementary mechanisms of action. In addition, this results in better tolerability and consequently, better treatment compliance.[12-14]

The *ASCOT* study[15] (*Anglo-Scandinavian Cardiac Outcomes Trial*) has indicated a significant reduction in all causes of mortality with the use of current medications for treating hypertension: calcium channel antagonists and angiotensin-converting enzyme inhibitors. It has also been demonstrated that a high incidence of adverse events may decrease treatment compliance. However, in the *LIFE*[16] study, angiotensin receptor antagonists proved to be better at reducing the risks related to cardiovascular events and they resulted in a lower rate of treatment discontinuation when compared to a beta-blocker.

In view of these data, we evaluated the importance of providing guidelines to patients via active telephone calls for blood pressure management and preventing treatment discontinuation in hypertensive patients. We used two treatment regimens with low-dose medications that were offered for free to avoid the influence of financial factors. We opted for one regimen called ''traditional'' based on diuretics and beta-blockers and another called ''current'' based on angiotensin II antagonists and calcium channel blockers.

METHODS

The study participants were selected at the Hypertension Unit, University of São Paulo General Hospital, Nephrology Division, University of São Paulo School of Medicine. The patients had essential hypertension and were able to receive telephone calls to be reminded of their medical appointments and be given guidance about hypertension. Patients were of both genders, from diverse ethnic backgrounds, over 18 years of age, and had body mass indices below 40 kg/m^2. The patients were enrolled in the study after signing a free and informed consent form. The study was approved by the Ethics Committee of the Board of Directors of the University of São Paulo School of Medicine.

Patients were excluded on several bases, including blood pressure <140/90 mmHg without antihypertensive medication, secondary hypertension, white-coat hypertension with systolic pressures ≥140 mmHg and/or diastolic pressures ≥90 mmHg at the doctor's office and awake mean systolic pressures <135 mmHg or awake mean diastolic pressures <85 mmHg without antihypertensive medication, malignant hypertension and patients with a previous history of hypersensitivity reaction to the study medications. Other exclusion criteria were as follows: pregnant women or nursing mothers, the presence of liver dysfunction evidenced by the patient's clinical history or by one of the liver function tests (levels twice the normal values for alkaline phosphatase, total bilirubin, aspartate amino-transferase), patients with clinical conditions that might interfere with the total conformity with the study or those who might have an increased risk for participating in the study, patients with a history of alcoholism, drug abuse or mental disorders that might invalidate the free and informed consent or limit the patient's ability to meet the protocol rules and patients who had participated in any other studies involving investigational drugs or drugs already marketed within the previous month before enrollment in this study or concomitantly with this study.

Blood Pressure Measurement

Blood pressure and heart rate measurements were performed on the right upper limb on sitting patients five times by the nursing staff using an appropriately sized cuff with a validated automatic oscillometric device (Dixtal, DX2710, São Paulo, Brazil).[17] The mean of the last two measurements was calculated and recorded if the difference between these measurements was less than 4 mmHg. If after the five measurements the difference between the last two was greater than 4 mmHg, the measurement was repeated until the difference between the two measurements was less than 4 mmHg. During the study, blood pressure measurements were always performed in the afternoon by the same nursing staff using the same device.

The diagnosis of hypertension was made when the mean values of the last two measurements were as follows: systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg with or without medication at the initial visit (Visit 0). Patients who were receiving antihypertensive medication at the initial visit and had a systolic pressure <140 mmHg or a diastolic pressure <90 mmHg were re-evaluated eight weeks after discontinuation of their medication and introduction of placebo; these patients were included in the study when the mean values included a systolic pressure ≥140 mmHg and/or a diastolic pressure ≥90 mmHg.

Controlled blood pressure was defined in two levels as (with the patient in the seated position) a systolic/diastolic pressure less than 140/90 or 120/80 mmHg.

All of the patients underwent Ambulatory Blood Pressure Monitoring (ABPM), which was performed with a validated oscillometric device (SpaceLabs 90207, SpaceLabs Inc, Richmond, WA, USA),[18,19] five weeks after the start of the placebo to eliminate cases of patients with white-coat hypertension and, in patients who did not receive placebo, to identify the white-coat effect.

According to clinical characteristics, the patients were assigned to two groups: a) ''uncomplicated''– hypertensive patients without complications and without other concurrent diseases and b) ''complicated''- patients with severe hypertension (mean diastolic pressure ≥110 mmHg with or without medication) or comorbidities such as diabetes mellitus, renal failure (serum creatinine >1.4 mg/dL), coronary insufficiency, congestive heart failure or prior history of cerebrovascular accident.

Patient Randomization

All patients, from both the complicated and the uncomplicated groups, were open-block randomized to receive active telephone calls (''phone calls'' group) or not to receive telephone calls (''no phone calls'' group) and to follow two treatment regimens, ''traditional'' or ''current''.

Thus, after the first visit and randomization, patients from the ''phone calls'' group were invited to enroll by telephone in a program called ''Biosintética Assistance'', supported by Biosintética Laboratory. The patients who subscribed started receiving active telephone calls from appropriately trained operators and also started receiving magazines with health-related information, which were sent periodically by mail. There were six contacts by telephone during the study. During phone calls, the patient was reminded to attend the next visit, and he/she was educated about hypertension and any necessary clarifications about his/her treatment. All patients randomized to the ''phone calls'' group were invited to attend occasional informative lectures with the participation of a multidisciplinary team.

At the initial stage of treatment (following eight weeks of treatment with placebo), the ''uncomplicated'' group received one of the following treatment regimens: a) ''traditional'' treatment with 6.25 mg 2x/day hydrochlorothiazide and 25 mg 2x/day atenolol; b) ''current'' treatment with 25 mg 2x/day losartan and 2.5 mg 2x/day amlodipine. If the blood pressure could not be controlled during the visits, the medication doses were doubled or another antihypertensive was added. The ''complicated'' group did not undergo the treatment period with placebo and was randomized to receive either ''traditional'' or ''current'' drug regimens similar to the ones administered to the ''uncomplicated'' group, though the specifics of each condition were carefully considered. The addition of other antihypertensive agents in the ''uncomplicated'' group and the specificities of the patient regimens in the ''complicated'' group were performed according to the guidelines from the V Brazilian Guidelines on Arterial Hypertension.[3]

All patients were instructed to take their medication every day at 7:00 AM and 7:00 PM, with a variation of up to one hour. A 12-month supply of the necessary medication was supplied to the patients by the physician at the end of the visit at no cost to eliminate the financial factor in this analysis; patients were given enough medication to last between visits. Patients were instructed to bring the remaining pills to their subsequent visits, at which time they were counted by the nursing staff without the patients' knowledge of this procedure.

Doctors' visits, preceded by the nursing staff visit, took place every eight weeks for 56 weeks and included measurements of blood pressure, heart rate and weight. The weight was checked with the patient wearing light clothes standing barefoot on a scale (model 2096PP, Toledo do Brasil, São Paulo, Brazil).

Study withdrawal was characterized by non-attendance to appointments for up to three months after the scheduled date. Patients who returned to the medical clinic within three months after the scheduled date were allowed to continue in the study and be evaluated in an unscheduled visit.

The tests performed during the placebo treatment and after 40 weeks of active treatments included the following: fasting glucose, urea, creatinine, total cholesterol, fractions of cholesterol, triglycerides, uric acid, total bilirubin, creatine phosphokinase (CPK), sodium (Na+), potassium (K+), hemoglobin, thyroid-stimulating hormone (TSH), alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotranferase (ALT) and urinary excretion of sodium in 24 h.

Statistical Analysis

Data were analyzed using an analysis of variance (ANOVA) according to the factor of controlled or uncontrolled hypertension. $P < 0.05$ was considered statistically significant.

RESULTS

The study included 398 patients. Of those, 44 were excluded for the following reasons: a) lack of enrollment in the Biosintética Assistance program (n = 17); b) body mass index >40 kg/m^2 (n = 6); c) secondary hypertension (n = 4); d) white-coat hypertension (n = 3); e) white-coat normotension (''masked hypertension'') (n = 3); f) alcohol use (n = 2); g) classification error (n = 4); h) refusal to do ABPM (n = 2); i) loss of blood pressure measurements from the first visit (n = 1); j) pregnancy (n = 1); k) death (n = 1). A total of 354 patients were evaluated.

There were no statistically significant differences in age, gender, skin color, body mass index, blood pressure or heart rate between the groups classified as: ''complicated'' (n = 175) and ''uncomplicated'' (n = 179); ''traditional'' (n = 176) and ''current'' (n = 178); ''phone calls'' (n = 108) and ''no phone calls'' (n = 246) (Table 1). In addition, no differences were seen in marital status, education or occupation.

a) Control of Blood Pressure

A marked reduction in blood pressure was seen in patients from both the ''complicated'' and ''uncomplicated'' groups (Table 2). The blood pressure was reduced by $19 \pm 10/20 \pm 14$ mmHg in the ''uncomplicated'' group and by $18 \pm 14/22 \pm 17$ mmHg (systolic/diastolic) in the ''complicated'' group ($p > 0.05$; n = 354).

The ''phone calls'' and ''no phone calls'' groups showed significantly lower blood pressures at the end of treatment ($p < 0.00001$). The ''traditional'' and ''current'' groups showed significantly lower blood pressures at the end of treatment (Figure 1).

Table 1 - Study groups demographics.

	Uncomplicated n = 179	Complicated n = 175	Traditional n = 176	Current n = 178	No Phone Calls n = 246	Phone Calls n = 108
Age (years)	53 ± 11	53 ± 11	54 ± 11	52 ± 11	54 ± 11	52 ± 11
Gender (%)						
Male	27	41	33	34	33	34
Female	73	59	67	66	67	66
Skin color (%)						
Whites	62	52	60	54	56	60
Non-whites	38	48	40	46	44	40
BMI (kg/m^2)	29 ± 4	29 ± 4	29 ± 4	29 ± 4	29 ± 4	29 ± 4
Blood Pressure at Randomization (mmHg)						
Systolic	155 ± 12	163 ± 24	159 ± 19	158 ± 19	159 ± 19	158 ± 19
Diastolic	91 ± 10	102 ± 20	96 ± 17	97 ± 16	97 ± 16	97 ± 17
Heart rate	80 ± 13	83 ± 13	81 ± 13	82 ± 13	82 ± 13	82 ± 13

Data are shown as mean $\pm$ s.d.; BMI = Body Mass Index; $p > 0.05$: ''complicated'' vs. ''uncomplicated'', ''traditional'' vs. ''current'', ''phone calls'' vs. ''no phone calls'' for age, gender, skin color and BMI.
Blood pressure at randomization: uncomplicated vs. complicated groups: systolic – t = 3.78, p = 0.0002; diastolic – t = 6.44, $p < 0.000001$; FC – t = 2.41, p = 0.016

Table 2 - Blood pressure (mmHg) at the beginning and end of the 12-month treatment in the ''uncomplicated'' and ''complicated'' groups, according to the ''traditional'' and ''current'' treatments and randomization into the ''phone calls'' and ''no phone calls'' groups.

Group	Randomization Visit	Final Visit
Uncomplicated (n = 179)	155±12/91±10	126±14*/73±11*
''Traditional'' Treatment (n = 90)	155±12/91±9	126±14*/71±11*
''Current'' Treatment (n = 89)	155±12/92±10	126±15*/74±11*
''No Phone Calls'' (n = 119)	156±13/91±10	127±16*/73±12*
''Phone Calls'' (n = 60)	154±11/92±9	125±11*/73±10*
Complicated (n = 175)	163±24/102±20	131±19*/78±14*
''Traditional'' Treatment (n = 86)	164±24/102±21	132±21*/77±16*
''Current'' Treatment (n = 89)	161±23/102±19	130±18*/78±12*
''No Phone Calls'' (n = 127)	162±23/102±19	132±20*/79±15*
''Phone Calls'' (n = 48)	163±25/103±22	127±18*/75±11*

Data are shown as mean±s.d.; *p< 0.00001 – Randomization Visit versus Final Visit.

Table 3 - Percentage of patients with controlled blood pressure at the beginning (randomization visit), at the next-to-last visit (visit 7) and at the end (visit 8-final) of the 12-month treatment period.

Group	Randomization Visit	Visit 7	Final Visit
''Uncomplicated''	0*/0**	90*/31	80/30
''Complicated''	16/6	66/31	67/28
''Traditional'' Treatment	8/3	75/32	73/31
''Current'' Treatment	11/3	81/30	74/27
''Phone Calls''	8/3	84/32	80/33
''No Phone Calls''	8/3	75/30	71/27
Total	8/3	78/31	74/29

Controlled blood pressure: < 140/90 mmHg/120/80 mmHg.
p >0.05, except:
- *Uncomplicated versus complicated: Randomization visit - χ^2_1 = 28.94; p<0.000001 (SBP<140/DBP<90)
- **Uncomplicated versus complicated: Randomization visit - χ^2_1 = 8.55; p = 0.0035 (SBP<120/DBP<80)
- Uncomplicated versus complicated: Visit 7 - χ^2_1 = 28.84; p<0.000001 (SBP<140/DBP<90)

The percentage of patients with controlled blood pressure (<140/90 mmHg) was also high at the end of treatment (74%). On the other hand, the percentage of patients with blood pressure reduced to <120/80 mmHg was only 29%. There was no difference in the percentage of patients with controlled blood pressure between the ''phone calls'' and ''no phone calls'' groups or in the reduction of blood pressure and the percentage of patients with controlled blood pressure among the ''traditional'' and ''current'' treatments. However, patients in the ''phone calls'' group (80%) had better blood pressure control than those in the ''no phone calls'' group (71%), though the difference was not statistically significant. The ''uncomplicated'' and ''complicated'' groups had statistically significant differences in the percentage of patients with controlled blood pressure (<140/90 mmHg) (80% vs. 67%, respectively; p<0.000001). At the next to last study visit (visit 7), 90%

and 66% of patients had blood pressure measurements <140/90 mmHg in the ''uncomplicated'' and ''complicated'' groups, respectively. However, there was no difference in the percentage of patients with blood pressure <120/80 mmHg (31% on the final visit in both groups, Table 3).

Among patients with a blood pressure <140/90 mmHg at the final visit, only 3% had received only one type of antihypertensive medication; most patients (56%) received 2 (34%) or 3 (22%) types of antihypertensive medication (Table 4).

b) Treatment Discontinuation

A significantly lower number of patients in the ''phone calls'' group quit the treatment compared to the ''no phone
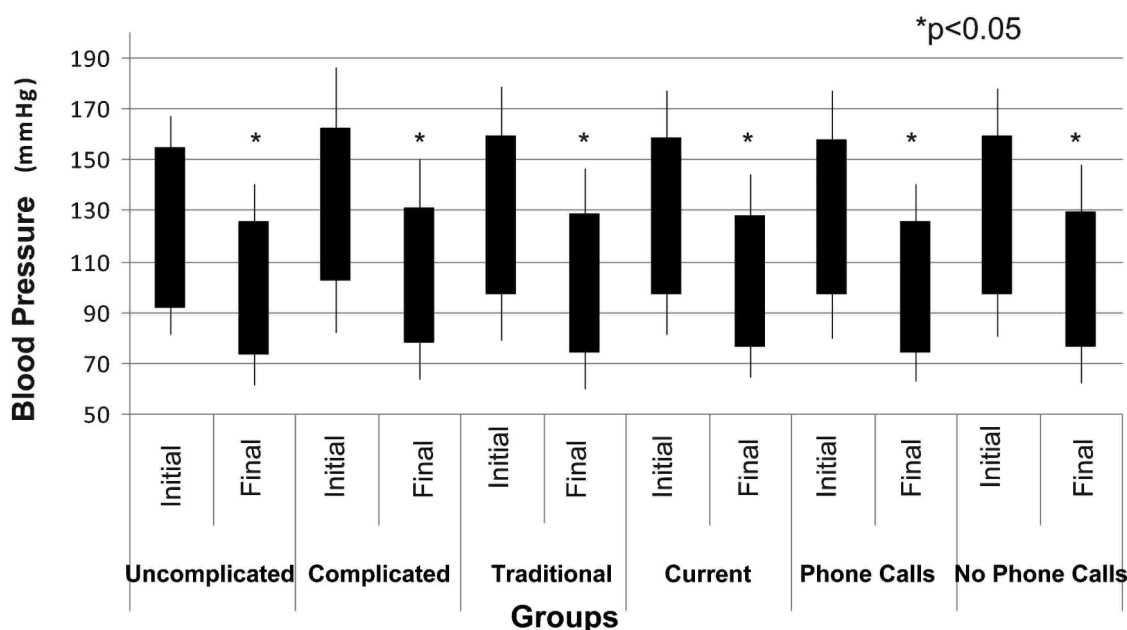
Figure 1 - IASH 2009 How to avoid discontinuation of antihypertensive treatment: the experience in São Paulo, Brazil.

Table 4 - Number of antihypertensive medications in use at the end of the study in patients who achieved control (<140/90 mmHg) of their blood pressure at the end of the 12-month study.

Number of Antihypertensive Medications	Blood Pressure <140/90 mmHg	Blood Pressure >140/90 mmHg	Total
01	3.2%	1.0%	4.2%
02	34.4%	5.0%	39.4%
03	21.9%	6.8%	28.7%
04	12.2%	6.8%	19.0%
05	3.9%	2.9%	6.8%
06	1.6%	0.3%	1.9%
Total	77.2%	22.8%	100%

Table 5 - Weight (kg) at the beginning and end of the treatment.

Group	Randomization Visit	Final Visit	P Value
"Uncomplicated"	72 $\pm$ 12	73 $\pm$ 13	0.39
"Complicated"	74 $\pm$ 15	76 $\pm$ 15	0.007
"Traditional" Treatment	74 $\pm$ 15	74 $\pm$ 15	0.09
"Current" Treatment	73 $\pm$ 13	74 $\pm$ 13	0.005
"Phone Calls"	74 $\pm$ 14	74 $\pm$ 15	0.13
"No Phone Calls"	73 $\pm$ 14	74 $\pm$ 14	0.018
Total	73 $\pm$ 14	74 $\pm$ 14	0.0008

Data are shown as mean $\pm$ s.d.

calls'' group (4 vs. 30, respectively; Figure 2). There was no difference in the percentage discontinuation in the ''complicated'' and ''uncomplicated'' groups or in the ''current'' and ''traditional'' treatment regimens (p>0.05).

c) Tablet Count

Patients in the groups: ''complicated'' and ''uncomplicated''; ''traditional'' and ''current''; ''phone calls'' and ''no phone calls'' did not show statistically significant differences in medication intake, as verified by counting the tablets returned at the visits. Compliance was over 85% at all visits. However, patients in the current + uncomplicated + phone call group had the highest rate of compliance (93%). The lowest rate of compliance occurred in the traditional + uncomplicated + no phone call group (85%) (p>0.05).

d) Body Weight

Blood pressure reductions occurred in the presence of increased body weight (baseline visit: 73 $\pm$ 14 kg; final visit: 74 $\pm$ 14 kg, p = 0.0008, Table 5).

e) Adverse Events and Laboratory Tests

Most of the adverse events that occurred during the study were of light or moderate intensity. Patients in the

''traditional'' group showed significantly more depression symptoms (5 vs. 0) and coughing (30 vs. 4) when compared with patients in the ''current'' treatment group. On the other hand, patients in the ''current'' group had a greater number of complaints of dizziness when compared to patients in the ''traditional'' treatment group (63 vs. 42, respectively).

Compared to patients in the ''uncomplicated'' group, patients in the ''complicated'' group presented a larger number the following symptoms: abdominal pain (19 vs. 8), sleepiness (32 vs. 10), cough (23 vs. 11), weakness (23 vs. 11) and blurred vision (6 vs. 0). Conversely, compared to patients in the ''complicated'' group, patients in the ''uncomplicated'' group presented a larger number of complaints such as pain (74 vs. 53) and headache (80 vs. 59). Patients in the ''phone calls'' group reported a 34% rate of symptoms, while a 66% rate of symptoms was reported by patients in the ''no phone calls'' group. The most frequently (>10%) found adverse events were as follows: headache (62.1%), unspecific pain (58.2%), dizziness (45.8%), edema (40.1%), fatigue (15.3%), sleepiness (14.4%), cough (13.3%), precordial pain (13.3%), weakness (11.9%), tachycardia (11.3%), insomnia (10.5%) and paresthesia (10.5%). There were 26 (8%) severe adverse events: death (5), unstable angina (4), acute myocardial infarction (1), transient ischemic attack (1), hypertensive encephalopathy (1), breast cancer (3), bronchospastic crisis (1), cholecysto-

Cumulative Proportion Surviving (Kaplan-Meier)
○ Discontinued the study   Others
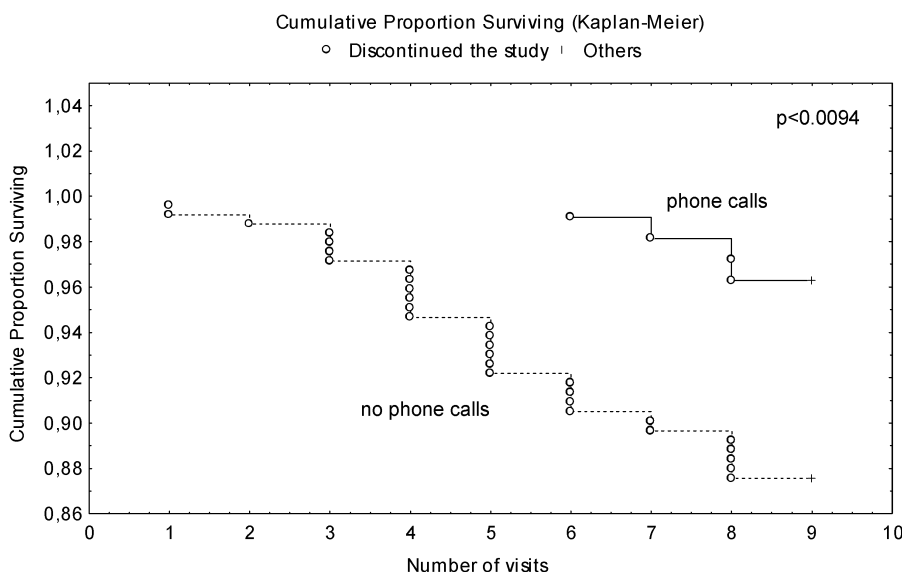
Figure 2 - Discontinuation of antihypertensive treatment.

pathy (1), diabetic decompensation (1), syncope (1), nephrectomy (2), trauma (2), peritoneal bypass (1), diarrhea (1) and gastrectomy (1).

The results of the laboratory tests performed in the beginning and end of the study are shown in Table 6. There was an increase in the 24-hour urinary sodium excretion from the beginning to the end of the study (120 ± 46 vs. 129 ± 45 mEq/L, respectively; p = 0.000036)

DISCUSSION

Adherence to a medication regimen is generally defined as the extent to which patients take medications as prescribed by their health care providers.[20] This can be classified into three aspects of the individual's behavior regarding his/her health: 1) take the medication correctly, 2) follow the professionals' instructions related to diets and lifestyle changes and 3) attend medical visits.[21]

The discontinuation of medication is considered the most serious type of noncompliance with treatment. In our study, the ''phone calls'' group showed a significantly lower percentage of patients who discontinued treatment compared with the ''no phone calls'' group. A meta-analysis of randomized studies[22] suggested that treatment discontinuation is effectively avoided by contacting the patient using letters, telephone calls or e-mails. Márques Contreras et al.[6] evaluated the efficacy of telephone and e-mail intervention for therapeutic compliance among 538 patients with mild to moderate hypertension and verified that the group that received phone calls showed higher compliance rates (96.2%) than the group that was only contacted by e-mail (91.3%) or the group that did not receive any intervention (69.2%). Similar data were found in a controlled study recently conducted by Bosworth et al.[7] in which the self-reported medication adherence was shown to increase by 9% in the group that had received behavioral and educational intervention (319 hypertensive subjects) through telephone calls versus 1% in the group that had not received intervention (n = 317).

Friedman et al.[23], through telephone calls associated with usual medical care for six months, compared hypertensive patients who received their usual medical treatment with those who used a monitoring and counseling system. Participants with compliance below 80% of the prescribed medication prior to enrollment in the study showed better compliance with the treatment when the telephone monitoring system was used than did patients who did not use the system (36% vs. 26%, respectively). On the other hand, participants with a compliance level above 80% prior to enrollment in the study did not show any change in compliance, and compliance was comparable in users and non-users of the telephone monitoring system.

In our study, regardless of the group to which they were randomized, patients showed compliance rates above 85% at all visits. However, we do not have data regarding medication compliance before enrollment in the study.

It is important to point out that treatment compliance is directly related to mortality. A study conducted by Wu et al.[9] randomized 442 non-compliant patients who took five or more medications for chronic illnesses to either receive or not receive telephone counseling. The objective was to investigate the influence of this advice for treatment compliance and patient mortality. The study verified that telephone counseling was associated with a 41% reduction of death risk after two years. These authors used scores to classify the levels of compliance of 1011 patients, and they showed that the lower the level of compliance, the higher the risk of mortality in the long term.

The influence of the initial selection of antihypertensive medication in regards to compliance with treatment was evaluated by Monane et al.[24] The authors verified that the use of newer antihypertensive agents, such as angiotensin converting enzyme inhibitors and calcium channel antagonists, was associated with a compliance $\geq 80\%$ when compared with thiazide diuretics in patients with cardiac morbidities and multiple visits to physicians. This may have been the result of better tolerability to newer classes of antihypertensive agents. However, in our study, there was no difference in tolerability between the ''traditional'' and ''current'' groups, which could explain the similar compliance rates in both groups. On the other hand, just like in Monane et al.[24] we found that fewer patients in the ''complicated'' group had their blood pressure under control in the final visit (67%), whereas in the next to last study visit, 90% of patients in the ''uncomplicated'' group and only 66% in the ''complicated'' group had blood pressure levels below 140/90 mmHg. This may be due to comorbidities and the use of other concurrent treatments.

The groups: ''complicated'' and ''uncomplicated''; ''traditional'' and ''current''; ''phone calls'' and ''no phone

Table 6 - Results of laboratory tests measured at the beginning and end of the study.

	Initial	Final	Test value	P value
Fasting Glucose (mg/dL)	108 ± 41	111 ± 41	1.82	>0.05
Urea (mg/dL)	32 ± 10	34 ± 16	3.83	= 0.00015
Creatinine (mg/dl)	0.9 ± 0.3	1.0 ± 0.4	5.52	<0.000001
Total Cholesterol (mg/dL)	199 ± 44	190 ± 38	5.07	= 0.000001
HDL Cholesterol (mg/dL)	49 ± 13	48 ± 14	1.19	>0.05
Triglycerides (mg/dL)	147 ± 123	152 ± 218	0.61	>0.05
Uric Acid (mg/dL)	5.1 ± 1.5	5.3 ± 1.8	3.90	= 0.00011
Sodium (mEq/L)	140 ± 3.2	139 ± 2.7	7.34	<0.000001
Potassium (mEq/L)	4.2 ± 0.5	4.2 ± 0.4	1.21	>0.05
Hemoglobin (g/dL)	14.4 ± 1.4	14.2 ± 1.3	4.73	= 0.000003
Alkaline Phosphatase (U/L)	79.7 ± 25.3	75.1 ± 22.7	5.29	<0.000001
ALT (U/L)	23.5 ± 10.6	26.6 ± 51.0	1.15	>0.05
AST (U/L)	24.4 ± 15.9	30.2 ± 92.5	1.18	>0.05
Sodium Urinary Excretion in 24 h (mEq/L)	119.6 ± 45.6	128.8 ± 45.3	12.81	= 0.000036

Data are shown as mean$\pm$s.d.

calls''showed significant reductions in blood pressure from the randomization visit to the final visit, as a high percentage of patients with good blood pressure control (BP <140/90 mmHg) in the total group (74%), regardless of an increase in body weight throughout the study.

In our study, the high percentage patients with controlled blood pressure at the end of treatment can be explained by the simple drug regimen, the simple drug acquisition provided by the physician at no cost at the end of each visit, a fixed team of physicians and nurses throughout the study period and the easy access to team members in cases of unexpected occurrences by means of unscheduled visits.

We observed that in the next-to-last study visit, the ''uncomplicated'', ''current'', ''traditional'', ''phone calls'' and ''no phone calls'' groups had more patients with controlled blood pressure when compared to the last visit. It is possible that during the last visit the patients were worried about continuing the treatment and receiving the medications.

Therefore, guidance provided to patients by means of active telephone calls, brochures and group workshops with healthcare professionals is an efficient strategy for reducing treatment discontinuation, the most severe type of non-compliance with treatment.

Perspectives

In an attempt to reduce non-adherence to antihypertensive treatment determinants in a developing country, we demonstrated that better blood pressure control was obtained through doctor's visits every two months with the same physician preceded by nursing staff visits with patients receiving all medication necessary for their treatment; this benefit was independent of comorbidities and the type of treatment used. Guidance provided to the patients through active telephone calls, brochures, group workshops with healthcare professionals and donation of all the required medications significantly reduced the treatment discontinuation rates.

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