

IMPACT IN THE REDUCTION OF COMPLICATIONS THROUGH A PERSONALIZED FOLLOW-UP STRATEGY TO ENSURE ADHERENCE TO ANTIHYPERTENSIVE THERAPY

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Abstract - The lack in continuity of antihypertensive treatment is one of the major common causes of uncontrolled high blood pressure and increased of adverse effects and medical costs associated to this disease. The current study aimed to investigate the relationship between a personalized strategy that guarantees the adherence to antihypertensive treatment and complications related to hypertension. To do so, 586 patients hypertensive patients attending primary care institutions in La Plata Argentina, were randomly assigned either to an intervention group that had regular and periodically follow up contact to check treatment adherence or to control group. Both groups received free of charge antihypertensive medicines. The adherence was assessed with the adherence evaluation scale of Girerd. The presence of complications of hypertension disease (stroke, angina pectoris, myocardial infarct, transient ischemic attack, heart failure, kidney failure, retinopathy and death associated to this disease) were checked monthly. Among the 293 patients included in the intervention group study 98.63 % (289/293) were adherents while only 49.14% (144/293) of the control group had continuity in the therapy. Comparing complications events developed by patients belonging to Intervention vs Control group after 24 month of follow up were for overall events 19.79% vs 27.98% (p<0.001), for stroke 0.34/1.02% (pNS); angina pectoris 4.09/6.48% (p 0.004), 0.68/1.02 (pNS), TIA 0/0.34% (p NS), heart failure 4.77 /7.16% (p0.003), while hospitalization associate to primary hypertension disease was 16.04/30.3% (p<0.001) respectively. We can conclude that a personalized strategy to guarantee hypertension treatment adherence reduce the hospitalization and several complication associated to this disease.

Keywords - Adherence, Hypertension, Treatment, Complications.

I. INTRODUCTION

High blood pressure is one of the most prevalent chronic diseases in the world that affects millions of people regardless of their race, ethnicity, or educational level.

Compared to developed countries, in low-to-middle-income countries, the incidence of arterial hypertension (AHT) is increased, and awareness, control of the disease and adherence to treatment are at low levels.

In Argentina, there is a prevalence of 39.8% of which has evidence that only 28% are treated and of these only between 7 to 43 % achieve the goal. When a AHT is not controlled, there is a high risk of multiple cardiovascular complications that worsen the prognosis and quality of life of the patient [1].

Among these complications are listed several events like stroke, myocardial infarcts, TIA, coronary disease, heart or renal failure, neuropathy, including mortality associated to this disease [2].

Several researches demonstrated that properly blood pressure control reduce the incidence of stroke, acute coronary syndrome, myocardial infarction, congestive heart failure, and cardiovascular death [3]. Since AHT therapy results essential to avoid these complications; adherence to AHT treatment requires efficient strategies to guarantee a proper antihypertensive regimen to control related undesirable events [4,5]. Adherence to treatment is better in patients with AHT compared to other chronic diseases. Good compliance with antihypertensive therapy is a multifactorial

process influenced by environmental factors, as well as the type of treatment (including dosing regimen), concomitant medications, clinical status, presence of co-morbidities, cost of treatment, and the doctor-patient relationship [6].

In order to demonstrate if a personalized strategy to improve AHT therapy adherence, and if this treatment compliance is associate in a reduction of high blood pressure complications, we initiated the present study.

II. MATERIALS AND METHODS

A. Type of Study

This is a Randomized Clinical Trial where

B. Universe and sample selection

The universe of population studied was all patient affected by arterial hypertension that attend the first level of the health system of La Plata, Argentina. A random sample of that universe was enrolled to be included in this study. For patient selection, the following formula was used to calculate the proportion of finite population to be included in the study:

$$n = \frac{NZ^2PQ}{d^2(N-1) + Z^2PQ}$$

where n is the size of the sample, N the total population, Z the value of z for the confidence level (1-alpha), p the expected proportion of complications associated with hypertension in the population and d absolute precision. A minimum of 500 people (250 per

group) to obtain data that were statistically significant (the incorporation of individuals to the two study groups exceeded the minimum mentioned). Including criteria was patients older than 18 years old, with uncomplicated blood hypertension and with classical treatment in course free of charge offered by the State (enalapril, losartan, amlodipine, hydrochlorothiazide, atenolol alone as monotherapy or in combination). Exclusion criteria were all patient with a history of complications due to arterial hypertension or with severe AHT that required other treatment than the one mentioned.

C. Groups of Study

After we identified potentially eligible patients from the medical record system and drug provision list, we proceed to a random stratify selection of patients in two groups (Control and Intervention groups). Randomization process was performed using a table of random number. Patients included in the project received an information package, information about the study, and an informed consent form. Patients belonging to Control group (CG) were observed in the usual medical care process by their primary healthcare (PHC) provider or their own GP. Treatments were carried out with free drugs obtained on request either in the PHC service (REMIAR or REMIAR-CUS Program). On the other hand, Intervention group (IG) was submitted to the intervention strategy designed for this study that is a personalized follow up of patients with a weekly contact (either physically, e-mail or by phone message contact) in order to remind the importance of treatment accomplishment and to check that adherence to the medication given by the same programs mentioned in control group.

D. Period of Study: Between 1st January 2016 to 31st December 2018.

E. **Variables of Study:** age, gender, weight, height, drug treatment, treatment adherence -measure by MAQ survey, access to health service, number of medical consultation, hospital admission, inpatient days, smoking status, basal cholesterol levels, diastolic and systolic blood pressure, neuronal, renal or cardiovascular complications events that demand consultation or hospital admission during the study period. All variables were measured in both groups.

F. **Endpoints:** Primary end point was treatment adherence; and Secondary end points were complications associated to diabetes disease.

G. **Statistical analysis:** We used descriptive statistics to summarize personal and clinical data. The impact of the intervention was tested in the continuity of treatment and in reduction of complication associate to AHT. We present regression coefficients, indicating the mean difference between the intervention and control group after adjusting for baseline variables.

III. RESULTS

Five hundred and eighty six patients were enrolled in the study. Two hundred and ninety were assigned to each group. General baseline data for both groups demonstrated non significant differences in the main variables to be study (Table 1). Baseline systolic blood pressure level was 143.52 ± 22.12 and 142.94 ± 19.24 and diastolic blood pressure was 90.14 ± 8.41 and 89.87 ± 7.95 for IG and CG respectively (table1).

Group	n	Age	Male/ Female (%)	SBP	DBP	Smoke habit (%)	Diabetes (% - n)	Years of Hypertension since diagnose
IG	293	60.72	46.41 /53.59	143.52	90.14	19.11 /80.89	4.09% (n12)	7.64
CG	293	61.04	45.39 /54.61	142.94	89.87	21.16 /78.84	4.77% (n14)	7.05

IG: Intervention Group; CG: Control Group; n: number of patients enrolled in the group of study; SBP: basal systolic blood pressure; DBP: diastolic blood pressure

Table 1. Patients basal data

IG: Intervention Group; CG: Control Group; n: number of patients enrolled in the group of study; SBP: basal systolic blood pressure; DBP: diastolic blood pressure

Patients were treated with free medication offered by the State government (REMIAR/REMIAR-CUS program). 61.43% of the patients received monotherapy as AHT medication (table2).

Group	Monotherapy (% - n)	ACEI (% - n)	ARB (% - n)	Thiazide (% - n)	CCB (% - n)	Beta Blockers (% - n)
IG	60.75 /178	27.98 /82	17.40 /51	3.07 /9	7.85 /23	3.75 /11
CG	62.11 /182	26.62 /78	16.72 /49	3.41 /10	8.87 /26	5.80 /17

IG: Intervention Group; CG: Control Group; n: number of patients enrolled in the group of study; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; (as monotherapy)

Table 2. Patients Treatment data

The percentage of treatment adherence was 98.63% for Intervention Group and 49.14 % for Control Group. Hospitalization for any cause associated to AHT was 16.04% and 30.03% ($p < 0.001$) for Intervention and Control group respectively. Complications data due to high blood pressure detected during 24 months of follow up period are available in the next table (table 3):

G	Overall (% - n)	Stroke (% - n)	Angina Pectoris (% - n)	MI (% - n)	TIA (% - n)	Heart failure (% - n)	Kidney failure (% - n)	Retino pathy (% - n)	Neuro pathy (% - n)	Death (% - n)
IG	19.79 /58	0.34 /1	4.09/12	0.68 /2	0 (n0)	4.77 /14	2.73 /8	3.75 /11	3.41 /10	0
CG	27.98 /82	1.02 /3	6.48/19	1.02 /3	0.34 /1	7.16 /21	3.07 /9	4.77 /14	3.75 /11	0.34 /1

G: Group; IG: Intervention Group; CG: Control Group; n: number of patients enrolled in the group of study; MI: Myocardial Infarct; TIA: Transient ischemic attack;

Table 3. Complications registered during the study period

G: Group; IG: Intervention Group; CG: Control Group; n: number of patients enrolled in the group of study; MI: Myocardial Infarct; TIA: Transient ischemic attack;

IV. DISCUSSION

Recognizing that the study groups selected for this work have similar characteristics and the baseline parameters do not have significant differences, it is interesting to note that even though the medication is totally free and available in Institutions of the First Level of Care of the Health System, only one 49% of patients have compliance in the indicated treatments. This point was already observed by our group in previous works [7]. That is to say that it is not enough simply to make available the free medication to guarantee therapeutic adherence.

Many factors may influence the adherence to antihypertensive therapy and they are correlated with: gender, race, marital status, age, educational attainment, socioeconomic, and cultural level [8-10]. In our work, the periodical contact with the patient was enough to guarantee almost a complete antihypertensive treatment adherence (98.63 %). This method is easy a cheap, and provides excellent results in terms of avoiding the consequences associated with uncontrolled hypertensive disease.

Because hypertension has no symptoms, it is common that people by this disease do not perceive the severity of the consequences of uncontrolled blood pressure levels.

Previous studies carried out by our team, showed that in chronic diseases, the perception and demand for care is low, and that only programs that contact patients in their homes are more successful in avoiding the events associated with these diseases [11, 12]. It is also worth to mention that in terms of pharmacological management, there were more than 60% of patients with monotherapy and that the most of them used ACEI and ARA 2 as first option drugs, reaching up to 45% between both options. Noteworthy, there was a low indication of thiazide diuretics as a main therapeutic option when it is well recognized that is one of the best therapeutic choice for the control of hypertension, especially in elderly population [13, 14].

Finally, it is essential to emphasize that the adherence to pharmacological treatment has achieved two years of follow-up, halving the need for hospitalizations, and 10% the cardiovascular complications associated with hypertension.

V. CONCLUSION

A strategy of personalized and periodical contact to

patients with high blood pressure by the health service was able to increased treatment adherence when compared with classical follow up based on patient's spontaneous contact with the health system (98.63% vs 49.14 %). This strategy was also able to reduce Hospitalization (16.04% vs 30.03% $p<0.001$) and complications due to hypertensive disease (19.7 vs 27.9 % - $p<0.001$).

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