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Research Article

Non-adherence to Drug Therapy for Hypertension is Critical and Underestimated in Mexican Patients: A Study from the First Contact Level

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Summary

Adherence, in a healthcare context, refers to the extent to which a person's behavior aligns with recommendations from a healthcare provider. This can involve taking medication as prescribed, following a specific diet, or adhering to lifestyle changes. Although it is known that adherence is critical and requires a special approach to health, in Mexico, there are few studies on this issue. We confirm the information collected from 786 patients using an original questionnaire (AFEC) in Spanish, previously validated. Perfect adherence was detected in only 179 (22.8%), good adherence in 334 (42.5%), and nonadherence in 452 (57.5%). The age, obesity, and number of comorbidities were significantly associated with non-adherence ($p < 0.05$). Special strategies to approach this critical problem in health need to be reconsidered in Mexico. Non-adherence may help explain the low control rate of Mexican patients and the high rate of cardiovascular mortality.

More Information

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Keywords: Hypertension; Adherence; Control rate; Mexico

Introduction

Hypertension is a contributing factor to premature death in Mexico and worldwide. Its overall prevalence is estimated at 30% ± 10 in subjects aged 20 years or older. In Mexico, the prevalence has been maintained for two decades (30%); however, the current population is ~ 130 million, therefore, in absolute numbers, the hypertensive population has grown very significantly [1-3].

In the context of healthcare, adherence is the degree to which a person's actions follow advice from a medical professional. This may entail taking prescription drugs as directed, adhering to dietary restrictions, or changing one's lifestyle [4].

The hypertension control rate remains inadmissibly low. In Mexico, control rates vary widely and may depend on many factors, including the type of social security, economy, adherence, and therapeutic inertia. In 2008, only 10.7% of all hypertensive patients had their blood pressure under control; currently, it ranges between 20 and 60%. (~36.1%) [5].

Optimal adherence to antihypertensive medication is essential for effective hypertension management and reducing the risk of premature cardiovascular death [5,6]. Despite the importance of therapeutic adherence in hypertension, the nonadherence rate is estimated to remain high. Few studies have been directed at this aspect in Mexico. Among the factors recognized as influential for optimal adherence are those described by the WHO as 5 dimensions: the first is about the health system itself, such as temperature, supply of medicines and quality of services; the second is concerning the patient, their age, gender, level of education, socioeconomic status, knowledge and perception of their disease; The third is related to the disease itself, its severity and the medical condition, situations that can greatly limit the patient. The fourth are the

factors related to the treatment itself, that is, its complexity, cost, and availability; and, fifthly, social aspects, ethnicity, family support, and lifestyles. To determine the degree of therapeutic adherence among patients treated for arterial hypertension in primary care units, a survey was carried out using the AFEC questionnaire [6].

Patients and methods

A total of 800 patients with hypertension under pharmacological treatment were included, and a therapeutic adherence questionnaire was applied. All patients come from government institutions where the drugs have no cost to the patient. AFEC is a Spanish adherence questionnaire, adapted and validated from traditional English versions (Table 1). It consists of 7 directed questions whose answer is negative or affirmative. Each question is worth one point if it has a negative answer, so that total or perfect adherence is given when 7 points are obtained, good adherence if > 5 points are obtained, and non-adherence if 5 or fewer points are obtained. To compare groups, adherence was defined as 6 or 7 points obtained and non-adherence if < 6 points were obtained. In addition, the type of treatment (monotherapy, dual, triple, or more) was questioned, as well as whether it was in a single pill combination (SPC) or separate. The presence of comorbidities such as diabetes, obesity, and dyslipidemia was also recorded (Table 2).

Statistical analysis

Descriptive and inferential statistical analysis was applied according to the number of groups to be compared and types of variables (quantitative or qualitative), with parametric or non-parametric tests depending on their distribution. A logistic regression model was applied to determine the variables associated with non-adherence in this study. A p - value ≤ 0.05 was considered significant [7].

Results

A total of 800 patients from 18 states of the Mexican

Table 1: AFEC Test (Spanish), to measure Adherence in hypertensive treatment.

#	Question	Answers
1	¿En el último mes olvidó tomar sus medicamentos para la Presión Arterial?	Sí = 0 No = 1
2	¿Le ha ocurrido alguna vez sentir que el medicamento le produjo malestar y por ello lo ha tenido que suspender?	Sí = 0 No = 1
3	¿A usted se le ha olvidado tomar el medicamento para su Presión en el último día?	Sí = 0 No = 1
4	¿A usted le fastidia tomar muchos medicamentos?	Sí = 0 No = 1
5	¿Cuándo sale de casa o viaja, a veces se le olvida llevar sus medicamentos para la presión?	Sí = 0 No = 1
6	¿Tomar varios medicamentos lo confunde y cuando duda, prefiere no tomarlo?	Sí = 0 No = 1
7	¿Le cuesta trabajo con frecuencia recordar si ya se tomó la pastilla de la presión?	Sí = 0 No = 1

7 points – Perfect adherence; More than 5 points – Good adherence; 5 points or less – Non-adherence

Table 2: General Characteristics of the Study Population on Adherence to Drug Therapy for Hypertension in Mexico (N = 786 Patients).

Variables	N (%) N = 786	Adherence Group N = 334	Nonadherence Group N = 452	p - Value
Adherence Scale (AFEC)				
Total (7 points)	179 (22.8)	----	----	
Good Adherence (6/7 points)	334 (42.5)	----	----	
Nonadherence (≤ 5 points)	452 (57.5)	----	----	
Age Group				
20–40 years old	60 (7.6)	21 (06.3)	39 (08.6)	0.05
41–60 years old	243 (30.9)	117 (35.0)	126 (27.4)	0.056
61–80 years old	349 (44.4)	164 (49.1)	185 (40.9)	0.053
>80 years old	134 (17.0)	32 (09.6)	102 (22.6)	0.004
Gender				
Female	463 (58.9)	200 (59.9)	263 (58.2)	0.07
Male	323 (41.1)	134 (40.1)	189 (41.8)	0.08
Diabetes Type 2	364 (46.9)	144 (43.1)	220 (48.7)	0.07
Obesity	445 (56.6)	163 (48.8)	282 (62.4)	0.001
Dyslipidemia	365 (46.4)	140 (41.9)	225 (49.8)	0.03
Drug Therapy				
Monotherapy	352 (44.7)	162 (48.5)	190 (42.0)	0.07
Dual Therapy	274 (34.9)	118 (35.3)	156 (34.5)	0.11
Triple Therapy	160 (20.4)	106 (23.5)	54 (16.2)	0.03

Adherence Scale Used: AFEC. 7 points = Total adherence; 6 or 7 points = Good adherence; ≤ 5 points = Nonadherence. The comparison between good adherence (6/7 points) *vs.* nonadherence (≤ 5 points) is shown under the columns.

Republic were included, all of them from the first level of medical care. 14 patients were eliminated due to incomplete data. There were 463 (58.9%) females and 323 (41.1%) males, 60 (7.6%) patients belonged to 20-40 age group; 243 (30.9%) to 41-60 y.o.; 349 (44.4%) to 61-80; and, 134 (170.0%) to ≥ 80 y.o. 117 patients had hypertension history of less than one year, and 669 had at least 3 years of hypertension diagnosis. Demographic details of the study participants and comparisons between adherent *vs.* non-adherent are described in Table 2.

Comorbidities were highly prevalent. 369 (46.9%) had diabetes; 445 (56.6%) had obesity; and 365 (46.4%) had dyslipidemia.

Regimen screen

In the present study, 179 (22.8%) patients were perfectly adherent to their antihypertensive treatment (7 points of AFEC test). Good adherence, defined as 6 or 7 points, was detected in 334/786 patients (42.5%), and 452/486 (57.5%) of the participants were not taking antihypertensive medications as prescribed (non-adherence). This might contribute to inadequate blood pressure control. Very poor adherence was defined with ≤ 4 points; thus, 310 (39.4%) patients obtained that score.

There was a significant ($p < 0.001$) association between hypertension control status (69%) and adherence in the study participants. Patients with poor adherence were most likely to be out of control (Odds Ratio 6.18; 95% CI of 2.70 - 11.19). The most frequent question related to non-adherence was "Do you mind taking a lot of medicines?" There were 444(56.5%). This is very important because 76% of patients had at least one associated comorbidity, which implies taking a greater number of drugs.

Access barrier

It is important to mention that the patients come from a government institution where the drugs have no cost to the patient. Access barrier was reported by 22.57% of patients, of which 78.62% of patients reported that it is difficult to find medication from time to time, as the pharmacy sometimes doesn't on enough medication. The consequence is that the physician has to temporarily change it to similar drugs and then back to the previously prescribed treatment.

Number of anti-hypertensive drugs

The clinicians ($n = 114$) were asked about the number of antihypertensive drugs that the patients were taking at the time of the AFEC survey. There were 352 (44.7%) patients who were on monotherapy, 274 (34.9%) were on dual therapy, and 160 (30.4%) triple therapy. There was an association between the number of drugs and adherence. However, patients who were taking a single combined pill performed better in taking medications than when they were treated separately. Thus, 87 (48.6%) with monotherapy had adherence versus 265 (43.6%) with monotherapy and nonadherence ($p = 0.10$). From patients with adherence ($n = 179$), 36.3% had dual therapy, while in the non-adherence group ($n = 607$), 34.4% had non-adherence ($p = 0.11$). Nevertheless, those patients taking triple therapy in a single tablet (mostly perindopril + amlodipine + indapamide) had the highest adherence rate, 106/160 (66.25%) (Table 2).

Age groups

Age was categorized by every 20 years from 20 years of age. It was observed that at extreme groups (20 - 40 y.o. and > 80 y.o.) the non-adherence rate doubles ($p < 0.004$). While in the 61-80 y.o. Group, it is similar to around 46% (Figure 1).

Regression analysis

Logistic regression analysis showed that the gender was not associated to non-adherence (Odds Ratio 0.82, 95% CI of 0.57 - 1.12) unlike groups of comorbidities (diabetes, obesity, dislipidemia) where in the bivariate model almost all reach significance, nevertheless in the stepwise regression model only obesity remained as the most significant (Odds ratio 1.52, 95% CI of 1.08 - 2.12) (Figure 2).

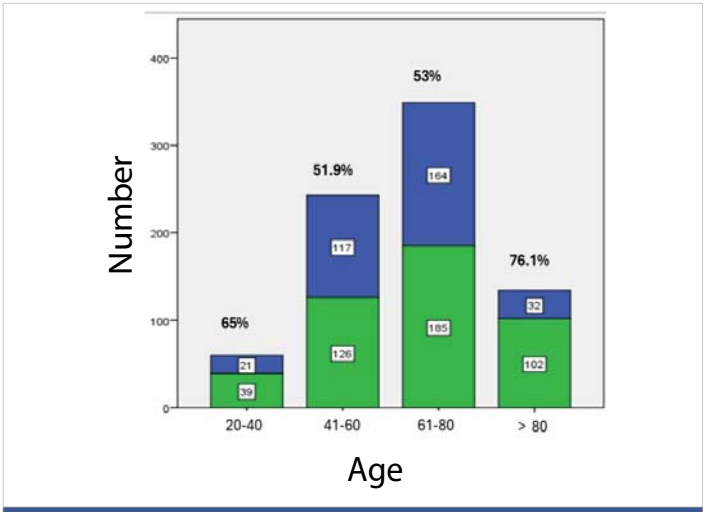

Figure 1: Rate of nonadherence by group of age group (N = 786). The extreme groups of age groups were associated with non-adherence ($p < 0.05$).

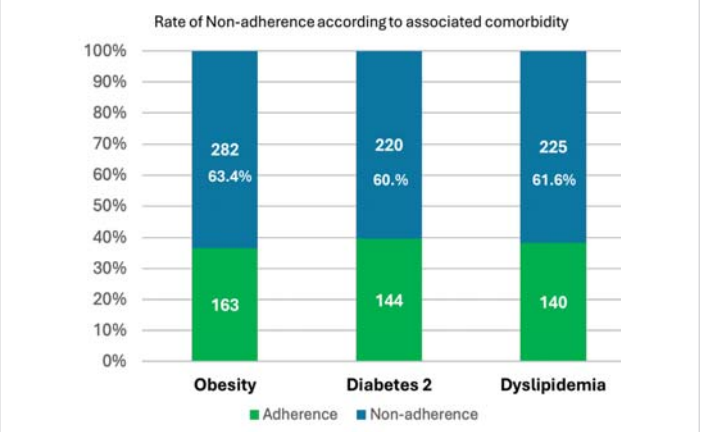

Figure 2: Rate of non-adherence by associated comorbidity.

Obesity remained the most significant variable even when incorporated into the stepwise logistic regression model, including age groups, sex, and type of treatment (single, dual, or triple). There was no significant difference in the number of antihypertensive medications or total medications being prescribed between adherent and non-adherent patients. Chi square analysis (p = 0.131) showed no association between the adherence pattern and the number of antihypertensive medications being prescribed. However, a single pill in dual or triple drug therapy was used in only 48% of patients. Most patients with triple therapy reached good adherence, most of them were taking perindopril, amlodipine, and indapamide in SPC Figure 3.

The odds ratio of having nonadherence according to selected comorbidities is shown in Table 3. A multiple logistic regression model allowed the estimation of the probability of having nonadherence according to the presence or absence of selected comorbidities Table 4.

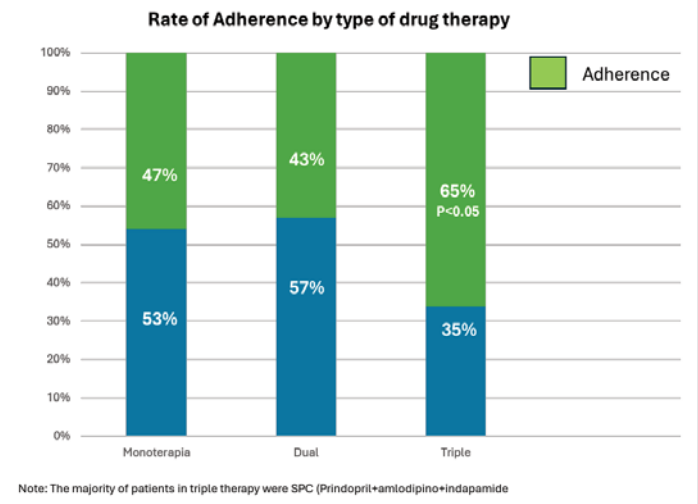

Figure 3: Adherence (green bar) rate according to the type of drug therapy.

Table 3: Odds Ratios of included comorbidities related to nonadherence in hypertensive patients (N = 786).

Variable	(OR)	95% (CI)
Obesity	1.52	(1.08 – 2.21)
DM2	1.37	(0.98 – 1.93)
DLP	1.38	(0.98 – 1.94)

OR: Odds Ratio; CI: Confidence Interval; DM2: Type 2 Diabetes; DLP: Dyslipidemia

Table 4: Probability of Nonadherence Based on Predictive Variables*

Predictive Variables			Probability
DM2	(OBS)	(DLP)	
Present	Present	Present	66%
Present	Present	Absent	52%
Present	Absent	Present	40%
Absent	Present	Absent	39%
Absent	Present	Present	38%
Absent	Absent	Present	38%
Present	Absent	Absent	37%
Absent	Absent	Absent	35%

Estimated probability of event = 1/(1 + e - (0.895+ 0.171(DM2) + 0.306(OBS)+ 0.194 (DLP); DM2, type 2 diabetes. OBS: Obesity; DLP: Dyslipidemia.

Discussion

The rate of blood pressure control depends on several factors [7-12]. The most important is an early and timely diagnosis, non-pharmacological measures, and lifestyle changes, but also an adequate pharmacological approach. The latter is related to the level of cardiovascular risk, presence of damage to target organs, and response to drugs. However, much progress has been made in therapeutic strategy with drugs, with combined therapy, preferably in a single pill, being accepted as the best strategy. Thus, the first step suggested by the ESH and ESC guidelines is dual therapy, where a renin-angiotensin blocker plus a thiazide-type diuretic or a dihydropyridine calcium antagonist is considered [13,14]. If the goal is not achieved within 4 weeks, it should be escalated to triple therapy with a renin-angiotensin system blocker (ACE inhibitor or ARB2) + calcium antagonist + thiazide-type diuretic (indapamide or chlorthalidone). If the control goal is not achieved, it is considered "resistant" and should be escalated to the specialist [14,15].

In Mexico, the RIHTA study showed that most patients living with high blood pressure are associated with an average of 4 to 5 risk factors [16]. This places the population at intermediate to high risk for the most part. More than half of patients with hypertension have target organ damage, with kidney involvement being very important. For this reason, great efforts are being made to break the inertia and promote the use of dual and triple therapy, preferably in a single pill. Unfortunately, despite already having combined treatments in the health sector, the control rate is still far from optimal. The average control rate according to national surveys is around 40%. This figure varies depending on the geographical region and the availability of resources.

In the years ahead, adherence to medication taking is going to remain a major issue. The cost of medicines and the real possibility for non-adherence, coupled with increasing longevity, mark this area of research as one of major importance.

Multiple strategies have been published for the detection of non-adherence and strategies to reduce it [17-19]. However, countries such as the USA report non-adherence rates of 50% [20]. These figures are truly alarming because about half of the patients do not take their pharmacological treatment adequately.

Cardiovascular mortality is perhaps declining in developed countries, but rather increases in developing countries [20]. Despite the availability of new effective and well-tolerated drugs enabling to control of blood pressure effectively in almost 60% of patients, according to clinical trials, hypertension remains the number one risk factor for the development of stroke, coronary heart disease, congestive heart failure, and chronic kidney disease. New invasive techniques, such as renal denervation and carotid baroreflex stimulation, have

become available to lower blood pressure in patients with resistant hypertension in addition to common drug therapies. Unfortunately, these techniques are not available in all medical centers. But the most serious thing is that situations such as adherence and persistence continue to have a high prevalence.

In our study, age was associated with non-adherence, and the highest rates were for the age groups of 20-40 years. And those with more than 80 y.o. Uchmanowicz B, et al. [21] showed that the variables of age, education level, and living with the family were statistically significant in explaining the adherence rates. Therefore, health professionals should pay more attention to how the patient perceives his or her illness and educate him or her on the issue of adherence and persistence. Unfortunately, in our country, there is no generalized strategy on adherence; in addition, it is very little measured. After 60 y.o. People suffer from various diseases, and for all of them, they must take medications, which generate polypharmacy, and then the patient frequently forgets to take their pills. We found that the greater the number of factors, the greater the probability of not taking medications properly [22,23] However, we notably detected that the risk factor that is most associated with non-adherence is obesity. Other authors have studied non-adherence in patients with obesity and arterial hypertension. Furthermore, sympathetic-nervous and renin–angiotensin–aldosterone systems, overactivity, emotional and psychiatric aspects are prevalent and need to be studied in this kind of patient. This comprehensive strategy can provide a personalized algorithm for managing hypertension in obesity within the context of "precision medicine" principles.

The more linked comorbidities a patient has, the more drugs they need to take. The number of comorbidities and the probability of non-adherence are shown in Table 4.

Conclusion

Non-adherence to antihypertensive drugs in Mexico is very high (57.5%). A holistic approach is required, where patient participation must be active. The high rate of non-adherence is associated with the low control rate. It increases risks, and health resources are not used properly. The use of combination drugs in a single pill was shown to improve adherence. Triple therapy in a single pill was the best strategy. Adherence is not only an issue that concerns the patient; physicians and health systems must focus more on this problem. Continuous education strategies for patients and their families should be part of the universal health system.

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