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Prescription patterns of antihypertensives in a community health centre in Mexico City: a drug utilization study

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ABSTRACT

Hypertension is highly prevalent; in Mexico, the 2012 National Health and Nutrition Survey reported a prevalence of hypertension of 31.5% in the adult population. Pharmacological treatment is the commonest intervention and has been shown to reduce cardiovascular mortality and morbidity, and total mortality. Accordingly, the type and number of antihypertensives used and the outcome — in terms of blood pressure (BP) control — are important. Therefore, our purpose is to learn the pattern of antihypertensive drug prescription and explore the determinants of BP control in an urban population in Mexico. A retrospective cross-sectional drug utilization study was conducted. Medical records from a community health centre were searched to identify those corresponding to patients diagnosed with hypertension; information upon antihypertensives used and control of the disease was carefully retrieved. A logistic regression model was built to know the main determinants of BP control. A sample of 345 clinical records of interest was identified. Most patients received antihypertensives (86.4%); the leading medications used were angiotensin-converting enzyme inhibitors, 63.8%; beta-blockers (26.5%), diuretics (19.8%), angiotensin-receptor blockers (15.8%) and calcium-channel blockers (6.4%). Only the age (≥ 55 years) and BMI (> 30) of the patients, and the age of the doctors (≥ 55 years), had an important influence on BP control. Obesity is a particular and important determinant of uncontrolled hypertension; it is worth to act on body weight, on an individual basis. As lack of control has been also tied to elderly doctors, an education programme could be envisaged.

INTRODUCTION

Hypertension is a highly prevalent cardiovascular risk factor worldwide due to the increasing longevity and prevalence of contributing factors, such as obesity [1]; it accounts for premature death, stroke, heart and renal disease. Lifestyle changes should be the initial approach to hypertension management and these include dietary interventions, weight reduction, tobacco cessation, physical exercise and stress management; pharmacological treatment of hypertension is, however, the most common and evident intervention and has been consistently shown to reduce the relative risk of cardiovascular mortality and morbidity, and total mortality [2,3].

In a systematic review, it has been estimated that, overall, 26.4% of the adult population in 2000 had hypertension and 29.2% were projected to suffer from this condition by 2025 [4]. In Mexico, the 2012 National Health and Nutrition Survey (ENSANUT) reported a prevalence of hypertension of 31.5% in the adult population [5,6]; previous estimates, in elderly populations, were even higher [7]. These figures are at the top in the world [8].

According to the previous national surveys, this prevalence has markedly increased up to the year 2006 [9] and since then, it has reached a plateau. As the rationale of the treatment is to achieve target blood pressure levels, the type and number of antihypertensives used and the outcome, in terms of blood pressure control, are important. Therefore, our purpose is to learn the pattern of antihypertensive drug prescription, and to explore the determinants of blood pressure control in an urban population in Mexico.

METHODS

For the purpose, a retrospective cross-sectional drug utilization study has been conducted. Community health centre medical records corresponding to January 2012 to December 2014 were carefully searched to identify those records belonging to over-20-year-old patients diagnosed with hypertension; incomplete records and those corresponding to pregnant women were not included. This community centre (TIII Portales) covers a population of 77 752 inhabitants in Mexico City. All relevant information was retrieved with a common template; particular attention was paid to demographics data, lifestyle habits, comorbidities, blood pressure and medications in the last visit to the

doctor. Also a survey was conducted to medical doctors attending these patients.

Patients with controlled hypertension were considered those with systolic pressure equal or below 140 mmHg and diastolic pressure equal or below 90 mmHg [10].

Statistics

Most of the results are expressed in frequencies and percentages; the two-tailed chi-square test was used to analyse differences in proportions, and the *t*-test was used to compare the means of two age groups. The relationship between the number of patients by doctor and the percentage of controlled patients was explored by linear regression analysis; the analysis of variance (ANOVA) was the method to test for the significance of that regression. A logistic regression model was built to know the main determinants of blood pressure control, and the goodness of fit was assessed by the Hosmer–Lemeshow test.

RESULTS

From January 2012 to December 2014, a total of 400 records of interest were identified; after discarding those not fulfilling inclusion criteria, we selected 345 clinical records; most patients received antihypertensive medications (86.4%; $n = 298$). The main characteristics of this sample are presented in *Table I*. Mean age in women was higher than in men (62.2 ± 12.9 years vs. 58.9 ± 13.6 years; $P = 0.029$). A number of patients presented several comorbidities and, consistently, also received other medications; overall, 96.8% had whatever medication and 38% had four or more medications.

In those having antihypertensives ($n = 298$), the leading medications used were angiotensin-converting enzyme inhibitors (ACEIs); 63.78% of all patients received a drug from this class; ACEIs were followed by beta-blockers (26.5%), diuretics (19.8%), angiotensin-receptor blockers (ARBs) (15.8%) and calcium-channel blockers (6.4%); no other classes of antihypertensives were used. The most commonly used ACEI was enalapril (105 of 190 for this class). Women did not receive more antihypertensives than men ($X^2_4 = 3.290$; $P = 0.511$) nor did they receive a significantly different type of antihypertensives: ACEIs ($X^2 = 0.324$; $P = 0.569$), beta-blockers ($X^2 = 2.430$, $P = 0.119$), diuretics, ($X^2 = 0.390$; $P = 0.532$), ARBs, ($X^2 = 0.530$; $P = 0.467$) or calcium-channel blockers ($X^2 = 0.004$;

Table I Sample of hypertensive patients studied ($n = 345$). Main characteristics

	Frequency (%)
Age, mean in years (SD)	61.2 (13.2)
Sex	
Men	107 (31.0)
Women	238 (69.0)
Education	
Illiterate	36 (10.4)
Elementary	116 (33.6)
Junior high school	69 (20.0)
Technical school	29 (9.4)
High school	38 (11.0)
College	31 (9.0)
Missing	26 (7.5)
Marital status	
Single	101 (29.3)
Married	142 (41.2)
Widowed	56 (16.2)
Divorced	28 (8.1)
Missing	18 (5.2)
Occupation	
Homemaker	163 (47.2)
Active worker	129 (37.4)
Unemployed	21 (6.1)
Retired	8 (2.3)
Missing	18 (5.2)
Lifestyle	
Smoker	52 (15.1)
Heavy drinker	8 (2.3)
Comorbidities	
Obesity	92 (26.7)
Diabetes	85 (24.6)
Dyslipemia	50 (14.5)
Venous insufficiency	40 (11.6)

$P = 0.951$). Of those medicated ($n = 298$), 72.1% were in monotherapy, the rest receiving more than one antihypertensive medication (two antihypertensives, 23.2%; three, 4.0%; and four, 0.7%); women did not receive a different number in combination than men ($X^2_3=1.780$; $P = 0.619$). Patients older than 55 years did not receive a higher number of antihypertensives compared with younger ones ($X^2= 1.390$; $P = 0.708$).

As for hypertension control, we had data upon 281 patients who had antihypertensives; of those, 105 (37.4%) were considered as controlled (men, 40.4%; women, 35.9%); no differences by sex were found ($X^2=0.529$; $P = 0.467$). The number of patients who are seen by a single doctor does not correlate with the percentage of hypertension control ($F = 0.008$; $P = 0.931$), neither the type (*Table II*; $X^2_3=2.712$;

$P = 0.438$) nor the number of medications in combination ($X^2_3=2.592$; $P = 0.459$). In a multivariate model, only the age (≥ 55 years) and BMI (>30) of the patients, and the age of the doctors (≥ 55) had an important influence on blood pressure control (*Table III*).

DISCUSSION

In our sample from a community-based health centre in Mexico City (*Table I*), most of the patients who had a diagnosis of hypertension were treated with antihypertensives, only 13.6% did not receive this medication; angiotensin-converting enzyme inhibitors concentrate almost three quarters of the prescriptions although beta-blockers (26.5%) and thiazide diuretics (19.8%) still had an important share. This pattern of prescriptions for antihypertensives had been previously observed in Mexico [7] and, taking into consideration the evolution in time, with some variation, is quite coincidental with that observed in other diverse countries such as Peru [11], Turkey [12], Portugal [13], Nigeria [14], Trinidad [15], Sweden [16] or Spain [17]. Thus, the current pattern of antihypertensive use in most of the countries would be that of a decline in the traditionally recommended medications, diuretics and beta-blockers, and an increase in newer medications such as ACEIs and ARBs; calcium-channel blockers would have a marginal role in this pattern. This is what is chiefly observed in our sample from Mexico City; it is worth mentioning that no prescription of an alpha-blocker was detected.

Although thiazide-type diuretics were recommended in previous guidelines as the preferred initial drug therapy for most patients with hypertension [18], subsequent data from important clinical trials [19–25] point to the need for a more open approach as different drug classes can reduce cardiovascular complications to a degree similar to that associated with diuretics. In addition, as generic preparations for each of these drug classes are now available [26], and there have been some successful negotiations of public procurement prices for patented medicines in Mexico [27], the cost advantage of diuretics has become much less of an issue.

In our sample, only a relatively small proportion of treated patients had more than one medication in whichever combination. However, in the majority of patients, two or more antihypertensive drugs are required to achieve target blood pressure levels and, as

Table II Patients treated for hypertension. Type of medications and hypertension control

Type ^{a,b}	Controlled (n = 105) n (%)	Uncontrolled (n = 176) n (%)	Total (n = 281) n (%)	χ^2 ; P
Diuretics	18 (17.1)	38 (21.6)	56 (19.9)	0.815; 0.367
Betablockers	32 (30.5)	42 (23.9)	74 (26.3)	1.482; 0.223
ACEIs	68 (64.8)	110 (62.5)	178 (63.3)	0.145; 0.703
ARBs	12 (11.4)	32 (18.2)	44 (15.7)	2.271; 0.132
Calcium-channel blockers	5 (4.8)	12 (6.8)	17 (6.0)	0.489; 0.484

^aPatients can combine medications from different types; as a result, the sum of the percentages is not 100. The most common combination was that of a diuretic and an ACEI (i.e. chlorthalidone plus captopril or enalapril, 15)

^bThe total distribution for individual medications was: For diuretics: furosemide, 10; spironolactone, 2; chlorthalidone, 43; hydrochlorothiazide, 5. For beta-blockers: metoprolol, 75; atenolol, 3; propranolol, 1; timolol, 1. For ACEIs: captopril, 84; enalapril, 105; ramipril, 1. For ARBs: candesartan, 3; irbesartan, 2; losartan, 31; telmisartan, 12. For calcium antagonists: dihydropyridines, 14 (amlodipine, 12; nifedipine, 2); diltiazem, 2; verapamil, 3.

Table III Risk factors accounting for a lack of hypertension control

Factors	Odds Ratio (95%CI)
Age (>55 years)	1.82 (1.02-3.25)
Obesity (BMI >30)	2.21 (1.27-3.83)
Doctor age (>55 years)	2.61 (1.51-4.52)

Hosmer and Lemeshow test = 7.772; P = 0.255

a result, several two-drug fixed-dose combinations have been introduced [28,29].

Less than half of the patients in our sample had their hypertension controlled (39.1%) (Table II); when referring to those treated with antihypertensives, the proportion barely varies (37.4%). These figures are consistent with that of 32.9% found in a geriatric centre in Monterrey [30] and with that of 45.4% observed in the National Survey in 2012; in the latter case, it was probably due to the fact that average age in the survey (42 years) and in our sample (61 years) was different, age being an important determinant for blood pressure control. In Spain, 36.1%, 41.4% and 46.3% of treated patients achieved blood pressure goals in 2002, 2006 and 2010, respectively [31]. The figures are still distant from those achieved in the United States, by the 2009 to 2010 time period; 47% of all hypertensive people and 60% of treated hypertensive people had blood pressure controlled [32]. Type, number or combination did not account for differences in the proportion of controlled patients.

We have explored several factors as related to hypertension control; among them, there were type and number of medications, sex, number or combinations, and also some factors associated with doctors. Finally, we have clearly identified age and obesity as two important factors which account for uncontrolled

hypertension; this is consistent with what has been previously identified in other studies in Mexico [33].

One of the limitations of this study is its retrospective character, as the information gathered was not intended for the purpose of the study; nevertheless, the clinical records were generally complete and we were able to carefully retrieve the most important data upon robust variables; thus, we have made available detailed information for our analysis. We completed the information from the patients with additional information from a survey directed to the attending medical doctors. This allowed us to build up a parsimonious model to predict control. It is as well possible that a unique measure of blood pressure can underscore the percentage of those patients considered as controlled. Another limitation would be representativeness; assuming our sample represents the hypertensive population of those covered by this community centre, the population of this borough is slightly older, wealthier and more literate than the rest of the Mexico; as the purpose of this study was not to know prevalence of hypertension but drug prescription patterns of use and determinants of uncontrolled blood pressure, it is likely that these differences in population would not highly modify the validity of our results.

In summary, we have consistently identified an evolving pattern of use of antihypertensives in Mexico of fewer diuretics and beta-blockers and more ACEIs and ARBs; in addition, we have observed no differences between men and women in the type, number and combination of these medications. As for blood pressure control, it has been observed that an older age and a BMI >30 of the patients, along with the age of the doctors, are important determinants; the knowledge of these factors may contribute to the use of individually tailored medication. Particular attention deserves

obesity; as this epidemic continues to rise, it is worth intervening on an individual basis on this problem. In Mexico, there are at the moment some interesting collective interventions to face this important problem of public health [34]. As lack of control has been also tied to elderly doctors, possibly with less updated knowledge than younger ones, an educational intervention targeted to these professionals could be envisaged. All in all, the results provided by this study allow suggesting some health interventions at different levels; in this regard, they can be considered as a standpoint for taking actions.

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REFERENCES

- WHO/ISH Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J. Hypertens.* (2003) **21** 1983–1992.
- Sundström J., Arima H., Jackson R. *et al.* Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of blood pressure reduction in mild hypertension: a systematic review and meta-analysis. *Ann. Intern. Med.* (2015) **162** 184–191.
- Blacher J., Halimi J.M., Hanon O. *et al.* French Society of Hypertension. Management of hypertension in adults: the 2013 French Society of Hypertension guidelines. *Fundam. Clin. Pharmacol.* (2014) **28** 1–9.
- Kearney P.M., Whelton M., Reynolds K., Muntner P., Whelton P.K., He J. Global burden of hypertension: analysis of worldwide data. *Lancet* (2005) **365** 217–223.
- Instituto Nacional de Salud Pública [INSP]. (2012). Encuesta Nacional de Salud y Nutrición (ENSANUT) 2012. http://ensanut.insp.mx/informes/ENSANUT2012_Resultados_Nacionales.pdf. Accessed, July 17th 2015.
- Campos-Nonato I., Hernández-Barrera L., Rojas-Martínez R., Pedroza-Tobías A., Medina-García C., Barquera S. Hypertension: prevalence, early diagnosis, control and trends in Mexican adults. *Salud Publica Mex.* (2013) **55**(suppl 2) S144–S150.
- García-Peña C., Thorogood M., Reyes S., Salmerón-Castro J., Curán C. The prevalence and treatment of hypertension in the elderly population of the Mexican Institute of Social Security. *Salud Publica Mex.* (2001) **43** 415–420.
- Kearney P., Whelton M., Reynolds P., Whelton H., Jiang H. Worldwide prevalence of hypertension. *J. Hypertens.* (2004) **22** 11–19.
- Barquera S., Campos-Nonato I., Hernández-Barrera L. *et al.* Hypertension in Mexican adults: results from the National Health and Nutrition Survey 2006. *Salud Publica Mex.* (2010) **52**(suppl 1) S63–S71.
- Chobanian A.V., Bakris G.L., Black H.R. *et al.* Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* (2003) **42** 1206–1252.
- Juárez-García M., Ortiz-Saavedra P.J., Gutiérrez-Fernán-Segarra L., Casas-Castañeda J. Pattern and costs of the antihypertensive treatment for ambulatory patients in a general hospital (In Spanish). *Rev Soc Peru Med Interna* (2008) **21** 17–21.
- Abaci A., Kozan O., Oguz A. *et al.* Prescribing pattern of antihypertensive drugs in primary care units in Turkey: results from the TURKSAHA study. *Eur. J. Clin. Pharmacol.* (2007) **63** 397–402.
- Furtado C., Pinto M. Anti-hypertensive drug utilization in Continental Portugal (1999–2004). *Portugal Rev Port Cardiol* (2006) **25** 273–292.
- Olanrewaju T.O., Aderibigbe A., Busari O.A., Sanya E.O. Antihypertensive drug utilization and conformity to guidelines in a sub-Saharan African hypertensive population. *Int. J. Clin. Pharmacol. Ther.* (2010) **48** 68–75.
- Clement Y.N., Ali S., Harripaulsingh S. *et al.* Drug prescribing for hypertension at primary healthcare facilities in Trinidad. *West Indian Med. J.* (2012) **61** 43–48.
- Bøg-Hansen E., Lindblad U., Ranstam J., Melander A., Råstam L. Antihypertensive drug treatment in a Swedish community: Skaraborg Hypertension and Diabetes Project. *Pharmacoepidemiol. Drug Saf.* (2002) **11** 45–54.
- Task force on Pharmacologic Approach of Hypertension in Primary Care (AFHAP). Selection of pharmacologic treatment of arterial hypertension in primary care. *Med Clin (Barc)* (2000) **114** 374–377.
- Mancia G., De Backer G., Dominiczak A. *et al.* 2007 Guidelines for the management of arterial hypertension: Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J. Hypertens.* (2007) **25** 1105–1187.
- Hansson L., Lindholm L.H., Ekblom T. *et al.* Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity in the Swedish Trial in Old Patients with Hypertension–2 study. *Lancet* (1999) **354** 1751–1756.
- Furberg C.D., Wright J.T., Davis B.R. *et al.* Major outcomes in high-risk hypertensive patients randomized to angiotensin converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* (2002) **288** 2981–2997.
- Pepine C.J., Handberg E.M., Cooper-DeHoff R.M. *et al.* A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease: the International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. *JAMA*(2003) **290** 2805–2816.

- 22 Dahlöf B, Sever PS, Poulter NR et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet* (2005) **366** 895–906.
- 23 Dahlöf B., Devereux R.B., Kjeldsen S.E. et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* (2002) **359** 995–1003.
- 24 Wing L.M., Reid M., Ryan P. et al. A comparison of outcomes with angiotensin converting–enzyme inhibitors and diuretics for hypertension in the elderly. *N. Engl. J. Med.* (2003) **348** 583–592.
- 25 Jamerson K., Weber M., Bakris G. et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N. Engl. J. Med.* (2008) **359** 2417–2428.
- 26 <http://www.cofepris.gob.mx/AS/Paginas/Registros%20Sanitarios/RegistroSanitarioMedicamentos.aspx>. Accessed, July 13th 2015.
- 27 Gómez-Dantés O., Wirtz V.J., Reich M.R., Terrazas P., Ortiz M. A new entity for the negotiation of public procurement prices for patented medicines in Mexico. *Bull. World Health Organ.* (2012) **90** 788–792.
- 28 Mancia G., Fagard R., Krzysztow N., Narkiewicz K., Redon J., Zanchetti A. 2013 ESH/ESC Guidelines for the management of arterial hypertension. *J. Hypertens.* (2013) **31** 1281–1357.
- 29 Wald D.S., Law M., Morris J.K., Bestwick J.P., Wald N.J. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 trials. *Am. J. Med.* (2009) **122** 290–300.
- 30 Cárdenas-Ibarra L., Salinas-Martínez R., Villarreal J.Z. Niveles de control de la presión arterial en pacientes ambulatorios ancianos. *Salud Pública de México* (2007) **49** 246–247.
- 31 Llisterra J.L., Rodríguez-Roca G.C., Escobar C. et al. Treatment and blood pressure control in Spain during 2002–2010. *J. Hypertens.* (2012) **30** 2425–2431.
- 32 Gu Q, Burt VL, Dillon CF, Yoon S. Trends in antihypertensive medication use and blood pressure control among united states adults with hypertension. The National Health and Nutrition Examination Survey, 2001 to 2010. *Circulation* (2012) **126** 2105–2114.
- 33 Mejia-Rodríguez O., Paniagua-Sierra R., Valencia-Ortiz M.R.-G. et al. , Factors associated with uncontrolled hypertension. *Salud Pública de México* (2009) **51** 291–297.
- 34 http://www.noalaobesidad.df.gob.mx/index.php?option=com_content&view=frontpage&Itemid=1.