Predictors of self-reported noncompliance with antihypertensive drug treatment: A prospective cohort study

Jean-Pierre Grégoire MPH PhD[1], Jocelyne Moisan PhD[1], Rémi Guibert MD MSc[2], Antonio Ciampi PhD[3], Alain Milot MD MSc[4]

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BACKGROUND: Persistence and compliance are different aspects of the broader concept of adherence to drug treatment. In a prior study, determinants of nonpersistence in a group of patients newly prescribed antihypertensive medications were examined.
OBJECTIVE: To determine noncompliance among those who were persistent with therapy.
METHODS: A prospective cohort study was conducted, in which individuals prescribed a new antihypertensive monotherapy were identified through a network of 173 pharmacies. Participants were interviewed by telephone twice during a three-month period. At the end of this period, individuals who reported still taking the medication initially prescribed were included in the analysis. Self-reported noncompliance was measured at three months. Data were analyzed using a multivariate logistic regression model.
RESULTS: Of 509 eligible participants, 118 (23.2%) reported noncompliance with their drug treatment. Noncompliance was significantly associated with the use of angiotensin-converting enzyme inhibitors (adjusted OR [AOR] 3.0; 95% CI 1.17 to 7.92) compared with the angiotensin II receptor blocker losartan, and with the belief that hypertension is not a risk factor for cardiovascular diseases (AOR 2.0; 95% CI 1.21 to 3.33). On the other hand, noncompliance was inversely associated with the use of more than four pills of medication per day (AOR 0.3; 95% CI 0.15 to 0.64).
CONCLUSIONS: Compliance with drug treatment could be improved by proper selection of medication, and by attempts to correct the false perceptions patients may have about hypertension. Further research is needed to better understand the clinical significance of a higher number of pills as a predictor of good compliance. Further research is also needed using different means of measuring noncompliance.

Key Words: *Compliance; Drugs; Health care delivery; Hypertension*

Les prédicteurs d'inobservation d'un traitement antihypertensif déclarée par le patient : Une étude prospective de cohortes

HISTORIQUE : La persistance et l'observation sont deux aspects différents du concept plus vaste de l'observance du traitement médicamenteux. Au cours d'une étude précédente, les déterminants de non-persistance au sein d'un groupe de patients à qui on venait de prescrire des antihypertensifs ont été examinés.
OBJECTIF : Déterminer l'inobservation chez les personnes qui persistaient dans leur traitement.
MÉTHODOLOGIE : Une étude prospective de cohortes au cours de laquelle les personnes à qui on avait prescrit une nouvelle monothérapie aux antihypertensifs a été repérée dans un réseau de 173 pharmacies. Les participants ont participé à une entrevue téléphonique trois fois pendant une période de trois mois. À la fin de cette période, ceux qui déclaraient toujours prendre le médicament prescrit à l'origine étaient inclus dans l'analyse. L'inobservation déclarée par le patient était mesurée au bout du troisième mois. Les données ont été analysées au moyen d'un modèle de régression logistique multivarié.
RÉSULTATS : Des 509 patients admissibles, 118 (23,2 %) ont déclaré une inobservation à leur traitement médicamenteux. L'inobservation était associée de manière significative au recours à des inhibiteurs de l'enzyme de conversion de l'angiotensine (RR rajusté [RRR] 3,0; 95 % IC 1,17 à 7,92) par rapport à l'antagoniste des récepteurs de l'angiotensine II losartan et à la conviction que l'hypertension ne s'associait pas à un facteur de risque de maladie cardiovasculaire (RRR 2,0; 95 % IC 1,21 à 3,33). Par contre, l'inobservation était inversement proportionnelle à l'utilisation de plus de quatre comprimés de médicaments par jour (RRR 0,3; 95 % IC 0,15 à 0,64).
CONCLUSIONS : L'observation du traitement médicamenteux pouvait être amélioré par le bon choix du médicament et par des tentatives de corriger les fausses perceptions éventuelles des patients au sujet de l'hypertension. D'autres recherches s'imposent pour mieux comprendre la signification clinique d'un grand nombre de comprimés comme prédicteur de bonne observation du traitement. D'autres recherches s'imposent également au moyen d'autres modes de mesure d'inobservation.

Cardiovascular disease remains the leading cause of mortality in the developed world. Despite evidence that blood pressure control may reduce premature cardiovascular mortality (1,2) and despite the availability of effective treatment for high blood pressure, a large proportion of identified hypertensive individuals do not have his or her blood pressure controlled (ie, diastolic blood pressure is greater than 90 mmHg or systolic blood pressure is greater than 140 mmgHg) (3-5).

Poor adherence to the recommended drug regimen constitutes a major barrier to adequate control of high blood pressure (3). Three different aspects can be differentiated within the broader concept of adherence (6). The first aspect is acceptance,

[1]*Faculty of Pharmacy and Population Health Research Unit, Université Laval, Québec City, Québec;* [2]*Mornington Peninsula Division of General Practice, Frankston, Australia;* [3]*Department of Epidemiology and Biostatistics, McGill University, Montréal;* [4]*Department of Medicine, Faculty of Medicine, Université Laval, Québec City, Québec*
Correspondence: Dr Jean-Pierre Grégoire, Population Health Research Unit, Centre hospitalier affilié universitaire de Québec, 1050 chemin Sainte-Foy, Québec City, Québec G1S 4L8. Telephone 418-682-7511 ext 4664, fax 418-682-7962, e-mail jean-pierre.gregoire@pha.ulaval.ca
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defined as the initial decision of the patient to agree to the treatment, fill the first prescription and obtain the first refill. The second aspect, persistence, describes the continued renewal of the prescription thereafter, in accordance with the treatment duration as agreed by provider and patient. The third aspect, compliance, refers to patients taking the treatment in accordance with other facets of the prescription, such as taking the prescribed dosage and at the prescribed time.

Various factors have been associated with nonadherence to antihypertensive treatment. These factors have varied from study to study. They generally include the choice of medication (7-15), some demographics (8,14,16,17) and health services factors (8,9). However, most studies focusing on this issue have looked at determinants of persistence (not compliance) (7,9,11,14,17) and most were secondary analyses of administrative databases (7-15,17). In these databases, important patient information, such as occupation, income, perception of health, and beliefs about the disease and its treatment, is seldom available. Consequently, causal associations studied are limited to the examination of an incomplete set of variables.

We conducted a prospective cohort study of individuals prescribed new courses of antihypertensive monotherapies, including individuals who had never been treated for high blood pressure and those switching from a prior treatment. In a previous analysis of the present cohort, we found discontinuation of initial medication use to be positively associated with the perception of side effects with initial medication, and inversely associated with insurance coverage for medication (18).

Because individuals who consume medication sporadically or at a reduced dose may do so for different reasons than those who discontinue their treatment (19), in the current study we evaluated the determinants of self-reported noncompliance among cohort members who had not discontinued their medication after three months of treatment. We examined the effect of an array of potential predisposing, enabling and reinforcing factors that may have affected their compliance with treatment.

METHODS

Study population

The initial cohort comprised individuals 18 years of age and older on newly prescribed antihypertensive monotherapies. From February 1996 to October 1997, hypertensive individuals who had acquired a first prescription of an angiotensin-converting enzyme inhibitor, a calcium channel blocker or an angiotensin II receptor blocker (at the time of the present study, losartan was the only angiotensin II receptor blocker available in Canada) were recruited through a network of 173 pharmacies across Canada. Pregnant women, individuals taking other antihypertensive medications at the same time, and those taking medications for chronic heart failure (eg, digoxin or furosemide) or angina (eg, nitrates) were excluded. To minimize selection bias, individuals who had been given samples of the study medications by their physician were also excluded because if they had experienced early side effects from the drugs, they might not have filled their prescriptions at the pharmacy. A total of 692 individuals were included in the initial cohort (11% from the Atlantic provinces, 57% from Quebec, 23% from Ontario, and 8% from the prairies or British Columbia).

Within an average of five days after their inclusion in the study and again at three months after study entry, a research assistant administered a structured telephone questionnaire to participants. At the three-month interview, participants were asked an open-ended question about their use of antihypertensive medications. Only cohort members who were still taking their entry medication at three months were included in the present study.

The present study was approved by Laval University's Ethics in Research Committee (Québec).

Data collection and variables

At the initial interview, information on potential predisposing, enabling and reinforcing factors was obtained (20). The predisposing factors were as follows: education level, occupation, family income, duration of hypertension, reasons for initiating the new treatment, history of hypertension drug use, number of symptoms due to health problems perceived the week before entering the study, comorbidities, perception of health, beliefs about hypertension and its treatment, and, finally, the perception of risk associated with the disease and the perception of the advantages in treating it. Participants were also questioned about the following enabling factors: specialty of the prescriber, use of a pill organizer, drug insurance coverage and social support. Lastly, information about two reinforcing factors was elicited from participants: satisfaction with information provided by physicians and pharmacists.

At the three-month interview, apart from asking participants about their use of antihypertensive medications, they were also asked about two enabling (barrier) factors: their perceived side effects from the study medications and the number of pills (tablets or capsules) they were taking daily.

To measure compliance with treatment, a structured four-item questionnaire available both in English (21) and French (22) was used. This questionnaire was made up of the following four questions: Do you ever forget to take your medicine?; Are you careless at times about taking your medicine?; When you feel better do you sometimes stop taking your medicine?; and, Sometimes if you feel worse when you take the medicine, do you stop taking it? Participants who answered yes to any of these four questions were deemed to be noncompliant.

Five independent variables were assessed using more than one question. Items pertaining to each of the following concepts were grouped together: beliefs about the efficacy of antihypertensive medication (two items), beliefs about hypertension as a risk factor for other diseases (five items), satisfaction with physician's care (three items) and satisfaction with pharmacist's care (two items). Moreover, social support using the three-item scale developed by Pearlin et al (23) was evaluated. Each resulting index was assessed for internal consistency using Cronbach's alpha. Principal component analyses were also carried out to confirm whether index scores were measuring only one factor. All index scores had alpha coefficients of 0.64 or higher, and all measured a single factor.

Statistical analysis

A descriptive analysis was carried out to determine the prevalence of noncompliance at three months according to the various study factors. The crude ORs and their 95% CIs were calculated to measure the association between each study variable and noncompliance. A multivariate logistic regression model was built applying a stepwise procedure to enter variables in the model (24). The model kept only variables that were statistically significant at the a priori level of 0.10. Multicolinearity was measured using the procedure described by Belsley et al (25). When there was colinearity between two variables, the variable showing the stronger association with noncompliance to drug treatment was kept in the

model. The analyses were conducted using SAS (version 6.12, SAS Inc, USA) (24).

RESULTS

Of 692 participants enrolled in the initial cohort, 665 (96.1%) were interviewed at three months. Of these, 509 (76.5%) reported still being on the initial medication and thus formed the study population. The characteristics of this population and the related prevalence of noncompliance are presented in Table 1. Participants had a mean age (± SD) of 58.6±12.7 years, and were predominantly women. More than one-half of the participants had never been pharmacologically treated for high blood pressure. Among those who had taken an antihypertensive medication in the past, 28% received the study medication because they had experienced side effects with their prior treatment. A majority of individuals (56%) received an angiotensin-converting enzyme inhibitor as the study medication, 32% a calcium channel blocker and 12% the angiotensin II receptor blocker.

A total of 118 participants (23.2%) reported not complying with their antihypertensive treatment. Of these, 105 (89.0%) reported that they had sometimes forgotten to take their medicine, 12 (10.2%) reported that they were careless at times in taking their medication, 17 (14.4%) reported that they had sometimes stopped taking their medication if they felt better and 11 (9.3%) reported that they had, on some occasions, stopped taking their medication if they felt worse.

Results from the multivariate, logistic regression model (Table 2) suggest that, compared with results from angiotensin II receptor blocker users, the odds of reporting noncompliance with their drug treatment were 2.33 times higher (95% CI 0.87 to 6.19) among individuals using calcium channel blockers and 3.04 times higher (95% CI 1.17 to 7.92) for those on an angiotensin-converting enzyme inhibitor. Participants who believed hypertension was not a risk factor for other diseases were also 2.00 times more likely to be noncompliant (95% CI 1.21 to 3.33) than those who believed it had a lot of effect. On the other hand, taking more than four pills of any medication daily was associated with better compliance with treatment (OR 0.30, 95% CI 0.15 to 0.64).

DISCUSSION

In our previous analysis of the present cohort (18), 24% of individuals discontinued their initial antihypertensive medication during the first three months. Our current analysis suggests that among those who persist, a similar proportion was noncompliant. Prior studies have also shown noncompliance with antihypertensive medication to be common. For example, in a secondary analysis of New Jersey's Medicaid program from 1982 to 1988, Monane et al (16) observed that, during a one-year period, 23% of new users of an antihypertensive medication had obtained their medication for less than 80% of the days. In another study performed using the Tennessee Medicaid Program database, Bailey et al (8) observed that 33% of medication refills were not obtained within 36 days of the last prescription, although enrollees could only obtain a 30-day supply of medication at one time. However, in the above-mentioned studies, compliance was measured using prescription refill patterns, which makes it difficult to differentiate noncompliant individuals from those who were nonpersistent.

In the past, the choice of antihypertensive medication has been reported to be associated with adherence to treatment. In the same Medicaid population mentioned above, Monane et al (9) found that people started on angiotensin-converting enzyme inhibitors or on calcium channel blockers were more likely to receive their medication for at least 80% of the days in a year than those started on thiazides. Using the Pennsylvania Medicaid Management Information system, Rizzo and Simons (10) observed that angiotensin-converting enzyme inhibitors, calcium channel blockers and beta-blockers were associated with higher levels of compliance than diuretics. Our findings are further evidence indicating that medication characteristics are associated with compliance with the treatment. These suggests that the use of angiotensin II receptor blockers may help patients to better comply with their treatment. This better compliance may be explained by the fact that patients on angiotensin II receptor blockers tend to perceive fewer side effects than those on angiotensin-converting enzyme inhibitors (26). For instance, in our initial cohort, dry cough was reported as a perceived side effect by 15% of patients initiated on angiotensin-converting enzyme inhibitors, whereas it was reported by only 5% of those initiated on the angiotensin II receptor blocker (26). On the other hand, noncompliance was not associated with the use of calcium channel blockers. This could, however, be explained by the lack of statistical power, as illustrated by the wide 95% CI around the adjusted OR.

In our study, participants who believed hypertension was not a risk factor for other diseases were more at risk of being noncompliant than the others. A similar result has also been reported by other researchers (27). This result is consistent with the Health Belief Model, which suggests that beliefs about a disease and its treatment predispose individuals to adhere to their drug treatment (28,29).

We found that using more than four pills a day was associated with better compliance. This result was unexpected. In the past, the complexity of a pharmacological treatment has been shown to be associated with the patient's failure to adhere to it (30,31). In the treatment of hypertension, compliance was improved when the dosage was simplified with the administration of a single daily dose (32-35). Studies have shown that the use of pill organizers (36), reminder messages (37) or both (34) had a positive effect on compliance with the medication. It has also been shown that, when compared with the use of one to three medications, using eight medications or more is associated with low compliance (9). However, in a recent study, Shalansky and Levy (38) observed that taking fewer medications was associated with lower compliance with chronic cardiovascular regimens, compliance being measured as the use of the drugs for at least 80% of the days over a 14-month period.

One possible explanation for this unexpected finding lies in the nature of the population we studied, namely, those who had not discontinued their medication after three months of treatment. Thus, the number of pills taken daily may constitute more of a barrier at an early stage of treatment but may be less important as people remain under treatment. Individuals persisting after three months of a complex treatment may have developed means to better manage their treatment, and they may do so more effectively than those prescribed less complex treatment. On the other hand, residual confounding factors cannot be ruled out. For example, because participants were asked to report the number of pills taken daily, they may not have reported the frequency of non-oral forms of medications.

TABLE 1
Characteristics of participants (n=509) according to self-reported noncompliance

Categorical variables	Participants (n)	Reported noncompliance (n)	P	Unadjusted OR	95% CI
Predisposing factors					
Sex					
Male	225	57	–	1.00	–
Female	284	61	0.307	0.81	0.53 to 1.22
Age, years					
18 to 50	131	37	–	1.00	–
51 to 60	124	26	0.179	0.67	0.38 to 1.20
61 to 70	128	29	0.303	0.74	0.42 to 1.31
≥71	101	21	0.195	0.68	0.36 to 1.23
Undisclosed	25				
Highest level of education completed					
Beyond high school	195	40	–	1.00	–
High school	221	49	0.681	1.10	0.69 to 1.77
Elementary	93	29	0.049	1.76	1.00 to 3.07
Main occupation					
Full-time work	176	46	–	1.00	–
Full-time housekeeping	88	21	0.689	0.89	0.49 to 1.61
Retired	177	35	0.156	0.70	0.42 to 1.15
Other	68	16	0.675	0.87	0.45 to 1.67
Annual family income					
$40,000 or more	180	38	–	1.00	–
$20,000 to $39,999	139	38	0.197	1.41	0.84 to 2.36
$0 to $19,999	136	34	0.415	1.25	0.74 to 2.11
Undisclosed	54				
Prior use					
New users	268	73	–	1.00	–
Prior discontinuers (no use in past 30 days)	79	17	0.309	0.73	0.40 to 1.34
Switchers (cause)					
Side effects with prior treatment	67	12	0.120	0.58	0.30 to 1.15
Uncontrolled blood pressure with prior treatment	55	7	0.027	0.39	0.17 to 0.90
Other	40	9	0.528	0.78	0.35 to 1.71
Perception of health					
Excellent or very good	235	58	–	1.00	–
Good, fair or poor	273	60	0.472	0.86	0.57 to 1.30
Undisclosed	1				
Beliefs concerning the efficacy of antihypertensive medication					
A lot of effect	153	38	–	1.00	–
Some effect	145	37	0.892	1.04	0.61 to 1.75
No effect	210	43	0.325	0.78	0.47 to 1.28
Undisclosed	1				
Beliefs concerning hypertension as risk factor for other diseases					
A lot of effect	172	32	–	1.00	–
Some effect	112	22	0.828	1.07	0.59 to 1.96
No effect	225	64	0.024	1.74	1.08 to 2.81
How much are you at risk of heart attack because of your hypertension if you follow your doctor's advice?					
No risk to moderate risk	424	98	–	1.00	–
High risk to very high risk	20	2	0.187	0.37	0.08 to 1.62
Do not know	65	18	0.420	1.27	0.71 to 2.29
How much are you at risk of a stroke because of your hypertension if you follow your doctor's advice?					
No risk to moderate risk	432	104	–	1.00	–
High risk to very high risk	13	2	0.474	0.57	0.13 to 2.63
Do not know	64	12	0.349	0.73	0.37 to 1.42
How much are you at risk of heart attack because of your hypertension if you do not do anything about it?					
No risk to moderate risk	88	23	–	1.00	–
High risk to very high risk	364	87	0.661	0.89	0.52 to 1.51
Do not know	57	8	0.087	0.46	0.19 to 1.12
How much are you at risk of a stroke because of your hypertension if you do not do anything about it?					
No risk to moderate risk	98	25	–	1.00	–
High risk to very high risk	365	87	0.731	0.91	0.55 to 1.53
Do not know	46	6	0.096	0.44	0.17 to 1.16

Continued on next page

TABLE 1 – continued
Characteristics of participants (n=509) according to self-reported noncompliance

Categorical variables	Participants (n)	Reported noncompliance (n)	P	Unadjusted OR	95% CI
Enabling factors					
Social support					
High	276	67	–	1.00	–
Low	219	46	0.390	0.83	0.54 to 1.27
Not reported	14				
Study medication prescribed					
Losartan	62	6	–	1.00	–
Angiotensin-converting enzyme inhibitor	283	78	0.005	3.55	1.47 to 8.57
Calcium channel blocker	164	34	0.058	2.44	0.97 to 6.14
Study medication prescribed by					
Family physician	448	104	–	1.00	–
Specialist	53	13	0.831	1.08	0.55 to 2.09
Undisclosed	8				
Side effects reported with study medication					
No	229	53	–	1.00	–
Yes	280	65	0.985	1.00	0.66 to 1.52
Use of a pill organizer					
No	447	107	–	1.00	–
Yes	62	11	0.281	0.69	0.35 to 1.36
Insurance coverage for antihypertensive medication					
No	68	17	–	1.00	–
In full or in part	433	99	0.698	0.89	0.49 to 1.61
Undisclosed	8				
Number of pills					
One or less	203	56	–	1.00	–
Two to four	209	52	0.533	0.87	0.56 to 1.35
More than four	97	10	0.001	0.30	0.15 to 0.62
Reinforcing factors					
Satisfaction with physician's care					
High	359	88	–	1.00	–
Low	141	27	0.201	0.73	0.45 to 1.18
Undisclosed	9				
Satisfaction with pharmacist's care					
High	459	108	–	1.00	–
Low	42	7	0.315	0.65	0.28 to 1.51
Undisclosed	8				

Continuous variables	Compliant, mean (SD)	Noncompliant, mean (SD)	P	Unadjusted OR	95% CI
Predisposing factors					
Symptoms due to health problems perceived the week before entering the study (n)	9.87 (6.96)	9.50 (6.51)	0.610	0.99	0.96 to 1.02
Duration of hypertension (months)	46.50 (81.14)	43.53 (72.15)	0.723	1.00	1.00 to 1.00
Enabling factors					
Illnesses other than hypertension (n)	0.61 (0.77)	0.56 (0.75)	0.560	0.92	0.70 to 1.21

This may have introduced bias if those under-reporting non-oral forms of medications were in greater proportion among noncompliant participants. Further research is needed to better understand the clinical significance of this finding.

One other important finding emerges from the present study. Determinants of self-reported noncompliance differ from those of discontinuation of use. In our previous paper (18), we reported that perceived side effects were positively associated with, and drug insurance coverage inversely associated with, discontinuation of the medication. We have also reported that patients' perceived benefits of a drug treatment may predict persistence with said treatment. By contrast, these three variables – perceived side effects, drug insurance coverage and perceived drug benefits – were not associated with self-reported noncompliance among those who were still on the initial treatment after three months. This result suggests that insurance coverage is important for long-term persistence with treatment but, for those who persist, it is not a factor that predicts compliance. It also suggests that side effects have an impact on discontinuation but, for those who persist with the medication despite its side effects, these will not be an important barrier to the use of the medication. Lastly, if perceived

TABLE 2
Multivariate logistic regression model of determinants of reported noncompliance with antihypertensive medication (n=509)

Determinant compliance	Participants (n)	Reported noncompliance (n)	P	Adjusted OR	95% CI
Study medication prescribed					
Losartan	62	6	–	1.00	–
Angiotensin-converting enzyme inhibitor	283	78	0.023	3.04	1.17 to 7.92
Calcium channel blocker	164	34	0.091	2.33	0.87 to 6.19
Beliefs concerning hypertension as a risk factor for other diseases					
A lot of effect	172	32	–	1.00	–
Some effect	112	22	0.628	1.17	0.62 to 2.19
No effect	225	64	0.007	2.00	1.21 to 3.33
Number of pills					
One or less	203	56	–	1.00	–
Two to four	209	52	0.660	0.90	0.57 to 1.43
More than four	97	10	0.002	0.30	0.15 to 0.64
Prior use					
New users	268	73	–	1.00	–
Prior discontinuers (no use in past 30 days)	79	17	0.414	0.77	0.41 to 1.44
Switchers (cause)					
Side effects with prior treatment	67	12	0.720	0.87	0.41 to 1.85
Uncontrolled blood pressure with prior treatment	55	7	0.082	0.46	0.20 to 1.10
Other	40	9	0.878	0.94	0.41 to 2.16
How much are you at risk of a stroke because of your hypertension if you do not do anything about it?					
No risk to moderate risk	98	25	–	1.00	–
High risk to very high risk	365	87	0.558	1.18	0.69 to 2.02
Do not know	46	6	0.072	0.40	0.15 to 1.09

benefits of a drug treatment seem to play a role in the patient's decision to continue the treatment, then perceived risks of the disease appear to be a key variable for motivating patients to take their medication appropriately. As recently noted by DiMatteo (39), "adherence might not be a unified construct". Our findings add evidence to this idea.

The present study has some limitations. First, in the absence of a gold standard for compliance measurement (39), clinicians must rely on methods with inherent limitations. We used a self-report questionnaire that has been validated against blood pressure control (21,22). The usefulness of this questionnaire is based on its specificity because patients reporting noncompliance are more likely to respond to strategies aimed at improving compliance (40). However, self-reported measures of compliance like the one used in the present study may exhibit poor agreement with those based on pharmacy refill patterns when measuring compliance with prescribed medications in general (41) or with cardiovascular medicines in particular (42), yet poor agreement between these two methods does not mean one is more valid than the other. Determinants identified in the present study could therefore be different had we used a different method to identify noncompliance. Second, that we were unable to identify more than three statistically significant determinants of noncompliance may be due to a lack of statistical power. Lastly, care should be taken before generalizing the results to other populations because the determinants of noncompliance may vary according to the disease being pharmacologically treated. Further research is needed using larger populations of patients. There is also a need to study the determinants of noncompliance with medication in other disease areas.

CONCLUSIONS

We designed the present study to assess, in a natural setting, the determinants of noncompliance with antihypertensive medications. We recruited partipicants through pharmacies, thus avoiding the selection bias likely to be introduced when physicians are asked to enroll patients for whom they are prescribing a new treatment. Furthermore, we were able to study many potential determinants that otherwise could not be examined using only the information generally available in administrative databases. Although we did not conduct the present study in the highly controlled environment of a randomized clinical trial, we minimized confounding bias by using multivariable modelling.

Our results suggest that among patients who persist with their initial antihypertensive drug treatment, their compliance with this treatment may be improved by an appropriate selection of medication, for instance, angiotensin II receptor blockers. Compliance may also be improved by addressing misleading perceptions patients may have about their disease. By discussing this issue with patients, both physicians and pharmacists may help them better manage their drug treatment.

Many patients do not take their antihypertensive medication as prescribed. As a consequence, the effectiveness of the treatment for reducing blood pressure may be jeopardized and its potential health benefit may be lost. There is an urgent need to develop, implement and assess strategies aimed at improving the appropriate use of medications by patients. To be successful, these strategies should target determinants such as those identified in the present study.

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REFERENCES

1. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. Lancet 1990;335:765-74.
2. Psaty BM, Smith NL, Siscovick DS, et al. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. JAMA 1997;277:739-45.
3. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206-52.
4. Joffres MR, Ghadirian P, Fodor JG, Petrasovits A, Chockalingam A, Hamet P. Awareness, treatment, and control of hypertension in Canada. Am J Hypertens 1997;10:1097-102.
5. Banegas JR, Rodriguez-Artalejo F, de la Cruz Troca JJ, Guallar-Castillon P, del Rey Calero J. Blood pressure in Spain: Distribution, awareness, control, and benefits of a reduction in average pressure. Hypertension 1998;32:998-1002.
6. Wahl C, Gregoire JP, Teo K, et al. Concordance, compliance and adherence in healthcare: Closing gaps and improving outcomes. Healthc Q 2005;8:65-70.
7. Jones JK, Gorkin L, Lian JF, Staffa JA, Fletcher AP. Discontinuation of and changes in treatment after start of new courses of antihypertensive drugs: A study of a United Kingdom population. BMJ 1995;311:293-5.
8. Bailey JE, Lee MD, Somes GW, Graham RL. Risk factors for antihypertensive medication refill failure by patients under Medicaid managed care. Clin Ther 1996;18:1252-62.
9. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effects of initial drug choice and comorbidity on antihypertensive therapy compliance: Results from a population-based study in the elderly. Am J Hypertens 1997;10:697-704.
10. Rizzo JA, Simons WR. Variations in compliance among hypertensive patients by drug class: Implications for health care costs. Clin Ther 1997;19:1446-57.
11. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: The importance of actual practice data. CMAJ 1999;160:41-6.
12. Conlin PR, Gerth WC, Fox J, Roehm JB, Boccuzzi SJ. Four-year persistence patterns among patients initiating therapy with the angiotensin II receptor antagonist losartan versus other antihypertensive drug classes. Clin Ther 2001;23:1999-2010.
13. Marentette MA, Gerth WC, Billings DK, Zarnke KB. Antihypertensive persistence and drug class. Can J Cardiol 2002;18:649-56.
14. Degli Esposti E, Sturani A, Di Martino M, et al. Long-term persistence with antihypertensive drugs in new patients. J Hum Hypertens 2002;16:439-44.
15. Bourgault C, Senecal M, Brisson M, Marentette MA, Gregoire JP. Persistence and discontinuation patterns of antihypertensive therapy among newly treated patients: A population-based study. J Hum Hypertens 2005;19:607-13.
16. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. Compliance with antihypertensive therapy among elderly Medicaid enrollees: The roles of age, gender, and race. Am J Public Health 1996;86:1805-8.
17. Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD. Persistence with treatment for hypertension in actual practice. CMAJ 1999;160:31-7.
18. Gregoire JP, Moisan J, Guibert R, et al. Determinants of discontinuation of new courses of antihypertensive medications. J Clin Epidemiol 2002;55:728-35.
19. Steiner JF, Earnest MA. The language of medication-taking. Ann Intern Med 2000;132:926-30.
20. Green LW, Kreuter MW. Health Promotion Planning: An Educational and Environmental Approach, 2nd edn. Mountain View: Mayfield Publishing Company, 1991.
21. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24:67-74.
22. Gregoire JP, Guibert R, Archambault A, Contandriopoulos AP. Medication compliance in a family practice. Can Fam Physician 1992;38:2333-7.
23. Pearlin LI, Lieberman MA, Menaghan EG, Mullan JT. The stress process. J Health Soc Behav 1981;22:337-56.
24. SAS Institute Inc. SAS/STAT User's Guide, Version 6, 4th edn. Cary: SAS Institute Inc, 1989.
25. Belsley D, Kuh E, Welsch RE. Regression Diagnostics: Identifying Influential Data and Sources of Collinearity. New York: John Wiley & Sons Inc, 1980.
26. Gregoire JP, Moisan J, Guibert R, et al. Tolerability of antihypertensive drugs in a community-based setting. Clin Ther 2001;23:715-26.
27. Levine DM, Green LW, Deeds SG, Chwalow J, Russel RP, Finlay J. Health education for hypertensive patients. JAMA 1979;241:1700-3.
28. Becker MH, Maiman LA. Sociobehavioral determinants of compliance with health and medical care recommendations. Med Care 1975;13:10-24.
29. Kirscht JP, Rosenstock IM. Patient adherence to antihypertensive medical regimens. J Community Health 1977;3:115-24.
30. Taylor DW, Sackett DL, Haynes RB, Johnson AL, Gibson ES, Roberts RS. Compliance with antihypertensive drug therapy. Ann N Y Acad Sci 1978;304:390-403.
31. Sclar DA, Chin A, Skaer TL, Okamoto MP, Nakahiro RK, Gill MA. Effect of health education in promoting prescription refill compliance among patients with hypertension. Clin Ther 1991;13:489-95.
32. Morgan TO, Nowson C, Murphy J, Snowden R. Compliance and the elderly hypertensive. Drugs 1986;31(Suppl 4):174-83.
33. Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybeck TR. The effect of prescribed daily dose frequency on patient medication compliance. Arch Intern Med 1990;150:1881-4.
34. Skaer TL, Sclar DA, Markowski DJ, Won JK. Effect of value-added utilities on prescription refill compliance and health care expenditures for hypertension. J Hum Hypertens 1993;7:515-8.
35. Farmer KC, Jacobs EW, Phillips CR. Long-term patient compliance with prescribed regimens of calcium channel blockers. Clin Ther 1994;16:316-26.
36. Rehder TL, McCoy LK, Blackwell B, Whitehead W, Robinson A. Improving medication compliance by counseling and special prescription container. Am J Hosp Pharm 1980;37:379-85.
37. Raynor DK, Booth TG, Blenkinsopp A. Effects of computer generated reminder charts on patients' compliance with drug regimens. BMJ 1993;306:1158-61.
38. Shalansky SJ, Levy AR. Effect of number of medications on cardiovascular therapy adherence. Ann Pharmacother 2002;36:1532-9.
39. DiMatteo MR. Variations in patients' adherence to medical recommendations: A quantitative review of 50 years of research. Med Care 2004;42:200-9.
40. Sackett DL. A compliance practicum for the busy practitioner. In: Haynes RB, Taylor DW, Sackett DL, eds. Compliance in Health Care. Baltimore: Johns Hopkins University Press, 1979:286-94.
41. Guenette L, Moisan J, Preville M, Boyer R. Measures of adherence based on self-report exhibited poor agreement with those based on pharmacy records. J Clin Epidemiol 2005;58:924-33.
42. Shalansky SJ, Levy AR, Ignaszewski AP. Self-reported Morisky score for identifying nonadherence with cardiovascular medications. Ann Pharmacother 2004;38:1363-8.