Monitoring one-year compliance to antihypertension medication in the Seychelles

Pascal Bovet,1 Michel Burnier,2 George Madeleine,3 Bernard Waeber,4 & Fred Paccaud5

Objective To examine the compliance to medication among newly diagnosed hypertensive patients screened from the general population of the Seychelles, a rapidly developing country.

Methods Among the 1067 participants to a population-based survey for cardiovascular risk factors, hypertension was discovered in 50 (previously unaware of having hypertension and having blood pressure ≥160/95 mmHg over 3 visits). These 50 patients were placed on a daily one-pill regimen of medication (bendrofluazide, atenolol, or a combination of hydrochlorothiazide and atenolol) and compliance to the regimen was assessed over 12 months using electronic pill containers. Satisfactory compliance was defined as taking the medication on 6 or 7 days a week on average (which corresponds to a mean compliance level of ≥86%).

Findings In the first month, fewer than half (46%) of the new hypertension patients achieved satisfactory compliance, and only about one-quarter (26%) achieved this level by the twelfth month. Compliance was better among the 23 participants who regularly attended medical follow-up, with nearly three-quarters of these patients (74%) achieving satisfactory compliance during the first month and over one-half (55%) by the twelfth month. There was a direct association between mean 12-month compliance level and having a highly skilled occupation; having good health awareness; and regularly attending medical appointments. In contrast, there was an inverse relationship between mean compliance level and heavy drinking.

Conclusion The low proportion of people selected from the general population who were capable of sustaining satisfactory compliance to antihypertension medication may correspond to the maximum effectiveness of medication interventions based on a screening and treatment strategy in the general population. The results stress the need for both high-risk and population approaches to improve hypertension control.

Keywords Antihypertensive agents/administration and dosage; Bendroflumethiazide/administration and dosage; Atenolol/administration and dosage; Hydrochlorothiazide/administration and dosage; Patient compliance; Longitudinal studies; Seychelles (source: MeSH, NLM).

Mots clés Antihypertenseurs/administration et posologie; Bendrofluméthiazide/administration et posologie; Aténolol/administration et posologie; Hydrochlorothiazide/administration et posologie; Observance prescription; Étude longitudinale; Seychelles (source: MeSH, INSERM).

Palabras clave Agentes antihipertensivos/administración y dosificación; Bendroflumetiazida/administración y dosificación; Atenolol/administración y dosificación; Hidroclorotiacida/administración y dosificación; Cooperación del paciente; Estudios longitudinales; Seychelles (fuente: DeCS, BIREME).


Voir page 37 le résumé en français. En la página 38 figura un resumen en español.

Introduction

Hypertension is a chronic condition that affects about 20% of adults in many industrialized countries (1) and seems to be even more prevalent in some developing countries (2, 3). In the Seychelles, for example, a rapidly developing country, the prevalence of hypertension was estimated to be greater than 30% (4, 5). The problem is compounded by the low compliance to antihypertension medication, even though the medication lowers blood pressure (BP) and reduces morbidity and mortality related to hypertension (6, 7). In outpatients, compliance to antihypertension medication ranges from 20% to 80% (7–9) and was estimated to be 56% in the Seychelles (based on a urinary marker, 10). Low compliance to medication is an inherent problem in the treatment of chronic, asymptomatic conditions and is one reason why hypertension may not be treated effectively with drugs (7, 9). Poor adherence to medication may also account for apparent resistance to therapy in more than one-third of patients (11–14).

Most hypertension compliance studies have measured adherence to therapy for only short periods of time (generally less than 3 months) and few have monitored compliance in patients in developing countries. In addition, most studies have included outpatients (i.e. patients attending health services regularly) so the potential of drug treatment at a population level is unclear. Most studies have also used transversal

1 Senior Lecturer, Institut Universitaire de Médecine Sociale et Préventive, rue du Bugnon 17, 1005 Lausanne, Switzerland (email: pascal.bovet@inst.hospvd.ch). Correspondence should be addressed to this author.
2 Professor, Division d’Hypertension et Médecine Vasculaire, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.
3 Registered Nurse, Unit of Prevention and Control of Cardiovascular Disease, Ministry of Health, Victoria, Seychelles.
4 Professor, Division de Physiopathologie, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.
5 Professor, Institut Universitaire de Médecine Sociale et Préventive, Lausanne, Switzerland.
measurements of compliance with poor precision and biases (15) and this is reflected in the wide variation in measured compliance rates.

A new method, the Medication Event Monitoring System (MEMS), records the date and time of each opening of a pill container (16–19) and allows longitudinal measurements of compliance. Although the container does not ascertain that the drug was actually ingested, it does provide a temporal history of presumptive drug taking. Using this system, we examined the one-year compliance of new hypertension patients — screened from the general population of the Seychelles — to the simplest medication regimen (one pill per day).

Methods

Setting

The Seychelles are a group of islands in the Indian Ocean, approximately 1800 km east of Kenya and 1800 km north-east of the island of Mauritius. The total population was 74 331 in 1994, 90% of whom lived on Mahe, the main island. Approximately two-thirds of the population are predominantly of African descent. Real gross domestic product (GDP) increased from US$ 2927 to US$ 5731 per capita between 1980 and 1999. In 1989 (4) and 1994 (5), surveys of the population aged 25–64 years found that 24.9–34.2% of men and 19.5–20.9% of women had BP ≥ 160/95 mmHg.

Selection of participants

To measure compliance to hypertension medication, we studied a subset of participants in a population-based cross-sectional survey of cardiovascular risk factors in the Seychelles in 1994. The 1994 study was approved by the Ministry of Health of Seychelles and detailed methods and general findings have been published (5). Briefly, a random age- and sex-stratified sample of the residents aged 25–64 years was drawn from the entire population of Mahe using computerized census data. Of the 1226 eligible subjects, 1067 participated in the study (504 men and 563 women), an overall participation rate of 87%. For all participants, a structured questionnaire on health, social variables, and knowledge about hypertension was completed in face-to-face interviews by a team of nurses who had previous experience in conducting surveys.

In the 1994 survey, BP values referred to the average of the second and third of three readings taken with a standard mercury sphygmonanometer at intervals of at least one minute. Among the 1067 study participants, 161 had BP readings ≥ 160/95 mmHg at the time of the survey and were unaware of having hypertension. From the 161 patients who had high BP at the first visit, 155 of them (96.3%) participated in further checks. BP values ≥ 160/95 mmHg were found in 74 (46.0%) and 50 (31.1%) subjects at their second and third visits, respectively.

Regimen for hypertensive patients

Participants in the compliance study were the 50 patients from the 1994 survey who had systolic/diastolic BP ≥ 160/95 mmHg on three separate medical visits and were previously unaware of having hypertension. All 50 patients received treatment for hypertension throughout the study period. During follow-up, patient BP was measured as an average of two readings taken at 1-minute intervals with a standard mercury sphygmonanometer. All patients gave free and informed consent to the treatment protocol.

Initially, the medication consisted of one pill per day of a randomly prescribed low dose of either a diuretic (bendroflumethiazide, 2.5 mg) or a beta-blocker (atenolol, 50 mg). If BP during follow-up was ≥ 160/95 mmHg, further treatments were: a full dose of the same medication (5 mg bendroflumethiazide or 100 mg atenolol); a low dose of the other medication; a full dose of the other medication; a low-dose combination of a diuretic and beta-blocker (25 mg hydrochlorothiazide and 50 mg atenolol (Tenoretic™, Astra-Zeneca, Grafenau, Switzerland)); and a full-dose combination (50 mg hydrochlorothiazide and 100 mg atenolol (Tenoretic™, Astra-Zeneca)). Pills were given in small bottles with a cap containing a microelectronics chip (MEMS-4, Aardex Ltd, Zurich, Switzerland) that recorded the date and time the bottle was opened. MEMS caps were changed at least once every six months for every patient.

Follow-up strategy

Follow-up medical visits were scheduled for 1 month later if BP was ≥ 160/95 mmHg; 2 months later if BP was <160/95 mmHg for the first time; 3 months later if BP was <160/95 mmHg more than once. During these visits all patients were repeatedly given advice on healthy lifestyles. None was excluded at the start of the study due to contraindications to the medication. Medical visits, blood tests, and medication were provided free of charge to the participants, consistent with the policy of the Ministry of Health of the Seychelles.

Attempts were made to arrange new appointments for patients who did not turn up to scheduled medical visits by making at least two telephone calls (at home, workplace, or neighbour’s home). The MEMS caps were recovered from the homes of patients who dropped follow-up.

Measuring compliance

Compliance to the one pill per day medication was measured as the number of days per unit time with one or more openings of the MEMS cap per day. Compliance was expressed in two ways: mean compliance was calculated as the number of days with one or more MEMS cap openings in the time period divided by the number of days in the time period (expressed as a percentage) or by category of compliance level. Satisfactory compliance was defined for a mean compliance of ≥ 86%, which corresponds to taking the medication on 6 or 7 days a week on average.

Differences in mean 12-month compliance between categories of selected variables were tested by t-test or ANOVA (analysis of variance). Two-tailed P-values ≤ 0.05 were considered significant. Analyses were performed with Stata for Windows, version 6.0 (Stata Corporation, College Station, TX, USA).

Results

Characteristics of participants

Of the 50 initial participants in this study, 33 were men (mean age ± SD: 46.8 ± 9.0 years) and 17 were women (49.6 ± 9.0 years). None reported serious side-effects from the medication. Some minor symptoms were noted, particularly headaches, but they did not provoke discontinuation of the medication. Out of 18 000 patient-days (50 patients multiplied
Compliance to antihypertension medication in the Seychelles

by 360 days), compliance data were unavailable for 630 patient-days (3.5%), mainly due to problems with batteries in the MEMS caps. The caps were opened twice a day in 282 patient-days and more than twice a day in 102 patient-days.

Of the 42 participants who attended medical follow-up for the 12 months of the study, 23 of them attended regularly (maximum delay of 4 days between scheduled and actual appointments for medical visits), and 19 attended irregularly (delay ≥5 days). Eight participants dropped follow-up before the twelfth month. Compliance was considered to be zero after dropping out. For patients with some missing MEMS data, the average 12-month compliance was calculated based on all months with available compliance data (no patient had missing MEMS data for more than six months).

The last medication prescribed to the 42 continuing participants on the twelfth month were: low-dose diuretic to 7 participants; full-dose diuretic to 8; low-dose beta-blocker to 9; full-dose beta-blocker to 8; low-dose combination to 2; and full-dose combination to 8.

Blood pressure measurements
Prior to treatment, the mean BP (± SD mmHg) of the 50 initial participants was 158 ± 15 / 10 ± 07 mmHg. There was no significant difference between the 42 continuing participants and the 8 who dropped follow-up. After one year of medication the mean BP for the 42 continuing participants had fallen to 145 ± 16 / 92 ± 8 mmHg. Within this group, the mean difference in BP between the first reading (before medication was started) and the last reading at month 12 was 16 ± 12 / 9 ± 6 mmHg for participants taking medication 6–7 days per week; 13 ± 5 / 9 ± 8 mmHg for those taking medication 4–5 days per week; and 7 ± 13 / 5 ± 6 mmHg for those taking medication 0–3 days per week. Differences between the highest and lowest compliance categories were significant both for systolic (P = 0.034) and diastolic (P <0.001) BP measurements.

Proportions of participants with selected compliance levels
The distribution of categories of compliance levels to the regimen over the 12-month study period is shown in Fig. 1 for all 50 initial participants. Those with satisfactory compliance (medication taken 6–7 days per week on average) decreased from 46% to 26% between the first and twelfth months, with most of the decrease taking place in the first 6–8 months. Notably, all participants with satisfactory compliance in the twelfth month were also in this category in the first month. Those with poor compliance (medication taken 0–4 days per week) increased from 26% to 32% over the same period.

Effect of regular follow-up
Among the participants who attended follow-up regularly, satisfactory compliance was found initially in a large proportion of participants (in 73.9% of participants), but in only 52.2% by the sixth month and 54.5% by the twelfth month. In contrast, among participants attending follow-up irregularly, satisfactory compliance was found only in 29.4% of the participants by the first month and 5.9% by the twelfth month (Table 1).

Similar findings appear when considering the mean levels of compliance in participants attending follow-up regularly or irregularly (Fig. 2). The mean compliance remained fairly high (e.g. 77% by the twelfth month) in participants attending regular medical follow-up but decreased sharply in participants attending follow-up irregularly.

Factors associated with compliance
Compared to other participants, the mean 12-month compliance was higher in the 31 skilled workers (63% vs 41%, P = 0.034); in the six participants who knew their BP before diagnosis (84% vs 50%, P = 0.028), in the six who thought current lifestyle was important for future health (81% vs 51%, P = 0.050), and, marginally, in the 37 reporting a daily alcohol intake of <100 g (60% vs 39%, P = 0.064).

The mean 12-month compliance was 76% in the 23 participants attending all medical visits with no visit delayed by more than four days, 63% in the eight participants with at least one visit delayed by 5–9 days, and 36% in the 11 participants with at least one visit delayed by ten or more days (P = 0.000).

Mean 12-month compliance was not significantly associated with sex, age, or level of education (secondary vs primary).

Discussion
The results of this study showed that only 26% of participants screened from the general population maintained satisfactory compliance to medication over a 12-month period (Fig. 1). This low proportion of people selected from the general population who were able to sustain satisfactory compliance to antihypertension medication may correspond to the maximum effectiveness of medication interventions based on a screening and treatment strategy in the general population. The low compliance results from the combination of a near-zero one-year compliance in approximately half of all new hypertensive participants who dropped or neglected medical follow-up and satisfactory compliance in approximately half of the participants who attended medical follow-up regularly during the 12-month period.

Compliance to medication decreased over time, particularly within the first 6 months (Table 1), suggesting that motivation fades rapidly, possibly because the disease is silent (13). Real or imagined discomfort from the medication may
compliance to medication people need to be provided with of treatment. Nevertheless, the data suggest that to boost 21
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participants in our study (54.6%, Table 1) who had satisfactory follow-up would probably be selected for in such studies.

outpatient studies, since patients who regularly attend medical medical follow-up (Table 1) may be comparable to those from

compliance of over 80% to newly prescribed antihypertension medication in the latter study, only one-third of these elderly people sustained compliance (12, 20, 24–26).

Factors in our study design which may influence compliance
Although follow-up in this study mimicked ordinary medical care and did not include special interventions to boost compliance, several factors may have inflated compliance to medication. The medication regimen, for example, was the simplest possible (one pill per day). Study participants were followed by the same medical professionals over the entire 1-year period and a substantial amount of time was spent with participants during medical follow-up visits. Also, participants rarely had to wait for appointments and those who missed a visit were invited at least twice to reschedule another visit. Finally, our study did not include the 13% of eligible people who did not participate in the initial survey and who are likely to be less health conscious than voluntary participants. On the other hand, some patients may have dropped medical follow-up to seek medical care elsewhere. Finally, the health care and medication were free of charge (consistent with the local policy), but it is unclear whether this enhances or decreases compliance to medication for chronic conditions.

Compliance in the Seychelles: developing- or industrialized-country levels?
The results of our study suggest that compliance to antihypertension therapy in Seychelles does not differ substantially from that in industrialized countries. Although it might have been expected that compliance would be lower in the Seychelles, because noncommunicable diseases such as hypertension may be perceived as less important health problems, the importance of cardiovascular disease (and hypertension in particular), has been largely recognized in the Seychelles, thanks to a countrywide prevention and control programme (4, 5, 24–26).

The effect of compliance on blood pressure levels
The decrease in BP was significantly greater in participants with satisfactory compliance compared to those with poor compliance, consistent with other studies (12). There were several reasons why the difference between the two groups was not even greater. Poorly compliant participants tend to take medication in the days preceding a clinical visit, a phenomenon known as “white coat” compliance (27), which could lead to an overestimation of the reduction in BP in this group. In addition, most participants in the study received only one active substance and the BP decrease was expected to be modest.

Table 1. Proportion of participants (n = 42) with selected levels of compliance to daily one-pill antihypertension medication, by month of follow-up and category of adherence to follow-up

<table>
<thead>
<tr>
<th>No. of days medication taken per week</th>
<th>Month of follow-up</th>
<th>1</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>6–7</td>
<td>73.9</td>
<td>29.4</td>
<td>52.2</td>
<td>22.2</td>
</tr>
<tr>
<td>4–5</td>
<td>17.4</td>
<td>35.3</td>
<td>26.1</td>
<td>22.2</td>
</tr>
<tr>
<td>0–4</td>
<td>8.7</td>
<td>35.3</td>
<td>21.7</td>
<td>55.6</td>
</tr>
</tbody>
</table>

A = percentage of participants (n = 23) who attended medical visits regularly.
B = percentage of participants (n = 19) who attended medical visits irregularly.

Also have contributed to the decline. The sharp decline in compliance during the first few months (Fig. 1) may have been exacerbated by the use of electronic caps, which tends to improve drug adherence per se at the start of treatment (12, 20, 27), leading to an artificially high compliance at the beginning of treatment. Nevertheless, the data suggest that to boost compliance to medication people need to be provided with both health education and practical advice promptly.

Compliance rates in other studies
Care must be taken when comparing results from compliance studies since most have been conducted in clinical settings that inherently include predominately health-conscious people, whereas our study involved participants selected from the general population. From a population-based perspective, our finding that 26% of all participants sustained satisfactory compliance is not largely different from findings in a population-based study of elderly North Americans. In the latter study, only one-third of these elderly people sustained compliance of over 80% to newly prescribed antihypertension medication, based on quantity of drugs dispensed (22).

Our findings for participants who regularly attended medical follow-up (Table 1) may be comparable to those from outpatient studies, since patients who regularly attend medical follow-up would probably be selected for in such studies. There is no significant difference between the proportion of participants in our study (54.6%, Table 1) who had satisfactory compliance at 12 months and regularly attended follow-up and the 56% of patients who complied to medication in a previous study in the Seychelles that monitored compliance (using a biological marker in urine among patients attending hypertension clinics) (10). Another study among outpatients that used the MEMS system also estimated that satisfactory compliance (≥ 80% prescribed pills taken) to antihypertension medication occurred in 53% of 93 African American patients with hypertension and moderately reduced renal function (followed once a month for 4–6 months) (23). In addition, among participants in our study who attended follow-up regularly, the mean twelfth-month compliance level of 77% (Fig. 2) was similar to the overall mean compliance level of 76% (range 53–85%) derived from a review of once-a-day antihypertension medication studies (9).

Fig. 2. Average compliance to a one-pill daily antihypertension medication by month of medical follow-up and category of adherence to follow-up

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Risk factors for low compliance

Several studies have investigated the risk factors associated with low compliance to treatment and appointments, and with poor treatment results (14, 28–32). In industrialized countries, male gender, young age, the initial drug choice, education level, living alone, unemployment, and living in big cities were commonly reported factors. Previously, we found that compliance in hypertension outpatients in the Seychelles was independent of the physician involved, but improved with patient’s level of education (10). In the present study, compliance was higher in people with skilled occupations, in those who were health conscious, and in those who regularly attended follow-up appointments. Compliance was lower in heavy drinkers. These results suggest that people of higher socioeconomic status adhere better to antihypertension treatment, which is not surprising, since a silent condition such as hypertension is likely to require an understanding of the long-term consequences to motivate compliance. The better compliance of participants who regularly attended medical follow-up suggests a simple indicator that clinicians could use in the management of their patients.

Problems of treating a condition which gradually leads to disease

The fact that only about one-quarter of participants screened from the general population was able to sustain satisfactory compliance underscores the difficulty of treating a silent medical condition over the long term. In addition, because even slightly elevated BP increases the risk of cardiovascular disease, only a small proportion of BP-related morbidity is attributable to patients with high BP levels, according to the classic prevention paradox (33). For example, in young American adults almost two-thirds of excess deaths attributable to BP are in people with BP levels <160/100 mmHg (34). The impact of antihypertension treatment is further diminished when low compliance is taken into account.

Conclusion

The low level of compliance to antihypertension medication found in this study, which is consistent with findings in other countries, emphasizes the need for population-wide primary prevention of elevated BP and cardiovascular disease (35). Such measures include educational, legislative, and fiscal actions to encourage the adoption of a healthy diet (particularly lower salt intake) and to increase facilities and opportunities for physical activity in leisure. It has been estimated in the Asia-Pacific region, for example, that reducing the population systolic BP by as little as 3% would prevent 15% of all stroke deaths and 6% of all coronary deaths (36). Nonetheless, antihypertension medication is among the most cost-effective high-risk interventions for noncommunicable diseases. Detection and treatment of hypertension must therefore be considered in both industrialized and developing countries, particularly for patients with other risk factors (6, 37). Less than optimal compliance in many hypertensive patients, such as found in this study, stresses the need to improve adherence to medication. Poor adherence to therapy is largely unrecognized in clinical practice and monitoring compliance could be a useful way of detecting poor adherence to medication as the cause of poor BP control, particularly in patients with high overall cardiovascular disease risk (12). These issues may be particularly critical in developing countries where antihypertension treatment can drain health care resources. More generally, the influence of knowledge, attitudes, and practices among patients and health professionals (e.g. how chronic disease is perceived and treated, and the role of traditional medicine) on compliance to medication should be examined and relevant measures taken accordingly.

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Conflicts of interest: Aardex Ltd (Zurich, Switzerland) provided the MEMS caps and Astra-Zeneca (Grafeneu, Switzerland) provided Tenoretic™ and Tenoretic mite™ but were not involved with data analysis or the writing of this manuscript.

Résumé

Surveillance de l’observance sur un an du traitement antihypertenseur aux Seychelles

Objectif Examinier l’observance du traitement pharmacologique chez des patients présentant une hypertension récemment diagnostiquée à la suite d’un dépistage de la population générale des Seychelles, un pays en développement rapide.

Méthodes Parmi les 1067 participants à une enquête en population sur les facteurs de risque cardio-vasculaire, une hypertension a été découverte dans 50 cas (chez des personnes qui ignoraient auparavant être hypertendues et dont la tension artérielle était égale ou supérieure à 160/95 mmHg lors de 3 visites). Ces 50 patients ont reçu une prescription pour un traitement consistant en la prise quotidienne d’un comprimé (bendroflumetide, aténolol ou association d’hydrochlorothiazide et d’aténolol), dont l’observance a été évaluée sur 12 mois au moyen de piluliers électroniques. L’observance était considérée comme satisfaisante si les patients prenaient en moyenne le traitement 6 ou 7 jours par semaine (ce qui correspond à une observance moyenne ≥ 86 %).

Résultats Le premier mois, moins de la moitié (46 %) des nouveaux patients ont atteint un niveau d’observance satisfaisant, et seuls un quart environ d’entre eux (26 %) atteignaient un tel niveau au douzième mois. L’observance était meilleure chez les 23 patients qui se présentaient régulièrement aux visites de contrôle, près des trois quarts d’entre eux (74 %) ayant suivi leur traitement de façon satisfaisante le premier mois et plus de la moitié (55 %) le douzième mois. Il existait une association directe entre l’observance moyenne sur 12 mois et l’exercice d’une profession hautement qualifiée, une bonne prise de conscience des problèmes de santé et l’assiduité aux rendez-vous médicaux. Il existait en revanche une association en sens inverse entre l’observance moyenne et la consommation excessive de boissons alcoolisées.
Seguimiento de un año de la observancia de la medicación antihipertensiva en las Seychelles

Objetivo
Analisar el grado de observancia de la medicación entre pacientes con diagnóstico reciente de hipertensión seleccionados a partir de la población general de las Seychelles, un país en rápido desarrollo.

Métodos
Entre las 1067 personas que participaron en un estudio poblacional de los factores de riesgo cardiovascular, se halló hipertensión (tensión arterial ≥ 160/95 mm Hg en tres visitas en personas que desconocían que sufrían hipertensión) en 50 casos. Se sometió a dichos pacientes a un régimen de un comprimido diario de medicación (bendrofluazida, atenolol, o una combinación de hidroclorotiazida y atenolol); para evaluar la observancia del régimen a lo largo de 12 meses los comprimidos se suministraron en envases electrónicos. La observancia satisfactoria se definió como la toma del medicamento durante un promedio de 6 a 7 días a la semana (lo que corresponde a un nivel medio de observancia ≥ 86%).

Resultados
Ese nivel satisfactorio de observancia fue alcanzado durante el primer mes por menos de la mitad (46%) de los pacientes con diagnóstico reciente de hipertensión, y al cabo de 12 meses el porcentaje se había reducido a sólo una cuarta parte (26%). El cumplimiento del tratamiento fue mejor entre los 23 participantes que asistieron regularmente a las visitas de seguimiento médico, entre los cuales casi las tres cuartas partes (74%) cumplieron satisfactoriamente el tratamiento durante el primer mes, y más de la mitad (55%) al cabo de 12 meses. Había una relación directa entre el nivel medio de observancia a los 12 meses y los siguientes factores: el desempeño de un trabajo que requería una alta competencia, una buena sensibilización en materia de salud, y la asistencia regular a las citas médicas. Por el contrario, se observó una relación inversa entre el nivel medio de observancia y la condición de bebedor empedernido.

Conclusion
La baja proporción de personas seleccionadas entre la población general que fue capaz de mantener una observancia satisfactoria de la medicación antihipertensiva podría corresponderse con la eficacia máxima de las intervenciones farmacológicas basadas en una estrategia de cribado y tratamiento de la población general. Los resultados obtenidos subrayan la necesidad de adoptar enfoques que apúnten tanto a grupos de alto riesgo como a la población para mejorar la lucha contra la hipertensión.

References
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