

Muscle relaxation and continuous ambulatory blood pressure in mild hypertension

Isaac Amigo, Ángela Fernández, Ana González and Julio Herrera
University of Oviedo

The objective of this study is to compare the effects of muscle relaxation on blood pressure (BP) and heart rate (HR) in medicated and unmedicated essential hypertensives using as dependent measures the ambulatory blood pressure monitoring (ABPM). Forty patients were randomly allocated to four different groups: relaxation medicated, relaxation unmedicated, control medicated and control unmedicated. Relaxation groups were superior to the control groups in reducing BP at post-treatment for systolic blood pressure (SBP) and HR and, at follow-up, for SBP and diastolic blood pressure (DBP). Relaxation training is of value in significantly reducing BP in medicated and unmedicated hypertensives and HR in unmedicated.

Relajación muscular y monitorización ambulatoria de la presión arterial en la hipertensión esencial ligera. El objetivo de este estudio es comparar los efectos del entrenamiento en relajación muscular sobre la presión arterial (PA) y la frecuencia cardíaca (FC) en pacientes hipertensos esenciales medicados y no medicados, tomando como variables dependientes la monitorización ambulatoria de la presión arterial (MAPA). Cuarenta pacientes fueron asignados al azar a cuatro grupos diferentes de tratamiento: relajación medicado, relajación no medicado, control medicado y control no medicado. Los grupos de relajación fueron superiores a los grupos control en cuanto a la reducción de la PA sistólica y la FC a la finalización del tratamiento y, en el periodo de seguimiento, mostraron mayores reducciones en la PA sistólica y en la PA diastólica. Se concluye que el entrenamiento en relajación parece efectivo para reducir la PA en pacientes hipertensos tanto medicados como no medicados y la FC en pacientes no medicados.

Treatment recommendations for mild hypertension are controversial, particularly as the potential side effects of the antihypertensive drugs may be significant (Houston, 1989; Swislocki, 1989). The U.S. Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (1993; 1997) recommends non-drug therapies as the initial treatment for individuals with mild hypertension. Although this group was not overly enthusiastic about relaxation therapies because in some studies no significant differences between the experimental group and the control group were found (Van Montfrans, Karmaker, Wieling & Dunning, 1990) there is strong evidence from a substantial number of studies that muscle relaxation training (Davison, Williams, Nezami, Bice & Dequattro, 1991; Johnston, 1991; Alexander, Schneider & Staggers, 1996; Boota, Varma & Singh, 1995; González y Amigo, 2000; Amigo, Fernández y González, 2001) can lower blood pressure (BP) by clinically significant amounts.

Up to the present time, no experimental studies have been carried out to determine how medication can affect the relaxation

training in blood pressure lowering, using the ambulatory blood pressure monitoring (ABPM). In addition, in most studies dealing with the psychological control of essential hypertension, the major focus has been on BP as the dependent variable. However, more attention is currently being devoted to heart rate (HR), as this has been related to the onset of hypertensive disease (Obrist, 1981) and with greater coronary heart-disease mortality (Thaulow & Erikssen, 1991).

The purpose of this study is to compare the effects of muscle relaxation training on BP and HR in medicated and unmedicated mild essential hypertensives using as dependent measures the ABPM.

Method

Subjects

Forty patients, twenty-four females and sixteen males, with essential hypertension participated in the study. All subjects were selected from the Hypertension Unit of Asturias General Hospital, Oviedo (Spain) and fulfilled the following requirements: (a) diagnosis of mild essential hypertension with diastolic blood pressure between 90 and 104 at the end of baseline sessions; (b) with a minimum duration of six months; (c) aged between 18 and 60 years; (d) absence of psychiatric disturbances; (f) no treatment for any other cardiovascular disease.

Apparatus

A DINAMAP 845-XT automatic sphygmomanometer was used for measurement of blood pressure and heart rate in hospital by the investigators in the clinic.

A SPACELABS 90202 ambulatory blood pressure monitoring was used for measurement of blood pressure and heart rate during 24 hours.

Measures

Fifty-four subjects were mailed invitations to attend a personal interview designed to introduce a non-pharmacological treatment for essential hypertension. After the details of the treatment were explained, those who agreed to participate, underwent the following baseline period of evaluation. After a resting period of five minutes, three separate measurements of blood pressure, with an interval of two minutes between each, were obtained for each subject. The mean of the last two measurements was considered as the score on the dependent variables (systolic and diastolic blood pressure and heart rate) for the session. The baseline period for all subjects lasted between 23 and 28 days, depending on the subjects' availability. During this period, four blood pressure and heart rate measurements were obtained for each subject. Those patients whose diastolic BP was between 90-104 were included in the study and submitted to the ABPM. Eight patients did not fulfil this requirement and were excluded from this study. In this way, no patient with white coat hypertension was included in the research, as was confirmed in the results of ABPM. Six patients refuse to participate in the study before being allocated at any group.

Procedure

Each of the 40 subjects was randomly assigned to one of the four following groups (Table 1): the unmedicated relaxation group (G1=10), unmedicated control group (G2=10), medicated relaxation group (G3=10), medicated control group (G4=10). All 40 subjects completed the study. Subjects in the medicated groups were treated with calcium antagonists and beta blocking agents. In the medicated relaxation group 7 subjects were taking beta blocking agents and 3 subjects calcium antagonists. In the medicated control group 5 subjects were taking beta blocking agents and 5 subjects calcium antagonists. The 40 participants signed a consent form detailing the measurement procedures and informing them that they would receive one of the two BP control programmes.

Table 1
Group characteristics

Group	Sex	Age (yr)
Unmedicated Relaxation	Female 4	Mean = 47.10 SD = 10.10
	Male 6	
Unmedicated Control	Female 7	Mean = 42.7 SD = 13.2
	Male 3	
Medicated Relaxation	Female 6	Mean = 46.8 SD = 11.01
	Male 4	
Medicated Control	Female 7	Mean = 54.5 SD = 8.2
	Male 3	

The decision as to which drug would be preferable to used was based on a variety of considerations and characteristics for each particular patient. Nevertheless, all drugs had the same therapeutic efficacy. Except for the therapist and the participants, all others involved in the study (doctor and nurses) were blinded with respect to the participants' treatment group, in order to the medical decisions would not be affected by the knowlegde of the treatment condition that each one of the patients was receiving.

Subjects included in the «relaxation groups» were exposed to a progressive muscular relaxation program of eight sessions, in addition to homework assignments aimed at providing self-control over stressful situations encountered in daily life. This involved eight one-hour weekly treatment sessions during which participants met individually with the therapist. Homework inter-session assignments included: daily practice of relaxation, subjective self-assessment of relaxation practice, and confrontation «in vivo» with stressful situations (Amigo, Buceta, Bueno & Becoña, 1991). (Table 2).

The patients in the control group also came to hipertensión unit 1 time a week for 8 weeks. Their BP were taken after 10 minute's rest on a couch. They were neither instructed in relaxation nor told their BP levels.

Statistical Analysis

Analysis of covariance, with pre-treatment BP or HR as the covariate, was used to test the treatment group differences in post-treatment and follow-up blood pressure readings. Analysis of covariance was made to test the effects of treatment as this reduces the bias caused by differences between groups that exist before the treatments are administered. A Student «t» test was used for the *post hoc* comparisons. Analysis of variance was used to test the treatment group differences in relation to weight, age, SBP, DBP and HR at referral during the first baseline session.

Results

Analysis of variance showed that the groups did not differ reliably with respect to weight, SBP, DBP and HR as measured at referral during the first baseline session. The participants' average body weight, measured at referral and at post-treatment, did not change over the study period, and no significant difference was found between groups. In relation to age, no significant difference between groups was found.

AMBULATORY BLOOD PRESSURE (24 hours, table 3)

Systolic blood pressure. Analysis of covariance revealed a treatment group difference on SBP (p<.000), at post-treatment. Subsequent analysis using a student A«t» test revealed significant differences between the unmedicated relaxation group and unmedicated control group (p<.052), between the medicated relaxation group and medicated control group (p<.006) and between the unmedicated relaxation group and medicated control group (p<.008). A Student «t» test showed that SBP decreased significantly in the unmedicated relaxation group (p<.000) and medicated relaxation group (p<.001). The unmedicated control group increased significantly SBP (p<.036). The results were similar at 6 month follow-up (p<.000). Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated con-

Table 2
Basic intervention procedure for subjects included in the group having the relaxation programme

Sessions work with therapist	Homework intersession assignments
1. – Brief explanation of the nature and goals of the programme – Training in progressive relaxation – Discussion about patients homework assignments	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Keeping record of stressful situations
2. – Brief discussion about homework assignments – Training in progressive relaxation – Setting imaginal scenes of low- intensity of stressful situations – Discussion about patients next homework	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Keeping record and self-rating of stressful situations
3. – Brief discussion about homework assignments – Setting imaginal scenes of medium-intensity of stressful situations – Training in progressive relaxation – Discussion about patients next homework	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Specific record and self-rating of stressful situations
4. – Brief discussion about homework assignments – Training in progressive relaxation – Confrontation in imagination with stressful situations of low and medium intensity, using the muscle relaxation – Discussion about patients next homework	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Confrontation in vivo with stressful scenes of low and medium intensity, using the muscle relaxation – Keeping record and self-rating of in vivo confrontation experience
5. – Brief discussion about homework assignments – Training in progressive relaxation – Confrontation in imagination with stressful situations of higher intensity, using the muscle relaxation	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Specific record and self-rating of stressful situations – Confrontation in vivo with stressful scenes of higher intensity, using the muscle relaxation
6,7,8. – Brief discussion about homework assignments – Training in progressive relaxation – Confrontation in imagination with scenes of high stress – Discussion with the patient about the behavioural skills learned during the training and the way of applying these skills in the future	– Daily practice of relaxation – Subjective self-assessment of relaxation practice – Self-monitoring and confrontation in vivo with stressful situations

trol group ($p < .013$), between the medicated relaxation group and medicated control group ($p < .000$) and between the unmedicated relaxation group and medicated control group ($p < .002$). A Student «t» test showed that SBP decreased significantly in the medicated relaxation group ($p < .01$).

Diastolic blood pressure. Analysis of covariance revealed no treatment group difference on DBP, at post-treatment. However, at 6 month follow-up revealed a treatment group difference on DBP ($p < .000$). Subsequent analysis using a student A«t» test revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .005$), between the medicated relaxation group and medicated control group ($p < .014$) and between the unmedicated relaxation group and medicated control group ($p < .024$). A Student «t» test showed that DBP decreased significantly in the unmedicated relaxation group ($p < .011$) and in the medicated relaxation group ($p < .004$).

Heart rate. Analysis of covariance revealed a treatment group difference on HR ($p < .011$), at post-treatment. Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .005$). A Student «t» test showed that HR decreased significantly in the unmedicated relaxation group ($p < .050$) and medicated relaxation group ($p < .027$). At follow-up, analysis of covariance revealed no treatment group difference on HR.

Table 3
Ambulatory Blood Pressure Monitoring and Heart Rate Data (24 hours)

Group	Pre-treatment mean (SD)	Post-treatment mean (SD)	Follow-up mean (SD)
(1) Unmedicated Relaxation			
SBP	141.5 (14.84)	127.7 (12.45)	128.2 (11.52)
DBP	90.1 (10.52)	80.6 (7.38)	78.8 (7.9)
HR	81.3 (12.95)	73.1 (5.74)	72.2 (6.76)
(2) Unmedicated Control			
SBP	134.3 (8.12)	138.2 (10.14)	141.2 (9.45)
DBP	86.5 (8.93)	87.5 (9.29)	89.5 (6.84)
HR	81.7 (8.12)	82.3 (7.12)	83.4 (6.6)
(3) Medicated Relaxation			
SBP	134.2 (12.73)	127.9 (11.23)	125 (9.78)
DBP	85 (10.31)	79 (7.62)	78 (7.62)
HR	76.8 (10.17)	71.9 (8.74)	71.5 (9.24)
(4) Medicated Control			
SBP	140.1 (16.99)	144.1 (12.03)	146.8 (11.02)
DBP	85.9 (10.18)	86.7 (11.15)	89.5 (11.08)
HR	71.6 (13.28)	74.4 (14.16)	77.1 (14.62)

AMBULATORY BLOOD PRESSURE (nocturnal from 24 AM to 6 AM, table 4)

Systolic blood pressure. Analysis of covariance revealed a treatment group difference on SBP ($p < .000$), at post-treatment. Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .025$), between the medicated relaxation group and medicated control group ($p < .015$) and between the unmedicated relaxation group and medicated control group ($p < .011$). A Student «t» test showed that SBP decreased significantly in the unmedicated relaxation group ($p < .000$) and medicated relaxation group ($p < .017$). The unmedicated control group increased SBP significantly ($p < .030$). The results were similar at 6 month follow-up ($p < .000$). Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .009$), between the medicated relaxation group and medicated control group ($p < .007$) and between the unmedicated relaxation group and medicated control group ($p < .015$). A Student «t» test showed that SBP decreased significantly in the medicated relaxation group ($p < .002$) and unmedicated relaxation group ($p < .017$). The unmedicated control group increased significantly the SBP ($p < .035$).

Diastolic blood pressure. Analysis of covariance revealed a treatment group difference on DBP, at post-treatment ($p < .000$). Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .010$). A Student «t» test showed that DBP decreased significantly in the unmedicated relaxation group ($p < .004$) and in the medicated relaxation group ($p < .012$).

Heart rate. Analysis of covariance revealed a treatment group difference on HR ($p < .001$), at post-treatment. Subsequent analysis revealed significant differences between the unmedicated relaxation group and unmedicated control group ($p < .002$). A Student «t» test showed that HR decreased significantly in the unmedicated relaxation group ($p < .047$) and medicated relaxation group ($p < .026$).

At follow-up, analysis of covariance revealed no treatment group difference on HR.

Medication

Subjects who had medication prescribed before treatment continued on it at post-treatment. At 6 month follow-up, however, four unmedicated control group subjects were started on medication and five medicated control group subjects increased their medication consumption by 50%. In contrast, six medicated relaxation group subjects reduced their medication consumption by 50%, and only one increased the medication.

Clinical relevance of the results

According to established criteria (Helgeland, 1980) significant clinical reductions were considered when systolic BP reduction is more than 10 mm Hg, diastolic BP drops more than 5 mm Hg and HR decreases by more than 5 beats by minute.

Seven subjects in the unmedicated relaxation group and 6 in the medicated relaxation group demonstrated marked clinical reductions in their SBP and/or DBP at post-treatment, while only 2 subjects in the unmedicated control group, and 1 in the medicated control group, did so. At the 6-month follow-up, 7 subjects in the unmedicated relaxation group and 8 in the medicated relaxation group demonstrated marked clinical reductions in their systolic and/or diastolic blood pressure at post-treatment, while only 2 subjects in the unmedicated control group, and nobody in the medicated control group, did so.

Concerning HR, 4 subjects in the unmedicated relaxation group and 5 in the medicated relaxation group demonstrated marked clinical reductions, while only 1 subject in the unmedicated control group, and one in the medicated control group, did so. At the 6-month follow-up, 5 subjects in the unmedicated relaxation group and 5 in the medicated relaxation group demonstrated marked clinical reductions in their HR at post-treatment, while only 2 subjects in the unmedicated control group, and nobody in the medicated control group, did so.

Discussion

The results of this study clearly demonstrate that relaxation training is of value in significantly reducing systolic blood pressure in medicated and unmedicated essential hypertension and heart rate in unmedicated hypertensives. These results of the relaxation groups were clearly superior to those observed in the control groups at post-treatment. At 6 month follow-up, these reductions persisted for systolic blood pressure and were significant for diastolic blood pressure, but not with respect to heart rate. In this study subjects were instructed to continue practicing relaxation techniques after finishing the treatment.

These data are in agreement with other studies employing similar programs and relaxation training (Patel, Marmot, Terry, Carruthers, Hunt & Patel, 1985; Irvine, Johnston, Jenner & Marie, 1986; Amigo, Gonzalez & Herrera, 1997) and which similarly showed significant reductions in SBP and/or DBP. However, the findings are not in agreement with other studies (Van Montfrans, Karemaker, Wieling & Dunning, 1990) in which has been used the ambulatory blood pressure monitoring. This can be explained because in our research the mean blood pressure levels of the subjects at the

Table 4
Ambulatory Blood Pressure Monitoring and Heart Rate Data
(From 24 AM to 6 AM)

Group	Pre-treatment mean (SD)	Post-treatment mean (SD)	Follow-up mean (SD)
(1) Unmedicated Relaxation			
SBP	134.9 (9.2)	122.1 (8.2)	122.6 (9.6)
DBP	82.5 (7.2)	75.7(9.8)	75.1 (8.1)
HR	68 (9.2)	61.1 (7.2)	61.4(10.5)
(2) Unmedicated Control			
SBP	128.8 (7.5)	134.2 (8.7)	137.5 (7.2)
DBP	82.5 (3.8)	84.9 (6.4)	85.7(6.3)
HR	77.3 (11.8)	79.4 (11.2)	80.4(8.5)
(3) Medicated Relaxation			
SBP	127.9 (8.2)	122.8 (10.1)	120.2 (10)
DBP	80.16(3)	74.7(8.0)	72.5 (8.9)
HR	71.6 (7.7)	65.5 (9.8)	65.1 (10.8)
(4) Medicated Control			
SBP	137.5 (7.5)	139.7 (8.7)	142.07.2)
DBP	81.9 (3.8)	84 (6.4)	85.7 (6.3)
HR	69.4 (11.8)	70 (11.2)	70 (8.5)

beginning of the treatment was higher. Furthermore, the results of BP and HR changes during the nocturnal period, between the 24 hours and 6 a.m. confirm the efficiency of the relaxation training. The reduction of the cardiovascular activity during the night can be especially healthy in the hypertensive patients that have a high cardiovascular risk, because the reduction of ABPM and most all its nocturnal component, is better correlated with cardiovascular prognosis (Yamamoto, Akiguchi, Oiwa, Hayashi & Kimura, 1998; Gueyffier, Cornu, Bossard, Mercier, Sebaoun & Jullien, 1999; Mallion, Baguet, Siche, Tremel & De Gaudemaris, 1999).

One issue frequently raised in similar research studies, centers on whether statistically significant results obtained during such experimental trials, have any clinical relevance with respect to long-term blood pressure reduction in essential hypertension. This study confirms the results of previous research (Amigo, González & Herrera, 1997) in which the reduction of SBP, DBP and HR had clinical significance for most subjects in the experimental groups.

With respect to HR, the reduction observed in the unmedicated relaxation group was greater than that observed in the unmedicated control group at post-treatment. Probably, no differences was found between medicated groups because of the effect of medication (beta-blockers) on HR. In any case, this is an important finding, based on research demonstrating the following: Mortality increases with increased HR at rest (Thaulow & Erikssen, 1991). Although anti-hypertensive drugs can lower the risk for cerebrovascular accidents and renal insufficiency, they are not effective in significantly reducing the incidence of angina or myocardial infarction (Houston, 1989; Helgeland, 1980). This may relate to the increased association between hypertension and glucose intolerance and/or insulin resistance, which are known coronary risk factors that anti-hypertensive medication can trigger (Houston, 1989; Swislocki, 1989). Finally, the hemodynamic models of hypertension demonstrate that this disorder follows an evolutionary deve-

lopment in which the initial changes result from an increase in cardiac output, which can be related to increased HR (Obirst, 1980). In this regard, others have observed that high resting HR was associated with high blood pressure after 32 years of follow-up (Gillum, Taylor & Anderson, 1981). This study found that participants with HR below the mean, had lower blood pressures on follow-up that averaged 10 mm Hg (SBP) and 5 mm Hg (DBP), compared to those with a HR above this distribution.

Based on these findings, we believe that additional research is required to further evaluate the efficacy of non-pharmacological treatment of mild hypertension on HR. From a hypothetical viewpoint, lowering this parameter could theoretically reduce the development of hypertensive disease and its consequences.

On the other hand, the results of the experimental groups (medicated and unmedicated) have shown specific changes in HR. Only the subjects belonging to the unmedicated relaxation group showed a significant reduction in HR at the end of the treatment. This can be explain because most of the subjects of the medicated relaxation group were taking beta-blockers. This drug provokes a significant decrease in HR, therefore it is possible that those patients that they were taking this type of medication had a lower HR and they would not be so responsive to HR lowering effects of muscle relaxation.

Finally, it is of interest to consider the effects of non-pharmacological approaches on the use of medication. The unmedicated experimental group resulted in a delay in pharmacological treatment, when compared to the unmedicated control group and six medicated relaxation group subjects reduced the medication consumption in a 50% while only one increased it. In addition to economic savings, this implies, prolonging the period of an improved quality of life, since antihypertensive drugs can have annoying side effects that interfere with this (Nies, 1975; Croog, Levine & Sudilovsky, 1988).

References

- Alexander, C.N., Schneider, R.H. & Staggars, F. (1996). Trial of stress reduction for hypertension in older African Americans II: sex and risk subgroup analysis. *Hypertension*, 28, 228-237.
- Amigo, I., Buceta, J.M., Bueno, A.M. & Becoña, E. (1991). Cognitive behavioural treatment for essential hypertension: A controlled study. *Stress Medicine*, 7, 103-108.
- Amigo, I., Gonzalez, A. & Herrera, J. (1997). Comparison of physical exercise and muscle relaxation training in the treatment of mild essential hypertension. *Stress Medicine*, 13, 59-65.
- Amigo, I., Fernández, A. & Gonzalez, A. (2001). Relajación muscular e hipertensión arterial: estudio controlado con pacientes medicados y no medicados. *Psicología Conductual*, 9, 131-140.
- Boota, A., Varma, R. & Singh A. (1995). Role of relaxation in hypertension. *Journal Indian of Academy Applied Psychology*, 21, 29-36.
- Croog, S.H. Levine, S. & Sudilovsky, A. (1988). Sexual symptoms in hypertensive patients: a report on a clinical trial. *Archives of Internal Medicine*, 148, 788-794.
- Davison, G., Williams, M., Nezami, E., Bice, T. & Dequattro, V. (1991). Relaxation, reduction in angry articulated thoughts and improvements in borderline hypertension and heart rate. *Journal of Behavioral Medicine*, 14, 453-468.
- Gillum, R.F., Taylor, H.L. & Anderson, J. (1981). Longitudinal study (32 years) of exercise tolerance, breathing response, blood pressure and lipids in young men. *Arteriosclerosis*, 1, 455-462.
- González, A. & Amigo, I. (2000). Efectos inmediatos del entrenamiento en relajación muscular progresiva sobre índices cardiovasculares. *Psicot-hema*, 12, 25-32.
- Gueyffier, F., Cornu, C., Bossard, N., Mercier, C., Sebaoun, A. & Jullien, G. (1999). Prognostic importance of ambulatory arterial pressure monitoring in France. Initial results of the OCTAVE study. *Archives Maladies d' Coeur et Vaiss*, 92, 1151-1157.
- Helgeland D. (1980). Treatment of mild hypertension: A five year controlled drug trial. The Oslo Study. *American Journal of Medicine*, 69, 725-743.
- Houston M.C. (1989). The risk cardiovascular. *American Heart Journal*, 117, 911-914.
- Irvine, M.J., Johnston, D.W., Jenner, D.A. & Marie G.V. (1986). Relaxation and stress management in the treatment of essential hypertension. *Journal of Psychosomatic Medicine*, 30, 437-450.
- Johnston, D.W. (1991). Stress management in the treatment of mild hypertension. *Hypertension*, 17(suppl III), III63-III68.
- Joint national committee on detection, evaluation and treatment of high blood pressure. The fifth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-V) (1993). *Archives of Internal Medicine*, 153, 154-183.
- Joint national committee on detection, evaluation and treatment of high blood pressure. The sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-VI) (1997). *Archives of Internal Medicine*, 157, 2413-2446.

- Mallion, J.M., Baguet, J.P., Siche, J.P., Tremel, F. y De Gaudemaris, R. (1999). Clinical value of ambulatory blood pressure monitoring. *Journal of Hypertension*, 17, 585-595.
- Nies, A.S. (1975). Adverse reactions and interactions limiting the use of antihypertensive drugs. *American Journal of Medicine*, 58, 495-503.
- Obrist, P.A. (1981). *Cardiovascular Psychophysiology: a Perspective*. New York: Plenum Press.
- Patel, C., Marmot, M., Terry, D., Carruthers, M., Hunt, B. & Patel, M. (1985). Trial of relaxation in reducing coronary risk: four years follow-up. *British Medical Journal*, 290, 1103-1106.
- Swislocki LM. (1989). Hypertension. *American Journal of Hypertension*, 2, 419-423.
- Thaulow, E. & Erikssen, J.E. (1991). How important is heart rate?. *Journal of Hypertension*, 9(suppl 7), S27-S30.
- Van Montfrans, G.A., Karemaker, J.M., Wieling, W. & Dunning, A.J. (1990). Relaxation therapy and continuous ambulatory blood pressure in mild hypertension: a controlled study. *British Medical Journal*, 300, 1368-1372.
- Yamamoto, Y., Akiguchi, I., Oiwa, K., Hayashi, M. & Kimura, J. (1998). Adverse effect of nighttime blood pressure on the outcome of lacunar infarct patients. *Stroke*, 29, 570-576.

Aceptado el 23 de agosto de 2001