

REVIEW

HYPERTENSION AND DEPRESSION

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Despite the high prevalence of depression and hypertension, the relationship between the two diseases has received little attention. This paper reviews the epidemiological, pathophysiological, and prognostic aspects of this association, as well as its implications for treatment. A Medline search was conducted using the following key words: depression, blood pressure, blood pressure variability, physical morbidity, hypertension, mood, stress, hypertension, antidepressive agents, and genetics, from 1980 to 2004. We found descriptions of increased prevalence of hypertension in depressed patients, increased prevalence of depression in hypertensive patients, association between depressive symptomatology and hypotension, and alteration of the circadian variation of blood pressure in depressed patients. There is considerable evidence suggesting that hyperreactivity of the sympathetic nervous system and genetic influences are the underlying mechanisms in the relationship between depression and hypertension. Depression can negatively affect the course of hypertensive illness. Additionally, the use of antidepressive agents can interfere with blood pressure control of patients with hypertension by inducing changes in blood pressure and orthostatic hypotension.

KEYWORDS: Depression. Cardiology. Hypertension. Blood pressure. Antidepressive agents.

Several studies have focused on the association between depression and cardiovascular diseases; however, the relationship between depression and hypertension has received less attention. Nevertheless, interactions between blood pressure (BP) and psychic factors have been observed. O'Hare observed that by asking hypertensive patients to talk about health problems or other life stresses, he could induce substantial increases in their BP, and while after resting quietly for 20 to 40 minutes, they had large drops in BP.¹ Over the next several decades, these observations were replicated many times by other investigators who also found that BP measurements by a doctor are frequently accompanied by marked increased BP and heart rate (HR). This increase (named the "white-coat" effect) is quite common and is believed to be a consequence of an

anxiety response to the doctor's visit.²

Since both hypertension and depression are highly prevalent, it is extremely important to better understand the relationship between them.

METHOD

This paper reviews the epidemiological, pathophysiological, and prognostic aspects of the association between hypertension and depression, as well as its implications for treatment. The method was a Medline search, which was conducted using the following key words: depression, blood pressure (BP), blood pressure variability (BPV), physical morbidity, hypertension, mood, stress, hypertension, antidepressive agents, and genetics, from 1980 to 2004.

RESULTS

Epidemiologic aspects

Both hypertension and hypotension have been observed in association with depression or depressive symptoms.

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Hypertension in depressive patients

An increased prevalence of hypertension in depressed patients has been described by Adamis and Ball.³ They studied the comorbidity between psychiatric and physical diseases in 75 elderly psychiatric inpatients, and found that depressed patients had more cardiovascular diseases and hypertension than other psychiatric patients.³ Nakagawara et al.⁴ also found an increased frequency of hypertension in depressed patients, but only in those with melancholic features.

A depressive mood has also been associated with higher BP levels,^{5,6} being positively associated with higher levels of systolic BP (SBP) and diastolic BP (DBP) in 24-hour BP monitoring of 54 subjects over 7 days.⁵ Additionally, significantly higher BP was found in 15 subjects with a clinical diagnosis of depression.⁵

Prospective studies have also suggested that depression may be a risk factor for the development of hypertension. In a study of 2992 normotensive subjects (25 to 64 years) who were followed for 6 to 7 years, to evaluate the prospective association between depressive symptoms and development of hypertension, high scores of depressive symptoms doubled the risk for hypertension, defined as a BP of 160/95 mm Hg or over, or a prescription of antihypertensive medications.⁷

Symptoms of depression and anxiety, measured by the General Well-Being Schedule were also associated with elevated risk of incident hypertension ($n = 3310$), and this effect was more pronounced in black women ($RR = 3.12$; 95% $CI = 1.24-7.88$) compared to white women ($RR = 1.73$; 95% $CI = 1.30-2.30$) or men ($RR = 1.56$; 95% $CI = 1.08-2.25$).⁸

Depression in hypertensive patients

Increased prevalence of depression has been described in hypertensive patients as well. Rabkin et al. found a 3-fold higher frequency of major depression in patients treated for hypertension.⁹

Hopelessness was associated with increased incidence of hypertension in 616 initially normotensive men, in a 4-year follow-up prospective study in Finland. Men reporting high levels of hopelessness at baseline were 3 times more likely to become hypertensive than men who were not hopeless, after adjustments for age, body mass index, baseline resting BP, physical activity, smoking, alcohol consumption, education, and parental history of hypertension.¹⁰

Hypotension and Depression

Conversely, the concept of a "hypotensive syndrome" emerged in the 1980s. It consisted of somatic symptoms such as tiredness, dizziness, headaches, with occasional minor psychiatric symptoms such as anxiety and depression.¹¹

Numerous treatments were tried, ranging from harmless tonics to digoxin, amphetamine, and ergotamine. Other associated symptoms included general fatigue, overexertion, psychosomatic symptoms, readiness to cry, feeling scared and panicky, feeling under strain, unable to enjoy normal activities, and unable to concentrate.¹¹⁻¹⁴ Several authors suggested that a primary psychiatric disorder such as depression could account for the symptoms of the syndrome and could be related to low BP as well.

There are also recent descriptions of low BP associated with depressive symptoms. In a study of 2723 elderly persons living in the community, hypotension was associated with increased depressive symptomatology, after adjustments for age, gender, and prescriptions for antihypertensives. Hypotensive subjects also had lower self-esteem.¹⁵

An inverse relationship between low diastolic BP (DBP) and depressive symptoms was demonstrated in a population study with 846 elderly men without a psychiatric diagnosis. Higher levels of depressive symptoms and more diagnosis of depression were found in those subjects with $DBP < 75$ mm Hg. Men with diastolic hypertension had more affective and somatic symptoms, such as fatigue, pessimism, sadness, and loss of appetite, weight loss, and preoccupation with health.¹⁶

Abnormal Circadian Blood Pressure Regulation

Abnormal circadian BP regulation has been associated with depression.¹⁷ Depressive symptoms were associated with a higher night/day systolic BP (SBP) ratio in 126 men who were without psychiatric diseases and medication-free.¹⁷ Autonomic nervous system dysfunction and abnormal hormonal regulation have been hypothesized to explain the results.¹⁷

In another study, self-reported depression was associated with higher SBP and DBP measurements and lower day/night BP ratios.¹⁸

Nevertheless, 24 h blood pressure monitoring revealed an increased mean 24 h SBP but normal nighttime BP level in a substantial subgroup of depressed inpatients, resulting in a high day/night BP ratio. The subjects had no hypertension but presented more cardiovascular reactivity during the day and difficulty in falling asleep in the evening.¹⁹ Additionally, less effective BP regulation in response to an orthostatic challenge has been associated with depression in 33 subjects.²⁰

Another indicator of poor BP regulation in depressive patients was the larger postprandial drop in systolic BP detected by Schwartz et al.²¹

There are also studies that failed to find an association between depression and BP. No significant differences in

BP were found between depressed and nondepressed psychiatric inpatients ($n = 1046$).²² The CARDIA Study (1996) examined cross-sectional relationships among depressive symptoms, anxiety, alcohol intake, and blood pressure in a sample of 4352 adults and found that depressive symptoms and anxiety were unrelated to BP.²³

Pathophysiology

Depression and Autonomic Nervous System (ANS)

The physiological mechanisms underlying the relationship between depression or anxiety and BP probably involve the effect of the sympathetic nervous system.^{23,24}

Data available at present show that sympathetic activation is a specific feature of essential hypertension, and it may play a pathogenic role in this disease. A metaanalysis showed that plasma noradrenaline, as an indirect marker of sympathetic tone, was elevated in patients with essential hypertension.²⁵ In addition, it was shown that the rate of noradrenaline spillover from sympathetic nerve terminals was sometimes increased in essential hypertension.²⁶ Additional data have emerged from direct measurements of sympathetic nerve traffic to skeletal muscle circulation using a microelectrode technique (microneurography). Most studies using this method have demonstrated increased sympathetic nerve activity in patients with essential hypertension. In contrast, patients with secondary hypertension did not differ from normotensive patients.²⁶

There is also reported evidence showing abnormal autonomic nervous system function in depression, specifically regarding increased sympathetic activity and poor vagal control. Several studies have examined cerebrospinal fluid (CSF), plasma or urinary levels of norepinephrine (NE) and its major central nervous system metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG). Plasma NE and/or MHPG levels have been reported to be elevated in depressive patients.²⁷⁻³⁰ Norepinephrine was significantly elevated in depressive patients compared with controls, although the rate of NE clearance from plasma was similar in both groups.³¹ Maes et al. measured the 24 h urinary excretion of noradrenaline (NA), adrenaline (A), dopamine (DA), and MHPG in depressed subjects. There were significant positive correlations between sleep disorders and NA, A, and DA excretion. The excretion of MHPG was negatively related to anxiety and hypochondriasis. It was suggested that these relationships between these symptoms and the dysfunction in the turnover of catecholamines could reflect the occurrence of a hyperarousal state in some major depressive disorders.³²

Other indicators of sympathetic nervous activity have also been studied in depressive patients. Lechin et al. found

higher heart rate increases during orthostasis and exercise periods and greater NA values in depressed patients, suggesting maximal neural sympathetic activity in them.³³ Bruno et al. assessed cardiovascular autonomic functioning in 22 unipolar depressive inpatients. Sympathetic cholinergic, alpha- and beta-adrenergic activity was assessed via the measurement of forearm blood flow (FBF) and the cardiac pre-ejection period (PEP). Significant negative correlations were found between depressive symptoms and FBF and significant positive correlations were found between depressive symptoms and PEP. It was concluded that the autonomic profile of depression is characterized by a decrease in central sympathetic cholinergic outflow, coupled with increases in alpha-adrenergic and in beta-adrenergic activity.³⁴ Diminished heart rate variability (HRV) also reflects increased sympathetic activity and decreased parasympathetic activity in depressive patients.³⁵⁻⁴⁰ Twenty-four hour ECG recordings were obtained from major depressive patients, normal controls, and medically healthy volunteer participants. High-frequency variability was markedly diminished in depressed patients, indicating that they may have an abnormality in parasympathetic nervous system activity.⁴¹ In another study, 380 acute myocardial infarction (MI) patients with depression and 424 acute MI patients without depression were compared. All but one HRV index remained significantly lower in patients with depression than in patients without depression, suggesting increased sympathetic activity and/or decreased parasympathetic modulation.³⁷ Increases in HRV were positively correlated with post-treatment Hamilton Rating Scale for Depression (HAM-D) scores after a therapeutic trial of various antidepressant medications.^{42,43} On the other hand, patients treated with mirtazapine or amitriptyline showed significant decreases in HRV after the treatment.⁴⁴

The hypothesis of hyperactivity of the sympathetic nervous system is not the only possible explanation for the relationship between depression and BP. Siever and Davis⁴⁵ proposed that the activity of neurotransmitter systems in affective disorders may be better understood as a reflection of a relative failure in their regulation, rather than simple increases or decreases in their activity. Thus, the impairment in the regulation of the noradrenergic system would be expected to disturb the individual affective responsiveness to external or internal stimuli. Stressful stimuli that episodically increase noradrenergic activity would be associated with dysphoric hyperarousal because this arousal would not be easily dampened by feedback mechanisms. Decreases in noradrenergic availability secondary to depletion by periodic excessive release could easily be seen as mediating anergic and vegetative symptoms. The exact configuration of these abnormalities might vary depending on the indi-

vidual and/or phase of the illness, so that appetite, sleep, and motor activity may be decreased or increased in depression.⁴⁵ Siever and Davis' theory seems very interesting and could explain the increased vulnerability for hypertension in depression. In addition, this theory is in accordance with the mixed BP findings in depressive patients.

Sloan et al. also associated autonomic control and BP to depression. Established psychological/behavioral risk factors for coronary artery disease (CAD), such as depression, hostility, and anxiety, are associated with diminished control of the heart, which may disinhibit pathogenic BP variability (BPV).⁴⁶ Blood pressure oscillates at high (0.15-0.5 Hz) and lower frequencies (0.02-0.15 Hz). An intact autonomically mediated cardiac control system, including baroreflexes, acts to buffer fluctuations in BP, especially in response to challenge. This increased BPV is harmful to the coronary arteries, contributing to plaque formation, plaque rupture, and acute coronary events. It is also related to greater left ventricular mass, higher urinary albumin excretion, carotid atherosclerosis, and cardiovascular morbidity in hypertensive subjects.⁴⁶ In CAD patients, depression was associated with low baroreflex sensitivity.⁴⁷

Stress and ANS

There is a considerable amount of data linking sympathetic nervous system hyperresponsivity to the development of hypertension. Hyperresponsivity is manifested by exaggerated HR and BP responses to psychological stimuli, experienced as engaging, challenging, or aversive.⁴⁸ One line of evidence suggesting a link between hyperreactivity and hypertension is the similarity between autonomically-mediated cardiovascular changes in the presence of borderline hypertension and those evoked in more reactive normotensive persons during certain types of behavioral events. Studies of hemodynamics in borderline hypertensive patients have shown an increased cardiac output, mediated by enhanced beta-adrenergic activity and decreased parasympathetic stimulation of the heart.¹

Patients with established hypertension have been observed to show greater HR and BP increases than normotensive subjects in response to behavioral events such as difficult mental arithmetical operations, or interpersonal interactions designed to arouse fear or anger or to expose personal conflicts.¹

Hyperreactivity seems to be related to psychosocial aspects. Elevation of BP was associated with certain personality traits, such as anger and its suppression, and also to unexpected unfortunate life events.^{49,50} Evidence about the relationship between these factors and hypertension also points to an autonomic nervous dysfunction.^{1,49}

Compared with nonhostile individuals, hostile subjects

manifest higher HR and BP responses to physiological stimuli, such as mental tasks, as well as higher ambulatory BP levels during daily-life activity. Evidence also suggests that hostile individuals are more likely to exhibit hypercortisolemia and high levels of circulating catecholamines, as well as diminished beta-adrenergic receptor function of mononuclear leukocytes, diminished vagal modulation of heart function, and increased platelet reactivity.⁴⁸

The "white-coat effect" was addressed by Grassi et al. by quantifying the sympathetic outflow to muscle and skin by microneurography. Measurements were performed in hypertensive subjects during a control period, during a visit by a doctor unfamiliar to the patient, and during a recovery period. The doctor's visit induced a sudden, marked, and prolonged BP and HR response, accompanied by a significant increase in skin and sympathetic nerve traffic, characterized by activation of the adrenergic nervous system.⁵¹

Interestingly, borderline hypertensive subjects with BP hyperreactivity also had higher negative affect scores after tasks, suggesting an association between depressive symptoms and hyperreactivity.⁵²

Studies have demonstrated that relaxation training and biofeedback can lead to significant in-clinic BP reductions. It is suggested that individuals reporting high levels of anxiety should be considered initially for relaxation training.⁵³ The BP lowering effects attributable to relaxation and biofeedback training were carried over to the working day.⁵⁴ Initial evidence suggests that the long-term effects of practice of these procedures are consistent with the decreased responsivity to plasma norepinephrine.⁵³ A follow-up study demonstrated that the advantage for relaxation training was maintained 15 months after treatment.⁵³ Nevertheless, the specific physiologic and neurohormonal mechanisms by which these effects are obtained are not known.⁵³

Genetic Vulnerability

It is also widely accepted that BP and susceptibility to hypertension are influenced by genetic factors.⁵⁵ Recently, twin, adoption, and family studies have suggested that genetic factors are important in the etiology of mood disorders.⁵⁶ Some studies have suggested that a shared genetic vulnerability could explain the relationship between depression and hypertension.

Grewen et al.⁵⁵ investigated whether parental history of hypertension (FH+) enhances the impact on ambulatory blood pressure (ABP) of depressed mood as indexed by the Beck Depression Inventory (BDI), (n = 314). Higher BDI scores were significantly associated with higher 24-hour ABP in FH+ subjects, but not in participants without parental history of hypertension (FH-). Relationships were sig-

nificantly stronger in those with 2 hypertensive parents vs. those with 1 vs. those with no hypertensive parents. In contrast, interaction was least predictive of BP levels during sleep, suggesting that the influence of depression on BP in FH- subjects is manifested during responses to everyday stresses and strains.⁵⁵

Subjects with a positive family history of hypertension exhibited higher tonic levels of BP and HR at rest, during mental stress tasks, and during recovery.⁵⁷ Individuals with positive family histories reported more depression during the tasks, suggesting that genetic and psychological factors are involved with cardiovascular hyperreactivity.⁵⁷

Rats that were genetically prone to hypersensitivity had a very high propensity for developing depression (learned helpless behavior). Moreover, hyporesponsive functioning of the hypothalamus–pituitary–adrenal (HPA) axis correlates with a propensity for learned helpless behavior.⁵⁸ Interestingly, the blockade of the renin–angiotensin system with the angiotensin converting enzyme inhibitor reversed the learned helplessness in rodents.⁵⁹ Additionally, several clinical investigations have suggested that captopril, an angiotensin-converting enzyme inhibitor exhibits antidepressant properties in humans, suggesting that the renin–angiotensin system may not only participate in the elevation of BP but may also contribute to depression, although its mechanism is unknown.⁵⁸

However, there are controversial findings. Depressive symptoms measured by the CES-D (Centers for Epidemiological Studies–Depression Scale) were associated with mean arterial pressure (MAP) in 87 monozygotic twin pairs and 86 dizygotic twin pairs.⁶⁰ Nevertheless, the association accounted for an environmental effect that was independent of genetic effects.⁶⁰ Another study found no association between depression and genetic polymorphisms related to vascular disease.⁶¹

Complications

Although there is no definitive evidence of an association between depression and development of hypertension, depression can impair the management and prognosis of hypertension.^{62,63}

An epidemiological study analyzed the longitudinal association between depressive symptomatology and BP control, stroke, and cardiovascular-related mortality in the elderly. This study demonstrated an increased risk of stroke among older patients with hypertension and high levels of depressive symptoms, and the association appeared to be a function of BP control, particularly in women.⁶²

Depression has also been associated with higher risk of stroke in the elderly. In a prospective study, depressive

symptoms were predictive of ischemic stroke in 901 subjects in a Japanese rural area during a 10-year period.⁶⁴ Wassertheil-Smoller et al.⁶³ detected that a significant excess risk of death and stroke or myocardial infarction was associated with an increase in depressive symptoms in patients with 60 years of age or more ($n = 4736$) and with systolic hypertension (SH), defined as SBP ≥ 160 mm Hg and DBP < 90 mm Hg.

Depression was independently associated with a substantial increase in the risk of heart failure among 4538 persons aged 60 years and older with isolated systolic hypertension in a study for which the average follow-up period was 4.5 years (RR = 2.59; 95% CI: 1.57–4.27).⁶⁵ Depressed persons also had higher SBP levels.⁶⁵

Depression independently increased the risk of mortality in the 4-year follow-up period of 2847 subjects with 55 to 85 years old.⁶⁶ The relative risk for mortality was 1.6 (95% CI: 1.0–2.7) in subjects with minor depression and cardiac disease, 1.5 (95% CI: 0.9–2.6) in subjects with minor depression without cardiac disease, 3.0 (95% CI: 1.1–7.8) in subjects with major depression and cardiac disease and 3.9 (95% CI: 1.4–10.9) in subjects with major depression without cardiac disease. A dose-response effect was demonstrated in that the more severe the depression, the higher the mortality risk.⁶⁶

Heightened susceptibility to platelet activation may be a mechanism underlying the increased risk of ischemic heart and cerebrovascular disease and/or mortality after MI in depression.⁶⁷ Hypertensive patients with higher scores on standardized depression rating scales showed significantly greater platelet reactivity following serotonin stimulation compared to patients with lower depression scores.⁶⁸

On the other hand, hypertension has been proposed as a risk factor for the development of depression. Neuroimaging studies reveal higher frequency of ischemic abnormalities in late-life depression.⁶⁹ According to the theory of vascular depression, these abnormalities could represent a vulnerability to depression.³

Antidepressive treatment

Another implication of the presence of depression in hypertensive patients is represented by the side effects of antidepressive agents. Tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOI's) have been associated with both reduction and elevation in systolic and diastolic BP.¹² Although serotonin selective reuptake inhibitors (SSRIs) produce fewer hemodynamic effects, hypertension in patients taking SSRIs has also been reported.¹² A metaanalysis of BP changes in patients treated with venlafaxine, imipramine, or placebo demonstrated a dose-

dependent increase in BP with venlafaxine treatment.⁷⁰ Sustained hypertension (defined as a resting diastolic BP value ≥ 90 mm Hg plus a ≥ 10 mm Hg rise above baseline diastolic BP for at least 3 consecutive clinical visits) was observed in 4.8% of patients treated with venlafaxine, 4.7% of those treated with imipramine, and 2.1% of those receiving the placebo. The largest increases (13.2%) occurred at doses ≥ 300 mg daily.⁷⁰ Interestingly, more than one third of the hypertensive patients also showed a spontaneous reduction in BP during continued venlafaxine treatment. Patients with a history of preexisting hypertension or pretreatment diastolic BP >90 mm Hg did not demonstrate a greater risk for developing drug-induced hypertension.⁷⁰ Another metaanalysis was performed using original BP data of 3744 patients with major depression studied in controlled clinical trials comparing venlafaxine, imipramine, and placebo. Venlafaxine and imipramine were associated with small, but statistically significant increases in supine diastolic BP. The effect of venlafaxine was dose-dependent as well and did not adversely affect the control of BP for patients with preexisting high BP. However, the BP elevations were persistent during continuation of therapy.⁷¹

Another study examined BP in 796 depressed patients taking fluoxetine 20 mg daily for up to 12 weeks. A modest reduction in SBP and DBP measures was observed. Patients pretreated with DBP <60 mm Hg showed a modest increase in mean DBP. Patients with preexisting cardiovascular disease, including hypertension, showed no significant BP changes.¹²

Potential of noradrenergic neurotransmission may be a mechanism by which antidepressants increase BP. In hy-

pertensive crises associated with MAOI therapy, high levels of unmetabolized tyramine or sympathomimetics trigger norepinephrine release from peripheral sympathetic neurons.⁷¹ A regional increase of cardiac noradrenergic activity may be the mechanism by which desipramine (a potent norepinephrine reuptake inhibitor) increases BP.⁷²

Another hypothesis is that central serotonergic transmission may have an essential role in BP regulation. The serotonin reuptake blockade could initiate a cascade of changes in central serotonin neurotransmission that results in an enhancement of autonomic tone.¹² Grubb et al. have consistently demonstrated that fluoxetine and sertraline can increase and stabilize low BP in patients with neurocardiogenic hypotension and also provide sustained prophylaxis against recurrent hypotension.⁷³⁻⁷⁶

In clinical terms, the risk of orthostatic hypotension (OH) during the tricyclic pharmacotherapy is far more important than elevations of BP. The MAOIs also cause relatively high rates of OH.⁷¹

The elderly are more vulnerable to OH. Occurrence of OH and its association with the complaint of dizziness was studied in depressive elderly women receiving nortriptyline 35 to 100 mg daily for 8 weeks.⁷⁷ Normotensive and hypertensive subjects (BP controlled with thiazide diuretics) were compared. BP and HR were assessed at baseline and at every 2 weeks, and a tilt-table test was performed before and after treatment. There was an increase in the SBP drop on orthostasis in both groups (the mean SBP drop was 10.5 mm Hg for hypertensive and 7.7 mm Hg for normotensive women) and an increase in HR (mean increase of 14 bpm) (Fig. 1). Orthostatic hypotension was observed in

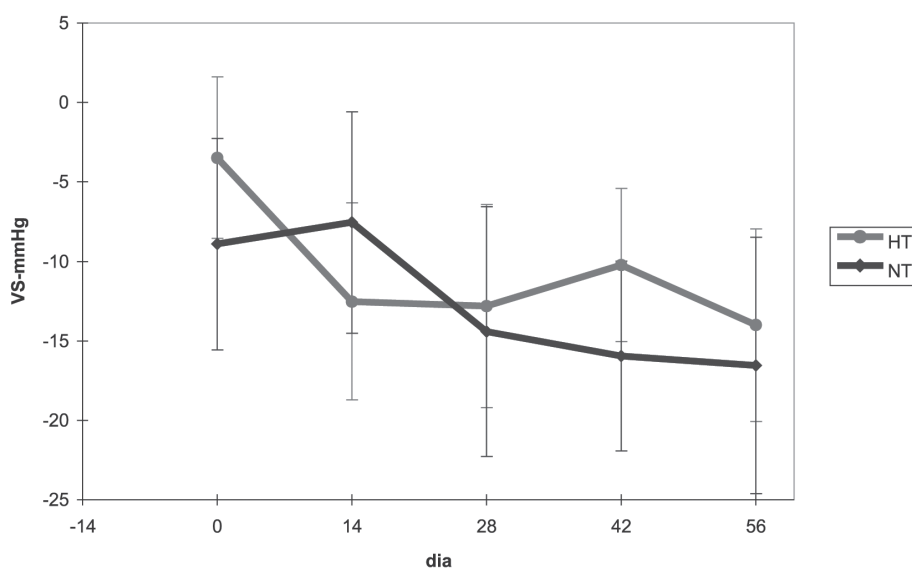


Figure 1 - Variation in systolic blood pressure at orthostasis (VS) during 8 weeks of treatment with nortriptyline. HT = hypertensive (21); NT = normotensive (22). Means and 95% confidence intervals (vertical bars). (Modified with authorization from Scalco MZ, Almeida OP, Hachul DT, Castel S, Serro-Azul J, Wajngarten M. Comparison of risk of orthostatic hypotension in elderly depressed hypertensive women treated with nortriptyline and thiazides versus elderly depressed normotensive women treated with nortriptyline. *Am J Cardiol.* 2000;85:1156-58).

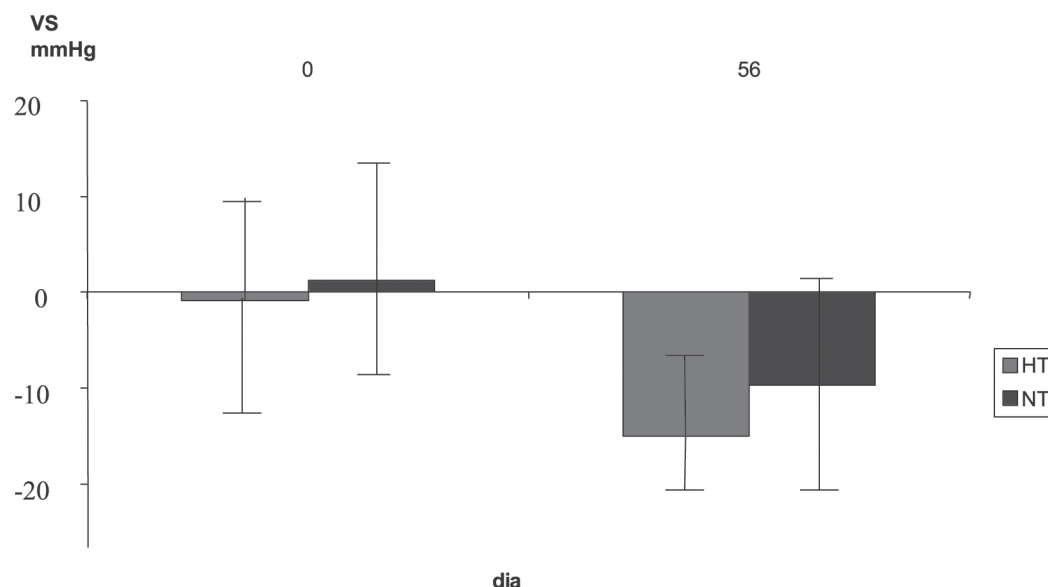


Figure 2 - Variation in systolic blood pressure at orthostasis during the tilt-table test before and after treatment. HT = hypertensive (19); NT = normotensive (21). Means and 95% confidence intervals (vertical bars). (Modified with authorization from Scalco MZ, Almeida OP, Hachul DT, Castel S, Serro-Azul J, Wajngarten M. Comparison of risk of orthostatic hypotension in elderly depressed hypertensive women treated with nortriptyline and thiazides versus elderly depressed normotensive women treated with nortriptyline. *Am J Cardiol.* 2000;85:1156-58).

21% of patients at baseline and in 33% after 8 weeks treatment. Results of tilt-table tests confirmed this increase in the frequency of OH after treatment (Fig. 2). There was no correlation between OH and subjective complaints of dizziness before or after treatment. Dizziness was reported by 53% and 38% of patients before and after treatment, respectively, suggesting that depression was probably involved with the frequency of complaints of dizziness.⁷⁷

Depressive patients have been considered to have a higher risk of OH while receiving tricyclic antidepressants compared to controls.⁷⁸ Autonomic dysfunction associated with depression could contribute to the vulnerability. Additionally, higher postprandial SBP drops have been described in the subsyndromal depressed elderly.⁷⁹

A reduction of the physiologic nocturnal drop of BP has also been reported in depressed elderly women during 8 weeks of treatment with nortriptyline. This could be explained by sympathetic hyperactivity leading to peripheral

vascular dilatation, suggesting that nortriptyline can affect BP in depressed elderly individuals.⁸⁰

CONCLUSION

The relationship between depression and BP is a complex issue. Published reports describe higher BP levels, higher incident hypertension, hypotension, and circadian variation abnormalities in depressed patients. Several causative factors have been proposed to explain this association, such as autonomic nervous system dysfunction, and more recently, genetic influences. The clinical relevance of this theme is clear, since depressive symptomatology is associated with poor BP control in hypertensive patients and with the development of complications of hypertension. Finally, extra care must be taken with depressive hypertensive patients to minimize the side effects on BP of antidepressants.

RESUMO

Scalco AZ, Scalco MZ, Azul JBS, Lotufo Neto F. Hipertensão arterial sistêmica e depressão. *Clinics.* 2005;60(3):241-50.

Apesar das altas prevalências de hipertensão arterial sistêmica e de depressão, o estudo da relação entre depres-

são e pressão arterial tem recebido pouca atenção da literatura. Nesse artigo são revisados os aspectos epidemiológicos, patofisiológicos, prognósticos e implicações no tratamento, relacionados à associação entre depressão e hipertensão arterial sistêmica. O método utilizado foi consulta ao banco de dados bibliográficos Medline, utilizando-se as

palavras chave *depression, blood pressure, blood pressure variability, physical morbidity, hypertension, mood, stress, hypertension, antidepressive agents e genetics*, no período de 1980 a 2004. Encontramos descrições de prevalência aumentada de hipertensão em pacientes deprimidos, prevalência aumentada de depressão em pacientes hipertensos, associação entre sintomatologia depressiva e hipotensão e alteração da variação circadiana da pressão arterial de pacientes deprimidos. Acredita-se que mecanismos envolvendo hiperatividade de sistema nervoso simpático e influências genéticas possam ser a base fisiopa-

tológica da relação entre depressão e hipertensão arterial sistêmica. Além disso, a presença de depressão pode piorar o curso da doença hipertensiva, e o uso de medicações antidepressivas pode induzir aumento de pressão arterial, diminuição de pressão arterial e hipotensão ortostática, dificultando o manejo de pacientes com hipertensão arterial sistêmica.

UNITERMOS: Depressão. Cardiologia. Hipertensão. Pressão arterial. Antidepressivos.

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