

ORTHOSTATIC INTOLERANCE AND PSYCHIATRIC MEDICATION. CLINICAL ASPECTS

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ABSTRACT:

Orthostatic intolerance is an important side effect and, sometimes, undervalued of psychiatric medication. Frequently, elderly patients with cardiovascular disease are diagnosed with depressive disorder and recommended treatment often causes hypotension.

Aim: To determine the role of antidepressant medication in the occurrence of orthostatic intolerance, orthostatic hypotension respectively.

Material and methods: The patients included in the study were selected from the cardiology clinic. After the anamnesis and a clinical and paraclinical examination and laboratory testing, an orthostatic tolerance test was performed. 40 patients were selected and they were divided into two groups, one with patients with known depressive disorder treatment and, a second group, with patients without psychiatric history.

Results and discussions: Differences in blood pressure determined in the supine and standing positions were significantly lower in the second group, the one with no history and no psychiatric medication compared with the first group.

Conclusions: It is important to carefully monitor the vital signs in these patients and to measure the blood pressure in the supine and standing positions at baseline and after starting specific therapy.

Keywords: orthostatic intolerance, orthostatic hypotension, psychiatric medication, active orthostatism

REZUMAT:

Intoleranța ortostatică este un efect secundar important și, uneori, subevaluat, al medicației psihiatrice. Frecvent, pacienții vârstnici cu boli cardiovasculare sunt diagnosticați cu tulburare depresivă și tratamentul recomandat, care, de multe ori, cauzează hipotensiune arterială.

Scop: De a determina rolul medicației antidepressive în apariția intoleranței ortostatice, respectiv, a hipotensiunii arteriale ortostatice.

Material și metodă: Pacienții incluși în studiu au fost selectați din clinica de cardiologie. După anamneză și un examen clinic și paraclinic și al analizelor de laborator, a fost efectuat un test de toleranță ortostatică. 40 de pacienți au fost selectați și au fost împărțiți în două grupuri, unul cuprinzând pacienții cu tratament cunoscut pentru tulburare depresivă și un al doilea grup, cu pacienții fără antecedente psihiatrice.

Rezultate și discuții: diferențele tensiunii arteriale determinate în pozițiile de clinostatism și ortostatism au fost semnificativ mai mici în al doilea grup, cel fără istoric psihiatric și fără medicație antidepressivă, comparativ cu primul grup.

Concluzii: Este important să se monitorizeze cu atenție semnele vitale la acești pacienți și să se monitorizeze tensiunea arterială în clinostatism și ortostatism la momentul inițial și după începerea tratamentului specific.

Cuvinte-cheie: intoleranță ortostatică, hipotensiune arterială ortostatică, medicamente psihiatrice, ortostatism activ

INTRODUCTION

Orthostatic intolerance is the result of an inadequate response to changing body position, namely the transition from supine to standing, a process that results in a series of responses regulated by the autonomic nervous system. Orthostatic hypotension, a form of orthostatic intolerance is defined as a reduction in systolic blood pressure at least 20 mm Hg and/or diastolic blood pressure decreased by at least 10 mm Hg from baseline within one minute, three or five minutes of the transition from supine to standing. (1) According to recent studies in hypertensive patients, diabetics or those with multiple system atrophy, reduced systolic blood pressure exceeding 30 mmHg for diagnostics. (1, 2)

Evaluation can be easily done during hospitalization, even bedside measurement of blood pressure and heart rate, initially supine and after that, in standing position. Another method used to determine the response to change in body position is passive method, namely the Tilt test. It is recommended that measurements be performed in the early morning when symptoms are more pronounced.

There are several types of orthostatic intolerance. The neurogenic forms are caused by a primary impairment of the autonomic nervous system like Parkinson's disease and multiple system atrophy. Nonneurogenic forms involve organs or systems that regulate homeostasis and in other cases may be caused by external factors such as drug use, alcohol and other substances (3). Drugs, however, are the most common causes of nonneurogenic orthostatic hypotension and may complicate or worsen neurogenic forms. There are many classes of medications that can cause orthostatic hypotension, including drugs used to treat cardiovascular diseases (nitrates, calcium channel blockers, ACE inhibitors, angiotensin II receptor blockers, and direct renin inhibitors, diuretics, β -blockers, α -blockers), anaesthetics, opioids, 5-phosphodiesterase inhibitors and therapies used in neurological or psychiatric impairment (in Parkinson disease, sedative hypnotics, antidepressants and antipsychotics). It is important for the clinician to know the potential hypotensive effect of this class of drugs in order to avoid the symptoms associated with cerebral hypoperfusion, excess mortality and, not at least, reduced adherence to treatment.

Orthostatic hypotension is a major side effect and sometimes undervalued of psychiatric medication. The clinical picture is dominated by dizziness, blurred vision and concentration difficulties, fatigue, tremor, balance disorder, and even loss of consciousness. Most exposed to such adverse effects are elderly patients, a special category being represented by institutionalized patients. (4 – 6) Some studies have shown an association between orthostatic hypotension and increased cardiovascular morbidity in coronary artery disease (7, 8) and stroke (9), and between the presence of orthostatic hypotension and mortality in the general population. (7, 10)

AIM

The aim of this study is to evaluate the secondary effects of psychiatric medication, particularly antidepressant treatment, regarding values of the blood pressure in the supine and standing position. Patients included in the study were selected from the cardiology clinic. After anamnesis and a complete clinical and paraclinic examination, an orthostatic tolerance test was performed.

MATERIAL AND METHODS

The 40 patients included in the study were aged between 43 and 82 years (mean age 54.8 years). They were divided into two groups, one with patients with known depressive disorder treatment and a second group, with patients without any psychiatric history. We selected 24 men (60 %) and 16 females (40 %). The first group consisted of 20 patients of which 6 (30 %) were men and 14 were women (70 %). The second group, the control group, consisted of 20 subjects of which 12 (60 %) were female and 8 (40 %) were male. In order to establish the diagnosis of inclusion, all patients were evaluated according to a preset protocol: history, clinical and paraclinical examination, including psychiatric consult.

RESULTS AND DISCUSSIONS

We compared the data obtained for the two groups. Statistical analysis aimed to see if there is any difference between the two groups after the orthostatic tolerance test is performed.

At the end of the study, it was found that the patients in the second group had smaller reductions in values of systolic, respectively diastolic blood pressure, after three minutes in standing compared with the first group (-23 ± 6 vs -27 ± 6 , $p = 0.03$; -18 ± 5 vs -22 ± 4 , $p = 0.003$) and five minutes of the test current (-21 ± 5 vs -27.7 ± 7 , $p = 0.003$; -15 ± 6 vs -18 ± 4 , $p = 0.04$). There were no significant differences between the studied groups in the first minute of orthostatic tolerance test (21 ± 4 vs 23 ± 3 , $p = 0.08$).

Frequently, elderly patients with cardiovascular disease are diagnosed with depressive disorders and recommended treatment often causes hypotension. Being a relatively common problem encountered in practice, it has been studied over time. For example, Craig described 50 cases of orthostatic hypotension in elderly patients and in 40 of them the cause was iatrogenic.

Diuretics have been identified as the main cause of orthostatic hypotension in these patients. After this, 26 % of cases were due to the assumption of benzodiazepines, 24 % antidepressants (amitriptyline, in particular) and 22 % parkinsonian drugs. (11) Antidepressants and antipsychotics may induce orthostatic hypotension through the inhibition of sodium, potassium and calcium channels in the synapses. Mechanisms through which tricyclic antidepressants may induce hypotension are well known: the blockade of postsynaptic α_1 receptors and, in the first phase of therapy, also the blockade of pre-synaptic α_2 receptors. (12, 13, 14) Antipsychotics, including chlorpromazine, clozapine and risperidone, frequently cause orthostatic hypotension, acting on α_1 postsynaptic receptors. Atypical neuroleptics seem to be frequently responsible for orthostatic hypotension, but data are limited. A systematic review on the association between the use of barbiturates and iatrogenic orthostatic hypotension is missing. Benzodiazepines can cause hypotension by decreasing left ventricular contractility and cardiac output.

CONCLUSIONS

Differences between blood pressure values determined in supine and standing positions were significantly lower in the second group, the one with no psychiatric medication compared with the first group. Patients with psychiatric diseases, with primary or secondary neurologic impairments, cardiovascular disease and older people, in general, are often treated with multiple medications and are at increased risk of symptomatic hypotension, due both to an adverse reaction to drug and as a result of a dysfunction of the autonomic nervous system.

A careful monitoring of vital signs and an evaluation of blood pressure in the supine and standing positions at baseline and after starting specific therapy it is required in neurological and psy-

chiatric patients, particularly in Parkinson's disease. Special caution it is needed during administration of psychoactive drugs for the elderly because they are more susceptible to negative secondary effects, both cardiovascular and neuro-psychiatric. It is also useful to know the associated comorbidities, such as diabetes or hypertension. The simultaneous presence of two or more drugs for the combined treatment often results in a synergistic or additive effect, which contributes to a significant reduction in blood pressure compared with the action of a single drug. Regarding the relationship between the number of vasoactive drugs and the blood pressure in the standing, a reduction in the number and type of hypotensive drugs is indicated, in order to reduce morbidity and mortality associated symptoms of orthostatic hypotension and selection of therapy associated with a low orthostatic hypotension.

Effective treatment of orthostatic intolerance can be a challenge. Orthostatic intolerance, a pathology located on the border of several medical specialties, is a condition sometimes difficult to treat and sometimes is severely affecting quality of life. The main therapeutic target is the improvement of symptoms in the transition from supine to standing and functional status of the patient, while reducing the risk of falls and syncope and less oriented to normalize blood pressure. It is known that an attempt to classify the blood pressure in some standards it is difficult to obtain and can be risky sometimes, causing nocturnal hypertension.

Individualized, personalized therapy is indicated. This requires medical education, implementation of nonfarmacological measures and, also, medication in some cases. Treatment should always start with the identification the cause and, if possible, reducing or discontinuing medications that may be causing symptoms or worsen the problem.

Nonfarmacological interventions can be tested in any order or combination based on patient indication, safety and comfort. It is important to correct hypovolemia (hydration, additional salt intake in carefully selected cases, elevating the head of the bed), the use of counter maneuvers, ingestion of cold water and avoid prolonged immobilization. In some cases, ultimately, it is advisable to associate medication (Midodrine).

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