

Erectile dysfunction in patients under antihypertensive treatment

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Acronyms

ACEI: angiotensin converting enzyme inhibitors

ARA-II: angiotensin-II receptor antagonists

ED: erectile dysfunction

HT: hypertension

IIEF: international index of erectile function

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ABSTRACT

Introduction: Hypertension (HT) and antihypertensive drugs can affect behavior, severity and response to treatment in erectile dysfunction.

Objective: To determine the influence of antihypertensive drug treatment on erectile dysfunction behavior.

Method: A descriptive and cross-sectional study was carried out, with 148 male patients attending the Therapy and Sexual Orientation Consultation in Santa Clara, Cuba. A sample of 63 patients between 20-60 years, hypertensive and with erectile dysfunction, receiving treatment for both diseases was taken. Data was obtained from reviewing medical records, sociodemographic variables, personal pathological history, drugs and erectile dysfunction severity (according to the International Erectile Function Index, IIFE) was analyzed.

Results: The highest number of patients with HT and erectile dysfunction were between 51-60 years (61.9%), 38.1% had diabetes mellitus and only 6.3% had a psychic illness diagnosis. 50.8% of the cases studied presented severe erectile dysfunction, and diuretics, angiotensin converting enzyme inhibitors and beta-blockers were the most used drugs for HT treatment; though hydrochlorothiazide alone ($p < 0.038$) or with atenolol ($p < 0.014$) showed statistically significant differences.

Conclusions: The use of hydrochlorothiazide monotherapy or combined with atenolol in patients with HT was associated with the onset and severity of erectile dysfunction.

Key words: Antihypertensive agents, Erectile dysfunction, Hypertension, Therapeutics

Disfunción eréctil en pacientes con tratamiento antihipertensivo

RESUMEN

Introducción: La hipertensión arterial (HTA) y los fármacos antihipertensivos pueden afectar el comportamiento, la gravedad y la respuesta al tratamiento de la disfunción eréctil.

Objetivo: Determinar la influencia del tratamiento farmacológico antihipertensivo en el comportamiento de la disfunción eréctil.

Método: Se realizó un estudio descriptivo y transversal cuyo universo de estudio lo constituyeron 148 pacientes masculinos que asistieron a la consulta de Terapia y Orientación Sexual de Santa Clara, Cuba. Se tomó una muestra de 63 pacientes

entre 20-60 años de edad, hipertensos y con disfunción eréctil que recibían tratamiento para ambas enfermedades. Los datos fueron obtenidos de la revisión de las historias clínicas, se analizaron variables sociodemográficas, antecedentes patológicos personales, fármacos y la gravedad de la disfunción eréctil (según el Índice Internacional de Función Eréctil, IIFE).

Resultados: El mayor número de pacientes con HTA y disfunción eréctil tenía edades entre 51-60 años (61,9%), un 38,1% padecía de diabetes mellitus y solo 6,3% tenía diagnóstico de alguna enfermedad psíquica. El 50,8% de los casos estudiados presentaba una disfunción eréctil grave y los fármacos más empleados en el tratamiento de la HTA fueron los diuréticos, los inhibidores de la enzima convertidora de angiotensina y los betabloqueadores; aunque únicamente la hidroclorotiazida sola ($p<0,038$) o con atenolol ($p<0,014$), mostró diferencias estadísticas significativas.

Conclusiones: El empleo de hidroclorotiazida en monoterapia o combinado con atenolol en pacientes con HTA se asoció a la aparición y gravedad de la disfunción eréctil.

Palabras clave: Antihipertensivos, Disfunción eréctil, Hipertensión arterial, Terapéutica

INTRODUCTION

Hypertension is a serious global health problem, affecting between 25-30% of the world population¹. Cuba is not exempt from this problem, and there is a high prevalence of it, ranging between 28-32% of the adult population². Its incidence increases with age, considering that more than half of people aged 60-69 years are hypertensive^{1,2}.

The antihypertensive agents most used universally and considered of first line in treatment are: diuretics –constitute the group of most prescribed drugs–, beta-blockers, calcium channel blockers, ACEI and more recently, angiotensin-II receptor antagonists (ARA-II)^{3,5}.

In general, antihypertensive agents are well tolerated, but may produce undesirable effects such as: hypotension, frequent urination, dizziness, sedation and sexual dysfunction, among others^{3,6}.

The ED erectile dysfunction (ED) is a common adverse effect with reversibility, which can follow the consumption of antihypertensive agents, mainly by the use of thiazide diuretics and beta-blockers⁶⁻⁸.

Like hypertension (HT), ED is highly prevalent. It is estimated to affect about 100 million people worldwide and it will affect 322 million by 2025⁹. Among the mechanisms involved in its pathogenesis, in hypertensive patients are: the severeness and duration of HT, age, and antihypertensive therapy¹⁰.

The ED is considered one of the greatest obstacles and dissatisfaction among those who receive antihypertensive treatment, because it can affect the

quality of life of men and treatment discontinuation¹¹. There is also a clear correlation between risk factors for HT and ED: age, smoking, alcoholism, diabetes mellitus, obesity and dyslipidemia^{10,12-15}.

In Cuba, there are few published studies that relate the behavior of ED with the consumption of drugs, specifically, antihypertensive agents. Those are the reasons that motivated the development of this research, with the aim of determining the influence of the antihypertensive treatment in the behavior of ED.

METHOD

A descriptive cross-sectional study was conducted in patients diagnosed with ED and HT, who went to the provincial reference consulting room of Therapy and Sexual Orientation, belonging to the *Hospital Universitario Gineco-Obstétrico Mariana Grajales Cello*, in Santa Clara, Cuba, from January to December 2014.

The population of study was constituted by 148 men who attended this consulting room and had ED diagnosis, from which a sample of 63 patients was selected by a non-probabilistic intentional sampling. The following inclusion criteria were taken into consideration:

- Male patient diagnosed with HT.
- Age between 18 and 60 years.
- Patients consuming antihypertensive agents, at

least in the past 3 months.

There were excluded patients with limiting health conditions like mental illness, (serious or crisis) benign and malignant prostate tumor diseases, and patients with anatomic abnormalities of the penis which obstructed erection.

Variables

The variables analyzed were: age, personal pathological records, medications, presence of ED and its severeness.

The diagnosis of ED and its severeness was made by applying the international index of erectile function (IIEF), developed by Rosen *et al.*¹⁶ and published in 1997, which consists in using 23 questions, where each item has the value of a point and according to the diagnostic criteria, it is classified: in severe (IIEF score <7), moderate (7≤IIEF <12) and slight (IIEF of 12-21).

Collection and processing of information

The data for the research were obtained from medical records and individual interviews. Its organization, analysis and summary, as well as the presentation of the results, were performed by using the statistical processor SPSS in its version 15.0. Tables and graphs were prepared, and descriptive measures, like frequency and percentage, were calculated. Comparison statistical tests of frequency and Chi square were employed.

Ethics

This research was developed following the ethical requirements for scientific research and with the consent of the Ethics Committee and the Scientific Council of the municipality of Santa Clara.

RESULTS

Some demographic factors can influence the onset of ED, but, no doubt, age is one that can mediate more in its behavior. As can be seen in **figure 1**, the

greater number of patients, affected by this situation, are in the age group of 51-60 (61.9%) and 41-50 years (34.9%).

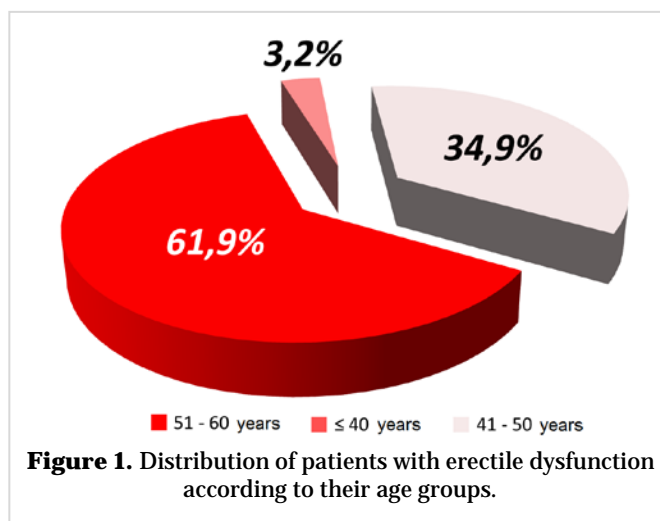


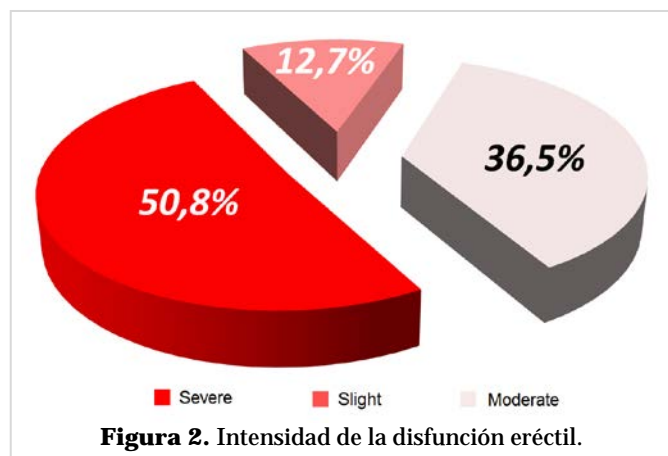
Figure 1. Distribution of patients with erectile dysfunction according to their age groups.

In **table 1** are shown the personal pathological records of the studied sample and it is also shown that, in addition to the HT present in all patients, there are other diseases, being the diabetes mellitus the most prevalent (38.1%). Although psychic diseases are frequently associated with ED, in this research was only present in 6.3% of patients.

Table 1. Personal pathological records of the studied patients (n=63).

Personal pathological records	Nº	%
Diabetes mellitus	24	38.1
Psychic diseases	4	6.3
Peptic ulcer	2	3.2
Bronchial asthma	1	1.6

From the cases studied, 50.8% presented severe ED (**Figure 2**), according to the score obtained by IIEF; this instrument is used to classify and determine the severeness or intensity of this sexual



disorder.

In **table 2** is shown the ratio between the antihypertensive agents employed by the patients studied and the intensity of ED. Diuretics, ACE inhibitors and beta-blockers were the most observed; but it

was only hydrochlorothiazide which showed a statistically significant difference ($p < 0.05$).

The patients' distribution in combinations of antihypertensive agents and its relationship with the intensity of ED (**Table 3**) shows that the combination which had the strongest association with the presence of severe ED was hydrochlorothiazide-atenolol ($p < 0.05$). This reinforces the negative influence of thiazide diuretics on erectile function, either as a single drug or in combination with other antihypertensive groups.

DISCUSSION

The vast majority of revised studies agree that age is an important factor in the occurrence of ED. In a publication of the National Health and Social Life Survey (NHSLs), which included a representative sample of men, the highest incidence of ED –as in this research– was found in the age group between

Table 2. Distribution of patients according to antihypertensive agents and intensity of the erectile dysfunction.

Drugs	Intensity of erectile dysfunction						Total Nº	p
	Slight		Moderate		Severe			
	Nº	%	Nº	%	Nº	%		
Hydrochlorothiazide	1	3.1	11	34.4	20	62.5	32	0.038
Captopril	5	21.7	8	34.8	10	43.5	23	0.254
Atenolol	1	4.7	6	28.6	14	66.7	21	0.160
Enalapril	2	12.5	6	37.5	8	50.0	16	0.995
Chlorthalidone	1	7.7	6	46.2	6	46.2	13	0.667

Table 3. Distribution of patients according to the combinations of antihypertensive agents and intensity of erectile dysfunction.

Drugs combination	Intensity of erectile dysfunction						Total Nº	p
	Slight		Moderate		Severe			
	Nº	%	Nº	%	Nº	%		
HCT - Atenolol	-	-	3	27.3	8	72.7	11	0.014
HCT - Captopril	1	9.1	5	45.4	5	45.4	11	0.345
HCT - Enalapril	-	-	1	16.7	5	83.3	6	0.215
Captopril - Chlorthalidone	1	20.0	2	40.0	2	40.0	5	0.598
Atenolol - Chlorthalidone	-	-	-	-	3	100	3	0.341

HCT: Hydrochlorothiazide

50-59 years¹⁷.

It is logical to notice that the highest proportion of patients with ED is in this age range, because according to the design of this study, all patients had HT diagnosis, a disease whose prevalence increases with age. When aging, considerable pathophysiological changes take place, which lead to an increase in the prevalence of both diseases^{18,19}. In addition, the evolution of HT, and its high levels, make that other changes are established in our body due to the resulting increased oxidative stress, inflammation, endothelial dysfunction and release of endothelins; all this make HT a risk factor not only for ED but also for other ailments^{14,18}.

These factors are involved in the mechanism by which HT can cause ED, as the oxidative stress and its effect on endothelial cells stimulate endothelial damage and affect vasodilatation of the vascular smooth muscle in arteries, arterioles and sinusoids where the cavernous bodies of the penis are included, which ultimately prevent it from the proper dilation and contribute with the appearance of ED in the hypertensive patient^{9,20}. In addition, the undesirable effects of antihypertensive agents on sexual activity can cause and worsen the ED^{7,8}.

Corugedo *et al.*¹⁸, in a study in Cienfuegos (Cuba), indicate that the prevalence of HT increases with age in men, with considerable changes between 35-44 years. Others note that the prevalence of ED in hypertensive men is greater than in normotensive¹⁹ and HT is present in 38-42% of men with ED; or, conversely, that approximately 35% of men with HT have some degree of ED.

The ED is usually associated with endocrine-metabolic diseases such as diabetes mellitus, and its prevalence in diabetic patients exceeds 50%; in addition, it is much higher when compared with the general population, as there are reported values ranging between 35-75%¹³. In Cuba, in individuals between 20-29 years old, it has a prevalence of 9% and increases to 90% in those who attain the age of 70²².

These observations, together with the fact that the ED is associated with other components of the metabolic syndrome, such as hypertension, abdominal obesity and dyslipidemia²³, –even without considering the overt hyperglycemia– they have directed to consider the hypothesis that the ED could be installed early in patients with metabolic syndrome, before the diagnosis of diabetes mellitus.

Psychiatric illnesses and their treatment are often associated with disorders in the sexual sphere. It is

known that hyperprolactinemia, caused by psychotropic drugs causes sexual dysfunction in both sexes. The type or class of antipsychotic can influence, for example, antagonists of dopamine receptors (D_2), such as haloperidol and risperidone, drugs considered to rise the most the prolactin levels; while atypical antipsychotics such as olanzapine, clozapine, quetiapine, among others of the same group, do not affect that much the prolactin levels in blood²⁴.

Shabsigh *et al.*² applied the IIFE to 1053 men aged 30 or more years, with diagnosis of associated risk factors such as: cardiovascular disease, hyperlipidemia, HT, diabetes mellitus and smoking, and notice that more than half (54%) presented moderate or severe ED.

In the EDOS study²⁶, held in Spain to assess the intensity of ED, which included a sample of 1029 patients with diagnosis and treatment for ED, about half presented severe ED, according to the rate applied, which coincides with our results.

As mentioned above, the prevalence of ED in hypertensive patients is higher than in normotensive. In the study by Manolis and Doulmas²⁷, after applying the IIEF-5 to 104 patients with HT, 62,2% were found to have some degree of ED; 45,2% severe, compared with only 10% of the general population of the Massachusetts Male Aging Study. Among the hypertensive patients, there was a high percentage of usage of beta-blockers and diuretics, which reinforces, once again, the high incidence of ED in those patients treated with these drugs^{7,8,27}.

Although practically all antihypertensive agents have been imputed, in some way, as inducers of sexual dysfunction, some have been more than others. Of the currently used, diuretics, beta-blockers, especially of first generation, noncardioselective as propranolol, and direct vasodilators are often the most incriminated. The calcium channel blockers, the ACEI and ARA-II are considered less hazardous in this regard; even, several studies attribute them beneficial effects on erectile function²⁸.

In a study that compared two groups of hypertensive patients with ED, one receiving thiazides and the other not, a higher incidence of severe ED among consuming thiazide diuretics was found; however, this research is not conclusive, as factors such as age and other endocrine-metabolic, psychotropic and toxic diseases may have also influenced as causal factors in patients receiving thiazides²⁹.

In clinical practice, it is often to find patients that

need to combine two or more drugs for controlling their blood pressure levels. Most combinations include low doses of thiazide that potentiate the effect of other antihypertensive agents^{7,8,30}.

The number of consumed drugs is associated with the severeness of ED. In a research published by Banks *et al.*²⁹, where they studied 37712 patients diagnosed with ED, 29% presented moderate or severe ED, associated with the consumption of two or more drugs. Therefore, they²⁹ and other authors^{31,32} suggest that the assessment of medication is an integral part of the ED's evaluation.

CONCLUSIONS

The studied hypertensive patients with erectile dysfunction used, mostly, hydrochlorothiazide in the treatment of their chronic disease. This diuretic alone, or combined with atenolol, had a significant statistical association with the severeness of this sexual disorder.

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