

REVIEW

THE EFFECT OF ANTIHYPERTENSIVE THERAPY ON HUMAN SEXUALITY

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Abstract

Aim: The aim was to analyse the effect of antihypertensive therapy on incidence of sexual dysfunction in patients with arterial hypertension. **Design:** a review study. **Methods:** In the period from 2000 to 2015 we searched licensed and freely available electronic databases: CINAHL EBSCOhost, ProQuest, Pubmed and Medline for relevant recherches of Czech and foreign sources. We set the following criteria: a study of least 100 participants and a minimum six-month follow-up. We excluded experimental and vaguely defined studies. From a total of 123 searches, 45 articles met the criteria. A review includes a total of 15 studies, six studies with a control group of healthy individuals, two cohort studies, six randomized trials and one case study with a control group. **Results:** The study analysis showed that beta-blockers and thiazide diuretics are the most detrimental in terms of incidence of sexual dysfunction. Angiotensin II receptor antagonists and angiotensin-converting enzyme inhibitors have a neutral or beneficial effect. **Conclusion:** The review article deals with the issue of patients' sexuality, focusing on the potentially negative effect of antihypertensive therapy on sexual function. Current scientific findings suggest that antihypertensive therapy increases the risk of occurrence of sexual dysfunction. Professional literature is more dedicated to the incidence of male sexual dysfunction, especially erectile dysfunction, than with female sexual dysfunction.

Keywords: hypertension, antihypertensive therapy, sexual function, sexuality, sexual dysfunction.

Introduction

Life satisfaction is conditioned by physical and mental health. Contemporary society at the beginning of the third millennium is characterized by lifespan prolongation, i.e. an aging population and an increase in cardiovascular diseases. Arterial hypertension is considered to be one of the most common diseases of the cardiovascular system. Due to its high occurrence in the population, the issue of this disease has become very topical (Berková, Berka, Topinková, 2014, p. 5–11). Sexuality is an important human need, that is everybody's right and an integral part of their personality (Šrenkel, 2013, p. 211). It is also a criterion that determines individuals' subjective satisfaction and affects each person's perception and feelings (Vique et al., 2006, p. 18). According to the Sexual Health and Overall Wellness Survey (the SHOW), conducted in nine European countries, sex is one of the highest priorities in 67% men and 57% women (Weiss, 2011, p. 3).

The prominent Czech sexologist, professor Zvěřina, (2010, p. 339) reports that sexual dysfunction (SD) is a disorder of sexual performance, characterized by insufficiency of one or more physiological components of sexual behaviour. Antihypertensive drugs are often discussed in connection with their negative effects on erectile function (Doumas et al., 2006, p. 2387–2392). A comprehensive German TRANSCEND, PROFESS and ONTARGET meta-analysis conducted in 2005–2010, in which patients were followed for up to five years, dealt with the problem of the effects of drugs on erectile dysfunction (ED). This study showed that only thiazide diuretics and older, in particular non-selective beta-blockers, induce erectile dysfunction (Bultas, Karetová, 2014, p. 287). Centrally acting alpha agonists and diuretics are involved in the deterioration of sexual function, and aldosterone receptor antagonist diuretic spironolactone is associated with ED and gynaecomastia (Conaglen, Conaglen, 2013, p. 42–46). In addition, the evidence available also suggests possible adverse effects of hypertension treatment on female sexual function. Doumas et al. (2006, p. 2387) point out that the prevalence of female sexual dysfunction (FSD) in women with essential hypertension versus

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normotensive women depends on the degree of hypertension, age and duration of antihypertensive treatment. There is a higher prevalence of SD in hypertensive women than in normotensive ones (Ma et al., 2011, p. S9; Martelli et al., 2012, p. 439). Women may experience a decrease in or absence of libido, inability to achieve orgasm (Steinke, 2005, p. 40–50) and a decrease in vaginal lubrication (Šrámková, 2013, p. 86).

Aim

The aim was to analyse the effect of antihypertensive therapy on incidence of SD and to find an association between antihypertensive therapy and SD, using relevant data from licensed and freely available electronic databases.

Methods

We chose a sensitive issue focusing on patients' intimate life with the aim of mapping the effects of antihypertensive therapy on individuals' sexual function and changes in sexuality which occur in patients treated for hypertension.

Eligibility criteria

The selection criteria chosen were: a study involving at least 100 participants and a minimum six-month follow-up. From the beginning we excluded studies which focused on evaluating the effects of drugs conducted by pharmaceutical companies, and experimental or vaguely-defined studies. We gradually excluded studies as recommended by PRISMA (see Scheme 1). From a total of 123 searches, 45 articles met the criteria.

Sources

Relevant data were used from licensed and freely available electronic databases: CINAHL EBSCOhost, ProQuest, Pubmed and Medline.

Search

The keywords 'hypertension', 'antihypertensive therapy', 'sexuality', and 'sexual dysfunction' were set as criteria for searching relevant sources in the time period 2000–2015.

Study selection and data analysis

The review includes a total of 15 studies: six studies conducted with a control group of healthy individuals, two cohort studies, six randomized trials, and a case study with a control group. There were eight studies on male sexual dysfunction (MSD) and seven studies on female sexual dysfunction (FSD). A total of 5,880 participants were included in the evaluated studies.

Results and discussions

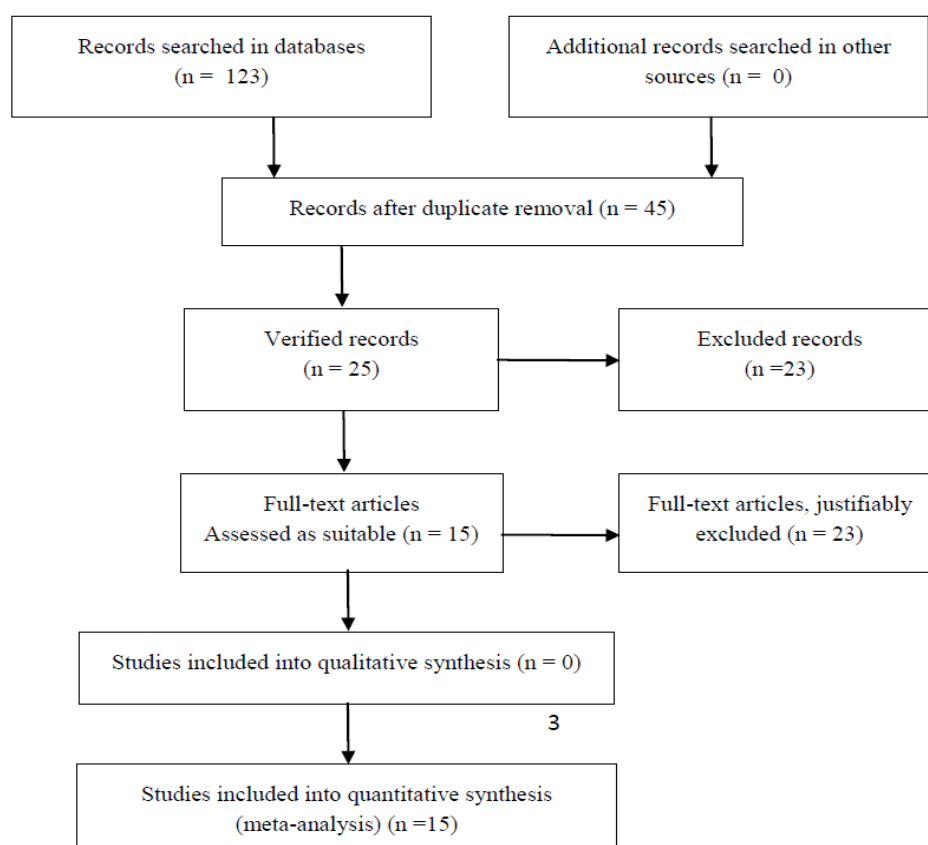
In professional, mainly foreign publications, considerable attention is paid to the relationship between antihypertensive therapy and SD. Chronic disease such as hypertension, or its pharmacotherapy, affects patients' sexual function (Steggall, 2007, p. 49–56). The main determinants involved in SD, both in men and women, are hypertension, age and antihypertensive therapy. Occurrence of SD is more frequent in hypertensive patients than in normotensive individuals (Manolis, Doumas, 2008, p. 2,074–2,084, Manolis, Doumas, 2012, p. 285–292). Sexuality disorders or SD in connection with hypertension treatment have subjective and objective characteristics. Subjective symptoms include problems with erections, or ejaculation, and objective symptoms include the strain on relationships with a partner (Sovová, Řehová, 2004, p. 76). In men, the side effects lead to a decrease in or loss of libido, erectile dysfunction, priapism, and premature or retrograde ejaculation. Women may experience a decrease in vaginal lubrication, low or absent libido and an inability to achieve orgasm (Steinke, 2005, p. 40–50).

From the searched literature, we included a total of 15 clinical studies in our review, (characterized in detail in Tab. 1 and Tab. 2) with a total of 5,880 participants, of whom 1,870 were women and 4,010 were men. Participants were followed up for at least six months. Standardized measuring scales and questionnaires were used in a total of nine studies. The most frequent measuring instrument was the International Index of Erectile Function (IIEF-5). Six clinical studies examined the effect of beta-blockers on sexual function; a total of five clinical studies examined the effect of pharmacologic antagonists angiotensin II; one study examined the effect of calcium channel blockers; and one study dealt with the effect of thiazide diuretics on occurrence of SD. The analysis of results shows that out of 15 clinical studies, 14 studies confirmed the negative effects of antihypertensive therapy or the treatment of the underlying disease (arterial hypertension) on participants' sexual function and only one clinical study showed a neutral or positive effect of treatment on prevalence of SD.

According to results of a randomized trial by Okeahialam and Obeka (2006, p. 638–640), in which a control group of normotensive participants was included, thiazide diuretics cause a higher prevalence of FSD, particularly in terms of decreased sexual desire. A total of five studies investigated which drug category of antihypertensive therapy results in a higher prevalence of SD. They evaluated beta-

blockers and angiotensin II antagonists. The comparison showed a deterioration in male sexual activity caused by beta-blockers (Fogari et al., 2001, p. 27–31, Fogari et al., 2002, p. 77–80) and a reduction in female sexual desire (Fogari et al., 2004, p. 77–81). The opposite result was found in a

randomized trial by Yang et al. (2013, p. 235–241), in which beta-blockers did not increase occurrence of SD. None of the five randomized trials indicate a higher prevalence of SD or a higher occurrence of ED due to treatment with angiotensin II antagonists.



Scheme 1 Flowchart – PRISMA recommendation

Results of occurrence of SD

An analysis of the searched sources (Tab. 1) suggests that antihypertensive therapy adversely affects participants' sexual function. Doumas et al. (2006, p. 2387–2392) point out that the prevalence of FSD in women with essential hypertension versus normotensive women depends on the degree of hypertension, age, and duration of antihypertensive treatment. Their conclusions are based on a study conducted on a population of active women using the Female Sexual Function Index (FSFI). The results showed that out of a total of 417 women (216 hypertensive women and 201 non-hypertensive women), SD occurred in 42% hypertensive women and in 19% normotensive women. The study concluded that there is a higher occurrence of FSD in women with essential hypertension compared with normotensive women (Doumas et al., 2006, p. 2387). There is a higher prevalence of SD in hypertensive

women, in particular decreases in vaginal lubrication and problems achieving orgasm (Duncan et al., 2000, p. 640–647). Kütmec and Yurtsever (2011, p. 56–63) examined sexual function in women with hypertension, which is classified as a chronic disease and is said to be an important factor affecting SD due to physiopathological changes in the vascular endothelium. An experimental study included 71 hypertensive women not suffering from any other chronic disease. A control group consisted of 85 healthy married women. SD occurred in 90% women with hypertension and in 41% healthy women. It was also found that prevalence of SD increases with age, but with higher education and income female sexual problems decrease (Ma et al., 2011, p. S9). The results of the evaluation of SD using FSFI in 160 hypertensive and 50 normotensive women show that FSD is more common in women with essential hypertension.

Table 1 Characteristics of clinical studies in relation of hypertension and antihypertensive therapy to prevalence of FSD

Source, year	Aim	Number of participants	Method	Results
Doumas et al. (2006)	To find the effect of beta-blockers on prevalence of FSD.	Data from 417 women, of whom 216 were treated with arterial hypertension and 201 were normotensive.	A study with a control group, using FSFI.	A significantly higher occurrence of SD ($p < 0.001$) in women with arterial hypertension.
Duncan et al. (2000)	To determine effect of antihypertensive therapy on prevalence of FSD.	3,312 medical records were examined, a total of 211 women, of whom 104 with arterial hypertension and 107 normotensive women were included into the study.	A study with a control group. A questionnaire with 47 items and a telephone interview. Statistical data processing using ANOVA at the level of significance 0.05.	Hypertensive women, irrespective of the type of therapy, reported, in direct correlation with age, a decrease in vaginal lubrication, less frequent orgasm and more frequent pain in comparison with normotensive women.
Duncan et al. (2001)	To examine the effect of antihypertensive therapy on prevalence of FSD.	Data from 640 women.	A study with a control group of healthy women, using 64-item SAQ.	The study confirmed a higher occurrence of SD in premenopausal women with arterial hypertension, especially a decrease in vaginal lubrication and problems with orgasm.
Fogari et al. (2004)	To compare the effect of two drug categories, angiotensin II antagonists and beta-blockers.	Data from 120 women.	A randomized trial.	In beta-blockers (atenolol) a significantly higher prevalence of SD was established in postmenopausal women (13.5%), especially in the area of decreased sexual desire.
Kütmeç, Yurtsever (2011)	To find a significant difference in prevalence of SD due to antihypertensive therapy in women with arterial hypertension in comparison with a control group.	Data from 156 women, of whom 71 were treated for arterial hypertension and 85 were normotensive.	A study with a control group of healthy women.	The study confirmed a higher prevalence of SD in women with arterial hypertension (90%) and in normotensive women (40%).
Ma et al. (2011)	To establish possible adverse effects of antihypertensive therapy on occurrence of SD.	Data from 210 women, of whom 160 were treated for arterial hypertension, and 50 were normotensive.	A cohort study, using FSFI.	The Chinese cohort study confirmed a significant result ($p < 0.001$), confirming a higher prevalence of FSD with arterial hypertension in 60.4% compared with normotensive women (26%).
Okeahialam, Obeka (2006)	To examine female sexuality, focusing on the effect of thiazide diuretics on occurrence of SD.	Data from 116 women.	A study with a control group of healthy women.	In women with arterial hypertension, 30.8% occurrence of SD was found in comparison with a control group of healthy women with 4.7%. Decreased sexual desire was the most common problem.

Fogari et al. (2004, p. 77–81) published a study examining the effect of treatment with valsartan and atenolol on the sexual behaviour of 120 menopausal women, aged 51–55, diagnosed with hypertension.

After 16 weeks of treatment they were asked questions from a ten-item self-assessment, covering aspects of desire, orgasm and coital activity. The results showed significant increase in sexual desire in

women treated with valsartan. The result of another randomized trial on evaluation of SD using FSFI, evaluated after 24 and 48 weeks of treatment with felodipine in combination with irbesartan, showed improvement of sexual function in the items of arousal and orgasm. Occurrence of SD also increased with age (Ma et al., 2011, p. S9). A Nigerian study focusing on the potential negative effects of thiazide diuretics on the occurrence of SD did not confirm a statistically significant occurrence of SD in hypertensive women compared with a control group of healthy individuals (Okeahialam, Obeka, 2006, p. 638–640).

The results of occurrence of MSD

Tab. 2 describes the studies searched which investigate the effect of antihypertensive therapy on MSD. Mittawae et al. (2006, p. 575–578) examined patients' health status using IIEF-5 with an emphasis on hypertension and the assessment of their sexual function. Of 800 patients, with a mean age of 59.2, 739 (92%) had regular sexual activity once or twice a week. Of these, 346 (44%) were diagnosed with ED. The results showed that the presence and treatment of hypertension may increase ED. The following year, Bener et al. (2007, p. 870–878) conducted a Qatari study from May to October. A total of 425 participants with hypertension, aged 30–75, were selected for this study. Of these, 296 (74%) participants agreed to be included in the study. The mean age was 54.8. Sexual function was assessed using IIEF, and ED occurred in 66% of patients. ED occurred in 196 (66.2%) of the 296 participants with hypertension, while in the control group of healthy individuals, ED was reported in 71 (23.8%) men out of a total of 298 participants. In participants with hypertension, 25% participants suffered severe ED, 29.1% moderate ED and 12.1% mild ED. Percentages of different domains of sexual activity were very significant, with a higher risk in hypertensive patients than in normotensive ones ($p < 0.001$). The results of the study showed that ED is more common in patients with antihypertensive therapy and that the frequency and severity of ED increases with age. The aim of a cohort study by Huang et al. (2014, p. e92794) was to assess erectile function in 1,531 Chinese men aged 40 to 80, classified as asexual and to further analyse the specific reasons for this condition. The conclusion of the study showed a higher prevalence of ED in 49.9% participants and prevalence of asexuality in 37.2% participants. Prevalence was significantly affected by participants' age, hypertension and diabetes mellitus. A Spanish study by Cuéllar de León et al. (2002, p. 521–526) aimed to define how consistent the inability

to achieve or maintain an erection sufficient to permit satisfactory sexual intercourse was and how closely this was associated with hypertension. This multicenter study was conducted in primary care educational centers. A total of 512 participants with hypertension were included in the study, of whom five were excluded due to incomplete questionnaires. Prevalence of ED in hypertensive patients was evaluated using IIEF-5. The study analysed factors associated with ED which were in direct relationship with disease and ED. Participants' mean age was 63.36 (the age range was 30–86). The prevalence of ED was 46.5%. No statistically significant occurrence of ED was established with age, but a high occurrence of ED was found in patients with hypertension. In the same year, another Spanish study was conducted by Guirao Sánchez et al. (2002, p. 290–296), which reached a similar conclusion, showing hypertension to be the main indicator of ED in 33.6%. The aim of a prospective, randomized study by Yang et al. (2013, p. 235–241) on 218 male participants was to establish whether the combination of calcium channel blockers with either angiotensin II blocker or beta-blockers could have similar effects on sexual function in hypertensive men. No statistically significant difference was found in occurrence of ED before and after the treatment in the two combination therapies. The results of the study even suggest that the combination of angiotensin converting enzyme inhibitors (ACEI) with angiotensin II may contribute to increased male sexual desire. The aim was to answer the question of whether antihypertensive therapy adversely affects sexual function and sexual life in men and women with arterial hypertension. A synthesis of all available data from clinical studies indicate that some studies confirm obvious side effects of antihypertensive therapy on sexual function, while others suggest the opposite. An analysis of the results did not reveal any negative effects of calcium channel blockers on sexual function. In fact, the results suggest the positive effects of this drug category on sexual function, namely increased sexual desire. Neither do ACEI cause a higher prevalence of SD. On the other hand, beta-blockers and thiazide diuretics have a significant negative impact on sexual function. A higher prevalence of SD was proved in these two drug categories. Men treated with beta-blockers (carvedilol, atenolol) report a decrease in sexual activity (Fogari et al., 2001; p. 27–31; Fogari et al., 2002, p. 77–80). The results of clinical research are unambiguous: beta-blockers have a negative impact on human sexuality and contribute significantly to the occurrence of SD.

Table 2 Characteristics of clinical studies in relation of hypertension and antihypertensive therapy to prevalence of MSD

Source, year	Aim	Number of participants	Method	Results
Bener et al. (2007)	To determine occurrence of ED, its severity or to find other SD in hypertensive and normotensive Qatari men.	Data from 594 men (age range 30–75). A total of 296 men were treated for hypertension and 298 were normotensive. Mean age was 54.8.	A case study with a control group using IIEF.	Of the 296 patients with hypertension, 196 (66.2%) suffered from ED. Of 298 normotensive men, 71 (23.8%) reported ED. A total of 25% hypertensive men suffered from severe ED, 29.1% had moderate ED and 12.1% had mild ED. The frequency and severity of ED increased with age.
Cuellar de León et al. (2002)	To define how consistent the inability to achieve or maintain an erection sufficient for satisfactory sexual intercourse is and how closely SD is associated with hypertension.	Data from 512 men. Mean age was 63.36 (age range 30–86).	A randomized study, using IIEF-5.	Prevalence of ED was 46.5%. A high occurrence of ED in hypertensive men.
Fogari et al. (2001)	To find the effects of two pharmacological preparations: valsartan (angiotensin II antagonist) and carvedilol (a beta-blocker) on sexual activity in men treated with hypertension in comparison with a control group of normotensive men.	Data from 120 males with newly diagnosed hypertension, age range 40–49, without any previous SD.	A study with a control group of healthy men. Participants were also administered a placebo.	Deterioration in sexual activity due to carvedilol (beta-blocker).
Fogari et al. (2002)	To compare the effects of valsartan (angiotensin II antagonist) and of atenolol (beta-blocker) on sexual activity in newly diagnosed, previously untreated men with essential hypertension.	Data from 110 men, age range 40–49.	A randomized study, participants were also administered a placebo. The statistical significance level was 0.05.	The results suggest the negative effect of atenolol on sexual activity. Beta-blocker therapy significantly reduced sexual activity (from 6.0 sexual episodes/month to 4.2 sexual episodes/month ($p < 0.01$) compared with placebo. Valsartan therapy caused a slight increase in male sexual activity. From a total of 5.8 sexual episodes/month to 7.4 sexual episodes/month ($p = 0.058$) compared with a placebo.
Huang et al. (2014)	To find prevalence of ED and to analyze the specific reasons for this condition.	Data from 1,531 Chinese men, age range 40–80.	A cohort study, using IIEF-5.	A higher prevalence of ED in 49.9% participants and prevalence of asexuality in 37.2% participants were found. Higher prevalence was significantly affected by participants' age, hypertension and diabetes mellitus.
Mittawae et al. (2006)	To evaluate prevalence of ED, its severity and to find other sexual functional domains.	Data from 800 Egyptian men treated for hypertension. The mean age was 59.2 +/- 2.3 yrs (age range 28–75).	A randomized trial, using IIEF-5.	Of a total of 800 men, 739 (92.3%) had regular sexual activity (once or twice per week) and 346 (43.2%) suffered from ED. Of the total number of men, 40 (5%) had mild ED, 96 (12%) moderate, and 210 (26.2%) severe ED. A highly statistically significant correlation between the duration of hypertension and mild ED was found.
Guirao Sánchez et al. (2002)	To identify factors associated with occurrence of ED.	Data from 125 men.	A randomized trial, using IIEF-5.	33.6% men with hypertension suffered from ED.
Yang et al. (2013)	To establish whether the combination of calcium channel blockers with either angiotensin II blocker or beta-blockers can have similar effects on sexual function in hypertensive men.	Data from 218 men.	A randomized trial.	A higher prevalence of ED was not found. The results suggest that the drugs felodipine (ACEI) and irbesartan (angiotensin II blocker) may be beneficial to sexual desire in hypertensive men, rather than a combination of felodipine (ACEI) and metoprolol (beta-blockers).

Furthermore, it was found that antihypertensive therapy has a significant impact on higher prevalence of ED (Guirao Sánchez et al, 2002, p. 290–296; Cuéllar de León et al., 2002, p. 521–526; Bener et al., 2007, p. 870–878; Huang et al., 2014, p. e92794). The opposite result regarding the effects of antihypertensive therapy on occurrence of ED is reported by Yang et al. (2013, p. 235–241). The fact that occurrence of SD correlates with age also attracted attention. A clinical randomized trial by Huang et al. (2014, p. e92794) included, in our opinion, sufficient participants to establish a statistically significant result. A relatively large number of the clinical studies searched included a control group of healthy subjects with which to compare the significance of occurrence of SD. Based on the data from clinical studies, we found that there is a higher prevalence of SD in women with arterial hypertension compared to normotensive women (Doumas et al., 2006, p. 2387–2392; Kütmeç, Yurtsever, 2011, p. 56–63; Ma et al., 2011, p. S9). At present, there still remain many open and unanswered questions regarding occurrence of SD in men and women with arterial hypertension

Conclusion

Chronic diseases, which include arterial hypertension, can restrict individuals' life in some ways and reduce life satisfaction. Current scientific findings suggest a higher risk of occurrence of SD during antihypertensive therapy. The literature shows that SD brings psychological problems, somatic complaints, emotional stress and social isolation. It causes relationship problems, significantly impairs the stability of a marriage or cohabitation and, not least, it reduces individuals' life satisfaction (Pastor et al., 2008, p. 1). We closely examined human sexuality and, based on analysis of the results, have come to significant conclusions, one of which is the fact that men and women show a statistically significant difference in occurrence of SD due to antihypertensive therapy. This could be explained from several interrelated perspectives. The literature states age, menopause, antihypertensive therapy and duration of treatment of arterial hypertension. Hypertensive men have the greatest difficulty achieving erection and the most problems with sexual activity. Women treated with antihypertensive therapy experience a reduced desire for sexual activity (libido), as well as problems with vaginal lubrication and attainment of sexual arousal. Furthermore, we can state that occurrence of SD correlates with age. We should not lose sight of the fact that quality health care specifies that we should do the right things at the right time to the right people

and thereby achieve the best possible results under current conditions (Gladkij et al., 2003, p. 364). Sexuality, as a basic human need, falls into the realm of nursing, where nursing professionals' knowledge of the potential negative effects of antihypertensive therapy may lead to more targeted patient education and, in turn, greater patient satisfaction.

Ethical aspects and conflict of interest

We declare that the research conducted within this review study does not constitute any conflict of interest and that the results were processed in compliance with ethical standards.

Author contribution

Concept and design (BB, YV), data collection (BB), data analysis and interpretation (BB, YV), drafting the manuscript (BB), supervision (YV), critical correction of the manuscript (BB, YV).

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