Section: General Medicine

Review Article

ANTI-HYPERTENSIVES AND SEXUAL DYSFUNCTION: A LITERATURE REVIEW

Pila R[1], Pillala R[2], Tiruvidula Reddy P[3], Kulkarni A[4]

[1,2]*Medical Student, Ramaiah Medical College, Bangalore, Karnataka, India.*
[3]*MBBS Intern, Ramaiah Medical College, Bangalore, Karnataka, India.*
[4]*Professor, Department of General Medicine, Ramaiah Medical College, Bangalore, Karnataka, India.*

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Corresponding Author:
Ritija Pila,
Medical Student, Ramaiah Medical College, Bangalore, Karnataka, India.
Email: ritija.pila@gmail.com

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ABSTRACT

Background: Hypertension is one of the leading causes of cardiovascular mortality worldwide and requires long-term pharmacological management for effective control. Although antihypertensive medications significantly reduce cardiovascular complications, several classes of these drugs have been associated with sexual dysfunction, thereby negatively affecting quality of life as well as treatment adherence. Sexual dysfunction in hypertensive patients may result from both hypertension itself and the adverse effects of antihypertensive therapy.

Objective: To review the association between antihypertensive medications and sexual dysfunction in males and females, with emphasis on prevalence, mechanisms, and the effects of different antihypertensive drug classes on sexual function.

Methods: A literature review was conducted using PubMed-indexed articles including review articles, randomized controlled trials, observational studies, and meta-analyses related to hypertension, antihypertensive therapy, erectile dysfunction, and female sexual dysfunction. Relevant studies published in English were included and analysed.

Results: The reviewed studies established that sexual dysfunction is commonly associated with antihypertensive therapy, particularly with thiazide diuretics and conventional beta blockers. Erectile dysfunction was the most frequently reported manifestation among hypertensive males, while hypertensive females commonly experienced decreased libido, impaired arousal, vaginal dryness, and reduced sexual satisfaction. Proposed mechanisms included endothelial dysfunction, impaired nitric oxide-mediated vasodilation, reduced genital blood flow, hormonal alterations, and psychological factors. In contrast, ACE inhibitors and angiotensin receptor blockers generally demonstrated neutral or beneficial effects on sexual function.

Conclusion: Sexual dysfunction is a significant yet underrecognized complication of antihypertensive therapy that adversely affects medication adherence and quality of life. Individualized antihypertensive selection and improved physician awareness are important for optimizing patient outcomes.

Keywords: Hypertension, Antihypertensive Drugs, Sexual Dysfunction, Erectile Dysfunction, Female Sexual Dysfunction, Beta Blockers, Angiotensin Receptor Blockers.

INTRODUCTION

Hypertension is one of the most prevalent chronic diseases worldwide and is an important risk factor of cardiovascular and cerebrovascular diseases.[1] Effective control of blood pressure significantly reduces the risk of complications such as myocardial infarction, stroke, therapies, long term treatment adherence remains a significant challenge in hypertensive patients. Among the various adverse

effects contributing to poor adherence, those related to sexual function are often under-recognized and underreported. Sexual dysfunction associated with antihypertensive therapies may lead to deterioration in patients' quality of life. Therefore, it is important for practitioners to become familiar with the wide variation in sexual side effects produced by antihypertensive agents and to discuss the potential occurrence of these side effects with their patients.[2] Sexual dysfunction in males includes disturbances in libido, arousal, erection, ejaculation, orgasm, and overall sexual satisfaction. Erectile dysfunction is particularly common with older agents such as thiazide diuretics and conventional beta blockers.[3] Studies have also shown that women may experience decreased lubrication, impaired arousal, and reduced sexual satisfaction.[4] In many cases, modification of the patient's drug regimen may help patients overcome certain specific sexual side effects experienced with treatments. Studies show that, losartan, an angiotensin II antagonist, is not typically associated with development of sexual dysfunction and may actually positively impact several indices of sexual function (erectile function, sexual satisfaction, and frequency of sexual activity) as well as perceived quality of life.[5] Existing studies often overlook Female Sexual Dysfunction, even when the prevalence is as high as 42.1%. This literature review aims to evaluate the association between antihypertensive drugs and sexual dysfunction, discuss the possible pathophysiological mechanisms involved, compare the effects of different antihypertensive drug classes, and highlight current evidence regarding clinical management and future research directions.

MATERIALS AND METHODS

Study Design

This literature review was conducted to evaluate the association between antihypertensives and sexual dysfunction

Data Source

A literature search was conducted using the PubMed database due to its comprehensive coverage of biomedical and clinical research literature.

Search Strategy

Relevant articles were searched using PubMed, Scopus, and Google Scholar using keywords such as ‘hypertension,’ ‘antihypertensive drugs,’ ‘sexual dysfunction,’ and ‘erectile dysfunction.

Inclusion Criteria

Studies included in this literature review were those involving adult hypertensive patients receiving antihypertensive therapy and establishing the association between antihypertensive medications and sexual dysfunction. Sexual dysfunction outcomes assessed included erectile dysfunction, decreased libido, ejaculatory disorders, orgasmic dysfunction, arousal disorders, and overall sexual satisfaction. Studies evaluating any class of antihypertensive agents, including diuretics, beta blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and centrally acting antihypertensive drugs, were considered. Original research articles, randomized controlled trials, cohort studies, case-control studies, cross-sectional studies, systematic reviews, and meta-analyses published in peer-reviewed journals were included.

Exclusion Criteria: None

Study Selection

- Titles and abstracts of retrieved articles were screened for relevance.
- Full-text articles of potentially eligible studies were then reviewed to determine suitability for inclusion
- Studies meeting the eligibility criteria were included in the final analysis

Data extraction:

Data extraction was performed systematically from all eligible studies. Relevant information collected included the author’s name, year of publication, study design, sample size, study population characteristics, type of antihypertensive medication evaluated, duration of therapy, assessment methods used for evaluating sexual dysfunction, and the main outcomes reported. Data regarding the association between specific antihypertensive drug classes and various forms of sexual dysfunction, including erectile dysfunction, decreased libido, ejaculatory disorders, orgasmic dysfunction, and overall sexual satisfaction, were extracted. Information related to proposed pathophysiological mechanisms, comparative drug effects, and clinical implications was also reviewed and summarized.

Outcomes of Interest:

- Anti-hypertensives
  1. Classification of antihypertensive drugs
  2. Types of antihypertensive drugs associated with sexual dysfunction
- Sexual dysfunction
  1. Effects of sexual dysfunction on quality of life and compliance rate
  2. Pathophysiology of dysfunction in males and females
- Association between antihypertensive drugs and sexual dysfunction
  1. Prevalence of sexual dysfunction among hypertensive patients
  2. Mechanism of male and female sexual dysfunction due to antihypertensive drugs
  3. Effect of ARBs and ACE inhibitors on erectile dysfunction
  4. Female Sexual Dysfunction among hypertensive females due to non-selective beta blockers.
  5. Management

RESULTS

The findings of the included studies have been discussed under the following headings: antihypertensive drugs and their association with

sexual dysfunction, the impact and pathophysiology of sexual dysfunction, and the association between specific antihypertensive drug classes and sexual dysfunction in hypertensive patients. The results in the literature are summarized below regarding the same.

Anti-hypertensives:

Classification of antihypertensive drugs:

Antihypertensive therapy is usually initiated as monotherapy following unsuccessful blood pressure control through lifestyle modifications. Combination therapy is commonly employed when adequate control is not achieved with a single agent. Effective reduction of blood pressure significantly decreases cardiovascular morbidity and mortality, with maintenance of systolic blood pressure below 130 mmHg shown to reduce complications like heart failure, diabetes mellitus, coronary artery disease, stroke, and other cardiovascular disorders. The response to antihypertensive monotherapy may vary depending on factors such as age and race.[6]

Several classes of antihypertensive medications are currently used in the management of hypertension. Thiazide and thiazide-like diuretics remain among the most commonly recommended first-line agents. According to the JNC 8 guidelines, thiazide diuretics may be used either alone or in combination with other antihypertensive drugs across different age groups and racial populations, except in patients with chronic kidney disease. Thiazide-like diuretics such as chlorthalidone and indapamide have demonstrated superior efficacy in reducing cardiovascular morbidity and mortality at relatively lower cost. Chlorthalidone is frequently preferred as an initial monotherapy agent due to its prolonged duration of action and effective blood pressure control.[7]

Thiazide diuretics exert their antihypertensive action primarily by inhibiting sodium reabsorption in the distal convoluted tubule through blockade of the sodium-chloride (Na/Cl) cotransporter. Although they may produce a minor effect on sodium transport within the proximal tubule, their principal site of action remains the distal tubule. The initial antihypertensive effect of thiazides is attributed to intravascular volume depletion and a consequent reduction in cardiac output. However, cardiac output gradually returns toward baseline within 6–8 weeks through compensatory autoregulatory mechanisms, while blood pressure reduction is maintained. Thiazide diuretics may also acutely activate the renin–angiotensin–aldosterone system, resulting in increased systemic vascular resistance that can attenuate the initial antihypertensive response. This compensatory activation tends to diminish with long-term therapy, and concurrent administration of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers may further enhance blood pressure control. In addition, thiazide-type diuretics exhibit modest vasodilatory properties, although the precise mechanisms underlying this effect remain incompletely understood.[8]

Loop diuretics are generally not considered first-line agents for uncomplicated hypertension; however, they are preferred in patients with reduced renal function, particularly when the estimated glomerular filtration rate is below 30 mL/min. They are also widely used in the management of oedema associated with congestive heart failure, hepatic disease, and renal disorders. Potassium-sparing diuretics such as spironolactone and eplerenone are commonly used in resistant hypertension, particularly as add-on therapy to multidrug regimens. However, caution is advised when these agents are combined with angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARB) due to the increased risk of hyperkalaemia.[6,9]

Calcium channel blockers (CCBs) are also recommended by the JNC 8 guidelines as first-line agents for the management of hypertension, either as monotherapy or in combination with other antihypertensive drugs, across different age groups and racial populations, except in patients with chronic kidney disease where ACE inhibitors or ARBs are preferred. Similar to thiazide diuretics, CCBs have demonstrated efficacy in reducing cardiovascular events, although their benefit in preventing heart failure is comparatively lesser. They are considered suitable alternatives in patients who are unable to tolerate thiazide diuretics. They are broadly classified into two groups: dihydropyridines and non-dihydropyridines. Dihydropyridines primarily exert potent vasodilatory effects with minimal influence on cardiac conduction and contractility, making them more commonly used in the treatment of hypertension. Amlodipine and nifedipine are among the most frequently prescribed drugs in this group. In contrast, non-dihydropyridines exhibit greater effects on cardiac conduction and myocardial contractility with relatively weaker vasodilatory action. Due to these properties, they are more commonly used in the management of arrhythmias and other cardiac conditions rather than in hypertension treatment. (The mechanism of action of CCBs is related to the inhibition of Ca2+ entry to the cells; this occurs by binding to the L-type voltage-gated calcium channels located in the heart muscle. This effect can cause peripheral vasodilation, which is seen mainly in dihydropyridines, or a negative inotropic effect on the heart muscle in non-dihydropyridines, inhibiting the sinoatrial and atrioventricular nodes, leading to slow cardiac contractility and conduction.[11]

ACE inhibitors and ARBs are the antihypertensives of choice for patients with heart failure and chronic kidney disease. They are indicated as first-line treatment for patients with chronic kidney disease with evidence of proteinuria. Beyond their antihypertensive effects, these drug classes possess significant cardioprotective properties, contributing to reduced cardiovascular morbidity and mortality in high-risk patients. Among ACE inhibitors, ramipril has been shown to reduce mortality, myocardial infarction, and stroke in patients with symptomatic

heart failure as well as in asymptomatic patients with reduced ejection fraction. Perindopril has also demonstrated decreased cardiovascular events among patients with stable coronary artery disease and preserved systolic function. Among ARBs, losartan has shown superiority over atenolol in reducing cardiovascular morbidity and mortality while providing effective blood pressure control. Furthermore, studies comparing ramipril and telmisartan have demonstrated comparable efficacy in patients with diabetes mellitus and heart failure, with telmisartan being associated with a lower incidence of angioedema. ACE inhibitors decrease blood pressure by inhibiting the angiotensin-converting enzyme; this causes a decline in the production of angiotensin II and increases the bradykinin level by inhibiting its degeneration, which leads to vasodilation.[9,10,12] ARBs work by blocking the binding of angiotensin II to the angiotensin 1 AT1 receptors, which inhibit the angiotensin II effect. In contrast to ACE inhibitors, ARBs do not affect the kinin levels.[6]

Beta-blockers are not indicated as primary treatment for hypertension They are associated with decreased cardiovascular morbidity and mortality when used in younger patients but are less protective in patients older than 65 and were noted to be associated with an increased risk of strokes They work by inhibiting the catecholamines from binding to the Beta 1, 2, and 3 receptors. Beta-1 receptors are found primarily in the heart muscle, beta-2 receptors are located in the bronchial and peripheral vascular smooth muscles, and beta-3 receptors appear in the adipose tissue of the heart. Cardio-selective beta-blockers (e.g., metoprolol succinate, metoprolol tartrate, atenolol, betaxolol, and acebutolol) inhibit only beta-1 receptors, causing fewer bronchospasms. By inhibiting the catecholamines binding to the beta receptors, the beta-blockers have a negative inotropic effect, which results in a decrease in the heart rate, which helps to reduce oxygen consumption.[6]

Direct vasodilators and centrally acting antihypertensive agents are generally reserved for patients with resistant hypertension who fail to achieve adequate blood pressure control with first-line therapies. Hydralazine may be added either alone or in combination with nitrates, particularly in patients with heart failure. However, its use is associated with reflex sympathetic activation and increased sodium and water retention; therefore, concomitant administration of beta blockers and loop diuretics is often necessary to minimize these adverse effects.[13] Clonidine, a centrally acting alpha-2 adrenergic agonist, is not commonly used as first-line therapy but may serve as an adjunctive agent in patients inadequately controlled on combination antihypertensive regimens. The transdermal formulation is generally preferred because it improves compliance and reduces the risk of rebound hypertension associated with abrupt discontinuation.[14] Minoxidil is considered in severe or refractory hypertension, particularly when treatment with hydralazine is unsuccessful. Although highly effective in lowering blood pressure, minoxidil commonly causes fluid retention and reflex sympathetic stimulation, often necessitating the concurrent use of loop diuretics and beta blockers. Alpha-adrenergic blockers are generally not recommended as first-line antihypertensive agents because they are less effective in reducing cardiovascular morbidity and mortality compared to other antihypertensive drug classes.[6,10]

Types of antihypertensive drugs associated with sexual dysfunction

Several classes of antihypertensive medications have been associated with sexual dysfunction, although the degree of impairment varies among different drugs. Sexual adverse effects commonly reported include erectile dysfunction, decreased libido, ejaculatory disorders, impaired arousal, and reduced sexual satisfaction. Among the antihypertensive agents, thiazide diuretics and conventional beta blockers have been most consistently implicated in the development of sexual dysfunction.[15-18]

Thiazide diuretics have frequently been associated with erectile dysfunction in hypertensive males. A study reported that thiazide diuretics were among the antihypertensive agents most commonly linked to impotence.[19] Similarly, in another study it was observed that thiazide-type diuretics represent one of the most prominent antihypertensive classes associated with erectile dysfunction. The proposed mechanisms include decreased penile blood flow secondary to volume depletion, vascular changes, and metabolic disturbances.[20]

Beta blockers, particularly older non-selective agents such as propranolol and atenolol, have also been strongly associated with sexual dysfunction. These agents may impair erectile function by reducing sympathetic nervous system activity, decreasing penile perfusion, and contributing to fatigue and depressive symptoms.[15,17] However, newer vasodilatory beta blockers such as nebivolol appear to exert neutral or even beneficial effects on erectile function because of nitric oxide-mediated vasodilation.[21]

Centrally acting antihypertensive agents, including clonidine and methyldopa, have also been associated with impaired sexual function. A study reported that centrally acting sympatholytic drugs may further worsen sexual dysfunction in hypertensive patients by suppressing central sympathetic outflow. Multiple studies also additionally highlighted the association between centrally acting agents and various forms of sexual dysfunction, including reduced libido and erectile impairment.[22,23]

In contrast, calcium channel blockers and angiotensin-converting enzyme inhibitors are generally considered to have neutral effects on sexual function. Angiotensin receptor blockers may demonstrate comparatively favourable effects, with several studies suggesting improvement in erectile function due to enhanced endothelial function and

improved penile blood flow following inhibition of angiotensin II-mediated vasoconstriction.[24]

Sexual dysfunction

Effects of sexual dysfunction on quality of life and compliance rate

The relationship of antihypertensive drugs have a long history of association with sexual dysfunction. Sexual dysfunction increases with age and is associated with physical and emotional symptoms. Sexual dysfunction is associated with impairment of quality of life and noncompliance.[33] Sexual dysfunction has been identified in multiple controlled trials to be a frequent accompaniment to antihypertensive therapy. Issues of cause and effect are confused because hypertension itself can cause sexual dysfunction. It seems probable, however, that use of certain classes of blood pressure-lowering agents, notably non-cardioselective beta blockers such as propranolol, thiazide diuretics such as chlorthalidone and centrally-acting adrenergic agonists, is associated with an increased risk of sexual dysfunction.[34] A multicenter randomized placebo-controlled clinical trial conducted among 697 patients with mild hypertension elucidated the effects of low-does antihypertensive therapee on quality of life and sexual function. The study found that Chlorthalidone caused a significant increase in erection-related problems in men compared to placebo, while Atenolol too caused sexual side effects they were fewer.[35] A systematic review of literature published between 1970 and 2012 evaluated the effects of various antihypertensive drug classes on sexual function. The review found that diuretics and older-generation β-blockers were commonly associated with sexual dysfunction thus lower treatment compliance.[36] A multicenter observational study assessed sexual interest and behavior among hypertensive women aged 60–80 years. The study found that difficulty achieving orgasm and lack of vaginal lubrication were the two most common sexual complaints. Scores on quality-of-life measures did not differ significantly between the sexual abstinent and active women at baseline.[37]
A prospective interventional study evaluated the effect of Losartan on sexual dysfunction in hypertensive men over a 12-week period. The study found that Losartan treatment improved sexual satisfaction, and the subjects reporting a high frequency of sexual activity improved from 40.5% initially to 62.3% after drug treatment. Improvement on quality of life was also demonstrated in 73.7% of subjects medicated with Losartan.[38]

Association between antihypertensive drugs and sexual dysfunction

Prevalence of sexual dysfunction among hypertensive patients

Several reports collectively spanning more than three decades indicate that 2.4%–58% of hypertensive males experience one or more symptoms of sexual dysfunction of varying degrees of severity during antihypertensive drug therapy. It is also true however, that hypertensive patients also experience sexual dysfunction prior to taking medication, when compared to normotensive subjects.
The large variations in the prevalence of sexual problems reported in the literature most likely reflect differences in study methodology (lack of control subjects), types of antihypertensive medications taken, the presence of confounding medications, age differences of study populations, and cultural and socioeconomic factors. In the clinical practice setting, the prevalence of sexual dysfunction is likely to be even higher than that reported in clinical trials because the personal nature of this problem often leads to an unwillingness of many patients and/or physicians to openly discuss this issue.[2]
Although most studies on sexual dysfunction have focused almost exclusively only on men[25], women with hypertension are also at risk of developing sexual dysfunction. According to a 1994 survey, sexually active women aged 60–80 years who were receiving antihypertensive medications (atenolol, enalapril, or isradipine) experienced sexual dysfunction, as manifested as a difficulty achieving orgasm, inadequacy of vaginal lubrication, and diminished libido.
However, in the absence of a control group of hypertensive women who were not receiving antihypertensive therapy, it is difficult to accurately assess the effect of antihypertensive medication on sexual functioning.[26]

Mechanism of male and female sexual dysfunction due to antihypertensive drugs

Antihypertensive drugs may contribute to sexual dysfunction through multiple vascular, neurohormonal, endothelial, and psychological mechanisms. These effects variable and depend on the class of antihypertensive agent and may affect both males and females. Sexual dysfunction associated with antihypertensive therapy mostly presents as erectile dysfunction, decreased libido, ejaculatory disturbances, impaired arousal, vaginal dryness, anorgasmia, and reduced sexual satisfaction.[27] In males, erectile function is highly dependent on adequate penile blood flow and nitric oxide-mediated vasodilation:
NO→cGMP→Smooth muscle relaxation→Penile er ection
Antihypertensive drugs may impair this pathway through reduced sympathetic activity, endothelial dysfunction, decreased penile perfusion, and hormonal alterations. Thiazide diuretics have been shown to contribute to erectile dysfunction through intravascular volume depletion, reduced penile blood flow, and probable zinc depletion affecting testosterone synthesis. Conventional beta blockers such as propranolol and atenolol may worsen erectile function by inhibiting sympathetic nervous system activity, decreasing cardiac output, and producing fatigue and depressive symptoms that negatively affect sexual performance.[15,19,27] Centrally acting

antihypertensive agents, including clonidine and methyldopa, may cause sexual dysfunction by suppressing central sympathetic outflow and reducing libido and arousal. In addition, spironolactone has been associated with erectile dysfunction and gynecomastia because of its antiandrogenic properties.[6]

In females, antihypertensive drug-induced sexual dysfunction is less extensively researched but is becoming increasingly recognized. Hypertension and certain antihypertensive medications may impair vaginal blood flow and lubrication through endothelial dysfunction and reduced availability of nitric oxide. This thereby results in decreased arousal, vaginal dryness, dyspareunia, and difficulty achieving orgasm. Beta blockers may additionally contribute to female sexual dysfunction through fatigue, depression, and reduced sympathetic stimulation, thereby negatively affecting libido and sexual satisfaction.[27]

Some studies also reported that psychological mechanisms also play an important role in both sexes. Anxiety regarding sexual performance, fear of cardiovascular complications during intercourse, depression, reduced self-esteem, and medication-related fatigue may further exacerbate sexual dysfunction in hypertensive patients receiving antihypertensive therapy.[15,19]

Conversely, certain antihypertensive agents such as angiotensin receptor blockers and nebivolol may exert beneficial effects on sexual function. Nebivolol enhances nitric oxide release and improves endothelial function, thereby facilitating penile vasodilation and erectile function. Similarly, angiotensin receptor blockers may improve genital blood flow through inhibition of angiotensin II-mediated vasoconstriction and reduction of oxidative stress.[17,27]

Effects of ARBs and ACE inhibitors on erectile dysfunction:

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are generally considered to have neutral or beneficial effects on erectile function when compared with other antihypertensive drug classes such as thiazide diuretics and conventional beta blockers. Several studies suggest that these drugs improve endothelial function, enhance nitric oxide availability, and improve penile blood flow, thereby exerting favourable effects on erectile function.[30]

Multiple studies have reported that angiotensin II (AII)maybe acting as a regulator of penile erection through contractile effects on corporal and vascular smooth muscle.[29] By blocking the effects of AII, ARBs and ACE inhibitors produces a dose-dependent increase in cavernosal pressure and relaxation of smooth muscle, and hence, development of an erection. These groups of drugs therefore offer a new therapeutic option to prevent and/or correct erectile dysfunction in patients with hypertension.[2] A 2019 systematic review and meta-analysis evaluated the efficacy of ARBs on erectile function in hypertensive men and reported significant improvement in sexual activity and erectile function among patients receiving ARB therapy.[31]

Losartan has been particularly associated with improvement in sexual satisfaction and frequency of sexual activity in hypertensive males with erectile dysfunction. Several studies demonstrated significant improvement in erectile function following losartan therapy independent of blood pressure reduction. Similarly, valsartan has demonstrated improvement in multiple domains of sexual function, including erectile function, sexual desire, and intercourse satisfaction.[27]

Overall, current evidence suggests that ARBs may represent a preferable antihypertensive option in sexually active hypertensive males experiencing erectile dysfunction, while ACE inhibitors are generally associated with minimal adverse sexual effects. These findings are clinically important because sexual adverse effects may significantly influence medication adherence and quality of life in hypertensive patients.[32]

FSD (Female Sexual Dysfunction) among hypertensive females due to non-selective beta blockers.

A prospective open-label randomized study evaluated the effect of nebivolol and bisoprolol on female sexual function in 300 hypertensive women aged 20–50 years. Sexual function was assessed using the Female Sexual Function Index (FSFI) over a 90-day follow-up period. The study demonstrated that females receiving nebivolol showed significant improvement in sexual function scores compared to the baseline values, whereas no significant improvement was observed in the bisoprolol group. It was theorised that non-selective and conventional beta blockers may contribute to female sexual dysfunction through reduced nitric oxide bioavailability, impaired genital blood flow, and decreased vaginal lubrication. Nebivolol demonstrated comparatively favourable effects because of its nitric oxide-mediated vasodilatory properties, which improve endothelial function and genital blood flow. Thus, the study concluded that switching hypertensive females experiencing beta blocker-associated sexual dysfunction to nebivolol may improve sexual function and overall quality of life.[40]

DISCUSSION

Antihypertensives

Classification of antihypertensive drugs

Although antihypertensive medications significantly reduce the risk of complications such as stroke, myocardial infarction, heart failure, and chronic kidney disease, their adverse effects on sexual function remain an important clinical concern. The present review demonstrates that both hypertension

and antihypertensive therapy contribute to sexual dysfunction through vascular, endothelial, neurohormonal, and psychological mechanisms. Among the different antihypertensive classes, thiazide diuretics and conventional beta blockers were found to be most strongly associated with sexual dysfunction, particularly erectile dysfunction in males. Thiazide diuretics may impair sexual function through reduced penile blood flow, volume depletion, and electrolyte disturbances, while beta blockers may decrease sympathetic activity and contribute to fatigue and depressive symptoms that negatively affect sexual performance. In contrast, ACE inhibitors and ARBs generally demonstrated neutral or beneficial effects on sexual function. ARBs such as losartan and valsartan have shown improvement in erectile function and sexual satisfaction, likely due to enhanced endothelial function and improved nitric oxide-mediated vasodilation.[6-8]

Calcium channel blockers were generally associated with minimal adverse sexual effects and are often considered as suitable alternatives in patients intolerant to other antihypertensive agents. Female sexual dysfunction, although less extensively studied, was also identified among hypertensive women, including decreased libido, impaired arousal, vaginal dryness, and reduced sexual satisfaction. An important finding of this review is the impact of sexual dysfunction on treatment adherence. Patients experiencing antihypertensive-induced sexual dysfunction may discontinue therapy or demonstrate poor compliance, resulting in inadequate blood pressure control and increased cardiovascular risk. Therefore, clinicians should consider the sexual side-effect profile of antihypertensive drugs while choosing a treatment plan.[6,11]

Types of antihypertensive drugs associated with sexual dysfunction

Sexual dysfunction is a common adverse effect associated with several classes of antihypertensive medications, although the severity varies among different drug groups. The most frequently reported manifestations included erectile dysfunction, decreased libido, ejaculatory disturbances, impaired arousal, and reduced sexual satisfaction. Multiple studies consistently identified thiazide diuretics and conventional beta blockers as the antihypertensive agents most strongly associated with sexual dysfunction.[3,15,19]

Several studies reported a significant association between thiazide diuretics and erectile dysfunction in hypertensive males. Weiss reported that thiazide diuretics were among the antihypertensive agents most commonly linked to impotence.[3] Similarly, it was also observed that thiazide-type diuretics are strongly associated with erectile dysfunction due to reduced penile blood flow, vascular changes, and metabolic disturbances.[20] Conventional beta blockers, particularly propranolol and atenolol, also demonstrated strong associations with sexual dysfunction. Corona et al. reported that older beta blockers may impair erectile function through decreased sympathetic nervous system activity, reduced penile perfusion, and associated fatigue and depressive symptoms.1 However, newer vasodilatory beta blockers such as nebivolol demonstrated comparatively favourable effects on erectile function because of nitric oxide-mediated vasodilation.[17]

Centrally acting antihypertensive agents including clonidine and methyldopa were also associated with impaired sexual function. A study reported that centrally acting sympatholytic agents may worsen erectile dysfunction and reduce libido by suppressing central sympathetic outflow.[3] In contrast, calcium channel blockers and angiotensin-converting enzyme inhibitors were generally associated with neutral effects on sexual function. Several studies additionally demonstrated that angiotensin receptor blockers may exert beneficial effects on erectile function by improving endothelial function and penile blood flow through inhibition of angiotensin II-mediated vasoconstriction.[31]

Sexual dysfunction:

Effects of sexual dysfunction on quality of life and compliance rate

Sexual dysfunction is a well-recognised adverse effect encountered with anti-hypertensive therapy which may significantly impair quality of life and adherence to therapy. Both hypertension itself and antihypertensive therapy may contribute to sexual dysfunction which makes it difficult to establish a direct causal relationship. Older anti-hypertensives agents such as thiazide diuretics and non-cardioselective beta-blockers have been proven to have a stronger association with sexual dysfunction. Chlorthalidone was consistently associated with increased erectile dysfunction in men and Atenolol also demonstrated sexual side effects, although less severe than Chlorthalidone which suggests variability among beta-blockers. Female sexual dysfunction among hypertensive patients is underreported but may include reduced vaginal lubrication and difficulty in achieving orgasm. The association between sexual dysfunction and reduced treatment compliance highlights the importance of addressing sexual health during antihypertensive therapy. Losartan and other ARBs may improve sexual satisfaction and quality of life, suggesting that certain antihypertensive classes may have protective or beneficial effects on sexual function. Switching patients from older antihypertensive drugs to ARBs may help improve adherence and overall patient satisfaction. In case of hypertensive patients, assessment of sexual function routinely helps clinicians identify adverse effects early and individualize antihypertensive therapy.[33,38]

Pathophysiology of dysfunction in males and females

A review article by Reffelmann T, Kloner RA exploring the pathophysiology of sexual dysfunction

in hypertensive patients receiving antihypertensive therapy highlighted endothelial dysfunction as the major underlying mechanism of sexual dysfunction, wherein chronic hypertension leading to vascular damage and impaired nitric oxide-mediated vasodilation in both systemic and penile vasculature. Reduced nitric oxide release from endothelial cells and nerve endings leads to inadequate relaxation of penile smooth muscle, thereby impairing penile blood flow and erection. Additionally, certain antihypertensive drugs, particularly thiazide diuretics and β-blockers further worsen sexual dysfunction through vascular and neurohormonal mechanisms such as impairment of vascular function and reducing penile blood flow in hypertensive patients already affected by endothelial dysfunction.

In case of beta blockers, additional depression in sympathetic activity and altered vascular hemodynamics may contribute to erectile dysfunction. On the other hand, angiotensin II receptor blockers may improve endothelial function and sexual performance due to the blockade of AT1 type receptors which reduced vasoconstriction and vascular dysfunction, thereby improving penile blood flow and erectile response. The review suggested that endothelial dysfunction and impaired nitric oxide-mediated vasodilation may also contribute to female sexual dysfunction leading to complaints such as decreased vaginal lubrication, reduced arousal, and difficulty achieving orgasm.[39]

Association between antihypertensive drugs and sexual dysfunction:

Prevalence of sexual dysfunction among hypertensive patients

The reviewed studies demonstrated a high prevalence of sexual dysfunction among hypertensive patients receiving antihypertensive therapy. Reports published over the past few years indicated that approximately 2.4%–58% of hypertensive males experience one or more symptoms of sexual dysfunction during antihypertensive treatment. Sexual dysfunction commonly presented as erectile dysfunction, decreased libido, ejaculatory disturbances, and reduced sexual satisfaction. However, several studies also observed that hypertensive patients may experience sexual dysfunction even before initiation of antihypertensive therapy, suggesting that hypertension itself contributes significantly to impaired sexual function through vascular and endothelial abnormalities.[3,17,27]

The wide variation in prevalence rates reported in the literature appears to be influenced by differences in study methodology, patient age, antihypertensive drug classes used, duration of therapy, associated comorbidities, and sociocultural factors. Several authors additionally suggested that the true prevalence of sexual dysfunction in clinical practice may be underestimated because both patients and physicians are often reluctant to discuss sexual health concerns openly.[2,3]

Most published studies have predominantly focused on male sexual dysfunction, particularly erectile dysfunction.25 Nevertheless, hypertensive women have also been found to be at increased risk of developing sexual dysfunction. A study reported that sexually active hypertensive women aged 60–80 years receiving antihypertensive medications such as atenolol, enalapril, and isradipine experienced impaired orgasm, inadequate vaginal lubrication, and diminished libido (26). Similarly, another study demonstrated that hypertensive women receiving antihypertensive therapy reported poorer sexual functioning compared to normotensive controls.[4] However, several studies emphasized that the absence of adequate control groups limits the ability to determine whether sexual dysfunction is primarily attributable to hypertension itself or to antihypertensive medications.[4,26]

Mechanism of male and female sexual dysfunction due to antihypertensive drugs

Several studies demonstrated that antihypertensive drugs case impairment in the physiological nitric oxide-mediated vasodilation through endothelial dysfunction, reduced sympathetic activity, decreased penile perfusion, and hormonal alterations. Thiazide diuretics were associated with erectile dysfunction due to intravascular volume depletion, vascular changes, and possible zinc depletion affecting testosterone synthesis. Conventional beta blockers such as propranolol and atenolol were also consistently associated with impaired erectile function because of reduced sympathetic nervous system activity, decreased cardiac output, and associated fatigue and depressive symptoms.[15,19,27] Centrally acting antihypertensive agents including clonidine and methyldopa demonstrated negative effects on libido and arousal through suppression of central sympathetic outflow. Additionally, spironolactone was associated with erectile dysfunction and gynecomastia because of its antiandrogenic effects.[6]

Female sexual dysfunction associated with antihypertensive therapy was comparatively less investigated but was seen to be increasingly recognized in the reviewed literature. Studies reported that hypertension and antihypertensive medications may impair vaginal blood flow and lubrication through endothelial dysfunction and reduced nitric oxide availability, resulting in decreased arousal, vaginal dryness, dyspareunia, and difficulty achieving orgasm.[27] Beta blockers were additionally associated with fatigue, depression, and reduced sympathetic stimulation that negatively affected female libido and sexual satisfaction. Psychological mechanisms were also found to contribute significantly to sexual dysfunction in both sexes. Anxiety regarding sexual performance, fear of cardiovascular complications during intercourse, depression, reduced self-esteem, and medication-related fatigue were identified as important contributing factors.[15,19] Conversely, angiotensin

receptor blockers and nebivolol demonstrated comparatively favourable effects on sexual function through improved endothelial function.[17,27]

Effects of ARBs and ACE inhibitors on erectile dysfunction:

The reviewed studies suggest that angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) demonstrate comparatively better effects on erectile function when compared with older antihypertensive agents such as thiazide diuretics and conventional beta blockers. Unlike antihypertensive classes commonly associated with sexual dysfunction, ACE inhibitors and ARBs generally exhibit neutral or beneficial effects on sexual performance due to their positive influence on endothelial function, nitric oxide availability, and penile blood flow.[30] Several studies identified angiotensin II as an important regulator of penile vascular tone through its contractile effects on corporal and vascular smooth muscle.[29] By inhibiting the renin–angiotensin–aldosterone system, ACE inhibitors and ARBs reduce angiotensin II-mediated vasoconstriction and promote cavernosal smooth muscle relaxation, thereby facilitating penile erection. A study also reported that blockade of angiotensin II may improve erectile function through dose-dependent increases in cavernosal pressure and improved endothelial-mediated vasodilation.[2] These findings support the role of ACE inhibitors and ARBs as potentially beneficial antihypertensive options in patients experiencing erectile dysfunction.

Among ARBs, losartan and valsartan demonstrated particularly favourable outcomes in hypertensive males with erectile dysfunction. Several studies reported improvement in erectile function, sexual desire, intercourse satisfaction, and overall sexual activity following ARB therapy, independent of blood pressure reduction.[27] Furthermore, a 2019 systematic review and meta-analysis demonstrated significant improvement in erectile function and sexual activity among hypertensive men receiving ARB therapy.[31]

The comparatively favourable sexual side-effect profile of ARBs and ACE inhibitors is clinically significant because sexual dysfunction is an important factor contributing to poor medication adherence and reduced quality of life in hypertensive patients. Consequently, these agents may represent preferable therapeutic options in sexually active hypertensive males, particularly in patients experiencing antihypertensive-induced erectile dysfunction. However, additional long-term prospective studies are required to further clarify the extent of their beneficial effects on sexual function across different patient populations.[32]

Female Sexual Dysfunction among hypertensive females due to non-selective beta blockers.

Beta-blockers may differentially affect female sexual function depending on their pharmacological properties. Conventional and non-selective beta-blockers appear to worsen sexual function by reducing nitric oxide availability and impairing genital blood flow, whereas nebivolol demonstrated comparatively beneficial effects due to its vasodilatory action mediated through nitric oxide release. These observations are in support of the hypothesis that endothelial dysfunction and impaired vascular perfusion play an important role in the pathogenesis of female sexual dysfunction among hypertensive women. Studies also highlight the need for clinicians to consider the impact of antihypertensive therapy on quality of life and treatment compliance when selecting medications, especially for female patients. The limited number of studies on female sexual dysfunction compared to male sexual dysfunction indicates the need for larger and more comprehensive studies in women.[40]

Management

Sexual dysfunction should be actively screened in hypertensive patients receiving antihypertensive therapy because patients often hesitate to report sexual symptoms voluntarily due to embarrassment or social stigma. Early identification may improve adherence and quality of life. Treatment regimens should be individualized to minimize adverse sexual effects while maintaining adequate blood pressure control as hypertension itself contributes to sexual dysfunction. Lifestyle modifications and switching antihypertensive medications may improve sexual function. ARBs such as losartan and valsartan demonstrated beneficial effects on erectile function, likely due to improved endothelial function, reduced angiotensin II-mediated vasoconstriction, and enhanced nitric oxide-mediated vasodilation. Psychological counselling and patient education are important parts of management, as anxiety, depression, and reduced self-esteem may further worsen sexual dysfunction in both males and females. Female sexual dysfunction requires greater clinical attention since signs and symptoms of female sexual dysfunction are often underreported and understudied in hypertensive women. A multidisciplinary and patient-centered approach is recommended, involving regular assessment of sexual health, individualized drug selection, cardiovascular risk reduction, and counselling to improve overall treatment compliance and quality of life.[38]

CONCLUSION

Sexual dysfunction is a significant yet frequently underrecognized adverse effect among hypertensive patients and may occur as a consequence of both hypertension itself and antihypertensive therapy. The reviewed literature demonstrates that different classes of antihypertensive medications exert varying effects on sexual function. Thiazide diuretics and conventional beta blockers were most consistently associated with adverse sexual effects, particularly erectile dysfunction, decreased libido, and impaired

sexual satisfaction. In contrast, angiotensin-converting enzyme inhibitors and especially angiotensin receptor blockers demonstrated comparatively neutral or beneficial effects on sexual function through improvement of endothelial function and penile blood flow. Although male sexual dysfunction, particularly erectile dysfunction, has been extensively studied, female sexual dysfunction remains comparatively underreported and insufficiently investigated and studied. this review integrates Hypertensive women may also experience impaired arousal, reduced lubrication, dyspareunia, and decreased sexual satisfaction associated with hypertension and antihypertensive therapy.

Sexual adverse effects significantly affect quality of life and may contribute to poor adherence to antihypertensive treatment, ultimately compromising blood pressure control and increasing cardiovascular risk. Therefore, clinicians should routinely assess sexual health while managing hypertensive patients and consider the sexual side-effect profile when selecting antihypertensive therapy. Individualized treatment strategies and improved physician–patient communication may help reduce treatment discontinuation and improve overall patient wellbeing. Further large-scale prospective studies are required to better understand the long-term effects of antihypertensive medications on sexual function in both males and females and to establish evidence-based management strategies for antihypertensive drug-associated sexual dysfunction.

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