Gender Differences in Prescribing Antihypertensive Drugs in a Public Hospital in Alkharj

Nehad J. Ahmed¹*, Menshawy A. Menshawy² and Ziyad S. Almalki¹*

¹Department of Clinical Pharmacy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia.
²Department of Medicinal Chemistry, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia.

Authors’ contributions

This work was carried out in collaboration among all authors. Author NJA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MAM and ZSA managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Hypertension is considered one of the most significant risk factors for mortality and morbidity worldwide. There are major clinical implications for gender-specific pharmacokinetics and pharmacodynamics. It is important to know the potential gender differences in hypertension treatment and to know the prescribing trends in male and female hypertensive patients in order to optimize the treatment of hypertension.

Aim: This is a retrospective study that aims to describe the difference in prescribing antihypertensive drugs between male and female patients.

Methodology: This is a retrospective study that includes the revision of patient electronic records of outpatients with hypertension in 2018 in Alkharj.

Results: The total number of prescribed antihypertensive drugs was 1838 drugs. The calcium channel blocker was the most commonly prescribed antihypertensive class (27.86%). The study showed that there are different patterns of antihypertensive drug use among hypertensive men and women and showed that female patients are more frequently treated with diuretics and less...
frequently with angiotensin-converting enzyme inhibitors and angiotensin receptors blockers than male patients.

**Conclusion:** Stratified guidelines and policies based on gender will be appropriate if more studies show a difference in the efficacy and safety of antihypertensive drugs between male and female patients. It is important to conduct more studies about these differences.

**Keywords:** Antihypertensive; differences; gender; prescribing; sex.

1. INTRODUCTION

Hypertension is considered one of the most significant risk factors for mortality and morbidity worldwide. It is responsible for the deaths of about 9 million people yearly [1]. Hypertension or high blood pressure was defined by the National Institute for Health and Care Excellence as a clinic blood pressure of 140/90 mmHg or higher confirmed by a subsequent ambulatory blood pressure monitoring daytime average (or home blood pressure monitoring average) of 135/85 mmHg or higher [2].

High blood pressure does not develop in older adults only it can occur also in younger adults. For example, in England 2015 over 2.1 million people less than 45 years old had high blood pressure [3]. It is important to diagnose and treat hypertension early because this will result in significant reductions in the risk of subsequent cardiovascular diseases [4,5]. Even with strong evidence for such treatment, studies suggest that several people remain sub-optimally controlled [6].

Previous studies have shown that women have a 50–70% greater risk of suffering from adverse drug reactions compared to men, and that about 60% of patients admitted to hospital with an adverse drug reaction are women [7,8].

There are other differences between women and men such as the differences in pharmacokinetics that make female patients in general more susceptible to dose-dependent adverse drug reactions [9]. Moreover, several factors influence the bioavailability and distribution of drugs, such as circulating plasma volume, the ratio of lean to fat tissue, and the number of plasma proteins binding the drug [10]. Furthermore, there are differences in body fat composition and in body mass between male and female patients that will affect the half-life of the medications [11].

In general, numerous medications are metabolized by enzymes of the CYP system. Sex differences have been shown regarding several enzymes such as CYP1A2, CYP2D6, CYP2E1, and CYP3A4 [12] but still, the studies on the clinical impact of these differences are inadequate [13]. Renal clearance is usually higher in men than in women [9]. Women may respond to cardiovascular medication differently than men [14].

Since women have slower gastric motility and intestinal transit than men, they may need to wait longer between food consumption and medication if a drug is to be taken on an empty stomach [15,16].

Several important reasons could explain gender-induced differences in blood pressure levels, blood pressure control, and antihypertensive treatment. They involve sex hormones, the renin-angiotensin-aldosterone and sympathetic nervous system, and arterial stiffness [17]. However, Data on the efficacy of antihypertensive therapy between genders are conflicting and further clinical research is needed to uncover potential gender differences in hypertension [18].

It is important to know the potential gender differences in hypertension treatment and to know the prescribing trends in male and female hypertensive patients. Therefore, this study aims to describe sex differences in prescribing antihypertensive drugs in a public hospital in Alkhari.

2. METHODOLOGY

This is a retrospective study that aims to describe the difference in prescribing antihypertensive drugs between male and female patients. The study includes the revision of patient electronic records of outpatients with hypertension in 2018 in Alkhari that is a governorate in central Saudi Arabia.

Inclusion criteria include outpatient prescriptions for hypertensive patients in 2018 so the prescriptions of patients who didn’t have hypertension, the inpatient prescriptions, and the
prescriptions before or after 2018 were excluded due to the availability of 2018 data only.

The data includes the most commonly prescribed antihypertensive classes, the most commonly prescribed antihypertensive drugs, the sex differences in prescribing antihypertensive classes, and the sex differences in prescribing antihypertensive drugs.

3. RESULTS AND DISCUSSION

The total number of prescribed antihypertensive drugs was 1838. Calcium channel blocker was the most commonly prescribed antihypertensive class (27.86%) followed by diuretics (21.16%) and Angiotensin-converting enzyme inhibitors (20.13%). Table 1 shows the prescribed antihypertensive groups.

Generally, 54.08% of the prescriptions were prescribed for female patients. Beta-blockers and Angiotensin-converting enzyme inhibitors were prescribed in male more than female patients. Calcium channel blockers, diuretics, angiotensin receptors blockers were prescribed more in female patients. The sex differences in prescribing antihypertensive classes are shown in Table 2.

Amlodipine was the most commonly prescribed antihypertensive drug (25.30%) followed by bisoprolol (13.98%). The 6 medications that were prescribed most commonly (amlodipine, bisoprolol, furosemide, lisinopril, captopril, and indapamide) form about 70% of the total prescribing medications for the treatment of hypertension. The prescribed antihypertensive drugs in 2018 are shown in Table 3.

Amlodipine, furosemide, captopril, indapamide, telmisartan, valsartan, metoprolol, perindopril, atenolol, methyldopa, losartan, and verapamil were prescribed for female patients more than male patients. Propranolol and irbesartan were prescribed equally. Bisoprolol, lisinopril, enalapril, hydrochlorothiazide, spironolactone, olmesartan, nifedipine, carvedilol, diltiazem, and hydralazine were prescribed for male patients more than female patients include. The sex differences in prescribing antihypertensive drugs are shown in Table 4.

Table 1. The frequencies and percentages of the prescribed antihypertensive groups in 2018

| Antihypertensive class                      | Number | Percentage |
|--------------------------------------------|--------|------------|
| Calcium channel blockers                   | 512    | 27.86%     |
| Diuretics                                  | 389    | 21.16%     |
| Angiotensin-converting enzyme inhibitors   | 370    | 20.13%     |
| Beta-blockers                              | 343    | 18.66%     |
| Angiotensin receptors blockers             | 202    | 10.99%     |
| Others                                     | 22     | 1.20%      |

Table 2. The sex differences in prescribing antihypertensive classes

| Medication                                | Male   | Female  |
|-------------------------------------------|--------|---------|
| Calcium channel blockers                  | (43.16)| (56.84) |
| Diuretics                                 | (43.70)| (56.30) |
| Angiotensin-converting enzyme inhibitors  | (50.27)| (49.73) |
| Beta-blockers                             | (53.64)| (46.36) |
| Angiotensin receptors blockers            | (39.11)| (60.89) |
| Others                                    | (18.18)| (81.81) |
| Total                                     | 844    | 994      |
|                                           | (45.92)| (54.08) |
Similarly, Zhao et al reported that sex differences in the prescription of cardiovascular medication exist among patients at high risk or with established cardiovascular disease in primary care and similar to the result of the present study, Zhao et al also reported that there is a lower prevalence of angiotensin-converting enzyme inhibitors prescription in women and a lower prevalence of diuretics prescription in men and that the lower use of angiotensin-converting enzyme inhibitors among women, relative to men, could be explained by women's higher use of diuretics [19]. Additionally, similar to the results of the present study, Lloyd-Jones et al. [20], Gu et al. [21], and Qvarnstrom et al. [22] reported that women were more likely to be on diuretics but less likely to be on angiotensin-converting enzyme inhibitors which are in line with the results of the present study. Similarly, a study of 36 000 patients with established coronary heart disease in the United States, showed that women were less likely than men to be prescribed with angiotensin-converting enzyme inhibitors, statins, or aspirin or at both acute and hospital discharge of coronary heart disease [23].

Wang et al. reported that in patients aged 18–44 years, angiotensin-converting enzyme inhibitors showed the best control rate in males, while calcium channel blockers were least effective. In patients aged 45–64 years, diuretics showed the best control rate in females, while calcium channel blockers were least effective [24]. Klungel et al. reported that the different patterns of antihypertensive drug use among hypertensive men and women seem irrational and that among those on monotherapy for hypertension, women were less likely than men to be using a β-blocker, a calcium antagonist, or an angiotensin-converting enzyme inhibitor than a diuretic [25].

Furthermore, similar to our results Möllsten et al stated that to treat hypertension in diabetic patients it seems that the first choices for men are more often angiotensin-converting enzyme inhibitor or angiotensin receptors blockers and for women diuretics and βeta blockers, even in patients with type 1 diabetes [26]. Likewise, Muiesan et al stated that differences have been described regarding the pattern of antihypertensive drug prescription and use in hypertensive men and women; women are more frequently treated with diuretics and less frequently with angiotensin-converting-enzyme-inhibitors and angiotensin-receptors blockers [27].

Table 3. The prescribed antihypertensive drugs in 2018

| Medication       | Number | Percentage |
|------------------|--------|------------|
| Amlodipine       | 465    | 25.30%     |
| Bisoprolol       | 257    | 13.98%     |
| Furosemide       | 180    | 9.79%      |
| Lisinopril       | 147    | 8.00%      |
| Captopril        | 135    | 7.34%      |
| Indapamide       | 105    | 5.71%      |
| Telmisartan      | 75     | 4.08%      |
| Enalapril        | 67     | 3.65%      |
| Valsartan        | 64     | 3.48%      |
| Hydrochlorothiazide | 56   | 3.04%      |
| Spironolactone   | 48     | 2.61%      |
| Olmesartan       | 37     | 2.01%      |
| Metoprolol       | 36     | 1.96%      |
| Nifedipine       | 35     | 1.90%      |
| Perindopril      | 21     | 1.14%      |
| Atenolol         | 18     | 0.98%      |
| Methyldopa       | 17     | 0.92%      |
| Propranolol       | 16    | 0.87%      |
| Carvedilol        | 16    | 0.87%      |
| Irbesartan       | 16     | 0.87%      |
| Losartan         | 10     | 0.54%      |
| Diltiazem         | 7      | 0.38%      |
| Hydralazine      | 5      | 0.27%      |
| Verapamil        | 5      | 0.27%      |
Table 4. The sex differences in prescribing antihypertensive drugs

| Medication      | Male   | Female  |
|-----------------|--------|---------|
| Amlodipine      | 191    | 274     |
|                 | (41.08)| (58.92) |
| Bisoprolol      | 145    | 112     |
|                 | (56.42)| (43.58) |
| Furosemide      | 84     | 96      |
|                 | (46.67)| (53.33) |
| Lisinopril      | 80     | 67      |
|                 | (54.42)| (45.58) |
| Captopril       | 66     | 69      |
|                 | (48.89)| (51.11) |
| Indapamide      | 32     | 73      |
|                 | (30.48)| (69.52) |
| Telmisartan     | 27     | 48      |
|                 | (36.00)| (64.00) |
| Enalapril       | 35     | 32      |
|                 | (52.24)| (47.76) |
| Valsartan       | 20     | 44      |
|                 | (31.25)| (68.75) |
| Hydrochlorothiazide | 29 | 27    |
|                 | (51.79)| (48.21) |
| Spironolactone  | 25     | 23      |
|                 | (52.08)| (47.92) |
| Olmesartan      | 20     | 17      |
|                 | (54.05)| (45.95) |
| Metoprolol      | 14     | 22      |
|                 | (38.89)| (61.11) |
| Nifedipine      | 25     | 10      |
|                 | (71.43)| (28.57) |
| Perindopril     | 5      | 16      |
|                 | (23.81)| (76.19) |
| Atenolol        | 6      | 12      |
|                 | (33.33)| (66.67) |
| Methyldopa      | 0      | 17      |
|                 | (0.00) | (100.00)|
| Propranolol     | 8      | 8       |
|                 | (50.00)| (50.00) |
| Carvedilol      | 11     | 5       |
|                 | (68.75)| (31.25) |
| Irbesartan      | 8      | 8       |
|                 | (50.00)| (50.00) |
| Losartan        | 4      | 6       |
|                 | (40.00)| (60.00) |
| Diltiazem       | 4      | 3       |
|                 | (57.14)| (42.86) |
| Hydralazine     | 4      | 1       |
|                 | (80.00)| (20.00) |
| Verapamil       | 1      | 4       |
|                 | (20.00)| (80.00) |
| Total           | 844    | 994     |

4. CONCLUSION

It can be concluded that there are different patterns of antihypertensive drug use among hypertensive men and women and that female patient are more frequently treated with diuretics and less frequently with angiotensin-converting-enzyme-inhibitors and angiotensin-receptors.
blockers than male patients. In the future, stratified guidelines and policies will be more appropriate if more studies showed a difference in the efficacy and safety of several antihypertensive drugs between male and female patients. More studies are needed to find the sex differences in prescribing antihypertensive drugs and to determine the antihypertensive drugs that could have better efficacy or safety profile in male or female patients.

**CONSENT**

It is not applicable.

**ETHICAL APPROVAL**

The data were collected after the study approval by IRB ethical committee with a log number 2019-0153E and analyzed using Excel software and after that, the descriptive data were represented as percentages and frequencies.

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**COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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