Original Article

DRUG UTILIZATION EVALUATION OF ANGIOTENSIN RECEPTOR BLOCKER (ARB) ALONG WITH THEIR ADRS IN A TERTIARY CARE HOSPITAL

MOHAMMAD RIYASAT[1], MD. SHAMIM[1,2*], JIGAR HARIA[3], MOHAMMAD DAUD ALI[4], MAHFOOZ HUSSAIN[1], MD. SARFARAZ ALAM[5], SARFARAZ AHMAD[6]

[1]Department of Pharmacy Practice, College of Pharmacy, Teerthanker Mahaveer University. Delhi Road, NH 24, Bagadpur, Uttar Pradesh 244001, India, [2]Department of Pharmacy, Lakhmi Chand Patwari Pharmacy College, Baghpat. SH 57, Khekra, Uttar Pradesh, 250101, India, [3]Department of Medicine, Teerthanker Mahaveer Medical College and Research Centre, Teerthanker Mahaveer University. Delhi Road, NH 24, Bagadpur, Uttar Pradesh 244001, India, [4]Department of Pharmacy, Mohammed Al-Mana College for Medical Sciences, Abdulrazaq Bin Hammam Street, Al Safa, Dammam 34222, Saudi Arabia, [5]Department of Pharmaceutics, College of Pharmacy, Jazan University, Jazan 45142, Saudi Arabia, [6]Department of Clinical Pharmacy, College of Pharmacy, Jazan University, Jazan 45142, Saudi Arabia
Email: shamimpharma@gmail.com

ABSTRACT

Objective: To evaluate the drug utilization of Angiotensin Receptor Blocker (ARB) along with their ADRs in a tertiary care hospital. And to monitor, report of adverse drug reaction and drug interactions, if any.

Methods: The patients who meet the inclusion and exclusion criteria were enrolled into the study. The pertinent data such as demographic details, drug name, dose, frequency, and laboratory data were gathered from medical records of the patient and results were analyzed.

Results: Total of 100 patients were included in this study, the maximum utilization of antihypertensive drug (ARB) was telmisartan (90%) and widely use of ARBs in the age group of 41-50 y. Total 32 ADRs were observed and most probable ADRs included headache (42.8%), Nausea (14.28%) and dizziness (12.5%).

Conclusion: Telmisartan was the most prescribed and utilized drug than the other drugs of ARBs. Maximum ADRs were noted in females, the most frequent ADRs headache, nausea and dizziness were reported. The majority of reactions were probable on causality assessment done by WHO-UMC and Naranjo's scale having mild severity. So it can be concluded that considering risk factors, prevention and management of ADRs can drastically improve the therapeutic outcomes of the patients.

Keywords: Antihypertensive drugs, Angiotensin Receptor Blockers (ARBs), ADRs, Drug utilization, Telmisartan, Olmesartan, Azilsartan

INTRODUCTION

Hypertension or elevated blood pressure (BP) is a most common problem felt by human in their daily life, mainly early adulthood and old age. It is not a disease in itself, but it is a serious medical condition that is significantly alarming signal for the heart and blood vessels related mortality and morbidity [1]. During 2010, Patients of Hypertension were estimated nearly 1.15 billion throughout the world. Mainly (two thirds) hypertensive patients were belonging from small and middle income nations [2]. During 2015, it has been estimated that hypertension is more prominent in male (1 in 4) in comparison to female (1 in 5) [3]. Globally including India, it has been projected that Hypertension is one of the main causes of death, studied in 2010 [4]. Worldwide targeted that decrease the occurrence of hypertension by 25% by 2025, out of all non-communicable diseases [5].

The latest report regarding cardiovascular risk factors within Saudi community describes that the occurrence of hypertension is 31.4% which is remarkably raised in comparison to previous study [4, 6-8]. Due to the increased burden of Hypertension in the Community of Saudi Arabia, its duty of Healthcare provider keeps them aware and come forward for early detection and treatment. Pharmacotherapy of hypertension efficiently suppress hypertension related mortality and morbidity [9]. The chief goal of antihypertensive treatment is to prevent morbidity and mortality related to hypertension. Ultimate number of patients with hypertension suggested single, two or more antihypertensive medications [1]. Angiotensin Converting Enzyme Inhibitors (ACEIs), Angiotensin receptor blockers (ARBs), Beta‑Blockers (BBs), Calcium channel blockers (CCBs), centrally acting, Diuretics and Vasodilators have all been revealed to reduce

problems of hypertension and may be used for early drug therapy [10, 11]. The Joint National Committee (JNC) during 2003 released series of guidelines endorses the proper antihypertensive therapy on the basis of best available evidence. The guidelines endorse Thiazide diuretics to be prescribed only or as part of combination treatment for most hypertensive patients deprived of compelling indications [11, 12]. Though, most latest published data indicated an increasing use of the more costly Angiotensin Converting Enzyme Inhibitors (ACEIs) and Calcium Channel Blockers (CCBs) in spite of the absence of evidence to support that they are superior to diuretics and beta blockers (BBs) in suppressing morbidity and mortality of heart diseases [13]. In spite of widespread broadcasting of the JNC guidelines, prescribing practices have long continued discrepant with recommendations [14]. Currently for the treatment of hypertension Saudi Arabia follows JNC 8 guideline [15]. Appropriate antihypertensive drug treatment is significant as the occurrence of hypertension has risen radically in the last three decades [16]. Somewhat deviance from evidence based guidelines in hypertension treatment contributes to the high cost of medicines and makes problems in providing affordable prescription drugs [17]. Improper prescribing is a noticed throughout the world challenging the health care delivery system [18]. Drug utilization studies (DUS) are potent investigative tools to determine the role of drugs in society [19].

Among all the antihypertensive drugs Angiotensin Receptor Blocker (ARB) are most commonly drugs used specially in hypertension along associated disease. Hence, the current study was conducted with as Drug Utilization evaluation of Angiotensin Receptor Blocker (ARB) along with their adverse drug reactions ADRs in a tertiary care hospital.

MATERIALS AND METHODS

Methodology

Study design

A Prospective, observational analysis of ADRs Patterns in patients with associated with ARBs used for treatment of Hypertension. All the observed data were captured in special designed form and data were utilized in calculation of different parameters.

Study site

Study were conducted in Cardiology outpatient department (OPD) of Teerthanker Mahaveer University (TMU) Hospital, Moradabad, Uttar Pradesh, 244001, India.

Duration of study

Study were conducted for a period of six months from 1st January 2018 30th June 2018.

Material used

Naranjo's Scale, Hartwig's severity scale, WHO-UMC ADR assessments scale used for assessment of causality assessment ADRs.

Inclusion criteria

• Patients who are diagnosed with hypertension and receiving ARBs.

• Patients with co-morbid disease such as diabetes mellitus, renal disease (stage 1 and 2) and coronary artery disease associated with hypertension.

Exclusion criteria

• Pediatric patients

• Pregnant patients

• Hypertensive patients not taking ARBs.

Sources of data

All the relevant and necessary data will be collected from Treatment charts, Case sheets, Laboratory report and Patients hospital admission records.

Data collection

Prior to conduction of study and data collection, study protocol has been approved by the Institutional Ethics Committee (Ethical approval number: TMMC and IEC/18/12). Information on age, gender, drugs prescribed and ADR information were recorded on special design form in Cardiology OPD by conducting a patient interview after their informed consent was obtained. All the data were archived kept as confidential.

Data analysis

All the data were analysed in terms of frequency (n) and percentage (%). All the data were analysed by using Microsoft Excel Version 2013.

RESULTS

Demographic characteristics of study participants

Among all Hypertensive patients visited at study center in which 100 patients were included in the study during entire period of study as per inclusion and exclusion criteria of subject the study. A total 100 patients were on ARBs therapy where the maximum number of patients were 33 (33%) belongs to the age group of 41-50 y. Males 49 (49%) and Females 51 (51%). the Most patients were found in non-smokers (69%). Details are available in table 1.

Table 1: Demographic characteristics of patients using ARBs (Telmisartan, Olmesartan and Azilsartan) antihypertensive drugs

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	49	49%
Female	51	51%
Age (years)		
31-40	20	20%
41-50	33	33%
51-60	20	20%
61-70	18	18%
71-80	9	9%
Social status		
Smokers	31	31%
Non smokers	69	69%

Indication with or without co-morbidities

A total 100 patients on antihypertensive therapy (ARBs) with or without co-morbidities, indicated with HTN (18%), HTN-IHD (28%), HTN-DM (17%), HT-hypothyroidism (5%), HTN-CVA (6%), HTN-COPD (3%) and HTN-others (23%).

Details are available in fig. 1.
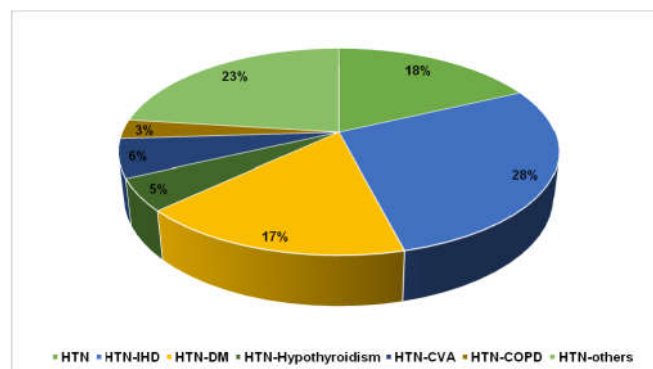
Fig. 1: Indication with or without co-morbidities

Utilization of ARBs (Telmisartan, Olmesartan and Azilsartan)

A total 100 patients were on antihypertensive therapy, ARBs were telmisartan (90%), Olmesartan (8%) and azilsartan (2%). In this study, the most common drug telmisartan drug was used. Details are available in fig. 2.

Utilization of ARBs with or without other antihypertensive drugs in patients

A total 252 prescriptions of ARBs (telmisartan, olmesartan and azilsartan) and ARBs with other class of antihypertensive drugs were used. The maximum number of 100 prescriptions (40%) in single therapy, 98 prescriptions (39%) in dual therapy, 51 prescriptions (20%) in triple therapy and 3 prescriptions (1%) in tetra therapy. A total 100 patients were on antihypertensive therapy (ARBs) where the dual therapy (41%) was the most common therapy used than the single (38%), triple (18%) and tetra (3%) therapies. Details are available in table 2.

Types of ADR produced by different ARBs among studied patients

A total 32 ADR were reported in this study where the most numbers of probable ADRs were include Headache 24 (42.8%), Nausea 8 (14.28%), Dizziness 7 (12.5%), Abdominal pain 5 (8.92%), Vomiting 4 (7.14%), Cough 4 (7.14%), Muscle pain 2 (3.57%), Fever 1 (1.78%) and Diarrhea 1 (1.78%). Details are available in table 3. A total 32 patients of ADRs of antihypertensive drugs (ARBs), the maximum numbers of ADRs were Telmisartan (88%), olmesartan (9%) and azilsartan (3%). Details are available in table 3.
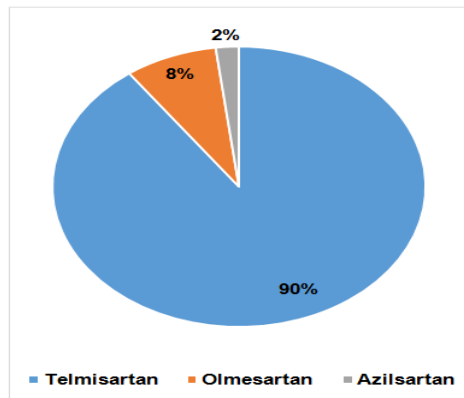

Fig. 2: Utilization of ARBs (Telmisartan, Olmesartan and Azilsartan) among studied patients

Table 2: Utilization of ARBs with or without other antihypertensive drugs in patients among studied patients

Therapy	ARBs and other antihypertensive drugs	No of prescriptions (n= %)
Single	Telmisartan	85
	Olmesartan	12
	Azilsartan	03
Dual	Telmisartan+Diuretics	42
	Telmisartan+CCBs	46
	Telmisartan+β blockers	1
	Telmisartan+αβ blockers	1
	Olmesartan+Diuretics	7
	Olmesartan+CCBs	1
Triple	Telmisartan+Diuretics+CCBs	38
	Telmisartan+Diuretics+Diuretics	3
	Telmisartan+Diuretics+β blockers	1
	Telmisartan+CCBs+β blockers	1
	Telmisartan+CCBs+α blockers	1
	Telmisartan+CCBs+α-β blockers	1
	Telmisartan+α-blockers+α-β blockers	1
	Olmesartan+Diuretics+Diuretics	2
	Azilsartan+CCBs+Diuretics	3
Tetra	Telmisartan+Diuretics+Diuretics+CCBs	2
	Telmisartan+Diuretics+CCBs+α blockers	1

Table 3: Types of ADR produced by different ARBs

ADRs experienced	Telmisartan	Interventions	Olmesartan	Interventions	Azilsartan	Interventions
Headache	22	Dechallenge	1	Symptomatic treatment	1	Symptomatic treatment
Nausea	6	Symptomatic treatment	2	Symptomatic treatment	Nil	-
Vomiting	4	Symptomatic treatment	Nil	-	Nil	-
Fever	1	Dechallenge	Nil	-	Nil	-
Diarrhea	1	Dechallenge	Nil	-	Nil	-
Dizziness	6	Symptomatic treatment	1	Symptomatic treatment	Nil	-
Cough	4	Dechallenge	Nil	-	Nil	-
Abdominal pain	5	Dechallenge	Nil	-	Nil	-
Muscle pain	2	Symptomatic treatment	Nil	-	Nil	-

Age distribution in ADRs

A total 32 patients of ADRs were on ARBs therapy where the maximum number of patients were 11 (34%) belongs to the age group of 41-50 y. A total 32 patients of ADRs of antihypertensive therapy, the maximum numbers of ADRs were found in females (56%) than males (44%). Details are available in table 4.

Severity of ADR and ADR assessment

WHO-UMC ADR assessments scale

Causality assessment was done according to WHO-UMC assessment scale in this study where the terms were Probable 23 (72%), Possible 9 (28%) and others 0 (0%). Details are available in table 5.

Naranjo's scale

The total 32 ADRs were reported in this study, causality assessment was done according to Naranjo's scale where the terms are Probable 21 (66%), Possible 11 (34%), Unlikely/Doubtful 0 (0%) and Definite 0 (0%). Details are available in table 6.

Hartwig's severity scale

To assess the severity of ADR, Hartwig's scale (level 1 to 2 = Mild, level 3 to 4 = Moderate and level 5 to 7 = Severe) was widely used for this purpose in this study. A total 32 ADRs were found and the terms (on the basis of their levels) of severity were Mild 12 (38%) and Moderate 20 (62%). Details are available in table 7.

Table 4: Age wise distribution of ADRs among studied patients

Age in years	No of patients	% of patients
31-40	4	12%
41-50	11	34%
51-60	6	19%
61-70	7	22%
71-80	4	13%
Gender		
Male	14	44%
Female	18	56%

Table 5: Naranjo's Scale WHO-UMC ADR assessments scale

Terms	No of patients	% of patients
Certain	Nil	Nil
Probable	23	72%
Possible	9	28%
Unlikely	Nil	Nil
Conditional/Unclassified	Nil	Nil
Unassessable/Unclassifiable	Nil	Nil

Table 6: ADRs description according to naranjo's scale

Terms	No of patients	% of patients
Probable	21	66
Possible	11	34
Unlikely/Doubtful	Nil	Nil
Definite	Nil	Nil

Table 7: ADRs description according to Hartwig's severity scale

Terms	No of patients	% of patients
Level 1	07	22
Level 2	05	16
Level 3	20	62
Level 4	NAD	NAD
Level 5	NAD	NAD
Level 6	NAD	NAD
Level 7	NAD	NAD

DISCUSSION

The details of our study reported that females are more dominated over males which revels previous study [20]. This might be due to sedentary types of daily life which makes them more vulnerable to the adverse effects of dosages forms and accelerate the chances of ADRs. Older patients experienced more ADR which was greater than 40 y with compare to younger ones that are fewer than 40 y which was also reported in other studies [21]. More ADRs are produced by Telmisartan 88% followed by Olmesartan and Azilsartan which also reveals to other studies conducted in Saudi Arabia [22]. Most common ADR is produced by Telmisartan i.e., Headache (22), Dizziness (6) and nausea (6), Olmesartan also shows Nausea (2) and headache (1) also but it was less in common comparison to Telmisartan. Azilsartan shows headache only in one patients however it also shows ADR in comparison to other ARBs.

ADR shows different types of causality as per causality assessment tools. According to WHO-UMC assessment scale were probable 23 (72%), Possible 9 (28%) and others 0 (0%). As per Naranjo's scale Probable 21 (66%), Possible 11 (34%), Unlikely/Doubtful 0 (0%) and Definite 0 (0%). As per Hartwig's severity scale (level 1 to 2 = Mild, level 3 to 4 = Moderate and level 5 to 7 = Severe) and severity were Mild 12 (38%) and Moderate 20 (62%).

CONCLUSION

Present study was designed and conducted in Indian hospital to monitor ADRs associated with ARBs used for treatment of Hypertension. The study finding showed that female was more prone to hypertension compared to male in the middle age group. Maximum ADRs observed with Telmisartan, followed by Olmesartan, and Azilsartan. Most of ADR were observed in this study were mild and

well tolerated by the patients. The main limitation of the mentioned study was the small sampled size and short duration study. So, I would suggest that more thorough study of special groups like paediatrics and pregnant women needs to be included in further study to identify strength of ADRs. And the outcome of therapy.

LIMITATIONS

In our study a small number of subjects were involved. Data from a larger number of subjects required to further assess the ADR appeared due to the use of ARB.

FUNDING

AUTHORS CONTRIBUTIONS

Mohammad Riyasat and Md. Shamim has proposed the idea, Dr. Mohammad Daud Ali developed the methodology and performed the analysis, interpretation of the obtained data. Mahfooz Hussain, Dr. Jigar Haria contributed the work in literature and data collection Dr. Md. Sarfaraz Alam wrote the manuscript. Dr. Md. Sarfaraz Ahmad supervised and assisted the whole study.

CONFLICT OF INTERESTS

None

REFERENCES

1. Tripathi KD. Antitubercular drugs. Essential of medical pharmacology, seventh edition. Jaypee Brothers Medical Publishers (P) Ltd, India. Essentials of Medical Pharmacology; 2013. p. 556.
2. Egan Brent M, Kjeldsen Sverre E, Grassi Guidoc, Esler Murray, Mancia Guiseppe. The global burden of hypertension exceeds 1.4 billion people. J Hypertens 2019;37:1148-53.
3. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005;365:217–23.
4. Saeed AA, Al-Hamdan NA, Bahnassy AA, Abdalla AM, Abbas MA, Abuzaid LZ. Prevalence, awareness, treatment, and control of hypertension among Saudi adult population: a national survey. Int J Hypertens 2011;2011:174135.
5. Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure related disease, 2001. Lancet 2008;37:1513–8.
6. Al-Hamdan N, Saeed A, Kutbi A, Choudhry A, Nooh R. Characteristics, risk factors, and treatment practices of known adult hypertensive patients in Saudi Arabia. Int J Hypertens 2011;168739. DOI:10.4061/2010/168739.
7. Al-Nozha MM, Abdullah M, Arafah MR, Khalil MZ, Khan NB, Al-Mazrou YY, *et al.* Hypertension in Saudi Arabia. Saudi Med J 2007;28:77-84.
8. Ahmed AM, Hersi A, Mashhoud W, Arafah MR, Abreu PC, Al Rowaily MA, *et al.* Cardiovascular risk factors burden in Saudi Arabia: the Africa Middle East cardiovascular epidemiological (ACE) study. Saudi Heart Assoc 2017;29:235–43.
9. Rimoy GH, Justin Temu M, Nilay C. Prescribing patterns and cost of antihypertensive drugs in private hospitals in dar es Salaam. East Cent Afr J Pharm Sci 2008;11:69‑73.
10. Gu Q, Paulose Ram R, Dillon C, Burt V. Antihypertensive medication use among
11. US adults with hypertension. Circulation 2006;113:213–21.
12. European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003;21:1011-53.
13. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, *et al.* Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 2003;42:1206–52.
14. Liu PH, Wang JD. Antihypertensive medication prescription patterns and time trends for newly diagnosed uncomplicated hypertension patients in Taiwan. BMC Health Serv Res 2008;8:133.
15. Guo JD, Liu GG, Christensen DB, Fu AZ. How well have practices followed guidelines in prescribing antihypertensive drugs: the role of health insurance. Value Health 2003;6:18-28.
16. Najla A Alshehri, Turky H Almigbal, Abdulaziz Alodhayani, Mohammed Ali Batais. Family and internal medicine resident's awareness of and adherence to the Joint National Committee 8 (JNC 8) hypertension guidelines: a crosssectional study. Biomed Res 2017;28:5572-9.
17. Rachana PR, Anuradha HV, Shivamurthy M. Antihypertensive prescribing patterns and cost analysis for primary hypertension: a retrospective study. J Clin Diagn Res 2014;8:19‑22.
18. Ali, Mohammad. Cost analysis and utilization of antihypertensive drug therapy in Saudi Arabia. J Pharm Health Services Res 2020. https://doi.org/10.1111/jphs.12372
19. Akhtar AK, Divya V, Pillai KK, Kiran D. Drug prescribing practices in pediatric department of a North Indian University Teaching Hospital. Asian J Pharm Clin Res 2012;5:146‑9.
20. Essential Medicines and Health Products Information Portal, World Health Organization. Available From: http://apps.who.int/medicinedocs/en/d/Js4882e/8.5.html [Last accessed on 19 Jul 2020].
21. Regitz Zagrosek V. Sex and gender differences in health-science and society series on sex and science. Eur Mol Biol Organization Repots 2012;7:596-603.
22. Ansari MS, F Al-otaibi. "Drug utilization based adrs monitoring of antihypertensive agents prescribed in al-quwayiyah general hospital, saudi arabia". Int J Pharm Pharm Sci 2018;10:22-6.
23. Amy Barreras, Cheryle Gurk Turner. Angiotensin II receptor blockers. Proc (Bayl Univ Med Cent) 2003;16:123–6.