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The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(6): 36-39

www.thepharmajournal.com
Received: 19-06-2015
Accepted: 21-07-2015

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Drug utilization study of antihypertensive drugs

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Abstract
Aim: The present drug utilization study was undertaken to study the pattern of the use of antihypertensives and appropriateness of their use in a teaching hospital.
Material and Method: Data was collected from 59 newly diagnosed hypertensive patients from the Medicine OPD. Male patients outnumbered the female patients in the study. 28 patients belonged to stage 1 hypertension and 31 patients belonged to stage 2 hypertension.
Result: When overall drug utilization was considered, irrespective of stage of hypertension/kind of therapy, it was diuretic (50.85%) which was most utilized followed by CCBs (45.76%), â-blockers (35.59%), ARBs (20.34%) and ACEIs (16.95%). This is in concordance with the JNC 7 guidelines.
Conclusion: DDD/1000/day was found to be more for amlodipine, ramipril and atenolol.

Keywords: amlodipine, antihypertensives, Ramipril

Introduction
Drug utilization study of antihypertensive Drugs Heart disease is the most common cause of death in hypertensive patients [3]. Hypertensive heart disease is the result of structural and functional adaptations leading to left ventricular hypertrophy, diastolic dysfunction, CHF, abnormalities of microvascular disease and cardiac arrhythmias. Individuals with left ventricular hypertrophy are at increased risk for CHD, stroke, CHF and sudden death. Hypertension is an important risk factor for brain The prescription order is an important therapeutic transaction between the prescriber and the patient. So it should be scientifically legible, unambiguous, adequate and complete. The prescription order is the most frequent outcome of the outpatient physician visit. Prescriptions containing errors communicate incompletely or inadequately
to the pharmacist and may have various detrimental consequences. Some errors will require the pharmacist simply to use additional professional judgment in the interpretation and execution of the prescription [1]. Bad prescribing habits lead to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient [2]. Various studies have been carried out to find out the impact of medication errors; but, the issue received maximum attention in the immediate years after the Institute of Medicine report 1999 was published [3].
Hypertension is the commonest disease posing a major public health challenge to the societies. It is one of the major risk factors for the cardiovascular mortality which accounts for 20 – 25% of all deaths. Hence there is a clear need to conduct drug utilization studies for antihypertensive drugs. Drug utilization studies of antihypertensive agents were conducted in many parts of the world [5-7]. Many guidelines for the management of hypertension are published [1]. A special consideration since long time has been given to the elderly with hypertension [4]. Even WHO has recommended such studies to be conducted in every part of the world. But in India utilization of antihypertensive agents is commonly studied as a part of utilization studies for all drugs [5]. Since the prescribing habit is likely to be influenced by several factors including the geographical ones, there is a clear need for such studies in our country. The present study was therefore undertaken to analyze the preparations given to the hypertensive patients in Krishna hospital which included only newly diagnosed patients attending the Medicine OPD. Treating hypertension has been associated with a 40% reduction in the risk of myocardia infarction [6].

Material and Method
As mentioned earlier this study was planned to identify the patterns of antihypertensive agents used in a teaching hospital. This study was done with the respect to the indications, dosage

schedules and combinations of antihypertensive agents with other drugs. This was a prospective and cross sectional study. The study was conducted in Krishna Hospital, Karad.

The proforma for collecting the data was designed for OPD patients and is shown in the annexure. The plan was to collect the newly diagnosed cases of hypertension from the medicine OPD for 1 year. Prescriptions given by the doctors belonging to the teaching staff and post graduate students were considered for the study. Prescriptions given by the internees were not included in the study. The prospective data was collected from Medicine OPD between 10.00am to 1.00pm on Wednesday and Friday in one week and Tuesday and Saturday in the next week for the given duration. This was done in order to attend the Medicine OPD of all the units without any bias and also not to hamper the teaching activities of the department. The data from these prescriptions were collected in the proforma.

The total duration of study was extended over a period of one year, starting from November 2009 to October 2010. During this period 59 prescriptions were obtained.

Data analysis

As mentioned above, data from 59 patients was obtained. A master chart was prepared. During the process, patterns of antihypertensive agents prescribed were studied. The Defined Daily Doses (DDDs) and Prescribed Daily Doses (PDDs) were calculated. DDD/1000/day was calculated according the formula given by WHO.

Results

As mentioned earlier, this study was done to analyze the prescriptions given to the hypertensive patients in the Krishna Hospital, Karad. Data from 59 prescriptions was collected from Medicine OPD. Out of the total 59 patients, 28 patients belonged to Stage 1 hypertension and the rest 31 patients belonged to stage 2 hypertension. Of the total 28 patients belonging to Stage 1 hypertension, 22 were males and 6 were females Among the 31 patients belonging to stage 2 hypertension 23 were males and 8 were females age and sex wise distribution of all the hypertensive cases belonging to the data. Overall male patients were dominating over the female patients in all the age groups.

Maximum patients were seen in the age group 61-70 years with respect to both the sexes. Totally 19 patients fall in this group out of which 15 were males and 4 were females. This was followed by the age group 31-40 years which contained 13 patients out of which 10 were males and 3 were females, followed by the age group 51-60 years

Observations and Results

which contained 11 patients out of which 10 were males and 1 was female, followed by the age group 41-50 years which contained 9 patients out of which 6 were males and 3 were females, followed by the age group 71-80 years which contained 5 patients out of which 3 were males and 2 were females and finally followed by the age group 81-90 years which contained 2 patients out of which 1 was male and 1 was female. The patients were classified into stages 1 and 2 as per the JNC 7 guidelines.

Stage 1 hypertension:

In the total 28 patients belonging to stage 1hypertension, 20 patients received monotherapy and the rest 8 patients received polytherapy. Out of the 20 patients who were receiving monotherapy, 9 (45%) patients received â-blockers, 8 (40%) patients received CCBs, 2 (10%) patients received ACE inhibitors and 1 (5%) patient received ARB. So the preferred antihypertensive agent as monotherapy in Stage 1 hypertension was â-blocker (45%) followed by CCB (40%)

Stage 2 hypertension

In Stage 2 hypertension there were totally 31 patients of whom 16 patients received monotherapy and the rest 15 patients received polytherapy. Of the16 patients who received monotherapy, 5 (31.25%) patients received â-blockers, followed by CCBs, ARBs & ACE inhibitors which were received by 3 patients each and finally 2 (12.5%) patients who received diuretics

Monotherapy vs Polytherapy

A comparison of monotherapy and polytherapy was made irrespective of the stage of hypertension and it was found that monotherapy was instituted to a total of 35(59.32%) patients and polytherapy was instituted in 24(40.68%) patients out of the total 59. Of the 24 patients who received polytherapy, 23 were receiving combination therapy while only 1 patient was receiving two drugs prescribed separately

Combination therapy

Of the 59 patients, combination therapy was given to a total of 23 patients. Out of these patients the combination of CCBs and diuretics emerged as the preferred combination accounting for 10 (43.48%) patients followed by a combination of two diuretics which accounted for 6 (26.09%) patients. This was followed by combinations of diuretics with ACE inhibitors and CCBs and ARBs which were received by 3 (13.04%) patients. 1 (4.35%) patient received diuretic and ARB combination therapy.

Hypertension with co-morbidities

The study also included the cases with the comorbidities like IHDs, type-2 DM and stroke. Out of the total 59 patients, 42 (71.19%) patients were not having any comorbidity while 9 (15.25%) patients were having hypertension with IHDs and 8 (13.56%) patients were having hypertension with type-2 DM. There was no case of hypertension with associated stroke.

1. Hypertension with type – 2 DM

As mentioned earlier there were 8 cases of hypertension who had associated type–2 DM. Of the various drugs prescribed to the patients having hypertension associated with type-2 DM, ramipril (ACEI) with hydrochlorothiazide (diuretic) was given to 3 (37.5%) patients, followed by ramipril (ACEI) which was given to 3(37.5%) patients. Amlodipine (CCB) with hydrochlorothiazide (diuretic) was given to 2 (25%) patients.

2. Hypertension with IHDs

There were totally 9 patients who had hypertension associated with IHDs. Out of these 9 patients, 7 patients received polytherapy and 2 patients received monotherapy. In the polytherapy the preferred combination was torsemide (diuretic) and spironolactone (diuretic) administered to 3 patients, this was followed by ramipril and metoprolol which were administered to 2 patients each. Both the drugs were not prescribed alone but along with other drugs. Hence they could not fall into the category of monotherapy. In monotherapy, 1 patient received felodipine and the other patient received olmesartan.

DDD VS PDD

The comparison between the Defined Daily Dose (DDD) and Prescribed Daily Dose (PDD) was done. It came to notice from the comparison that for many patients the PDD was lesser than the DDD. These drugs were atenolol, amlodipine, losartan, furosemide, torsemide, hydrochlorothiazide, spironolactone. For some drugs the PDD was equal to the DDD, these were nebivolol and felodipine. For some drugs the PDD was more than the DDD, they were telmisartan, olmesartan, ramipril. The PDD of ramipril and amlodipine was in close proximity with the DDD. For the combination drugs the information of DDD was not available. Information for metoprolol in the S-enantiomer form and extended release form was also not available through information for plain metoprolol was available. In the study metoprolol was prescribed either in the S-enantiomer form or the extended release form. Hence DDD/1000 persons/day could not be calculated for metoprolol.

Discussion

In this study, the recommendations made by JNC 7 guidelines were used for classifying patients into stages 1 and 2 [7]. The blood pressure that was recorded in the case sheets of the patients was taken into account as it was measured either by an intern or a post graduate student. The blood pressure was measured by the indirect method by using a mercury sphygmomanometer. The appearance of Korotkoff sounds was taken as systolic blood pressure and total disappearance of these sounds (Phase V) was taken as the diastolic blood pressure as the muffling of the sounds (Phase IV) will give higher blood pressure levels. The BP was recorded only on the recumbent position.

The data from the newly diagnosed patients was collected in the proforma, the sample of which is shown in the annexure. During the study period 59 newly diagnosed patients were found. As per the JNC 7 guidelines they were classified into stages 1 and 2 of hypertension. Single antihypertensive agent was used for a maximum number of patients (35 out of 59).

Selection of antihypertensive agent

As per the JNC 7 guidelines the therapy should be started with a thiazide type diuretic for most of the cases. Other drugs that may be considered are ACEI, ARBs, CCBs orâ-blockers or a combination therapy. In stage 2 hypertension a combination therapy should be preferred. Usually a combination of thiazide type diuretic with ACEI or ARB or â-blocker or CCB should be preferred. In the study â-blockers and CCBs were the frontline drugs as monotherapy in both stages of hypertension. Among the combination therapies, a combination of CCB and diuretic [8] (43.48%) and a combination of two diuretics (26.09%) were preferred combination therapies.

If the overall drug utilization frequency was considere then diuretics were the preferred drugs with 50.85% utilization followed by CCBs with 45.76%, â-blockers with 35.59%, ARBs with 20.34% and ACEI with 16.95% utilization. This is in concordance with JNC 7 guidelines. But a similar kind of study which was conducted in Punjab University by Tiwari H *et al*. showed the utilization of CCBs and beta blockers to be more than diuretics [9]. This suggests a growing interest in the use of diuretics as an antihypertensive agent. Another similar study which was conducted at St. John's Medical College by Xavier D MN *et al*. reported the wide use of CCBs in hypertension [10].

Antihypertensive drug combinations

The initiation of the therapy with more than one drug increases the likelihood of achieving BP goal in a more timely fashion. Sometimes it becomes necessary to add a second or even a third drug if proper response has not been obtained by a single drug. But the combinations should always be additive and valuable. The use of multidrug combinations often produces greater BP reduction at lower doses of the component agents, resulting in fewer side effects.

JNC 7 guidelines has recommended the use of following drug combinations

1. ACEIs and CCBs
2. ACEIs and diuretics
3. ARBs and diuretics
4. Â-blockers and diuretics
5. Centrally acting drug and diuretic
6. Diuretic and diuretic

As mentioned earlier JNC 7 guidelines clearly suggest that thiazide type diuretics should be used as the initial therapy for most patients, either alone or in combination with one of the other classes (ACEIs, ARBs, BBs, CCBs). Selection of one of these other agents as initial therapy is recommended when a diuretic cannot be used or when a compelling indication is present that requires the use of a specific drug like post myocardial infarction, chronic kidney disease [9].

Among the combination therapies recorded in the study, all the combination therapies were in synchrony with that suggested by the JNC 7 guidelines except the combination of CCB and ARB. Also the documentary evidence is lacking for0 combination therapy of CCB and diuretic. Diuretics potentiate all other antihypertensives (except dihydropyridines) and prevent development of tolerance to these drugs by not0 allowing the expansion of plasma volume [10].

Hypertension with associated co-morbidities

The co-morbidities that were included in the study were IHDs, DM and stroke. There were totally 9 patients of hypertension who were found to be having associated IHDs and there were 8 patients of hypertension who were found to be having associated DM. Not a single hypertensive case was found during the study that had previous attack of stroke.

1. Hypertension with IHDs

As mentioned there were 9 patients who had hypertension with associated IHD. Out of these 7 patients received polytherapy and 2 patients received monotherapy. Among the polytherapy the combination of torsemide (diuretic) and spironolactone (diuretic) was commonly prescribed, this was followed by ramipril and metoprolol which were administered to 2 patients each. Both the drugs were not prescribed alone but along with other drugs. Hence they could not fall into the category of monotherapy. In monotherapy, 1 patient received felodipine and the other patient received olmesartan.

2. Hypertension with type – 2 DM

As mentioned earlier there were 8 cases of hypertension who had associated type–2 DM. Of the various drugs prescribed to the patients having hypertension associated with type-2 ramipril (ACEI) with hydrochlorothiazide (diuretic) was given to 3 (37.5%) patients, followed by ramipril (ACEI) which was given to 3 (37.5%) patients. Amlodipine (CCB) with hydrochlorothiazide (diuretic) was given to 2 (25%) patients.

Overall drug utilization

When overall drug utilization was considered, irrespective of stage of hypertension/kind of therapy, it was diuretic (50.85%)

which was most utilized followed by CCBs (45.76%), â-blockers (35.59%), ARBs (20.34%) and ACEIs (16.95%).

DDDs and PDDs

In this study the concept of Defined Daily Dose (DDD) and Prescribed Daily Dose (PDD) were used. It was found that PDDs for many drugs were lesser than DDDs. These results are due to the differences in the therapeutic approaches among the clinicians even though other factors like age and sex of the patient, concurrent diseases and economical factors are contributing. No drugs were found to be prescribed by the generic name. Prescribing of drugs by the generic names would have reduced the cost of prescription. All the drugs were found to be prescribed by the brand names.

Evaluation of drug usage

On evaluating the drug prescribing trend in the study, the antihypertensives which were in synchrony with the WHO Essential drug list were amlodipine, enalapril and hydrochlorothiazide [10]. The antihypertensives which were in concordance with the National Essential drug list were amlodipine, atenolol, enalapril, losartan and hydrochlorothiazide.

Conclusion

Prescribed Daily Dose (PDD) was calculated for all the drugs except metoprolol and it was found that the Prescribed Daily Dose was lower for many drugs than the Defined Daily Dose. DDD/1000 persons/day was calculated using the WHO formula. The DDD/1000/day was also much less than the earlier studies due to the long duration of study and the lower PDDs. DDD/1000/day was found to be more for amlodipine, ramipril and atenolol.

Conflict of interest: No conflict of interest

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