Original Research Article

Prescription audit of antihypertensive drugs used in stroke patients in a tertiary care teaching hospital

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Received: 30 October 2021
Revised: 27 November 2021
Accepted: 29 November 2021

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ABSTRACT

Background: Stroke is considered as one of the important reasons of death and disability worldwide. A rational use of medications is needed to prevent the recurrence and the disease related complications.

Methods: The current study is a prospective observational study. All stroke cases, with patients above the age of 25 and treated with antihypertensive agents were included in the study. A total of 189 patients were found suitable for inclusion in the study. Using a suitably designed data collection form, all pertinent data such as patient demographics, prescribed medicines, drug interactions and adverse drug reactions were collected from the patient's case file, nurses' charts, and medication charts. Prescription pattern of antihypertensive drugs were obtained. The causality of the ADR was assessed using the Naranjo causality assessment scale and reported in the institution where the study was conducted.

Results: Majority of patients included in the study were in the age group of 61-70 years. The incidence of stroke in this study was more in males than in the females. Ischemic stroke (72%) was more prevalent when compared to Hemorrhagic stroke. Among the antihypertensive agents, calcium channel blockers (32%) were the most commonly prescribed class of drugs. In our audit, drug related problems were observed in 27% of the cases which included cases with improper dose (3 cases), contraindications (4 cases), major drug interactions (20 cases), and adverse drug reactions (17 cases). Most of the prescriptions were legible. Drug related problems had a great impact on the overall stroketherapy.

Conclusions: The drug related problems are a relevant aspect to be considered when treating patients with stroke and it can arise irrespective of adherence to guidelines.

Keywords: Stroke, Antihypertensive agents, Prescription audit, Drug interactions, Adverse drug reactions

INTRODUCTION

Stroke is a medical condition in which the blood supply to the brain is decreased leading to cell death. The different types of stroke include ischemic stroke, hemorrhagic stroke and transient ischemic attack. The main cause of hemorrhagic stroke is increased blood pressure. Transient ischemic attack is an acute loss of neurological function caused by ischemia. The etiology of stroke includes high blood pressure, smoking, heart disease, diabetes mellitus, high lipid levels and the use of some medicines.[1] Among men, the prevalence of stroke is comparatively high in early adulthood, but the prevalence increases in women in old age. There are numerous risk factors associated with stroke, it can be modifiable (diet, comorbid conditions) and non-modifiable (age, race). The risk factors for stroke are complicated and include hypertension, atherosclerotic disease, hyperlipidemia, atherosclerosis of extracranial and intracranial blood

vessels and atrial fibrillation. Preventive therapy is done on the basis of identifiable risk factors (smoking, obesity) related to thestoke.[2]

Hypertension is a modifiable risk factor associated with stroke. Hypertension management in stroke is determined by timing, the type of stroke, concurrent medical condition and pharmacologic variables. Hypertension and stroke is tightly related and several factors need to be considered prior to initiating blood pressure control among stroke patients. The commonly used antihypertensive agents in stroke include nicardipine, labetalol, sodium nitroprusside, nitroglycerine, enalapril and hydralazine. Sodium nitroprussideis not an ideal agent for blood pressure reduction due to its unpredictable dose-response relationship, risk of rebound hypertension and its potential for raising the intracranial pressure.

Drug-drug interactions are defined as when two or more drugs interacting in such a way that the effectiveness or toxicity of one or more drugs is altered on the administration of the other. In stroke patients, drug interactions are most commonly observed with corticosteroids and aspirin, antibiotics and anticoagulants, aspirin and clopidogrel, corticosteroids and amlodipine, calcium channel blockers and angiotensin converting enzyme inhibitors. The quality of prescribing and dispensing can be improved by monitoring for drug interactions.[3] Adverse drug reactions are the noxious and unintended response to a drug that occurs at doses normally used in man for prophylaxis, diagnosis, therapy or modification of a physiological function. Casualty assessment of adverse drug reactions may be undertaken in different settings including hospitals and clinics, academics, pharmaceutical industry and regulatory bodies. Different causality assessment scales have been used and the most commonly used scales are the WHO scale and the Naranjo scale. The Naranjo scale classifies the adverse drug reaction into definite, probable, possible or doubtful and is obtained upon analyzing a set of questions, which examines factors such as the temporal association of drug administration and event occurrence, an alternative cause of the events, drug levels and previous patient experience with the medication. Most of the antihypertensive drugs such as amlodipine, verapamil and metoprolol cause adverse drug reactions like pedal edema, constipation, and headache.[4] Adverse drug Reaction monitoring and reporting assist in addressing the risk associated with the uses of these drugs.[5] Prescription audit is an important tool to analyze the rationality of a prescription. Rational use of drug is important to ensure the quality of treatment and ensuring adequate outcomes to therapy.[6] An ideal prescription should include, patients' demographic details, date, clinical diagnosis, clearly specifying the name of the drug using the generic name, formulation with the dose, frequency of administration, total quantity to be supplied or duration of treatment and the prescriber's signature.[7] Prescription audit serves as a tool to monitor, evaluate

and suggest appropriate modifications in prescribing practices and to ensure rationalized therapy.[8] The parameters analyzed in prescription audit includes; patient demographic details (including the patient name, age, body weight, sex, date of prescription received); clinical diagnosis) prescribing standards (including the dose, dosage form, generic name, brand name, duration of treatment and time of administration); prescriber's name and signature.[9] The irrational prescription, improper dispensing and improper medicine use will lead to increased treatment cost and can reduce the efficacy of the treatment.[10] Proper patient counselling should be given to every patient whenever possible thereby ensuring the proper drug use and hence aid in rationalized drug therapy.

METHODS

Study design

This was a prospective observational study done at the general wards of neurology department of Father Muller Medical college and hospital, Mangalore, for a period of 6 months (October 2018 to April 2019).

Study population

The study included patients with a minimum age of 25 years who were diagnosed with stroke and hypertension with or without other co morbidities and treated with antihypertensive agents, willing to give consent were included in the study. Patients who were pregnant or with incomplete case sheets were excluded from the study. The Patients were enrolled, based on the inclusion and exclusion criteria.

Sample size calculation

The Sample size was calculated based on the evidences from literature search as well as considering prevalence of Stroke cases in the hospital. The sample size was calculated based on the formula;

$$n = Z^2 P(100-P)/e^2$$

Sample size was calculated at 95% confidence level and at 5% margin of error (e) and Z=1.96. A sample size of 189 was determined by using the formula. Hence a total of 189 patients were included in the study.

Study procedure

The objectives of the study was to audit the prescriptions containing anti-hypertensive drugs in stroke patients, monitoring of drug-drug interactions, monitoring and assessment of the adverse drug reactions among antihypertensive agents. Suitably designed data collection forms were used to collect the data. Daily visits were made to general wards and collected the data needed for the study from patient case sheets and from other relevant

sources. For the prescription audit, we analyzed the parameters like, patient demographic details, clinical diagnosis, medications, dose, dosage form, duration of treatment, time of administration, use of unauthorized abbreviations, legibility, doctors' name and signature. Drug interactions were checked using clinirex software and correlated with the available research articles. The adverse drug reactions identified were reported to the hospital immediately and analyzed using Naranjo causality assessment scale and documented. The collected data were analyzed using appropriate statistical methods.

Statistical analysis

The data was collected and documented electronically on Microsoft Excel (2013) worksheets. Descriptive statistics (frequency, percentage) was used; tables and figures were used as appropriate.

RESULTS

A total of 189 patients were included in the study based on the inclusion and exclusion criteria and after analyzing the prescriptions, the following data were obtained. The mean age of the patients diagnosed with stroke was found between±65 years (Table 1).

Table 1: Age wise distribution in the study population.

Age (years)	Number of patients	Percentage
40 and below	5	2.6
41-50	22	11.6
51-60	43	22.8
61-70	64	33.9
71-80	35	18.5
Above 80	20	10.6
Total	189	100

Table 2: Gender wise distribution of study population.

Gender	Number of patients	Percentage
Female	83	43.9
Male	106	56.1

Table 3: Prevalence of stroke.

Types of stroke	Number of patients	%
Ischemic stroke	137	72
Hemorrhagic stroke	38	21
Transient ischemic attack	14	7

The study showed the occurrence of stroke were higher in males (n=106) than females (n=83) (Table 2). The incidence of ischemic stroke (n=137) occurring to the patients was more compared to hemorrhagic stroke (n=38) and transient ischemic attack (n=14) (Table 3).

Dual antihypertensive drugs (n=61) were prescribed in most of the cases. In the dual therapy of antihypertensive drugs calcium channel blockers were commonly prescribed in the treatment (Table 4). In the study, 44 drug related problems were identified. Among these 34 obtained from antihypertensive drugs (Table 5). The total drug related problems were divided into 4 categories; those are improper dose, contraindication, major drug interactions and adverse drug reactions.

Table 4: Prescription pattern of antihypertensive drugs in stroke.

Class of antihypertensive agents	Number of patients	Percentage
Diuretics	12	6
Calcium channel blockers	59	32
Angiotensin receptor blocker	15	8
Alpha agonists	8	4
Beta blocker	21	11
Ace inhibitors	10	5
Alpha blocker	4	2
Combinational	61	32

Improper dose

Tablet clonidine was prescribed with improper dose in 3 cases. The recommended initial dose for clonidine is 50-100 mcg twice daily and the maintenance dose is 200 mcg to 600 mcg orally per day in divided doses. Monitoring is required when this drug is prescribed for patients with renal impairment. In 3 of the cases analyzed, patients with chronic kidney disease with a glomerular filtration rate of 14ml/min, 11ml/min and 6ml/min were prescribed doses of tablet clonidine 100 mcg (two tablets at a time) three times a day, tablet clonidine 100 mcg (two tablets at a time) three times a day and tablet clonidine 100 mcg (one and a half tablet at a time) three times a day respectively.

Contraindications

Tablet telmisartan should be avoided among patients with severe deterioration of the renal function. Among 4 cases, tablet telmisartan (20 mg, once daily) was prescribed for the treatment of hypertension among patients with severely deteriorating renal function.

**Table 5: Drug related problems identified.**

Type of drug related problems	Number of cases drug related problems identified among antihypertensive agents	Total number of cases drug related problems identified on overall stroke therapy
Improper dose	3	3
Contraindications	4	4
Major drug interactions	12	20
Adverse drug reactions	15	17

Major drug interactions

A total of 20 severe drug interactions were observed (12 with antihypertensive agents and 8 with other therapeutic agents used in stroke therapy). Major drug interactions observed were clonidine and labetalol (n=5), clonidine and metoprolol (n=3), potassium chloride and telmisartan (n=4), insulin and levofloxacin (n=1), warfarin and aspirin (n=1), insulin and ciprofloxacin (n=1), aspirin and enoxaparin sodium (n=5).

Adverse drug reactions

Among 189 cases, adverse drug reactions were observed in 17 cases (15 adverse drug reactions with antihypertensive agents and 2 with the other therapeutic agents used in stroke therapy). The causality of the adverse drug reactions observed was assessed using the Naranjo causality assessment scale. All the adverse drug reactions were belongs to "possible" category (score: 1-4) includes, ramipril-dizziness (n=1), enalapril- hypotension (n=1), furosemide-hyponatremia (n=1), amlodipine-hyponatremia (n=5), telmisartan-dizziness (n=1), losartan-hyponatremia (n=1), mannitol-hyponatremia (n=2), cilinidipine-hypotension (n=3), ceftriaxone-diarrhoea (n=1), enoxaparin sodium hematuria (n=1).
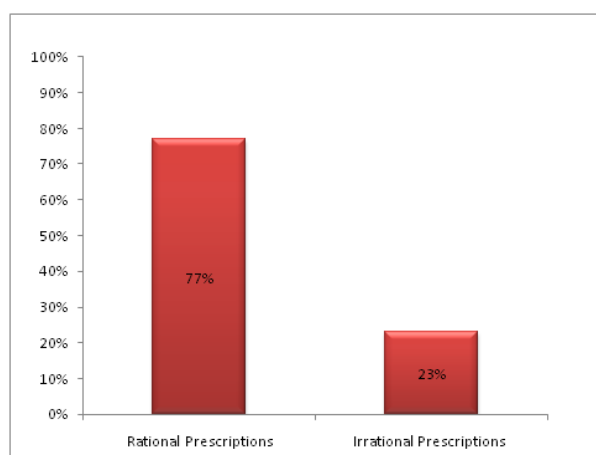
Figure 1: Rationality of prescriptions.

Legibility of prescriptions

The subjective observation of the prescriptions found that a total of 147 prescriptions (78%) were legible with ease and 42 prescriptions (22%) were legible but difficult to read.

Rationality of prescriptions

77% (145 prescriptions) of the prescriptions were rational and 23% (44 prescriptions) of the prescriptions were irrational. The irrational prescriptions had a great impact on overall stroke therapy (Figure 1).

DISCUSSION

Prescription audit plays an important role in identifying the drug related problems and ensuring the rationalized therapy in stroke patients. The present study revealed that stroke was more prevalent in the age group of 61 to 70 years (33.9%), which is in concordance with the study conducted by Margaret et al which reported that over 70% of the stroke cases occur at the average age of 65. Also, age is an important risk factor for stroke.[11] The number of male patients (56.1%) in our study was slightly higher than the female patients (43.9%), similar to the results obtained in the epidemiological study conducted by Peter et al where the male stroke incidence rate was 33% higher than the females. Stroke tends to be more severe in women, with a 1 month case fatality of 24%.[12]

In this study, we found that the prevalence of ischemic stroke (72%) was more compared to hemorrhagic stroke (21%). With higher mortality rates, the hemorrhagic stroke also has lesser incidence of recurrent stroke. This data is in agreement to the results obtained by Marc et al where the percentage of ischemic stroke in the study population was approximately 87% compared to the hemorrhagic stroke with 13%.[13] High blood pressure in stroke can be treated medically by the use of antihypertensive and modification of the lifestyle. Our study revealed that calcium channel blockers (32%) and combination therapy (32%) are the commonly prescribed antihypertensive agents. These observations were in agreement with the study conducted by Gupta et al which concluded that calcium channel blockers (39%) were the most prescribed monotherapy agent and the dual therapy included a combination of diuretics, ACE Inhibitors, adrenergic receptor blockers, calcium channel blockers, and beta blockers.[14]

The practice of assessing for drug-related problems represent the categorization and identification clinical problems related to the use of medications in the clinical practice and is essential to enhance the safety and efficacy of the medication. Our study population, the drug-related problems associated with stroke therapy was found among 23% of the patients (18% of drug related problems were associated with antihypertensive agents and 5% with other therapeutic agents used in stroke treatment). The drug related problems included cases with improper dose, contraindications, major drug interactions, adverse drug reactions. This can be correlated with the study conducted in 108 patients by Celin et al in which the drug-related problems were identified to occur at a frequency of 1.54 per patient.[15]

Drug interaction is one of the major factors to be considered before initiating a therapeutic regimen. There are various potential mechanisms through which a drug interaction might occur. These may lead to an increase or decrease in the beneficial or adverse effects of the prescribed drug/s. In our study, we identified a total of 20 cases (10.5%) with major drug interactions. These observations can be correlated with the study conducted by Venkateswaramurthy et al and an audit conducted by Megha et al in which it was found that among the 200 prescriptions for stroke patients, 20% of drug interactions were major, 60% were moderate and 20% of the drug interactions were minor.[16,17]

In our study, we identified 17 cases (15 cases with antihypertensive agents and 2 cases with other therapeutic agents used in stroke therapy) with probable adverse drug reactions among which 8% (15 cases) of adverse drug reactions were associated with antihypertensive agents used in stroke therapy. Calcium channel blockers were the highest class of drugs associated with adverse drug reactions, followed by diuretics, ARBs, ACE Inhibitors, and beta blockers. A study conducted by Pandel et al showed that calcium channel blockers were the most frequent drug class associated with ADRs among the antihypertensive drugs.[18]

The present study identified 77% (145 prescriptions) of the prescriptions were rational indicating proper adherence to the guidelines while prescribing. Also, proper monitoring of the drugs was also done in order to minimize the drug related problems and adverse reactions. Our results were similar to the ones concluded by Bashir et al about rational and irrational prescribing in different government and private health care centres of Punjab and they suggested that almost 45% of the prescriptions were rational. The study also highlighted the importance of a mutual relationship among the medical healthcare professionals like doctors, pharmacist, nurses, physiotherapist, nutritionist and other technicians to provide optimal rational and drug therapy to patients. In this study we identified that irrational prescriptions had a significant impact in the healthcare outcomes which can be concorded the study conducted by Basher et al which suggested that irrational use of drugs leads to adverse drug reactions and other complications.[19]

CONCLUSION

Prescription audit has its importance in clinical practice in identifying the drug related problems and enhancing the quality of treatment. Drug related problems are common in hospitalized settings and can arise due to improper drug prescription. The major identified drug related problems included improper dose, contraindications, major drug interactions and adverse drug reactions. Prescription audit enables the proper review of prescription which is useful in identifying many serious prescription related problems like usage of unauthorized abbreviations, improper refilling of prescription and other improper practices. Rational use of medication is important in providing a better quality of treatment. Pharmacist's intervention plays a major role in identifying the drug related problems and avoiding the complications associated with drugs in the overall therapy. About 77% of prescriptions were identified as rational through our prescription audit. Rationalized therapy can be achieved only when physician, pharmacist, nurses and all other health care professionals coordinate with each other in every aspects of the drug therapy.

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