A PROSPECTIVE STUDY TO EVALUATE THE PRESCRIBING PATTERN OF DRUGS IN PATIENTS WITH ISCHEMIC STROKE AND ROLE OF MEMANTINE IN POST- STROKE APHASIC

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ABSTRACT
Stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and / or signs of focal, and at times global (applied to patients in deep coma and those with subarachnoid hemorrhage), loss of cerebral function with symptoms lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin. This was a prospective observational study, which included 63 patients who were admitted in Pushpagiri Medical College Hospital. Patients prescribing pattern were evaluated from the case files and the clinical outcome were evaluated by using National Institute of Heart Stroke Scale (NIHSS) and Modified Rankin Scale (MRS). The language function of the aphasic patients were assessed by using Benson’s classification and their quality of life were evaluated by using Stroke Specific- Quality of Life (SS-QOL). Majority of the stroke patients was prescribed with Antiplatelet, Neuroprotective, Antihypertensive and Dyslipidemics. The clinical outcome, language function and quality of life of the patients were improved, indicating the effectiveness of Memantine on the language of post- stroke aphasic patients. The study confirm that post- stroke aphasia treatment with memantine 5mg and 10mg could have significant valuable effects on the neurological consequences of stroke and language function improvement of the study population.
**KEYWORDS:** Stroke, Prescribing pattern, Incidence, Clinical outcome, Post-stroke aphasia, Memantime.

**INTRODUCTION**

Stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and those with subarachnoid hemorrhage), loss of cerebral function with symptoms lasting for more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.\(^1\) Stroke can either be ischemic (88% of all strokes) or hemorrhagic (12% of all strokes).\(^2\)

Stroke are common in India. It is the leading cause of long term disability in adults, with 90% of survivors having residual deficits. Moderate to severe disability is seen in 70% of survivors. The American Heart Association estimates that there are 4.7 million survivors of strokes in the United States. Stroke incidence increases with age, especially after age 55, resulting in an increased stroke incidence due to aging of the population.\(^3\)

The physicians are often typically creating the choice on which drug to decide on during a patient-by-patient basis. In the present study, we have assessed the prescribing patterns of Neuro-physicians to identify the selection of a drug over another and what changes are made once a stroke happens in these patients. The rationality is of utmost importance because the irrational use will cause misuse, underuse or overuse of medications. The drug treatment strategy involved with choosing medication like thrombolytics, anticoagulants, antihypertensive (angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, and diuretics), blood lipid lowering agents (statins), antiplatelet medication (aspirin and clopidogrel), and cerebral activators. It is also suggested to select a route and dosage form of medication to own the best therapeutic effects to manage stroke.\(^4\)

The AHICPR Post- Stroke Rehabilitation Clinical Practice Guidelines defines aphasia as “the loss of ability to communicate orally, through signs, or in writing, or the inability to understand such communications (Klein, 1995). Darley (1982) noted that aphasia is generally described as impairment of language as a result of focal brain damage to the language dominant cerebral hemisphere. The incidence of post- stroke aphasia ranges from 40 to 60 per 100,000 per annum. Roughly 250,000 persons live with aphasia in the UK. Post- stroke aphasia is associated with more severe strokes, higher mortality, decreased rate of functional
recovery, and health-care cost. Patients are more likely to seek medical help earlier, and to receive thrombolysis compared to patients with no aphasia.\cite{5}

Memantine is a non-competitive antagonist of the N-methyl D-aspartate (NMDA) type of glutamate receptor, which are located ubiquitously throughout the brain. It regulates activity throughout the brain by controlling the amount of calcium that enters the nerve cell, a process essential for establishing an environment required for information storage. Over stimulation of the NMDA receptor by excessive glutamate allows too much calcium into the cell, disrupting information process. Blocking NMDA receptor with memantine may protect the neurons from the effect of excessive glutamate without disrupting normal neurotransmission.\cite{6}

The present study was performed to assess the usefulness of memantine in post-stroke aphasia and to assess the quality of life and also the clinical outcome of acute ischemic stroke patients. Neurological function was assessed by the NIHSS (National Institute of Heart Stroke Scale) and MRS (Modified Rankin Scale) score. This scale could be used as a clinical stroke assessment tool to evaluate and document neurological status in acute stroke patients. The NIHSS and MRS is valid for predicting patient’s outcome and can serve as a measure of stroke severity. Additionally, this stroke scales may serve as a data collection tool for planning patient care and could provide a common language for information exchanges among healthcare providers.\cite{7}

The aim of the study is to evaluate the trends in prescribing pattern of drugs in patients with acute ischemic role and to assess the role of memantine in post-stroke aphasia.

**Objectives include**

- To assess the prescribing pattern of acute ischemic stroke
- To assess the clinical outcome of stroke
- To assess the usefulness of memantine in post-stroke aphasia and to assess the quality of life.
- To estimate the incidence of stroke.

**MATERIALS AND METHODS**

**Study design**

Prospective observational study.
Study site: Study was conducted in the Neuro-medicine department of Pushpagiri Medical College Hospital, Thiruvalla.

Study period: This study was conducted for a period of 6 months (January 2018 to June 2018).

Study sample: 63 patients diagnosed with acute ischemic stroke with aphasia.

Source of data and materials: Patients prescriptions, patient case sheets, data collection form, NIHSS Score, MRS Score, Stroke Specific Quality of Life (SS-QOL), Benson’s classification.

Inclusion criteria: Patients diagnosed with acute ischemic stroke with aphasia, male and female patient of age 18 yrs. and above, those who give consent voluntarily to participate in the study.

Exclusion criteria: Patients who are not willing to give consent, hyper reactivity to memantine or any ingredients in the tablet formulation, hemorrhagic stroke patients.

Method of data collection: The study was carried out after taking approval from institutional ethics committee. The informed consent of patients was taken prior to the study. A standardized data collection form was prepared and necessary data were collected which includes the demographic details, socio- economic status, past medical history, past medication history, current medication. The clinical outcome were evaluated by using NIHSS & MRS scores. The usefulness of memantine in post- stroke aphasia is evaluated by using Benson’s classification and NIHSS. The quality of life of aphasic patients were evaluated by using SS-QOL. The patient’s score were monitored at the first visit. During the second visit, scores were checked again and assessed the outcome. Prescribing pattern of drugs was collected from their medical records and evaluated the rationality of the prescribing practices using WHO prescribing indicators. All the information regarding to the study were collected from the case records and discussions conducted with the inpatients and bystanders during the ward rounds, with the support of the physician.

Ethical consideration: The institutional ethics committee clearance was obtained (IEC No is PCP/E1/01A/03/ 2018), after that started the study. Informed consent was obtained from all patients who met the inclusion criteria were enrolled for the study.
RESULTS AND DISCUSSION

**Figure 1:** Distribution of Patients Based on Age.

Fig. 1: It was clear that majority of the patients were in the 60-70 year age group.

**Figure 2:** Distribution of Patients Based on Gender.

Fig. 2: shows that, greater proportion (70%) of the study population belonged to the male sex.

**Figure 3:** Distribution of Patients Based on Social History.

Fig. 3: indicate that majority of the study population were smokers.
In this study, total number of prescription was 451; average number of drugs per prescription was 7.15 and the percentage of drugs prescribed by generic name was 30% (table 1). M.B.C. Ferreira et al[8] revealed that average number of drugs per prescription varies from 10 – 13 and polypharmacy is common in stroke patients and less percentage of drugs were prescribed in generic name.

Table. 1: Analysis of prescription in acute ischemic stroke.

<table>
<thead>
<tr>
<th>Prescribing indicators</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription analyzed</td>
<td>63</td>
</tr>
<tr>
<td>Total number of drugs per encounter</td>
<td>451</td>
</tr>
<tr>
<td>Average number of drugs per encounter</td>
<td>7.15</td>
</tr>
<tr>
<td>Percentage of drugs prescribed by generic name</td>
<td>30%</td>
</tr>
<tr>
<td>Percentage of encounters with an antibiotic prescribed</td>
<td>17.46%</td>
</tr>
<tr>
<td>Percentage of encounters with an injection prescribed</td>
<td>36.50%</td>
</tr>
<tr>
<td>Percentage of drugs prescribed from formulary</td>
<td>29.49%</td>
</tr>
</tbody>
</table>

In the present study, most of the patients were prescribed with antiplatelet drugs like clopidogrel (46.83%) and aspirin (36.70%) followed by neuroprotective like memantine (91.30%) and donepezil (8.69%), antihypertensive like clinidipine (21.66%), losartan (15%) and amlodipine (10%). The most commonly prescribed dyslipidemics were atorvastatin (72.72%), gastro intestinal drugs were pantoprazole (73.91%), antiepileptic were levetiracetam (37.5%), anti-psychotropic were fluoxetine (40%) were also prescribed in recruited patients (Fig. 4).

![Figure 4: Prescription pattern of drugs used in stroke patients.](image-url)

The present study showed that, among the 63 patients there was a significant improvement on the basis of the measuring scales i.e, by means of the NIHSS Score (more moderate
neurological impairment (54%) to mild neurological impairment (28.5%), P value <0.0001) (Fig.5) and MRS Score (severe disability (19%) to no significant disability (15.8%), P value <0.0001) (Fig. 6).

![Graph showing clinical outcome on the basis of NIHSS score.](image)

**Figure 5: Clinical outcome on the basis of NIHSS score.**

![Graph showing clinical outcome on the basis of MRS score.](image)

**Figure 6: Clinical outcome on the basis of MRS score.**

Memantine is a NMDA receptor antagonist which is used in post-stroke aphasia. The language problems such as impairment in fluency (63.5%), comprehension (46%), naming (82%), reading (76.2%), writing (46%) and repetition (82.6%) (Fig.7). Hence, the study showed that neuroprotective effects of memantine improved aphasia severity and also their quality of life increased from 14.14% to 18.18% ( P value <0.0001) (Fig.8). In the study by Berthier et al also studied memantine in post- stroke aphasia and reported its effectiveness.
Figure 7: Language assessed on the basis of Benson’s classification.

Figure 8: Assessment of quality of life in post-stroke aphasia.

Table 2: Incidence of acute ischemic stroke.

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of new cases of stroke (6 months)</td>
<td>90</td>
</tr>
<tr>
<td>Number of people in that population (6 months)</td>
<td>979</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Table 2 shows that incidence was found to be 0.091. Most common age group individuals experiencing stroke were between 40-60 yrs. (63.33%) followed by people whose age range between 60-80 yrs. (37%). These findings were in concordance with the study of Wadhwani j et al[9] and Celin A et al[10] where stroke incidence was higher in age group 41-60 yrs and 51-60 yrs. whose age range between 60-80 yrs (37%).

CONCLUSION

Stroke is a neurologic deficit and it occupies the top most burdens. The incidence rate of stroke was found to be 0.091. The use of medications differs with hospitals and physicians.
Various types of drugs were used depending upon the illness. The study reported various medicines prescribed in acute ischemic stroke patients like antiplatelet, neuroprotective, antihypertensive, dyslipidemics, neurotonic and anticoagulants. The study showed that the cognitive functions and outcome of the acute ischemic stroke patients were improved. The study confirm that post-stroke treatment with memantine 5mg and 10mg could have significant valuable effects on the neurological consequences of stroke and language function improvement of the study population, hence their quality of life also were improved.

ACKNOWLEDGEMENTS
I would like to thank Dr Sheetal S, neurologist, Pushpagiri Medical College Hospital, Thiruvalla for his immense support and guidance for the success of the thesis work and also all the members of Pushpagiri College of Pharmacy.

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