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Research article

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Drug utilization 90% in patients with acute hemorrhagic stroke to assess adherence to standard anti-hypertensive treatment

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ABSTRACT

The early management of hypertension in hemorrhagic stroke affects the extent of brain injury and patient suffering's. This study conducted at civil hospital Nashik, describes antihypertensive treatment in acute hemorrhagic stroke do not adhere to standard treatment, DU 90% not achieved. As in first 30 patients no patients were prescribed with recommended drugs, interim analysis was performed on 16% of sample size. Antihypertensive drugs were prescribed as single drug or in combination, Cap Nifedepin (40%) was most frequently prescribed single drug.. Calcium Channel Blockers were preferred with or without combination with beta-blocker agent; Mean cost per patient treated was 2280₹.

Keywords: Hemorrhagic Stroke, Emergency Hypertension, Drug Utilization 90%

INTRODUCTION

In 2001 out of all deaths CVA accounted for 5.5 million i.e. 9.6% deaths worldwide. Whereas in year 2005, 5.7 million deaths recorded, 87% of these deaths were in low income countries¹. Stroke was second leading cause of death and fourth leading cause of disability worldwide in 2007. It was estimated that two third of deaths occurred in developing country, 40% of patients were less than 70 years of age. In developed countries approach to the patient with acute stroke is changing as a stroke survivor develops prolonged disability and restriction in activity which needs support of other person to survive [2, 3]. Potential therapeutic benefits can be achieved by managing emergency hypertension in hemorrhagic CVA, within 48 hours with easily titratable agents to avoid further complications [4, 5].

Intravenous preparations require continuous blood pressure monitoring unless leads to persistent lowering in BP. oral formulation have limitation as difficult to administer in acute phase of stroke, act irreversibly. Slow release preparation need to be administered by crushing for nasogastric administration destroys its delayed action. Sublingual nifedepin is frequently used in management of hypertension; which is neither safe nor efficacious should always be avoided in this condition; it may result in rapid fall in blood pressure.

There are four agent that reduce blood pressure in a easily titratable fashion and do not lead to increase in intracranial pressure, these are Labetalol, Esmalolol, Enalaprilat and Nicardipine [6, 7]; There is recent evidence that the transdermal administration of nitrates is convenient

alternative that does not reduce cerebral blood flow in acute stroke [8]. Out of all four antihypertensive agents Esmalolol is in India's essential drug list, Nicardipine is not available in India. Labetalol and Enalaprilat are available but in high cost.

Subject Selection

Subject Inclusion Criteria

- Confirmed clinical diagnosis of stroke and confirmed by CT scan or MRI Findings.
- Patient had blood pressure ≥ 190 mmHg at the time of admission.
- Male or female above 18 years age.

Exclusion Criteria

- Previous cranial neurosurgical interventions.
- H/O Immune deficiency or any psychotic Disorder any end stage of sickness as HIV/Diabetic renal or metabolic failure / Cirrhotic Liver Disease.
- Patient transferred from other institute after 48 hours of stroke management.

METHODOLOGY

A Prospective study was conducted to assess prescribed antihypertensive in hypertensive emergencies in hemorrhagic stroke patients admitted to Intensive care unit of Civil Hospital, Nashik. Patient was screened from IPD records

fulfilling Inclusion and Exclusion criteria. Participants were included in the study if they fulfill inclusion exclusion criteria. Subjects were excluded if they had end stage of sickness. Patient's basic demographic and other information was collected from the IPD record and was recorded in case record form.

1. Does patient had history of hypertension; on which anti-hypertensive medication?
2. Does patient had discontinued treatment in past?

Confidentiality statement

Information about study patients was kept confidential and managed according to the regulatory requirements.

RESULT

This interim analysis report is prepared on the basis of 16% of sample; Total 72 patients were screened out of 72; 30 patients fulfilled inclusion exclusion criteria. Interim Analysis was performed at enrolment of 16% of sample size; in all 30 patients Enrolled recommended drugs were not used.

Demographic Distribution

Out of 30 enrolled patients 11 were female. Mean Age of study participants is 59 years,

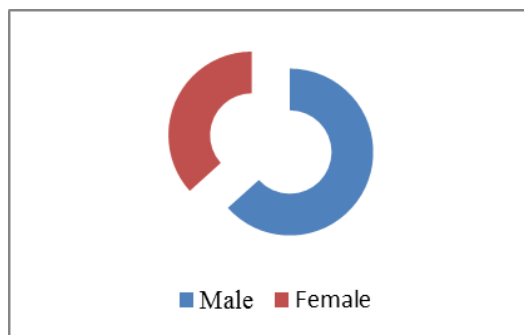


Fig. A

Number of Days Patient Hospitalized

Mean number of Civil Hospital stay was 8.5 days; two patients were transferred to Private

hospital. 21 patients had history of hypertension, Red Color represents death occurred. Four death were recorded represented in dark color (fig. b)

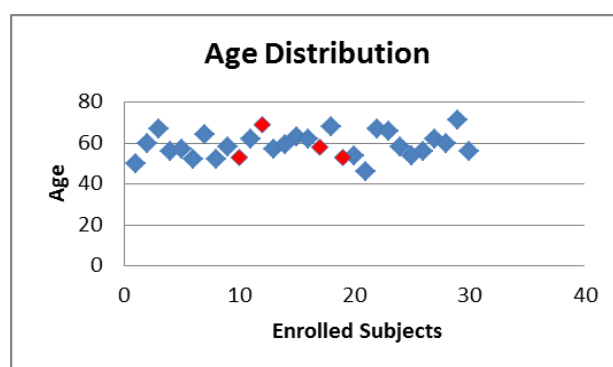


Fig B

Prescribing Indicator

The average number of Drugs per prescription was 5.3. Percentage of Drugs prescribed by Generic name was 79% (fig. c). Generic Drugs are preferred not only antihypertensive but also other drugs e.g. Antibiotics, Antacids etc., In cost assessment we have found that most of Prescribed branded drugs

were available in Civil hospital . Antihypertensive drugs were prescribed as single drug or in combination, Cap nifedepin (40%) was most frequently prescribed drug second most frequently prescribed drug was NTG Infusion (20%). Calcium Channel Blockers were preferred with or without combination with Beta-Blocker Agent (Fig. d).

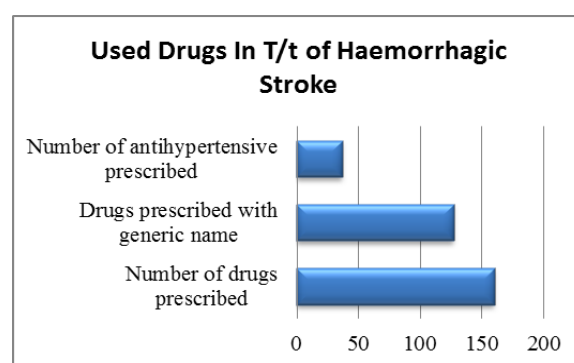


Fig C

Core Indicator

Table 1.1 shows DDD of used drugs and corresponding Utilization in this study. The DDD is

the assumed average maintenance dose per day for a drug used for its main indication in adults.

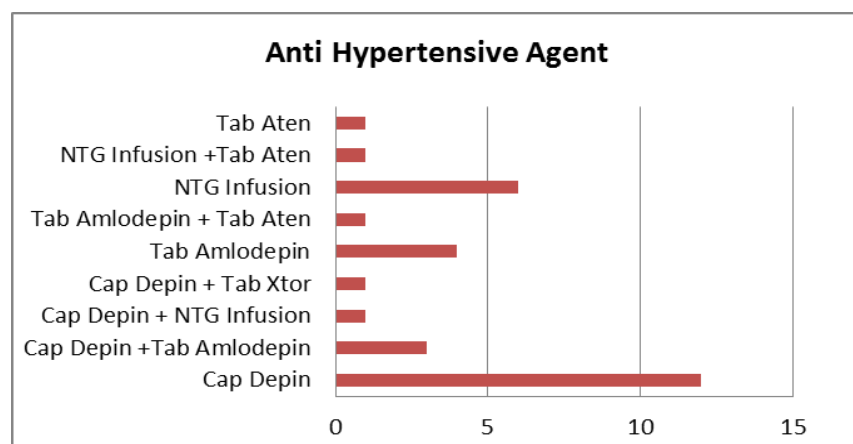
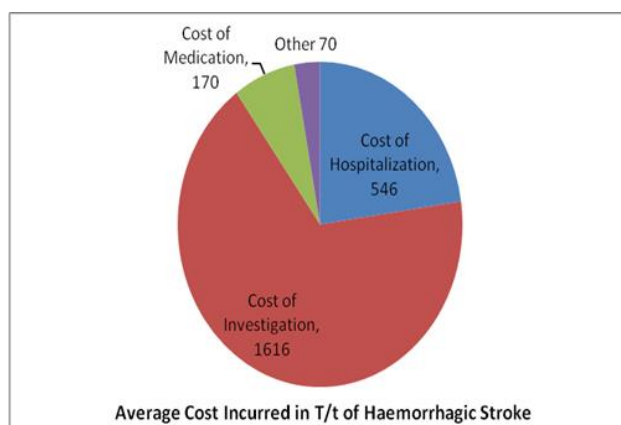


Fig D

Cost Assessment

Cost Assessment was done on interviewing patient relatives and with available bills. Hospital Stay, Investigation charges, Other (Ambulance charge) was evaluated from civil hospital charge list. Mean Cost per patient was 2280 ₹. Cost was subsidized for below poverty line patients. Cost of

Investigation was relatively high due to CT scan/ MRI Scan (Fig. e). Highest cost incurred was 4200₹ and lowest cost incurred was 0 ₹. ICU Stay per day was 200 ₹, Cost of CT Scan was (1200 ₹) and MRI Scan (2500 ₹). For subsidized subjects cost of CT scan and MRI Scan was reduced to half. Average Cost per patient was 2230 ₹.



DISCUSSION

We have found that prescribed drug for management of hypertensive emergencies in hemorrhagic stroke do not contain recommended drugs. As calculated sample size was 220, recommended drugs were not prescribed in first 30 enrolled patients; hence interim analysis was performed on 16% of sample size.

Mean age of study participants was 59 years; Out of 30 enrolled patients 11 were female. Average number of hospital stay was 8.5 days. 21 patients had history of hypertension. Antihypertensive drugs were prescribed as a single drug or in combination; CCB's were preferred with or without combination of beta-blocker. Sublingual nifedepin (40%) was most frequently prescribed single drug. 79% of drugs were prescribed with generic name. Mean cost per patient was 2280; Cost of investigation was relatively high (1616) because of CT scan and MRI scan. We were not

able to assess efficacy and safety of sublingual nifedepin due to early termination of study.

In case of severely elevated blood pressure rapid reduction may cause shift in Auto-regulatory system in cerebral vessel which is likely to be associated with morbidity therefore Blood pressure must be reduced in controlled manner [9, 11]. In patients of stroke gradual lowering in BP leads to frequent improvement of neurological symptoms [7]. Increased BP is associated with worst outcome as it may cause hematoma expansion in first 78 hours (Erin M et.al.). As blood pressure management should be more aggressive in Hemorrhagic stroke than Ischemic stroke. Sublingual route should be avoided with unpredictable pharmacodynamic effect in Hemorrhagic stroke [9]. In Australia Australian Drug Evaluation Committee (ADEC) have strongly recommends withdrawing Sublingual nifedepine capsule after receiving reports of hypotension on inadvertently receiving Capsule instead of tablets [10].

Table 1.1

S.No.	Drugs Used	ATC Code	DDD	Drug Used (%)
1	Labetalol	C07AG01	0.6 gm	0 %
2	Esmolol	C07AB09	2.5 gm	0%
3	Nifedepin	C08CA05	30 mg	40%
4	Amlodepin	C08CA01	5 mg	27%

5	Nitroglycerine	CO1DA02	50 mg	26%
6	Atenalol	C07	75 mg	7%

There are multicentre studies in haemorrhagic stroke patients with use of antihypertensive drug.

- In BEST trial they used Atenolol, Propranolol and placebo in 302 patients. Deaths were common in Beta-blocker group, Neurological Improvement was seen in placebo group; there was no difference in length of hospital stay in all three groups.
- INTERACT Prospective randomized trial patients were enrolled with Intra Cranial hemorrhage, Hematoma growth is attenuated with rapid intensive BP reduction after ICH. Patients were divided in standard care (BP Lowering Strategy) and treatment group (Intensive care) standard care group have shown accentuation of hematoma growth but no significant difference in death in both group [12].
- A Prospective dose-escalation study was performed in 60 patients of ICH Rapid, intensive BP reduction after ICH was feasible and safe¹³.
- A Prospective observational study in 432 patient of sub-archenoid hemorrhage, intracranial hemorrhage, ischemic stroke were enrolled; this study found that minimum recorded blood pressure and excessive blood pressure reduction may contribute to mortality after stroke [14].
- A Retrospective study in 100 patients of Intra cranial hemorrhage the risk of early neurologic deterioration in ICH begins to increase as SBP falls below 123mmHg [15].
- COSSACS Prospective randomized trial 763 patients were enrolled of Ischemic Stroke and Intracranial hemorrhage continuing antihypertensive treatment after acute stroke reduced BP; there was no significant difference in 2-week death or dependency.

- SCAST Prospective randomized trial in 2004 patients of Ischemic stroke, intracranial hemorrhage; there was a trend toward increased vascular events and worsening functional outcome in patients started on candesartan after acute stroke.

Hypertensive emergency in Acute hemorrhagic stroke is considered to be life threatening; therefore choice of antihypertensive should be of proven safety and efficacy. In our study we have found that prescribed antihypertensive do not contain recommended drugs.

Drugs play an important role in improving human health and in promoting wellbeing .To produce the desired effect, they have to be used rationally. The irrational use of drugs is a common occurrence throughout the world. Drug prescriptions form a very important point of contact between the doctors and the patients.

Despite fact, our study showed that irrationality in drug use, larger studies need to be planned to explore efficacy and safety with CCB's and Beta blockers. Even though the use of sublingual depine is controversial; this study fail to evaluate the outcome in relation to drug prescribed.

CONCLUSION

There is need to develop guideline for use of drugs in emergency management of HTN in hemorrhagic stroke. Mean cost per patient treated was 2280₹. Physician should choose recommended drugs; with due respect to outcome while treating narrow therapeutic conditions.

Further studies need to be planned with larger sample size, considering in-depth analysis of Outcome & Cost influenced due to use of recommended drugs.

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