

RESEARCH ARTICLE

Study of drugs used in cerebral edema in patients with stroke at a tertiary care center

Praveen Kumar B¹, Scandashree K², Padmaja Udaykumar¹

¹Department of Pharmacology, Father Muller Medical College, Mangalore, Karnataka, India, ²Department of Pharmacology, Mysore Medical College & Research Institute, Mysore, Karnataka, India.

Correspondence to: Padmaja Udaykumar, E-mail: padmajaundaykumar@gmail.com

Received: August 07, 2016; **Accepted:** August 07, 2016

ABSTRACT

Background: Various medical and surgical measures have been evolved to treat the raised intracranial pressure (ICP). Medical management mainly involves osmotic agents (glycerol and mannitol), diuretics, and corticosteroids to reduce raised ICP. It is not presently clear whether the routine use of mannitol, glycerol, and corticosteroids results in increased survival and decreased dependency in stroke patients. **Aims and Objectives:** To study the practice pattern of drugs used in the management of cerebral edema in stroke. **Materials and Methods:** The retrospective medical records of stroke patients receiving treatment from July 2013 to February 2013 at Fr. Muller Medical College Hospital were reviewed. Data regarding anti-cerebral edema drugs prescribed, co-prescribed drugs was collected from the records. Demographic data, age, gender, hospital medical records number, data regarding anti cerebral edema drugs, co prescribed medicines, clinical outcome in terms of improved/dead/discharged against medical advice, etc., were recorded. Patients above 18 years of age of either sex diagnosed with CVA and on treatment were included in the study. Data were analyzed using suitable statistical methods. **Results:** According to our study results, drugs were generally not used for the management of cerebral edema. Mannitol was the most common drug used in the management of cerebral edema in stroke (34.93%), followed by furosemide (26.5%), corticosteroids (8.46%), glycerol in 7.23%, and others including torsemide or aldactone (10.84%). Various combinations of these drugs were used. **Conclusion:** Various combinations of anti-edema drugs were used, no standard protocol was followed, and treatment was highly individualized. Predicting clinical outcome needs development of uniform protocols and further studies to standardize the practice of using drugs to manage cerebral edema routinely in stroke.

KEY WORDS: Stroke; Cerebro Vascular Accident; Cerebral Edema

INTRODUCTION

Stroke is the second leading cause of death and mortality worldwide next to the heart diseases, which is mainly due to raised intracranial pressure (ICP) and its consequences.

There are two main types of stroke, viz., (a) Ischemic, and (b) Hemorrhagic. Hemorrhagic stroke involves bleeding within the brain due to various causes like uncontrolled hypertension and aneurysms. Two types of hemorrhagic stroke exist viz., (a) Intracerebral and (b) Subarachnoid. Both are associated with brain tissue damage due to rupture of cerebral artery within or on the surface of the brain respectively. Ischemic stroke - two types: (a) Thrombotic and (b) embolic. Together accounting for 85% of stroke.^[1]

The raised ICP in ischemic stroke is due to vasogenic edema. And in hemorrhagic stroke, it is due to a mass effect and surrounding vasogenic edema. Various medical and surgical

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.0824619082016	

National Journal of Physiology, Pharmacy and Pharmacology Online 2016. © 2016 Padmaja Udaykumar et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or for any purpose, provided the original work is properly cited and states its license.

measures have been evolved to treat the raised ICP. Medical management mainly involves osmotic agents (glycerol, mannitol), diuretics, and corticosteroids to reduce raised ICP.

The majority of these agents are found to be ineffective in reducing brain edema, and their efficacy has not been proved by a randomized controlled trial.^[2] Many studies were conducted to assess the effect of corticosteroids, mannitol, and glycerol but they failed to give good results in reducing ICP.^[3-5]

Despite this, the American Heart Association recommended mannitol in its guidelines for the management of spontaneous intracerebral hemorrhage with progressively increasing ICP and clinical deterioration due to the mass effect.^[6]

In practice, mannitol, glycerol, and steroids are widely used in acute stroke worldwide.^[2]

It is not clear whether the routine use of mannitol, glycerol, steroids results in increased survival and decreased dependency in stroke patients.^[7]

In India, there is no consensus or guidelines about the anti-edema therapy in acute stroke.

Recently a study showed high diversity and uncertainty in using anti-cerebral edema drugs among general physicians and neurophysicians.^[2]

Hence, we studied the practice pattern of drugs used in cerebral edema therapy in our hospital for the management of stroke.

Objectives

- To study the pattern of use of drugs in cerebral edema drugs at a tertiary care center.
- To find the clinical outcome of the anti-edema drugs therapy in current use for stroke.

MATERIALS AND METHODS

Retrospective hospital records based study was conducted at Fr. Muller Medical College Hospital, Mangalore. Information of patients admitted to the hospital from July 2013 to February 2013 with stroke or cerebrovascular injury was included in the study. The medical records of stroke patients receiving treatment including demographic data, age, gender and hospital record numbers, data regarding anti-cerebral edema drugs prescribed, co-prescribed drugs, and discharge summary were collected from their records. The study was initiated after approval by institutional ethics committee.

Inclusion Criteria

- Patients aged >18 years newly diagnosed with cerebrovascular injury.
- Hospitalized patients.

Exclusion Criteria

- Old cases of stroke
- Patients on corticosteroids
- Patients on diuretics
- Patients with other comorbid conditions such as congestive heart failure, renal failure, and cirrhosis of liver
- Past history of head trauma.

Clinical Outcomes

Discharge summary was checked for final clinical status of the patient at the time of discharge and categorized as follows:

- Patient improved and discharged
- Patient died
- Patient discharged against medical advice (DAMA) or lost to follow-up.

Statistical analysis was performed using the suitable statistical test in SPSS Software Version 23. $P < 0.05$ was considered statistically significant.

RESULTS

Most of the patients were of 60-79 years (43%). Ischemic stroke appears more with 65% in males in our study. Hypertension and diabetes mellitus appear to be associated in most of the cases of stroke.

Mannitol is the most common drug used in the management of cerebral edema in stroke (34.93%), followed by furosemide (26.5%), corticosteroids (8.46%), glycerol (7.23%), and others including torsemide or aldactone (10.84%) (Figure 1).

Mannitol was the preferred intravenous osmotic diuretic, furosemide was preferred loop diuretic, and dexamethasone was preferred corticosteroid and glycerol the preferred oral osmotic diuretic (Figure 2).

Anti-edema drugs were used in 41% of cases only.

Among them, in 29.41% of cases single drug (monotherapy), mannitol (17.64%) was most commonly used, followed by glycerol (2.94%), furosemide (5.88%) and corticosteroid (2.94%).

In 52.49% cases, a combination of above drugs was used mannitol + furosemide combination was most commonly used (35.29%) followed by mannitol + glycerol and others.

In 14.70% cases, three-drug combination was used; mannitol + glycerol + dexamethasone was most common (8.82%) followed by mannitol + glycerol + furosemide combination (Table 1).

In 2.94% cases, all four drugs were used.

In total 84 patients included in the study, 34 patients (40.96%) were given any one or combinations of the anti-edema drugs. Remaining 49 patients (59.03%) were not given any of the above drugs.

Among the patients receiving the above drugs, 20 patients (58.8%) improved and were discharged, 10 patients died (11.76%) due to the failure of treatment and 4 patients (29.41%) were discharged against medical advice whose outcome is unknown (Table 2).

Among the patients not receiving the above drugs 39 patients (79.59%) improved and were discharged, 6 patients died (12.24%) due to the failure of treatment and 4 patients (11.76%) were discharged against medical advice whose outcome is unknown.

Clinical outcome (improvement, death, DAMA) of stroke patients treated with anti-edema drugs did not show statistical significance when compared with patients without anti-edema treatment ($P = 0.83, >0.05$).

Further outcome of patients treated with two drug combination, i.e., mannitol + furosemide when compared with three drug combination, i.e., mannitol + furosemide + corticosteroid did not show statistical significance ($P = 0.385, >0.05$).

DISCUSSION

This was a retrospective study to understand the trend of use of drugs used in the management of cerebral edema in stroke. Drugs were generally not used for the management of cerebral edema and when used, it was mostly mannitol and furosemide, either alone or in combination. The treatment of stroke with anti-edema drugs showed no significant change in our study. Response of ischemic stroke appears better compared to hemorrhagic stroke. No standard protocol was used, and the treatment was highly individualized. Parenteral steroid dexamethasone was used only in severe cerebral edema and severe intracranial bleeding. An addition of dexamethasone did not improve significantly the clinical outcome.

There are various limitations of the study and it was an attempt to do an initial study to assess the need for further study in the subject, done in small sample size. Only anti-edema drugs were taken into consideration, ideally co-prescribed drugs should have been considered for evaluation. The clinical outcome was taken only as improved, death or lost

to follow-up (discharged against medical advice), as it was a retrospective study and the data was limited. It could have been more informative if the assessment of clinical improvement

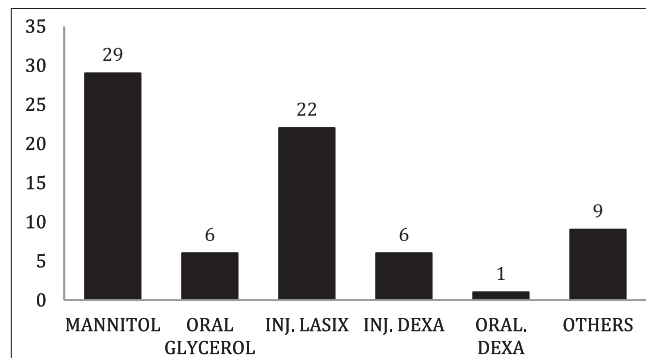


Figure 1: Prescription pattern

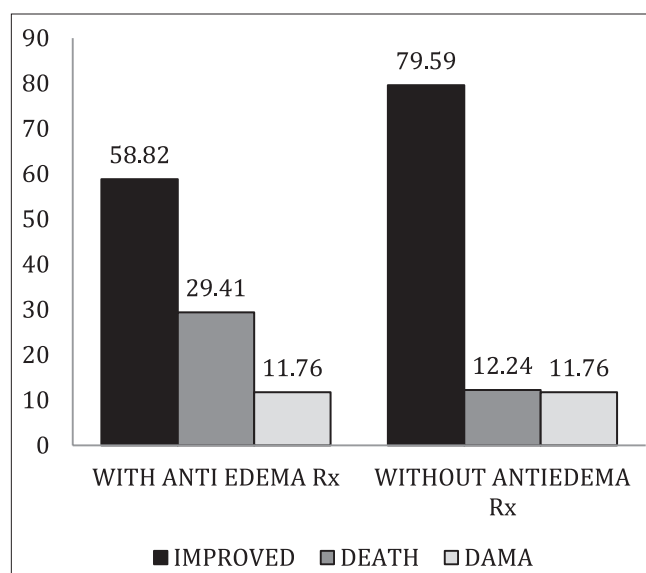


Figure 2: Clinical outcome

Table 1: Prescription pattern

Drugs	Numbers (%)
Monotherapy 29.41%	
Mannitol	6 (17.64)
Glycerol	1 (2.94)
Furosemide	2 (5.88)
Dexamethasone	1 (2.94)
2 drug combination therapy 52.94%	
Mannitol+furosemide	12 (35.29)
Mannitol+glycerol	1 (2.94)
Torsemide+aldactone	4 (11.94)
Glycerol+aldeactone	1 (2.94)
3 drug combination therapy 14.70%	
Mannitol+glycerol+dexamethasone	3 (8.84)
Mannitol+glycerol+furosemide	2 (5.88)
4 drug combination therapy	
Mannitol+furosemide+glycerol+dexamethasone	1 (2.94)

Table 2: Comparison of clinical outcome

Total 84 patients included	Improved	Death	DAMA
Anti-edema drugs used 34 post stroke (40.96%)	20 patients -58.82%	10 patients -11.76%	4 patients – 29.41%
Anti-edema drugs not used 49 post stroke (59.03%)	39 patients -79.59%	6 patients- 12.24%	4 patients- 11.76%

on clinical scale could have been done in prospective study. However, the study gives a glimpse into the facts of further need for the study in this regard. Predicting clinical outcome needs development of uniform protocols and further studies to standardize the practice of using drugs to manage cerebral edema routinely in stroke.

CONCLUSION

According to our study results, drugs were generally not used for the management of cerebral edema. When used, it was mannitol and Lasix, either alone or in combination was used most commonly. Predicting clinical outcome needs development of uniform protocols and further studies to standardize the practice of using drugs to manage cerebral edema routinely in stroke.

REFERENCES

1. Elfaki AS, Hamad M. Clinical profile and management of stroke at elobeid Hospital, West Sudan. *Woodpecker J Med Sci.* 2013;2(1):6-9.
2. Kalita J, Misra UK, Ranjan P. Prescribing pattern of antiedema therapy in stroke by neurologists and general physicians. *Neurol India.* 2004;52:191-3.
3. Berezcki D, Liu M, Prado GF, Fekete I. Cochrane report: A systematic review of mannitol therapy for acute ischemic stroke and cerebral parenchymal hemorrhage. *Stroke.* 2000;31(11):2719-22.
4. Pongvarin N, Bhoopat W, Viriyavejakul A, Rodprasert P, Buranasiri P, Sukondhabhant S, et al. Effects of dexamethasone in primary supratentorial intracerebral hemorrhage. *N Engl J Med.* 1987;316(20):1229-33.
5. Yu YL, Kumana CR, Lauder IJ, Cheung YK, Chan FL, Kou M, et al. Treatment of acute cerebral hemorrhage with intravenous glycerol. A double-blind, placebo-controlled, randomized trial. *Stroke.* 1992;23(7):967-71.
6. Broderick JP, Adams HP Jr, Barsan W, Feinberg W, Feldmann E, Grotta J, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke.* 1999;30(4):905-15.
7. Famularo G. The puzzle of neuronal death and life: Is mannitol the right drug for the treatment of brain oedema associated with ischaemic stroke? *Eur J Emerg Med.* 1999;6(4):363-8.

How to cite this article: Kumar BP, Scandashree K, Udaykumar P. Study of drugs used in cerebral edema in patients with stroke at a tertiary care center. *Natl J Physiol Pharm Pharmacol* 2017;7(2):151-154.

Source of Support: Nil, **Conflict of Interest:** None declared.