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A STUDY ON EFFICACY OF CITICOLINE AND EDARAVONE IN ACUTE ISCHEMIC STROKE

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Abstract:

Background: *Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide. Citicoline and Edaravone are neuroprotective agents with distinct mechanisms of action.*

Objective: *To compare the efficacy of Citicoline and Edaravone in patients with AIS using the National Institute of Health Stroke Scale (NIHSS) and Modified Rankin Scale (mRS).*

Methods: *A prospective hospital-based study was conducted at KIMS Hospital, Rajahmundry, Andhra Pradesh, India, between September 2022 and March 2023. Seventy-four patients diagnosed with AIS were randomized into two groups: Citicoline (n=35) and Edaravone (n=39). Clinical data, vascular risk factors, NIHSS, and mRS scores were assessed at baseline, discharge, day 14, and day 30. Statistical analyses included Levene's test, descriptive statistics, and post-hoc comparisons.*

Results: *Males predominated in both groups (63% Citicoline, 62% Edaravone). The majority were aged 61–70 years. Diabetes (36%) was the most common vascular risk factor. Both groups showed significant improvement in NIHSS and mRS scores from baseline to day 30. However, Edaravone demonstrated greater efficacy with significantly lower mean NIHSS (0.41 ± 0.88) and mRS (0.42 ± 1.06) scores at day 30 compared to Citicoline (NIHSS 2.37 ± 7.05, mRS 0.92 ± 0.73; $p<0.05$).*

Conclusion: *Both agents improved outcomes, but Edaravone was superior in reducing stroke severity and disability within 30 days. Larger multicenter trials with long-term follow-up are warranted.*

Keywords: *Acute ischemic stroke, Citicoline, Edaravone, NIHSS, Modified Rankin Scale, Neuroprotection*

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INTRODUCTION:

Acute ischemic stroke (AIS) is one of the main causes of death and disabilities in the world. Stroke occurs due to an obstruction in brain circulation, leading to neuronal damage with resultant neurological deficit.[1] Except for individuals who undergo immediate measures, all patients are destined to be fully, partially, or temporarily dependent on others, eventually imposing a serious socioeconomic burden on society due to lengthy rehabilitative therapy, caregiver selection, and lost productive time. Even though, they can be treated acutely, most patients are left with anatomical defects leading to functional deficits.[2]

Following ischemic stroke, there is this cascade of thousands of events: excitotoxicity, oxidative stress, inflammation, and apoptosis, so that the ongoing neuronal damage can progress further.[3] Reperfusion strategies restore blood flow, but without acting directly on secondary injury processes; while thrombolysis and mechanical thrombectomy are the modalities of reperfusion. Neuroprotective therapies will ultimately save neurons, preserve brain function, and help in recovery, particularly at an early stage after stroke onset.[4]

Edaravone works as free radical scavenger to reduce oxidative stress and prevent the progression of neuronal damage. Citicoline stabilizes neuronal membranes and supports repair by phospholipid synthesis and through modulation of neurotransmitter systems.[5] Both agents have been used as adjuncts in the treatment of AIS but have never been thoroughly assessed for their comparative efficacy in improving neurological and functional outcomes.[6]

Some clinical studies suggest that Edaravone might have a slight advantage in neurological and functional recovery, especially in the early phases, whereas Citicoline results have been somewhat inconsistent.[7] Differences in terms of study design, patient population, and follow-up duration have restricted definitive conclusions from being placed. This uncertainty underlines the need for studies capable of comparing these agents head to head to determine which treatment confers short-term benefit.[8]

Since post-stroke disability poses such a great burden and evidence is contradictory about Citicoline, it is therefore clinically important to evaluate the relative efficacies of Edaravone and Citicoline.[9] This study seeks to directly compare the effects on neurological and functional recovery in patients suffering from acute ischemic stroke, especially in the very first month. The results of this study may allow for the optimization of early management strategies and pave the way in decision-making toward better outcome and independence of patients.[10]

METHODOLOGY:

Study Design and Setting

This was a hospital-based, prospective, comparative observational study conducted in the Department of Neurology, KIMS (Bollineni) Hospital, Rajahmundry, Andhra Pradesh, India. The study protocol was reviewed and approved by the Institutional Ethics Committee (approval number: VIPS/DPP/IRB/05/2022-23). Written informed consent was obtained from all participants or their legally authorized representatives before enrollment.

Study Duration

The study was carried out over a period of six months, from 15th September 2022 to 15th March 2023.

Study Population

All patients admitted to the Neurology Department with a confirmed diagnosis of acute ischemic stroke and initiated on either Citicoline or Edaravone therapy were screened for eligibility.

Inclusion Criteria

- Patients aged ≥20 years.
- Patients presenting with clinical symptoms of acute ischemic stroke confirmed by radiographic evidence.
- Patients willing to provide informed consent or whose caretakers consented on their behalf.

Exclusion Criteria

- Patients diagnosed with intracranial hemorrhage.
- Pregnant or lactating women.
- Patients below 20 years of age.
- Patients unwilling to participate in the study.

Sample Size and Grouping

A total of 74 patients who met the inclusion criteria were enrolled. They were randomized into two groups:

- **Citicoline group (n=35):** Received Citicoline therapy.
- **Edaravone group (n=39):** Received Edaravone therapy.

Intervention and Drug Administration

- **Citicoline:** Administered at a dose of 500 mg twice daily (oral or parenteral) for a duration of 4 weeks.
- **Edaravone:** Administered as 30 mg intravenous infusion over 60 minutes, every 12 hours, for 14 days.

All patients received standard supportive and symptomatic care as per institutional stroke management protocols.

Data Collection Tools

Data was collected using a structured data collection form, and supplemented by:

- Patient medical records (register number, demographics, clinical and laboratory details, comorbidities, and social habits).
- Direct patient or caregiver interviews.
- Validated stroke assessment scales:
  - **National Institute of Health Stroke Scale (NIHSS):** Used to quantify neurological impairment.
  - **Modified Rankin Scale (mRS):** Used to assess functional disability and recovery outcomes.

Study Variables

- **Baseline variables:** Age, gender, height, weight, BMI, sociodemographic profile, chief complaints, comorbidities, and vascular risk factors (diabetes, hypertension, smoking, history of prior stroke, congestive heart failure).
- **Outcome variables:** Improvement in neurological function measured using NIHSS and functional recovery assessed by mRS at four time points:
  - Day of admission (DOA)
  - Day of discharge (DOD)
  - Day 14 follow-up
  - Day 30 follow-up

Outcome Measures

- **Primary outcome:** Change in NIHSS score from baseline to day 30.
- **Secondary outcome:** Change in mRS score from baseline to day 30.

Statistical Analysis

Data was entered in Microsoft Excel and analyzed using SPSS/SAS. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequency and percentages.

- **Levene's test** was applied to evaluate homogeneity of variances.
- **Post-hoc Student-Newman-Keuls test** was applied to detect pairwise differences in outcomes within groups. A p-value of <0.05 was considered statistically significant.

RESULTS:

A total of **74 patients** with acute ischemic stroke were screened and randomized into two treatment groups: **Citicoline (n=35)** and **Edaravone (n=39)**.

Gender Distribution

Out of 35 patients in the Citicoline group, 22 (63%) were male and 13 (37%) were female. In the Edaravone group, 24 (62%) were male and 15 (38%) were female. Overall, males constituted 62.2% of the total population, indicating that stroke was more common among men in this study cohort.

Table 1. Gender Distribution of Patients

Gender	Citicoline n (%)	Edaravone n (%)	Total n (%)
Male	22 (63%)	24 (62%)	46 (62.2%)
Female	13 (37%)	15 (38%)	28 (37.8%)
Total	35 (100%)	39 (100%)	74 (100%)

Age Distribution

Patients were grouped into five age categories. The **61–70 years age group** was most affected (32.4%), followed by **41–50 years (29.7%)** and **51–60 years (20.3%)**. The least affected groups were 71–80 years (10.8%) and 81–90 years (6.7%).

Table 2. Age Distribution of Patients

Age Group (Years)	Citicoline n (%)	Edaravone n (%)	Total n (%)
41–50	12 (34%)	10 (26%)	22 (29.7%)
51–60	4 (11%)	11 (28%)	15 (20.3%)
61–70	9 (26%)	15 (38%)	24 (32.4%)
71–80	6 (17%)	2 (5%)	8 (10.8%)
81–90	4 (12%)	1 (3%)	5 (6.7%)
Total	35 (100%)	39 (100%)	74 (100%)

Vascular Risk Factors

The most common risk factor was **diabetes mellitus (36%)**, followed by **smoking (33%)**, **previous stroke (16%)**, **hypertension (12%)**, and **congestive heart failure (3%)**.

Table 3. Vascular Risk Factors

Risk Factor	No. of Patients	Percentage (%)
Previous Stroke	18	16%
Diabetes Mellitus	40	36%
Hypertension	13	12%
Smoking	36	33%
CHF	3	3%

Neurological Outcomes (NIHSS)

The **mean NIHSS score in the Citicoline group** was 26.14 at admission, decreasing to 12.37 at discharge, 5.77 at day 14, and 2.37 at day 30. In the **Edaravone group**, NIHSS decreased more rapidly, from 24.49 at admission to 7.95 at discharge, 3.46 at day 14, and 0.41 at day 30.

- **Levene's Test:** Citicoline (p=0.203, not significant), Edaravone (p<0.001, significant).
- **Post-hoc Student-Newman-Keuls Test:** Confirmed significant, steady reductions in NIHSS over time in both groups.

Table 4. Mean NIHSS Scores

Time Point	Citicoline (Mean ± SD)	Edaravone (Mean ± SD)
Admission (DOA)	26.14 ± 7.30	24.49 ± 5.71
Discharge (DOD)	12.37 ± 7.75	7.95 ± 3.81
Day 14	5.77 ± 7.04	3.46 ± 2.61
Day 30	2.37 ± 7.05	0.41 ± 0.88

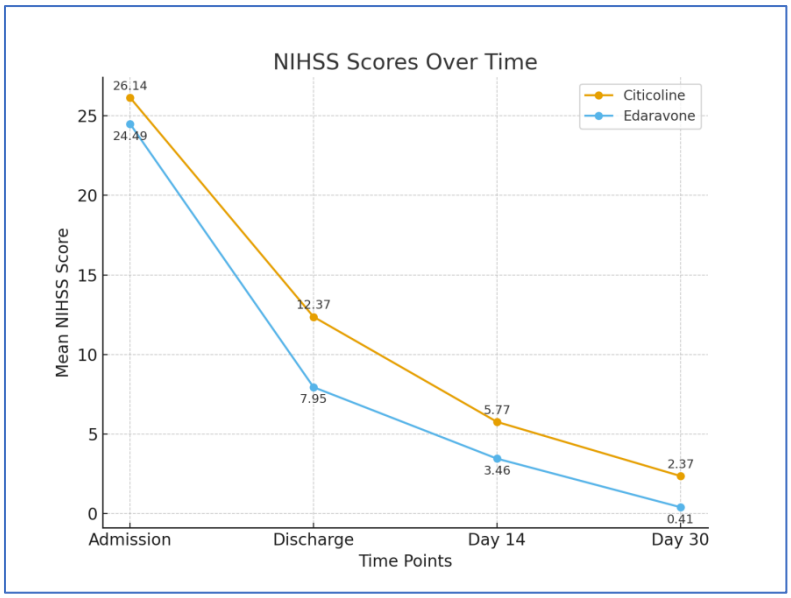

Figure 1 : Mean NIHSS Scores over time

Both groups demonstrated significant improvement, but **Edaravone showed faster recovery and lower residual deficits by day 30**.

Functional Outcomes (mRS)
The **mean mRS score in the Citicoline group** was 4.87 at admission, improving to 3.15 at discharge, 2.18 at day 14, and 0.92 at day 30. In the **Edaravone group**, mRS decreased from 4.80 at admission to 3.69 at discharge, 2.03 at day 14, and 0.43 at day 30.

- **Levene's Test:** Citicoline (p=0.096, not significant), Edaravone (p=0.009, significant).
- **Post-hoc Test:** Confirmed consistent reduction in mRS scores across all time points for both groups.

Table 5. Mean mRS Scores

Time Point	Citicoline (Mean ± SD)	Edaravone (Mean ± SD)
Admission (DOA)	4.87 ± 0.34	4.80 ± 0.58
Discharge (DOD)	3.15 ± 0.67	3.69 ± 0.93
Day 14	2.18 ± 0.64	2.03 ± 0.95
Day 30	0.92 ± 0.74	0.43 ± 1.06

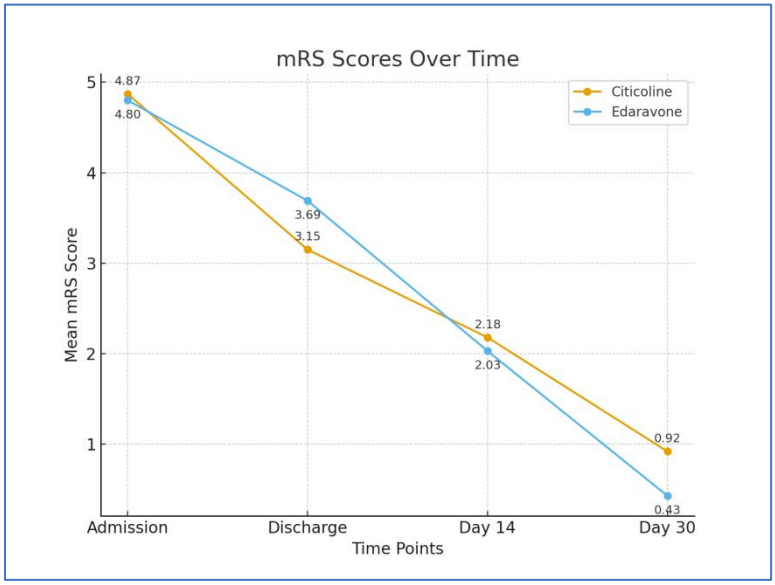

Figure 2 : Mean mRS Scores over time

Both groups achieved significant functional recovery, but **Edaravone patients had superior outcomes by day 30**, with most regaining near-complete independence.

Overall Interpretation

- Stroke was more prevalent among **males and elderly patients (≥60 years)**.
- **Diabetes and smoking** were leading vascular risk factors.
- Both Citicoline and Edaravone significantly improved neurological (NIHSS) and functional (mRS) scores.
- **Edaravone consistently demonstrated greater and faster improvement** compared to Citicoline, as confirmed by statistical analysis.

DISCUSSION:

In our study, the majority of patients with acute ischemic stroke were males (62%), and the most affected age group was 61–70 years. This demographic pattern is consistent with global data, where male sex and older age remain dominant risk factors for stroke incidence and recurrence. [11] Additionally, diabetes mellitus was the most prevalent vascular risk factor (36%), highlighting its strong contribution to ischemic pathology. Chronic hyperglycemia in diabetes promotes endothelial dysfunction, oxidative stress, and accelerated atherosclerosis, thereby increasing susceptibility to ischemic injury. [12] These findings emphasize the importance of addressing modifiable risk factors such as diabetes and smoking in primary prevention strategies. Our demographic profile reflects the growing burden of stroke in India's aging population, underscoring the need for

early detection and risk management to mitigate long-term disability and mortality.

Both Citicoline and Edaravone groups demonstrated significant reductions in NIHSS scores from baseline to day 30, reflecting neurological recovery. However, the Edaravone group exhibited a sharper decline (mean 24.48 to 0.41) compared to Citicoline (mean 26.14 to 2.37). This superior effect of Edaravone is consistent with clinical studies showing that its antioxidant properties attenuate reperfusion injury and neuronal apoptosis, leading to improved neurological outcomes Similar comparative work by Mitta et al. demonstrated that patients treated with Edaravone achieved significantly lower NIHSS scores at 3 months compared with Citicoline or standard therapy. The consistent NIHSS improvement across studies suggests that Edaravone's early neuroprotective role is clinically meaningful, particularly when administered promptly. These findings support its use as a frontline adjunct in acute ischemic stroke, especially in resource-constrained settings where timely reperfusion therapies are not always feasible.[13,14]

Functional recovery, as assessed by mRS, also favored the Edaravone group, which achieved a mean reduction from 4.80 to 0.42, compared to Citicoline's decline from 4.87 to 0.92. This outcome highlights Edaravone's ability not only to reduce acute neurological deficits but also to improve functional independence within the first month. These results resonate with previous reports from Japanese and Indian cohorts, where Edaravone significantly enhanced activities of daily living and overall disability scores. [15] Conversely, large randomized trials like ICTUS found no significant functional benefit with Citicoline, despite its widespread use. Taken together, our findings suggest that while both drugs contribute to functional recovery, Edaravone provides superior outcomes in the short term. However, longer follow-up studies are needed to determine whether these early advantages translate into sustained disability reduction over 3–6 months.[16,17]

CONCLUSION:

This study demonstrates that both Edaravone and Citicoline significantly improve neurological and functional outcomes in patients with acute ischemic stroke. Stroke was more prevalent among males and individuals aged 61–70 years, with diabetes mellitus and smoking identified as the leading vascular risk factors. While both treatment groups showed meaningful reductions in NIHSS and mRS scores over 30 days, Edaravone consistently provided faster and greater improvement, resulting in near-complete functional independence in most patients by the end of the follow-up period. These findings highlight Edaravone's early neuroprotective and functional benefits, supporting its use as an effective adjunct in acute stroke management. Nonetheless, longer-term studies are warranted to determine whether these short-term advantages translate into sustained reduction in disability and improved quality of life.

CONFLICT OF INTEREST:

None.

REFERENCES:

1. Hasan TF, Hasan H, Kelley RE. Overview of Acute Ischemic Stroke Evaluation and Management. Biomedicines. 2021 Oct 16;9(10):1486.
2. Musuka T.D., Wilton S.B., Traboulsi M., Hill M.D. Diagnosis and management of acute ischemic stroke: Speed is critical. Can. Med. Assoc. J. 2015;187:887–893
3. Kuriakose D, Xiao Z. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. Int J Mol Sci. 2020 Oct 15;21(20):7609.
4. Su Z, Ye Y, Shen C, Qiu S, Sun Y, Hu S, Xiong X, Li Y, Li L, Wang H. Pathophysiology of Ischemic Stroke: Noncoding RNA Role in Oxidative Stress. Oxid Med Cell Longev. 2022 Sep 12;2022:5815843
5. Lee BJ, Egi Y, van Leyen K, Lo EH, Arai K. Edaravone, a free radical scavenger, protects components of the neurovascular unit against oxidative stress in vitro. Brain Res. 2010 Jan 11;1307:22-7.
6. Song Y, Bei Y, Xiao Y, Tong HD, Wu XQ, Chen MT. Edaravone, a free radical scavenger, protects neuronal cells' mitochondria from ischemia by inactivating another new critical factor of the 5-lipoxygenase pathway affecting the arachidonic acid metabolism. Brain Res. 2018 Jul 1;1690:96-104.
7. Chen C, Li M, Lin L, Chen S, Chen Y, Hong L. Clinical effects and safety of edaravone in treatment of acute ischaemic stroke: A meta-analysis of randomized controlled trials. J Clin Pharm Ther. 2021 Aug;46(4):907-917.
8. Gareri P, Castagna A, Cotroneo AM, Putignano S, De Sarro G, Bruni AC. The role of citicoline in cognitive impairment: pharmacological characteristics, possible advantages, and doubts for an old drug with new perspectives. Clin Interv Aging. 2015 Sep 3;10:1421-9.
9. Li M, Huo X, Chang Q, Liu X, Zhang J, Mao Z. Efficacy analysis of neuroprotective drugs in patients with acute ischemic stroke based on network meta-analysis. Front Pharmacol. 2024 Nov 7;15:1475021.

10. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation. 2019;139(10):e56-528.
11. Banerjee, T. K., & Das, S. K. Fifty years of stroke researches in India. Annals of Indian Academy of Neurology. 2016;19(1):1-8.
12. Mitta M, Goel D, Bansal KK, Puri P. Edaravone - citicoline comparative study in acute ischemic stroke (ECCS-AIS). J Assoc Physicians India. 2012 Nov;60:36-8.
13. Sadi AM, Khadeeja M, Periera LJ, John C, Lakshmi R, Soumya VC. A Comparative Study of Stroke Outcomes in Patients Receiving Edaravone and Citicoline. Indian J Pharmacy Practice. 2025;18(4):404-9.
14. Ogawa Y, Akiyama H, Horii T, Mihara K. Association between edaravone use and activities of daily living in older patients with atherothrombotic stroke: an observational study using Japanese real-world data. BMC Geriatr. 2025 Jan 15;25(1):31.
15. Dávalos A, Alvarez-Sabín J, Castillo J, Díez-Tejedor E, Ferro J, Martínez-Vila E, Serena J, Segura T, Cruz VT, Masjuan J, Cobo E, Secades JJ; International Citicoline Trial on acUte Stroke (ICTUS) trial investigators. Citicoline in the treatment of acute ischaemic stroke: an international, randomised, multicentre, placebo-controlled study (ICTUS trial). Lancet. 2012 Jul 28;380(9839):349-57
16. Wang Y, Li M, Jiang Y, Ji Q. Comparative efficacy of neuroprotective agents for improving neurological function and prognosis in acute ischemic stroke: a network meta-analysis. Front Neurosci. 2025 Jan 6;18:1530987.
17. Sadi, Aleena & Maitheen, Khadeeja & Periera, Laveena & John, Cijy & Ramachandran, Lakshmi & Chandrasekharan, Soumya. (2025). A Comparative Study of Stroke Outcomes in Patients Receiving Edaravone and Citicoline. Indian Journal of Pharmacy Practice. 18. 404-409.