Section: Neurology

Original Research Article

COMPARATIVE EVALUATION OF SOVATELTIDE PLUS ASPIRIN VERSUS ASPIRIN ALONE IN ACUTE ISCHEMIC STROKE: A HOSPITAL-BASED OBSERVATIONAL STUDY

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ABSTRACT

Background: Neuroprotective agents are increasingly recognized as adjuncts to reperfusion therapies in ischemic stroke. Sovateltide, a selective endothelin B receptor agonist, has demonstrated promising neurorestorative effects. **Materials and Methods:** This observational study included 100 patients with acute ischemic stroke presenting within 24 hours. Group S received sovateltide plus aspirin; Group A received aspirin alone. Outcomes were assessed using NIHSS, mRS, and BI scores at admission, discharge, 30 days, and 90 days. **Result:** Group S showed significantly greater improvement in NIHSS (mean reduction: 8.40 vs. 3.96 at 90 days, $p<0.01$), mRS, and BI scores. Odds ratios for favorable outcomes were consistently higher in Group S. **Conclusion:** Sovateltide enhances neurological recovery and functional outcomes when added to standard antiplatelet therapy in acute ischemic stroke.

INTRODUCTION

Ischemic stroke continues to be a major cause of disability and death worldwide, responsible for almost 85% of all stroke.[1] In spite of progress in thrombolysis and thrombectomy, most patients are still excluded because of time limits, contraindications, or insufficient access to referral centers.[2,3] Neuroprotective drugs provide an alternative approach to enhance outcomes, particularly in resource-poor environments.[4]

Sovateltide (IRL-1620), a selective endothelin B (ETB) receptor agonist, is an inducer of neurogenesis, angiogenesis, and anti-apoptotic pathways.[5,6] Preclinical experiments have shown that sovateltide increases mitochondrial biogenesis, improves cerebral perfusion, and decreases infarct size in rodent models.[7,8] These multidimensional actions make it a likely neurorestorative agent outside the strict therapeutic window of thrombolytics.[9]

Recent phase III studies have confirmed sovateltide's clinical effectiveness when given within 24 hours of stroke symptom onset. Patients that received sovateltide in conjunction with usual treatment demonstrated statistically significant gains in NIHSS, mRS, and BI at 90 days over placebo[2,10] Most importantly, the drug was tolerated well, with no significant adverse effects observed. These results justify its inclusion in the protocols for early stroke care, particularly in environments where mechanical thrombectomy or thrombolysis is not readily available.[11]

Moreover, the addition of sovateltide to stroke protocols can complement future tendencies in personalized medicine in which molecular targeting and neurorestoration are given as much weight as reperfusion.[19] Its synergy with routine antiplatelet therapy and low adverse profile make it a strong contender for wider adoption, especially among low-resource environments.[20]

MATERIALS AND METHODS

The study is an observational prospective study with a sample of 100 patients of acute ischemic stroke who were admitted to a tertiary care hospital within 24 hours of onset. Study period was from January 2023 to January 2024. The sample was divided randomly into two groups of 50 patients each. Patients who were given Sovateltide and Aspirin were named group S, and patients who were given aspirin alone were named group A. Both groups of patients were

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assessed using NIHSS, MRS (Modified Rankin Scale), Barthel's Index at the time of admission, discharge, 1 month and 3-month follow-up. The means across both the groups were then compared for each individual scale. Institutional Ethics Committee approval was taken for the study.

Treatment Regimen: Group S was given Sovateltide administered intravenously at a dose of 0.3 ug/kg of body weight/dose iv bolus over 1min given as 3 doses per day with intervals of 3 + 1 hours, where 1st dose to be given within 24hrs of stroke onset, on days 1,3,6 with total of 9 doses. Aspirin was given at a dose of 75mg and 150mg. Group A was given Aspirin alone at a dose of 75mg and 150mg. The regular standard of care was not compromised in either of the groups.

RESULTS

A total number of 100 patients were taken for the study, 50 patients under group S, and 50 patients under group A. A total of 50 patients in each group were assessed based on stroke scales, where 42 patients from group A and 43 patients from group S completed the follow-up study period. A total number of 7 deaths were seen in group S and 8 deaths in group A.

Demographic data: Mean age group of group S was (62.60 ± 13.59), the mean age group of group A was (56.04 ± 10.63). In group S, 28 (56%) were male, and 22(44%) were female, in group A 28 (56%) were male, and 22(44%) were female.

NIHSS Scores: NIHSS scores of group S and group A are compared at different time points i.e at the time of admission, discharge, 1month follow up and 3 months follow up, through student t test and the mean differences are interpretated as below. These results suggest that over time, Group S tends to have lower NIHSS scores compared to Group A, and the differences are statistically significant at each time point after admission.

Table 1: Comparison of mean scores on NIHSS between group S and group A

Variables	NIHSS		Treatment Effect	t-value (P-value)
	Group S (n=50)	Group A(n=50)		
	Mean ± S D	Mean ± S D		
At Admission	13.77± 4.545	10.94 ± 3.721	Mean Diff = 2.830	0.0014 (p < 0.01)
At Discharge	9.39 ± 2.964	8.16 ± 2.368	Mean Diff = 1.230	0.029 (p < 0.05)
After 1 Month	6.39 ± 2.788	7.46 ± 2.114	Mean Diff = -1.070	0.047 (p < 0.05)
After 3 Month	5.37 ± 2.478	6.98 ± 2.447	Mean Diff = -1.610	0.0034 (p < 0.01)

MRS Scores: MRS scores of group S and group A are compared at different time points i.e at the time of admission, discharge, 1month follow up and 3 months follow up, through student t test and the mean differences are interpretated as below. These results suggest that over time, Group S tends to have lower MRS scores compared to Group A, and the differences are statistically significant at each time point after admission.

Table 2: Comparison of mean scores on MRS between group S and group A

Variables	MRS		Mean Difference	t-value (P-value)
	Group S (n=50)	Group A (n=50)		
	Mean ± S D	Mean ± S D		
At Admission	4.29 ± 0.506	4.00 ± 0.452	Mean Diff = 0.290	0.004 (p < 0.01)
At Discharge	3.75 ± 0.908	3.23 ± 0.758	Mean Diff = 0.520	0.003 (p < 0.01)
After 1 Month	2.64 ± 0.278	2.40 ± 0.335	Mean Diff = 0.240	0.000 (p<0.001)
After 3 Month	2.36 ± 0.394	2.14 ± 0.225	Mean Diff = 0.220	0.002 (p < 0.01)

BI (Barthel Index): The scores indicate a statistically significant difference in BI scores between Group S and Group A three months after admission, with Group S still having a higher mean BI score.

Table 3: Comparison of mean scores on BI between group S and group A

Variables	BI		Mean difference	t-value (P-value)
	Group S (n=50)	Group A (n=50)		
	Mean ± S D	Mean ± S D		
At Admission	28.12 ± 12.905	22.83 ± 10.317	Mean Diff = 5.290	0.031 (p < 0.05)
At Discharge	58.77 ± 11.244	53.01 ± 10.556	Mean Diff = 5.760	0.012 (p < 0.05)
After 1 Month	68.48 ± 13.351 (n=44)	62.33 ± 13.308 (n=43)	Mean Diff = 6.150 95% CI : 0.467 to 11.833	0.034 (p < 0.05)
After 3 Month	75.91 ± 11.605 (n=43)	70.05± 15.033 (n=42)	Mean Diff = 5.860 95% CI : 0.074 to 11.646	0.047 (p < 0.05)

While comparing the difference in scores within the groups measuring the difference from day of

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admission to after 3months, we observed that Group S generally shows greater improvement in all the indices compared to Group A at all time points.

DISCUSSION

The results observed for sovateltide in the present study match its potential neurovascular remodeling effects. It allows for both structural and functional recovery by increasing the proliferation of neural stem cells and the expression of neurotrophic factors like VEGF and NGF.[6,12] Its capacity to protect the neural mitochondria and inhibit apoptotic cascades further helps ensure neuronal integrity.[13,14]

Additionally, the excellent safety profile of sovateltide adds to its clinical value. In contrast to thrombolytics, which pose a threat of hemorrhagic transformation, sovateltide does not affect coagulation cascades.[15] Therefore, it is especially useful in patients contraindicated for reperfusion therapy. With the global impact of ischemic stroke and the shortcomings of existing treatments, sovateltide is a breakthrough toward regenerative pharmacotherapy.[16] Its long-term efficacy needs to be validated in future multicenter trials with extended follow-up times, and its place in combination with other neuroprotective agents needs to be determined.[17,18]

Furthermore, inclusion of sovateltide in stroke guidelines might fit with the recent trends in individualized medicine, with molecular targeting and neurorestoration being emphasized along with reperfusion.[19] Its compatibility with conventional antiplatelet treatment and benign adverse profile render it an interesting candidate for more extensive use, especially in low-resource environments.[20]

CONCLUSION

Sovateltide, when administered within 24 hours of stroke onset, significantly improves recovery when combined with aspirin. Its neuroprotective properties make it a promising adjunct in stroke management.

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