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A Comparative study of citicoline vs cerebroprotein hydrolysate in ischemic and haemorrhagic stroke

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Introduction

Neuroprotection is a broad term that refers to pharmacological and non-pharmacological treatments used to halt the cellular events in the ischemic cascade, forming the theoretical basis for many of the acute stroke therapies. Currently available treatment options for stroke patients are clearly unsatisfactory. Newer neuroprotective therapies like Cerebroprotein hydrolysate & Citicoline act at multiple levels in the brain by inhibiting apoptosis. Study was done to compare the clinical efficacy of Cerebroprotein and Citicoline in stroke.

Materials and Methods

Present study was conducted in 100 patients divided into four groups of 25 patient each. Group I & II included ischemic and Group III & IV included haemorrhagic stroke patients. Group I and III were treated with Citicoline and group II and IV with Cerebroprotein. Patients were evaluated from time of admission upto 12 weeks.

The primary outcome was determined by Barthel Index (B.I.) and Modified Rankin Scale (MRS). Patients were diagnosed on basis of CT/MRI.

Observations

Groups	Mean score of barthel index at admission & 12 wks	Mean score of modified rankin score at admission & 12 wks
GROUP-1	13 & 93	5 & 2
GROUP-2	13 & 86	5 & 2
GROUP-3	10 & 70	5 & 3
GROUP-4	10 & 65	5 & 3

In Group-I mean B.I. and MRS score at admission & at 12 wks was 13 & 93 and 5 & 2, compared to Group-III where mean B.I. and MRS were 10 & 70 and 5 & 3 respectively.

In Group-II mean B.I. and MRS score at admission & at 12 wks was 13 & 86 and 5 & 2, compared to Group-IV where mean B.I. and MRS were 10 & 65 and 5 & 3 respectively.

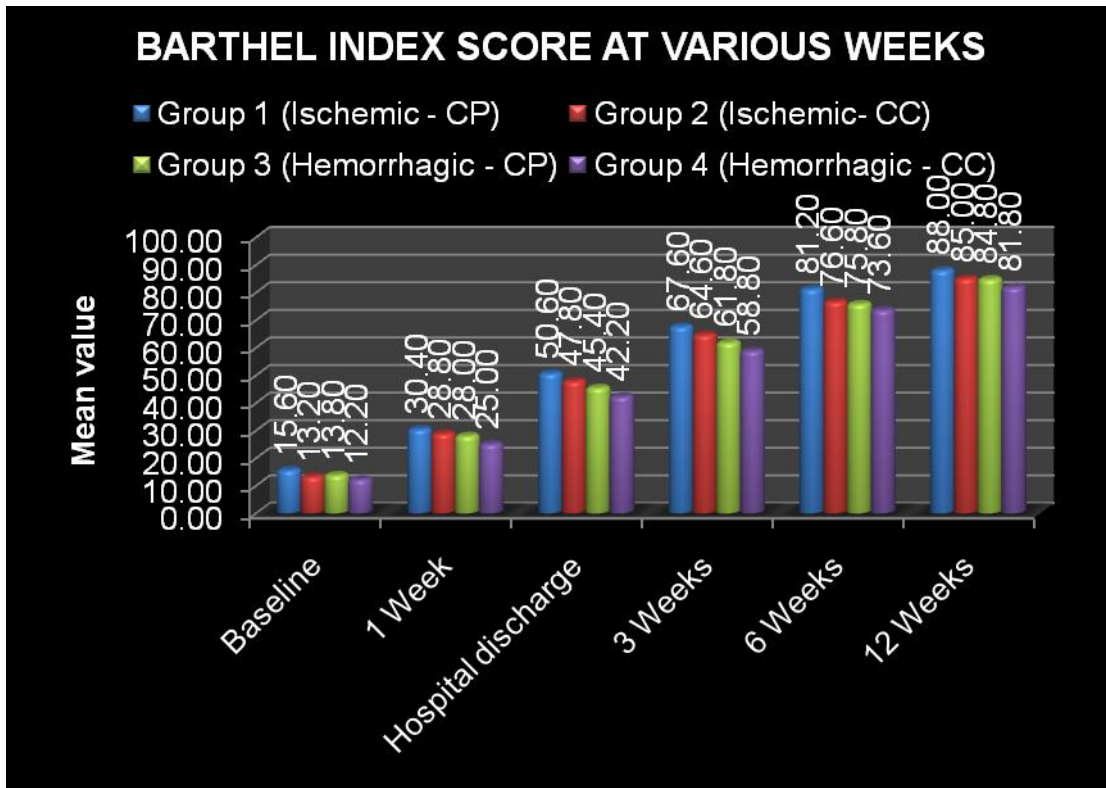
Barthel Index was one of the Primary end point of recovery in stroke patient used in this study. Recovery in stroke patient in each group were studied using Barthel Index. In all patients in each of the four groups Barthel Index score was calculated at Baseline, one week, at discharge from hospital, at 3weeks, at 6 weeks and 12 weeks.

Barthel index score improved from 15.60±5.60 at Baseline to 88.00±7.73 after 12 weeks in Ischemic stroke patients treated with Cerebroprotein Hydrolysate in Group1(Ischemic-CP) and from 13.20±4.30 at Baseline to 85.00±9.12 after 12 weeks in Ischemic stroke patients treated with Citicoline of Group 2

(Ischemic-CC). Barthel index score improved from 13.80±6.00 at Baseline to 84.80±11.59 after 12 weeks in Hemorrhagic stroke patients treated with Cerebroprotein Hydrolysate in Group 3 (Hemorrhagic-CP) and from 12.20±5.22 at Baseline to 81.80±12.73 after 12 weeks in Ischemic stroke patients treated with Citicoline in Group 4 (Hemorrhagic-CC).

The values of Barthel index within each group in all the four groups were statistically significant ($p < 0.05$) which shows effectiveness of the drugs used from baseline upto 12 weeks. The Barthel Index score when compared between different groups, i.e between Group 1 (Ischemic-CP) and Group 2 (Ischemic-CC) and between Group 3 (Hemorrhagic-CP) and Group 4 (Hemorrhagic-CC) were statistically non-significant ($p > 0.05$). There is no difference in efficacy of both the drugs given to the patients of different groups.

Figure 1: Barthel index score at various weeks



Modified Rankin Scale was used to scale the Primary end point of recovery in stroke patient used in this study. Recovery in stroke patient in each group was studied using Modified Rankin Scale. In all patients in each of the four groups, Modified Rankin Scale was used at Baseline, one week, at discharge from hospital, at 3 weeks, at 6 weeks and 12 weeks. Values of Modified Rankin Scale are given in Fig No.2

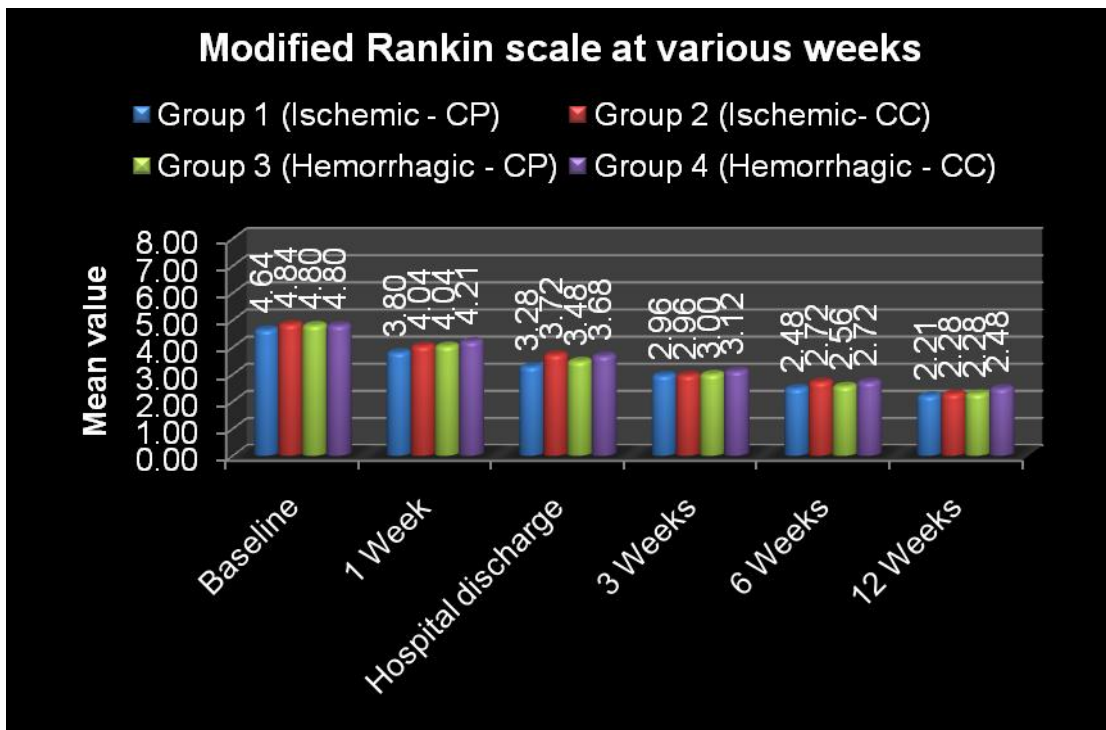
Modified Rankin scale improved from 4.64 ± 0.4 Baseline to 2.21 ± 0.4 at 12 weeks in Ischemic stroke patients treated with Cerebroprotein Hydrolysate Group 1 (Ischemic-CP). Mean improved from 4.84 ± 0.3 Baseline to 2.28 ± 0.4 at 12 weeks in Ischemic stroke patients treated with Citicoline Group 2 (Ischemic-CC). p-value is significant at hospital discharge patients.

Modified Rankin scale improved from 4.80 ± 0.43 Baseline to 2.28 ± 0.6 at 12 weeks in Hemorrhagic

stroke patients treated with Cerebroprotein Hydrolysate Group 3 (Hemorrhagic-CP) and from 4.80 ± 0.5 Baseline to 2.48 ± 0.5 at 12 weeks in Hemorrhagic stroke patients treated with Citicoline Group 4 (Hemorrhagic-CC).

The values of Modified Rankin Scale within each group in all the four groups were statistically significant ($p < 0.05$) which shows effectiveness of the drugs used from baseline upto 12 weeks. The Modified Rankin Scale when compared between different groups, i.e between Group 1 (Ischemic-CP) and Group 2 (Ischemic-CC) and between Group 3 (Hemorrhagic-CP) and Group 4 (Hemorrhagic-CC) were statistically non-significant ($p > 0.05$). There is no difference in efficacy of both the drugs given to the patients. There was no statistical significant difference in recovery of patients treated in all the four groups, p value was > 0.05 .

Figure 2: Modified rankin scale at various weeks



Discussion

The present study was conducted in 100 patients of ischaemic and haemorrhagic stroke. Patients of hemorrhagic and ischemic stroke were given cerebroprotein hydrolysate and Citicoline intravenously. Patients in all groups were duration

matched as far as possible. The maximum number of patients were in the age group of 51-60 years and 61-70 years in both the groups. The mean age of patients who were included in the study was more than 55 years in all the age groups. This is consistent with the pattern seen in study by Sapna E et al¹, who reported that the median age of

stroke patients was 67 years. The no. of patients who had middle cerebral artery involvement in this study was 71 and the no. of patients who had anterior and posterior cerebral artery involvement were 15 & 14 respectively. This pattern showed that middle cerebral artery involvement was common than anterior and posterior artery involvement in stroke patients which were consistent with the patterns in the study of Yee Sien Ng et al².

The no. of patients who had hypertension in this study was 77 and the no. of patients who did not have hypertension were 23 out of the 100 patients. This pattern was consistent with a recent study conducted in Gujarat by RP Eapen et al 2009³. It was found that modifiable risk factors such as hypertension (40%), alcoholism (35%), smoking (28%) are the commonest cause of stroke. Similar observations were observed by Gorecick et al⁴ and Golssteen et al⁵.

The efficacy variable which was applied in the study was changes in the scores of Barthel index and modified rankin scale(MRS) at various weeks which monitored improvement in daily activities at various weeks. Scores were calculated at baseline and the end of first week, at hospital discharge, at 3 weeks, at 6 weeks and at hospital discharge. In Ischemic stroke patients of Group 1 (Ischemic-CP) the mean Barthel index score and MRS at the end of 1st week were 30.40 & 3.80, and at hospital discharge the mean Barthel index score and mRS were 50.60 & 3.28, the mean Barthel index score and mRS were 67.60 & 2.96 at the end of 3 weeks, and at 6 weeks the mean Barthel index score and mRS were 81.20 & 2.48, and at the 12 weeks the mean Barthel index score and mRS were 88.00 & 2.21 respectively. Ischemic stroke patients of Group 2 (Ischemic-CC) the mean Barthel index score and MRS at the end of 1st week were 28.80 & 4.04, and at hospital discharge the mean Barthel index score and mRS were 47.80 & 3.72, the mean Barthel index score and mRS were 64.60 & 2.92 at the end of 3 weeks, and at 6 weeks the mean Barthel index score and MRS were 76.60 & 2.72, and at the 12 weeks the mean Barthel index score and mRS were 85.00 & 2.28. Similar observations were made by Davlos A et al⁶, Clark et al⁷, Clark et al⁸.

Hemorrhagic stroke patients of Group 3 (Hemorrhagic-CP) the mean Barthel index score and MRS at the end of 1st week were 28.00 & 4.04, and at hospital discharge the mean Barthel index score & mRS were 45.40 & 3.48, the mean Barthel index score and MRS were 61.80 & 3.0 at the end of 3 weeks, and at 6 weeks the mean Barthel index score and MRS were 75.80 & 2.56, and at the 12 weeks the mean Barthel index score and mRS were 84.80 & 2.28. In Hemorrhagic stroke patients of Group 4 (Hemorrhagic-CC) the mean Barthel index score and MRS were at the end of 1st week was 25 & 4.21, and at hospital discharge the mean Barthel index score and MRS were 42.20 & 3.68, the mean Barthel index score and mRS were 58.80 & 3.12 at the end of 3 weeks, and at 6 weeks the mean Barthel index score and MRS were 73.60 & 2.72, and at the 12 weeks the mean Barthel index score and MRS were 81.80 & 2.48. The mean improvement in Barthel index score at the end of 12 weeks was more than 50. These observations were consistent with the observations made by Heiss et al⁹, where the median improvement in the Barthel index score at the end of 12 weeks was more than 30. Similar observations were made by Haffner et al¹⁰ and Skvortsova et al¹¹.

In previous studies Cerebroprotein hydrolysate and Citicoline have been compared with placebo. The above results are consistent with studies done by Heiss et al⁹, where in the primary end point was Barthel index at the end of 12 weeks, showed 44.0% responders in the cerebroprotein hydrolysate group and 45.9% responders in the placebo group. The p-value being 0.57 which was not significant. Similar observations were made by Ladurner et al¹² where no significant superiority of cerebroprotein was seen as compared to placebo at the primary end point.

Similarly in the citicoline group, Clark et al⁸ found that citicoline was not superior to placebo in stroke patients at the end of 12 weeks by using Barthel index scores (Barthel 95: placebo 77%; citicoline 69%). The observations in the above study were in accordance with our study results which showed citicoline not superior to cerebroprotein at the primary end point of treatment.

References

Conclusion

Stroke is a global health problem, both in developed and developing countries with hypertension being the most important risk factor. Hypertension is the important risk factor in the community, its management is far from satisfactory. Patients of ischemic and hemorrhagic stroke who received cerebroprotein, their mean

Barthel index score at baseline were 15 & 13 and at the 12 weeks score were 88 & 84 and Modified Rankin Scale at baseline were 4.64 & 4.80 and at 12 wks were 2.21 & 2.28 showing that patients receiving cerebroprotein hydrolysate had significant improvement in functional outcomes of the patients.

Patients of Ischemic & hemorrhagic stroke who received Citicoline mean Barthel index score at baseline were 13 & 12 and at the 12 weeks score were 85 & 81 and Modified Rankin Scale at baseline were 4.84 & 4.80 and at 12 wks were 2.28 & 2.72 showing that patients receiving Citicoline had significant improvement in functional outcomes of the patients.

Patients of ischemic and hemorrhagic stroke who received cerebroprotein their mean Barthel index score at baseline were 15 & 13 and at the 12 weeks score were 88 & 84 and Modified Rankin Scale at baseline were 4.64 & 4.80 and at 12 wks were 2.21 & 2.28 showing that patients receiving cerebroprotein hydrolysate had significant improvement in functional outcomes of the patients.

It was also observed that at the end of 6th weeks and the end of 12 weeks cerebroprotein hydrolysate was not superior to citicoline i.e at the primary end point of study cerebroprotein hydrolysate was equivocal with citicoline in terms of functional outcomes.

This study concludes that Cerebroprotein Hydrolysate is equivocal to Citicoline in terms of functional outcome of stroke.

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Conflict of interest: None declared

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