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Role of citicoline in the management of mild head injury

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Abstract : Mild head injuries can cause functional disabilities resulting in economic loss. **Post concussion syndrome** is seen in 15-45% of these patients. Cytidine-5'-diphosphocholine (citicoline) is known to improve cognitive dysfunction. This study was undertaken to evaluate the effect of citicoline on the number of working days lost and on post concussion symptoms following mild head injury in adults, in a randomized, prospective, single blind study. Following informed consent, adults with mild head injury (Glasgow coma score of 13-15, <24 hours) were randomized, using a computer generated randomization table, to receive either citicoline (1 gram/day) or placebo for one month. The parameters evaluated at one month were number of working days lost, Glasgow outcome score, presence of post concussion symptoms and the Rivermead head injury follow up questionnaire (**RHFQ**) scores. The groups were compared using Pearson chi-square test and fisher's exact test. The groups were well matched with respect to age, gender, GCS and mode of injury. There was no difference in the number of working days lost between the groups (P=0.061), Glasgow outcome score (P=0.281), Rivermead head injury follow up questionnaire scores (P=0.667) and the post concussion symptoms (P=0.3) between the groups. Compared to placebo, one gram/day of citicoline for one month in patients with mild head injury did not reduce either the number of working days lost, or the post concussion symptoms. There was no difference in the quality of life between patients taking citicoline and placebo.

Keywords: mild head injury, citicoline, post concussion symptoms.

INTRODUCTION

Mild head injury accounts for about 70%-90% of traumatic brain injuries[1,2]. Most of the patients do not require admission, outcome will be largely favourable in them and they return to the pretrauma level of functioning within a few days or weeks[3]. A small cohort of patients experience multiple, persistent ongoing symptoms following injury with significant functional disabilities[4]. **Mild head injuries** (**MHI**) can cause disabilities in young and productive people of the society causing economic loss[2].

Mild head injury is associated with multiple cognitive and behavioral sequels. Post concussion syndrome refers to a constellation of symptoms, which can be categorized into cognitive (decreased memory, attention and concentration), somatic (headache, fatigue, insomnia, dizziness, tinnitus, sensitivity to noise or light), and affective (depression, irritability and anxiety) groups[3,4]. Treatment of this condition is a subject of ongoing research. This also gains importance in view of increasing compensation/litigation problems arising in cases of mild head injury[5]. Many pharmacological agents like naltrexone, amphetamine, amantadine, and buspirone have been used to treat this condition with limited success[5,6,7,8]. Though most of the patients' experience these symptoms initially, follow up studies have shown that they resolve over a period of 3 months and certainly by 12 months in a majority of them[9].

Cytidine-5'-diphosphocholine is known to be beneficial in cerebral ischemia, stroke, severe traumatic brain injury (TBI), Alzheimer's and Parkinson's disease[10]. It reduces phospholipaseA2 stimulation, preserves the neuronal membrane component phosphotidylcholine, and it also reduces free fatty acid accumulation[10]. Levin conducted a preliminary study in 1991 and reported improvement in post concussion symptoms in a small cohort of patients with MHI, when treated with citicoline[11]. Though Citicoline is being used in moderate and severe head injury, the role of this drug in MHI has not been defined. There seems to be paucity in scientific data regarding the use of this drug in MHI Hence an attempt was made to systematically evaluate the role of citicoline in MHI.

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MATERIALS AND METHODS

This was a prospective, placebo controlled, randomized, single blind study conducted in a tertiary level hospital. Patients with MHI were recruited for the study if older than 15 years and presented within 24 hours of trauma. A written and informed consent was obtained from them or their available nearest relatives. Patients with systemic injuries, previous history of head injury and pregnancy were excluded. **Mild head injury** was defined as any blunt blow to the head with a GCS of 13-15, with or without loss of consciousness, with or without amnesia, and without focal neurological signs[4,12].

Study Protocol: Patients were randomized into drug and placebo groups using a computer generated randomization chart. A detailed history was obtained, injuries were recorded, and CT head was obtained only if necessary. One gram per day of citicoline was given to the patients in the drug group for a month. Placebo was given to the rest of the patients. Follow up data was obtained by telephonic interview after a period of 1-3 months. The Rivermead head injury follow up questionnaire (**RHFQ**) was used to assess the problems after MHI[5,13]. other outcome variables assessed were the number of working days lost and the Glasgow outcome scale (GOS) [14]. The number of working days lost included both the bed disability days and days of restricted activity. The presence or absence of post concussion symptoms at 1 month was noted.

Statistical analysis: Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS for windows). Between-group differences for continuous data were analyzed using the student's t-test for normally distributed independent samples. Between-group comparisons of proportions were made with Pearson chi-square test and fisher's exact test. A p-value d" 0.05 was considered statistically significant.

RESULTS

Sixty-two patients were included in the study. Of these, 29 were randomized to the drug group, and 33 to the placebo group. Among those injured, 40(65%) of them had a road traffic accident and 9(15%) had history of assault. Forty-three (69%) of them had loss of consciousness and 8(13%) had amnesia for the event. A CT head was obtained in one-fourth of the patients. Linear skull fracture was a common finding. Follow up data was obtained by telephonic interview after a period of 1-3 months. Forty-four of them could be followed up i e n=44(71%). **The patients not available for follow-up were no different from the one who were available in terms of age (p=0.228), sex (p = .375), type of injury (p=.520) and GCS (p=1.0).** Also the drug and the placebo groups were well matched in terms of age, gender (table-1), GCS (p=0.15) and mode of injury (p=0.889). Mean age at injury was 37 (+/-14.663) years in the drug group and 36(+/-17.797) years in the placebo group. Number of days lost ranged from1- 53 days. Mean number of working days lost was 27 days in the drug group (+/-18.8) and 18 days in the placebo group (+/-15.416). No statistical difference was noticed at analysis (T-test, p-0.061).None of our patients had to change their job due to MHI. Persistent headache was seen in 8 (36%) of the patients in the drug group and 6 (27%) of the patients in the placebo group. The analysis of the other post concussion symptoms was as given in the table 1. None of them were statistically significant at analysis. Analyzing the RHFQ, 15(68%) in the drug group and 18(82%) in the placebo group noticed no changes in quality of life before and after trauma (Independent sample T-test, p =0.859).the mean total score on RHFQ in the drug group was 1.75 and in the placebo group was 1.28(p=0.667). There was no difference in the 1 month GOS between groups (Chi-square test, p-0.281).

Table 1: Post concussion symptoms

Symptoms	Drug group (n=22)	Placebo group (n=22)	P value
Headache	8 (36%)	6 (27%)	0.747
Sleep abnormalities	5 (23%)	2 (9%)	0.412
Dizziness	7 (32%)	6 (27%)	1.000
Poor concentration	2 (9%)	1 (5%)	–
Personality changes	–	1 (5%).	–

DISCUSSION

Our finding is that Citicoline did not reduce the number of working days lost in cases of mild head injury. Also, there was no improvement in post concussion symptoms. Citicoline has been useful in the management of moderate and severe head injury, is known to hasten neurological recovery, reduce hospital stay and improve intellectual and motor deficits[10]. Previous study by Levin had 14 patients randomized to the drug and placebo group and were given one gram of citicoline and placebo for a month. One month post concussion symptoms

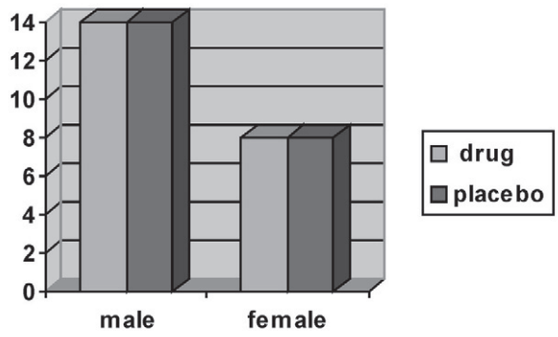

Fig 1: Comparison of the gender between the groups

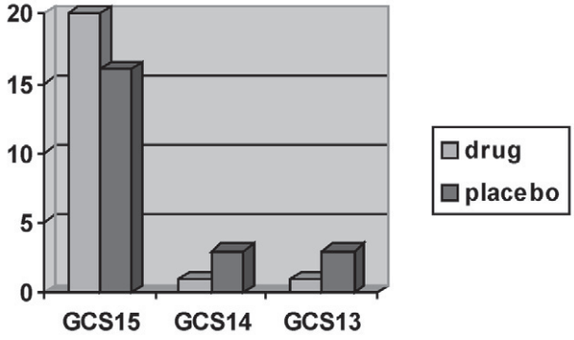

Fig 2: The GCS between the groups

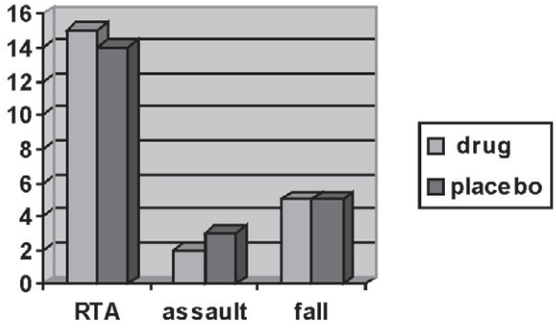

Fig 3: Mode of injury

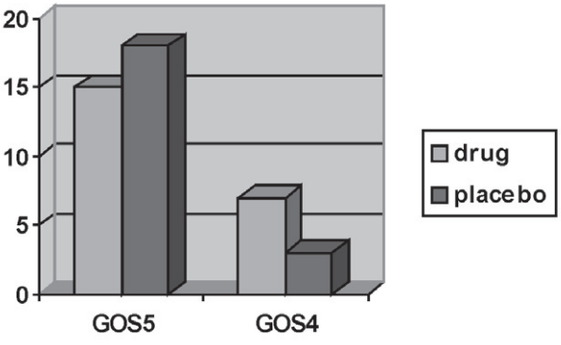

Fig 4: GOS between the groups

were evaluated, which revealed improvement in the drug group. Neuropsychiatric assessment for memory, fluency and attention had shown trend towards improvement[11]. Neuropsychiatric assessment was not performed in our patients, and as a result we may have missed some aspects of post MHI cerebral dysfunction and the effect of citicoline on such deficits. Majority of our patients were of GCS 15 and probably there is not much of a disarray in the pathway where citicoline works and the neurological damage is minimum in these minimally injured patients The present study involved more number of patients than the previous study but in the context of the large prevalence of MHI, further large sampled studies with long term follow-up is required.

CONCLUSION

Citicoline neither reduced the post concussion symptoms, nor the number of working days lost when used in mild head injury.

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