ORIGINAL ARTICLE

The use of cerebroprotein hydrolysate in dementia: A case series of 25 cases seen in a tertiary general hospital

Mosam Phirke, Avinash Desousa, Nilesh Shah, Sushma Sonavane, Anup Bharati

Department of Psychiatry, Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India

ABSTRACT

Background: Cerebroprotein hydrolysate (Cerebrolysin) is a pharmacological and neurotrophic agent that has been used widely in the management of various forms of dementia.

Purpose: The present paper presents a retrospective chart review of 25 patients with dementia visiting a tertiary general hospital psychiatry unit who received cerebroprotein hydrolysate as an add on treatment for dementia.

Materials and Methods: Twenty-five patients were administered 20 doses of cerebroprotein hydrolysate intravenously at a dose of 60 mg in 250 ml normal saline over 1-2 h after a test dose on 20 consecutive days. The cognitive assessment was done before the first injection and after the last dose using the Adenbrook's Cognitive Examination-Revised (ACER) and the Mini Mental Status Examination (MMSE).

Results: There was significant improvement in scores on the ACER and MMSE, although the final scores remained in the dementia range. None of the patients experienced any major side effects.

Conclusions: Cerebroprotein thus is a useful pharmacological option in the management of dementia and warrants further study and exploration.

Key words: Adenbrook's cognitive examination-revised, cerebrolysin, cerebroprotein hydrolysate, dementia, mini mental status examination

INTRODUCTION

Dementia is a neuropsychiatric disorder of late life manifesting as memory loss, cognitive dysfunction and behavioral symptoms that arise due to a neurodegenerative mechanism occurring in the neurons seen all together or independently.[1] Of the various types of dementia encountered in clinical practice, dementia of Alzheimer's type and dementia of vascular origin are the commonest varieties.[2] Dementia has a significant impact on the wellbeing and quality of life of elder patients and the caregivers who look after these patients.[3] Currently, most studies and meta-analyses show only a modest efficacy for the use of anticholinesterases and other similar agents recommended to alter the course or progression of Alzheimer's disease.[4] Cerebroprotein hydrolysate (Cerebrolysin, Lupin Pharma) is a newer pharmacological agent which is reported to be neurotrophic in nature and manufactured synthetically by the standardized enzymatic breakdown of lipid-free porcine brain proteins.[5] It has reported that cerebroprotein via certain mechanisms enhances neurogenesis, neuronal survival, and neuronal plasticity while also having a neuro-immunotrophic mechanism of action.[6] There are anecdotal case reports in the literature where cerebroprotein has been reported to be of some benefit in traumatic brain injury[7], certain forms of dementias[8] and extrapontine myelinosis.[9] In this report, we present the data of 25 patients who did not respond to anticholinesterases and were treated with cerebroprotein.

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MATERIALS AND METHODS

Patients and relatives were informed and educated about cerebroprotein hydrolysate, its pharmacological

Corresponding Author:
Dr. Avinash Desousa, Carmel, 18, St. Francis Road, Off S. V. Road, Santacruz West, Mumbai - 400 054, Maharashtra, India.
E-mail: avinashdes888@gmail.com

make up, dosage schedule and role in the management of dementia, along with the probable side-effects reported in the literature. Written informed consent was taken from every relative before starting the treatment as all our patients were not cognitively fit to consent for treatment. A test dose of cerebroprotein hydrolysate was given prior to stating the treatment and any allergic reactions were watched for. Twenty-five patients who were diagnosed as having dementia of various types based on Diagnostic and Statistical Manual for Classification of Psychiatric Disorders-IV TR criteria[10] who were following up in outpatient department were administered 60 mg equivalent of cerebroprotein hydrolysate intravenously as a slow infusion in 250 ml of normal saline over 1-2 h once daily for 20 consecutive days as inpatients. In our institution an intravenous therapy or intramuscular therapy like cerebroprotein is given in an inpatient setting. Admission is done for the ease of the patient and observation of any untoward effects like drug allergy etc., that may have arisen. The medication was made available to the patients at half the market price through a non-governmental organization in the institution. The patient's cognitive assessments were done using the Adenbrook's Cognitive Examination-Revised (ACER)[11] and Mini Mental Status Examination (MMSE).[12] These scales were administered twice viz. prior to starting cerebroprotein hydrolysate therapy and at the end of the course of 20 injections to assess the outcome. Author 1 did the initial rating and Author 5 did the final rating, but no blinding was followed. Patients who wished to continue the therapy further were offered medication at the same concessional rate and had the option of doing so. If they wished to continue therapy, the second course of 20 injections was offered after a gap of 1-month. The second course was also offered in an inpatient setting and not considered for the present analysis. Most patients were on concomitant medication for other neuropsychiatric symptoms. Most of the patients were on concomitant medication as well. 21 patients (84%) were on donepezil 5 mg/day, 4 were on quetiapine 25-50 mg at night for insomnia and 3 were on risperidone (2-3 mg per day) for aggressive behavior and anger. All these medications were started and were being taken by the patients for at least 6-8 weeks prior to the start of cerebroprotein therapy. Sixteen patients were on antihypertensive medications (telmasartan, amlodipine, and losartan) while 6 were on oral hypoglycemic agents (metformin and pioglitazone).

This retrospective study was discussed in the department review committee.

RESULTS

Majority of the patients were male (21 out of 25). All patients were aged above 65 years with the age range being 68-89 years and the mean age being 77.44 (standard deviation [SD]-5.42) years. A majority of patients had mixed dementia (Alzheimer's + vascular) (n = 12; 48%). Seven patients had pure vascular dementia while 6 had Alzheimer's dementia. The mean ACER scores at the start of therapy was 14.92 (SD = 4.04; range 9-22) and at the end of the course of therapy was 35.32 (SD = 5.46; range 22-43) [Table 1]. The mean MMSE scores at the start of therapy was 11.48 (SD = 1.36; range 10-14) and at the end of therapy was 18.84 (SD = 1.4; range 16-21) [Table 1]. The changes in ACER scores (t = 26.43, df = 23, $P < 0.0001$) and MMSE (t = 25.86, df = 23, P = 0.0001) were statistically significant.

It is worthwhile noting that the changes in scores were modest and cannot be said to have a major change in cognitive abilities of the patient, but there were certain areas of improvement that were appreciated by the relatives. Four patients regained bladder control, which was a big relief to the caregivers while aggression and anger reduced markedly in 2 patients each. One patient who was highly disinhibited and used to disrobe in public stopped that particular behavior while another patient who was sarcastic and used to pass hurtful comments (post the onset of dementia) stopped doing the same. No major side-effects were noted in any of the patients. Few patients complained of mild dizziness immediately after the injection which subsided within half an hour of the injection, and no medications were given to counter the same. The episodes of dizziness happened in the same patients and happened only during the first 3 injections. Only one patient developed a mild fever after the first injection, which was managed by Paracetamol alone. He then continued the further course uneventfully.

DISCUSSION

Various forms of dementia are collectively responsible for increased morbidity and mortality in the geriatric population.[13] Cerebroprotein hydrolysate is the first drug with neurotrophic factors which are small proteins that exert survival promoting and trophic action on neuronal cells.[14] It consists of short biological peptides, which act like endogenous neurotrophic factors. Neurotrophic activity can be detected up to 24 h after a single injection.[15] It is the only medication indicated

Table 1: Analysis of the 25 patients treated with cerebroprotein

Case number	Age	Sex	Dementia subtype	Time of assessment	Change seen (ACER)	Change seen (MMSE)	Major area of change
1	74	Male	Vascular	Beginning	10	11	Cognition
				End point	24	18	
2	77	Male	Alzheimer's	Beginning	12	10	Cognition
				End point	33	19	
3	73	Male	Vascular	Beginning	13	10	Cognition
				End point	34	17	Bladder control
4	68	Male	Vascular	Beginning	15	13	Cognition
				End point	39	18	Aggression
5	70	Male	Mixed	Beginning	11	12	Cognition
				End point	34	18	
6	82	Male	Mixed	Beginning	20	14	Cognition
				End point	43	20	Disinhibition
7	83	Male	Alzheimer's	Beginning	11	11	Cognition
				End point	29	16	
8	81	Female	Alzheimer's	Beginning	12	12	Cognition
				End point	31	19	Bladder control
9	79	Male	Mixed	Beginning	13	12	Cognition
				End point	33	21	
10	77	Male	Mixed	Beginning	9	10	Cognition
				End point	22	17	
11	87	Male	Mixed	Beginning	10	10	Cognition
				End point	28	18	Anger
12	86	Male	Mixed	Beginning	17	12	Cognition
				End point	37	18	Sarcasm
13	89	Male	Mixed	Beginning	19	14	Cognition
				End point	41	20	
14	78	Female	Vascular	Beginning	19	11	Cognition
				End point	37	19	Self-care
15	74	Female	Vascular	Beginning	12	10	Cognition
				End point	34	19	
16	76	Male	Alzheimer's	Beginning	23	13	Cognition
				End point	38	20	
17	77	Male	Vascular	Beginning	22	13	Cognition
				End point	40	19	
18	72	Male	Mixed	Beginning	12	11	Cognition
				End point	33	18	Bladder control
19	70	Male	Mixed	Beginning	16	10	Cognition
				End point	39	20	Anger
20	72	Male	Mixed	Beginning	18	12	Cognition
				End point	43	20	Aggression
21	76	Male	Mixed	Beginning	10	9	Cognition
				End point	35	17	Bladder control
22	77	Female	Vascular	Beginning	13	12	Cognition
				End point	38	20	
23	78	Male	Alzheimer's	Beginning	10	10	Cognition
				End point	37	19	
24	79	Male	Alzheimer's	Beginning	12	12	Cognition
				End point	40	20	Sleep
25	81	Male	Mixed	Beginning	15	13	Cognition
				End point	41	21	

ACER: Adenbrook's cognitive examination-revised, MMSE: Mini mental status examination

in dementias that acts at a neuronal level unlike others that act at neurotransmission and neurotransmitter levels. In our case series, we continued the medications that patients were on and improvement that was not noticed earlier was seen after starting cerebroprotein therapy. We were also surprised to see improvement in areas of bladder control (4 cases), anger, aggression, sarcasm and disinihbition that was not seen so far in these cases. Whether this was due to cerebroprotein or due to spontaneous remission shall remain a matter of debate. We agree that the changes in cognition and memory seen with cerebroprotein was mild to moderate and yielded scores within the dementia range itself, but still the change in scores were noteworthy. No major side-effects were seen in our case series unlike that reported by others which included headache, nausea,

dizziness, vomiting, and flushing.[16] Cerebroprotein is currently available in an intramuscular variant for ease of administration and earlier was available in an intravenous formulation alone. It is worthwhile that a combination of this drug with the other current available treatments in dementia be further explored in clinical practice. Further longitudinal studies with large groups of patients of varied subtypes of dementia are warranted.

The study is marred by its limitations as it was restricted to 25 patients in a case series rather than trial format. The study was an open one and no blinding was done. There was no control group for the study as well. The raters are not being blind to the assessments could have induced an element of bias in the final rating.

REFERENCES

1. Valenzuela MJ, Sachdev P. Brain reserve and cognitive decline: A non-parametric systematic review. Psychol Med 2006;36:1065-73.
2. Dewey ME, Saz P. Dementia, cognitive impairment and mortality in persons aged 65 and over living in the community: A systematic review of the literature. Int J Geriatr Psychiatry 2001;16:751-61.
3. Etters L, Goodall D, Harrison BE. Caregiver burden among dementia patient caregivers: A review of the literature. J Am Acad Nurse Pract 2008;20:423-8.
4. Plosker GL, Gauthier S. Cerebrolysin: A review of its use in dementia. Drugs Aging 2009;26:893-915.
5. Hartbauer M, Hutter-Paier B, Skofitsch G, Windisch M. Antiapoptotic effects of the peptidergic drug cerebrolysin on primary cultures of embryonic chick cortical neurons. J Neural Transm 2001;108:459-73.
6. Bae CY, Cho CY, Cho K, Hoon Oh B, Choi KG, Lee HS, *et al.* A double-blind, placebo-controlled, multicenter study of Cerebrolysin for Alzheimer's disease. J Am Geriatr Soc 2000;48:1566-71.
7. Karia S, Mahajan PT, Shah N, Sonavane S, De Sousa A. Cerebroproteinhydrolysate in traumatic brain injury. Mednifico J 2014;2:34-5.
8. Karia S, Majlikar R, De Sousa A, Shah N. Cerebroproteinhydrolysate in extra pontine myelinosis: A case report. Int J Sci Res Publ 2014;1:1-2.
9. Panisset M, Gauthier S, Moessler H, Windisch M, Cerebrolysin Study Group. Cerebrolysin in Alzheimer's disease: A randomized, double-blind, placebo-controlled trial with a neurotrophic agent. J Neural Transm 2002;109:1089-104.
10. American Psychiatric Association. Diagnostic and Statistical Manual for Classification of Psychiatric Disorders. 4th ed. Text Revised (DSM-IVTR). New York: American Psychiatric Publishing; 2000.
11. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The Addenbrooke's Cognitive Examination Revised (ACE-R): A brief cognitive test battery for dementia screening. Int J Geriatr Psychiatry 2006;21:1078-85.
12. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
13. Agüero-Torres H, Fratiglioni L, Guo Z, Viitanen M, Winblad B. Mortality from dementia in advanced age: A 5-year follow-up study of incident dementia cases. J Clin Epidemiol 1999;52:737-43.
14. Xiao S, Yan H, Yao P. The efficacy of cerebrolysin in patients with vascular dementia: Results of a Chinese multicentre, randomised, double-blind, placebo-controlled trial. Hong Kong J Psychiatry 1999;2:13-9.
15. Plosker GL, Gauthier S. Spotlight on cerebrolysin in dementia. CNS Drugs 2010;24:263-6.
16. Wei ZH, He QB, Wang H, Su BH, Chen HZ. Meta-analysis: The efficacy of nootropic agent Cerebrolysin in the treatment of Alzheimer's disease. J Neural Transm 2007;114:629-34.

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