

CASE REPORT

A Case Report on the Use of An Acetylcholinesterase Inhibitor (Donepezil) in Traumatic Brain Injury

GS Samuel; MBBS, MRCP (UK), YS Ng; MBBS, MRCP (UK)

Department of Rehabilitation Medicine, Block 6 Level 9, Singapore General Hospital, Outram Road Singapore 169608

SUMMARY

Traumatic Brain injury (TBI) is one of the most common causes of death and disability worldwide, with recent interest in the use of cholinomimetics in the treatment of TBI patients for cognitive impairments. Our patient who suffered TBI was started on a trial of an acetylcholinesterase inhibitor (Donepezil) for five weeks. Cognitive and memory testing with the Mini-Mental State Examination (MMSE) and Functional Independence Measurement (FIM) showed some degree of improvement: The three item recall component of MMSE improved and the FIM Memory score increased from 1 (Complete dependence) to 6 (Functional independence). Subjective assessment of his behaviour in the ward also showed improvement. This suggests that donepezil may help improve memory and behaviour of moderately severe traumatic brain injury patients, although more research in this direction should be undertaken.

KEY WORDS:

Traumatic brain injury, acetylcholinesterase inhibitor, donepezil, memory, cognition.

INTRODUCTION

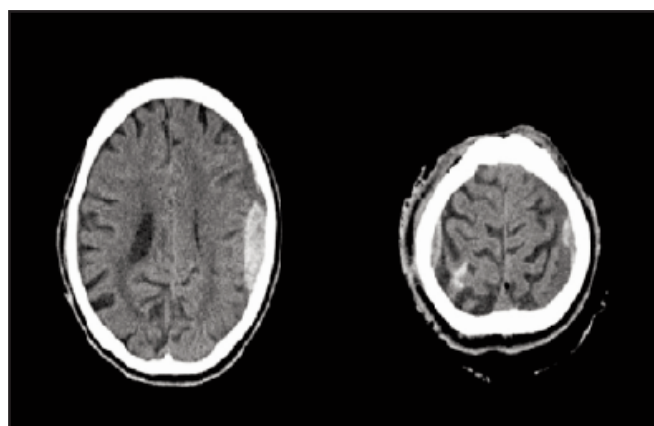
Traumatic Brain injury (TBI) is one of the most common causes of death and disability worldwide¹. Advances in neurosurgical intervention and critical care reduce fatalities but brings significant challenges of patients with cognitive deficits needing long-term care¹. We describe one such case below and review the use of cholinomimetics in treatment of cognitive impairments.

Background

Our patient is a 75 year old retired Chinese man who was independent in his activities of daily living (ADLs) prior to TBI. He is left lobe dominant. He has diabetes mellitus and a previous left striatocapsular lacunar infarct with good functional recovery. Past medical records showed he had no significant limb weakness or cognitive deficits; He had mild receptive dysphasia only.

His TBI resulted from repeated blunt head trauma assault with a chair. He was conscious on arrival in A&E and his Glasgow Coma Scale (GCS) Score was 11, indicating moderately severe of TBI. Emergent CT demonstrated multiple intracranial haematomas with mass effect particularly over the left fronto-temporo-parietal region. This is illustrated in Figures 1. He had subsequent bilateral

burrhole surgery to relieve raised intracranial pressure. Multiple skull fractures were treated conservatively.



Figures 1. Computed Tomography of the initial injury: The image on the left demonstrates a left fronto-temporo-parietal haematoma with mass effect at the level of the lateral ventricles. The image on the right shows a left parietal subdural haematoma and a right epidural haematoma near the vertex.

He was transferred to a dedicated rehabilitation unit after 44 days of acute neurosurgical care including a lengthy stay in the neurological intensive care unit for treatment of post-operative pneumonia and weaning from orogastric tube feeding in view of the multiple facial fractures.

Neuropharmacological Intervention

Donepezil (An acetylcholinesterase inhibitor) was started approximately eleven weeks after the initial injury and continued for five weeks total duration. We started at 5 milligrams (mg) of donepezil per day as a night dose during the first week. Donepezil was then increased to 10 mg per day for 4 more weeks.

There were no adverse effects reported, specifically: Nausea, dry eyes or constipation. Weekly checks of serum electrolytes were normal.

Progress in Rehabilitation

We used the mandarin version of the Mini Mental State Examination (MMSE) to assess general cognition. The MMSE significantly correlates with storage and recall aspects of memory².

This article was accepted: 2 May 2013

Corresponding Author: Geoffrey Samuel,, Department of Rehabilitation Medicine, Block 6 Level 9, Singapore General Hospital , Outram Road Singapore 169608 Email: samuelgeoffrey23@gmail.com

Ability to perform daily functional tasks was assessed using the Functional Independence Measurement (FIM). The FIM is an 18 item assessment tool of general Activities of Daily Living (ADL) performance ranging from 1 (Complete dependence) to 7 (Full independence) for a given task. The FIM score has a motor domain (13 items) and a cognitive domain (5 items)³. Outcomes were scored before and after administration of donepezil.

Our patient improved from a total FIM score of 81 before treatment (Denoting moderate ADL assistance) to a score of 101 after (Indicating minimal care needed). Table 1 illustrates the cognitive FIM score over the duration of our patient's rehabilitation admission. Of note, the memory FIM score improved from 1 to 6. The most gain was after the period of starting donepezil with an improvement of 3 points from week 9 to 12.

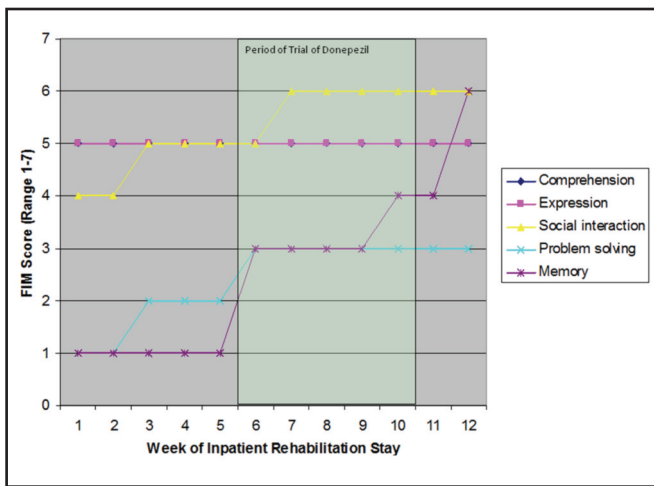


Table 1. Weekly Cognitive FIM score charted by a multidisciplinary team. A score of 6 and above indicates functional independence for that ADL; 5: Supervision; 4: Minimal Assistance; 3: Moderate assistance; 2: Maximal assistance; 1. Complete Dependence.

The MMSE score at the start of treatment was 21 out of 28, and the score at the end of treatment was 20. The one point decrease in the post treatment score is attributable to the orientation and calculation components of the MMSE.

Subjectively, our patient's behaviour improved two weeks after donepezil initiation. By Week 5 of treatment with donepezil, he was able to ambulate with supervision to the pharmacy. He could recall a list of three items after a 10 minutes interval (He previously could not perform this task). Undesirable behaviour such as irritability was also reported to be decreased.

Our patient's behaviour improvements were sustained after discontinuing donepezil for the remaining 2 weeks of inpatient rehabilitation and at outpatient clinic review 2 months later. His MMSE score 2 months after discharge was 21 and memory FIM score was 6. His caregiver commented that our patient's behaviour remained much as it was at the point of discharge.

DISCUSSION

Traumatic brain injury has 2 components- the initial mechanical trauma and secondary injury from dysregulation of neurotransmitters. Treatment with neuropharmacological agents is directed mainly at controlling this second aspect which often is associated with behaviour and memory issues in the recovery of patients. The medial temporal lobe and hippocampus are the regions of the brain important in the formation of memory and are abundant in cholinergic receptors. Thus the choice of an anticholinesterase inhibitor to increase brain acetylcholine levels.

A review of cholinomimetics for the treatment of cognitive impairment following TBI suggests that donepezil may be effective in improving cognition⁴. The suggested minimal efficacious dose of donepezil is 5mg daily^{4,5}. Donepezil's effect is dose dependent and studies have reported better response at 10mg daily dosing^{4,5}. Steady state distribution is reached in tissues by 14 to 21 days of initiation of donepezil therapy⁴. Thus a trial of five weeks total duration would be adequate to assess the effects of donepezil on our patient's memory, cognition and behaviour.

Over the course of his 12 week stay in rehabilitation, our patient's memory FIM score improved from 1 to 6. The most gain was after the period of starting donepezil with an improvement of 3 points from the fourth week of starting donepezil. The overall gain in memory is significant and connotes clinical improvement from total assistance with memory tasks to a level of independent functioning. Differentiating between the natural progression of our patient's recovery versus the benefit from donepezil is difficult. Nonetheless, given the more rapid improvement in his memory component after starting donepezil, it is possible that adding donepezil may have contributed to his memory improvement.

Although our patient's MMSE showed no overall significant change over the course of our patient's inpatient rehabilitation stay, the 3 item recall component was better after treatment than before.

Extrapolating the results for our patient, it is possible that use of anticholinergic agents may benefit patients with moderate TBI in terms of their memory and behaviour. These results seem present even if therapy is started late in the course of treatment.

Supporting the above conclusion, meta-analysis on the use of donepezil in the treatment of TBI yielded the following results: 5 studies examined donepezil (Using small sample sizes of 4-26 patients) of mild, moderate or severe TBI patients. Treatment with donepezil showed significant improvements in objective assessments of attention, memory and general cognition⁵.

CONCLUSION

This case study illustrates the sequelae of cognitive and behavioural deficits suffered by TBI patients and possible intervention to ameliorate this. More research needs to be

done to investigate the efficacy of treatment with cholinomimetic agents but the initial data is promising.

REFERENCES

1. Lee KK, Seow WT, Ng I. Demographical Profiles of Adult Severe Traumatic Brain Injury Patients: Implications for Healthcare Planning. *Singapore Med J* 2006; 47(1):3 1-36.
2. Lei F, Chong MS, Lim WS, Ng TP. The Modified Mini-Mental State Examination test: normative data for Singapore Chinese older adults and its performance in detecting early cognitive impairment. *Singapore Med J* 2012; 53(7): 458.
3. Dodds TA, Martin DP, *et al.* A validation of the functional independence measurement and its performance among rehabilitation inpatients. *Arch Phys Med Rehabil* 1993 May; 74: 531-6.
4. Whitlock JA Jr. Brain injury, Cognitive Impairment, and Donepezil. *J Head Trauma Rehabil.* 1999 Aug; 14(4): 424-7.
5. Wheaton P, Mathias JL, Vink R, *et al.* Impact of Pharmacological Treatments on Cognitive and Behavioral Outcome in the Postacute Stages of Adult Traumatic Brain Injury: A Meta-Analysis. *Journal of Clinical Psychopharmacology* Volume 31, Number 6, December 2011: 745-757.