Memantine improves attention and verbal episodic memory in Parkinson’s disease dementia and dementia with Lewy bodies: A double-blind, placebo-controlled, multicentre trial

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BACKGROUND

- The CDR System is an integrated set of automated tests of attention and memory designed for repeated use in clinical trials.
- The system has identified a characteristic profile of attentional impairment including notable fluctuations which are shared by patients with dementia with Lewy bodies and Parkinson’s disease dementia (1).
- The current consensus guidelines for diagnosis of dementia with Lewy Bodies (DLB) and Parkinson’s disease dementia (PDD) identify deficits to attention as core features in both conditions, and cite the CDR System data (2,3).
- In the major therapeutic trials to date in both dementias, the CDR System has detected significant benefits with rivastigmine on various aspects of attention (4-7).
- The present study evaluated the effects of memantine in DLB & PDD.

METHODS

- This was a parallel group, double-blind, placebo-controlled, multicentre trial of memantine.
- 21 DLB and 30 PDD patients were assessed prior to dosing and again at 12 and 24 weeks.
- CDR System tests of attention (simple and choice reaction time) and word recognition (immediate and delayed) were administered.
- The tasks were secondary measures and not included in the original study publication (8).

RESULTS

- Compared to placebo, memantine significantly improved choice reaction time (CRT) and the accuracy of both immediate and delayed word recognition (all p<0.02); with Cohen’s d effect sizes of between 0.56 and 0.57.
- The improvement in CRT was accompanied by a trend for improved accuracy on the task, and speed was numerically improved with memantine on the word recognition tasks.
- At baseline, compared to healthy age-matched controls, patients with DLB and PDD showed deficits to CRT and the recognition accuracy scores.
- Memantine reduced these initial deficits by between 45% and 47%.
- The analysis models included a term for the interaction of type of dementia with effects of treatment, but none of these approached significance for any measure. Thus the improvements with memantine occurred in both DLB and PDD.

CONCLUSIONS

- These are the first therapeutic improvements with memantine having clinically relevant effect sizes in either DLB or PDD on validated automated cognitive tests of attention and episodic memory.
- They directly support the improvement in the primary study outcome, the clinical global impression of change (CGIC) of 0.7 points, which had an effect size of 0.52 (8).
- Every measure from every CDR System test moved in the direction of improvement with memantine.
- These data support the rationale in the therapeutic dementia trials of using validated cognitive tests with established sensitivity for the detection of beneficial treatment effects.
- The analysis models included a term for the interaction between type of dementia with effects of treatment, but none of these approached significance for any measure. Thus the improvements with memantine occurred in both DLB and PDD.

REFERENCES


CONCLUSION

- Memantine improved attention and verbal episodic memory in Parkinson’s disease dementia and dementia with Lewy bodies, showing clinically relevant effect sizes in both conditions. This was a parallel group, double-blind, placebo-controlled, multicentre trial. Lancet Neurology 2009; 8: 613–618.