Long Term Clinically Meaningful Change In Verbal Repetition Following Cholinesterase Inhibitor Treatment Can Be Detected Early

Kenneth Rockwood,1,2 Matthew Richard1 Arnold Mitnitski1,2 1DGI Clinical Inc., Halifax, NS Canada; 2 Dalhousie University, Halifax NS Canada.

BACKGROUND

Verbal repetition (repetitive stories, questions) is a common, troubling, but comparatively under-studied problem in people with Alzheimer’s disease (AD). Clinically meaningful change in verbal repetition following cholinesterase inhibitor treatment can track the overall treatment effect.1 Exactly when in the treatment course such an effect might be discerned is less clear. Here, we evaluated how soon after treatment might a change in verbal repetition be identified, and whether the effect was sustained.

OBJECTIVES

1. To evaluate to what extent can early user reporting indicate change in verbal repetition?
2. Are any early impacts sustained?

METHODS

452 patients and their care partners at a Canadian tertiary care Memory Clinic were asked to target 4 verbal repetition (repetitive stories, questions) as a goal area. At each visit, symptoms were tracked using a 7 point scale anchored at 0 (no change) to +/-3 (very much better/worse).

Time-to-event (improvement/worsening) was defined as the time from entry to the first non-zero score. 128 patients tracked both change in symptoms and the Mini-Mental State Examination (MMSE) score and had a median time of 456 days until final follow-up visit. The time-to-event distribution was calculated using the Kaplan-Meyer estimator. Between group (improved/ worsened) differences were calculated using the log rank test, significant at p<0.05.

Severity of impairment was defined by clinical diagnosis ("Cognitive Impairment, Not Dementia" – CIND, Mild Dementia, Moderate Dementia) and the Global Deterioration Scale. Clinically meaningful MMSE change was defined as ± 5 points.

RESULTS

Table 1. Sample Demographics

| Age | % Female | 55% | MMSE | 23.1 (4.5) | Stage | 3.9 (1) | PSMS | 7.3 (3.9) | ADL | 15.2 (5.9) |

Table 2. Contingency tables of change in verbal repetition in relation to last visit change (top, n=128) and in relation to MMSE change (bottom, n=128). Median time interval between first and last visits was 244 days.

• Patients who reported improvement in verbal repetition were found to do so significantly sooner than patients who reported worsening of the symptom (p=0.001, log rank test)

Fig 1. Distribution of initial tracking score changes

Fig 2. Time until initial tracking score change for those who improved (blue, n=80) and those who worsened (red, n=48)

Fig 3. Time until initial change in verbal repetition of those who improved (top) and those who worsened (bottom) by severity of cognitive impairment

CONCLUSIONS

1. The first indication of improvement or worsening in verbal repetition can shed light on a patient’s long- term condition. Amongst patients reporting worse verbal repetition, fewer than 25% will ever improve. Amongst patients reporting improved verbal repetition, two thirds will remain improved for a median of 456 days.

2. The longer a patient reports “no change” in their verbal repetition symptom, the higher the probability that their condition will ultimately become worse.

3. These patterns appear to hold at all initial grades of severity, from CIND to moderate dementia.

LIMITATIONS

Only CIND to Moderate dementia patients were analysed.

REFERENCES


ACKNOWLEDGEMENTS

The research is supported by the Canadian Institutes of Health Research (CIHR), the Fountain Innovation Fund of the QEII Foundation and the Dalhousie Medical Research Foundation. DGI is supported by the National Research Council-Industrial Research Assistance Program (NRC-IRAP), the Atlantic Canada Opportunities Agency (ACOA), and Innovateuk.