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RESEARCH LETTER

Rivastigmine in the treatment of dementia in Alzheimer's disease in adults with Down syndrome

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The neuropathology of Alzheimer's disease is reported to occur in virtually all adults over the age of 40 years with Down syndrome (DS). Studies confirm that age-specific prevalence rates of dementia in Alzheimer's disease (DAD) are markedly higher in the DS population than the general population—55% for those aged 60–69 years (Prasher, 1995). The widely accepted hypothesis for this association, is the affects of the triplication of the amyloid precursor protein gene on chromosome 21 and the ensuing 'amyloid-cascade theory'.

Although there is no cure for DAD, a number of anti-dementia drugs have been developed which may slow the rate of decline and in some cases improve symptomatology. These include donepezil and galantamine (anticholinesterase inhibitors), rivastigmine (an anticholinesterase and butyrylcholinesterase inhibitor) and memantine (a N-methyl-D-aspartate antagonist). Randomised controlled trials have demonstrated the efficacy of such drugs in the general population. Although there are reports highlighting the role of donepezil in DAD in the DS population (Kishnani *et al.*, 1999; Lott *et al.*, 2002; Prasher, 2004), there are no reports on the use of rivastigmine.

Medical records of patients with DS diagnosed as having DAD according to ICD-10 (WHO, 1993) criteria, seen in the Memory Clinic between January 2002 and December 2003 and treated with rivastigmine were audited. The diagnostic process involved a standard psychiatric interview with carers and the patient, the ICD-10 Symptom Checklist for Mental Disorders (WHO, 1994) to detect psychopathology, a mental state examination, haematological and biochemical screens and where necessary, magnetic resonance imaging to exclude intracranial pathology.

As per NICE (2001) guidance, monitoring was undertaken with standardized measures. Baseline assessments of: (i) global functioning was made using the Dementia Questionnaire for Mentally Retarded Persons (DMR); (ii) non-cognitive and behavioural problems, using the Neuropsychiatric Inventory (NPI) and (iii) changes in adaptive behavior, using the Adaptive Behavior Scale (ABS). These have been used in other research (Prasher, 2004). Rivastigmine was started at 1.5 mg twice daily and gradually increased up to 12 mg a day over 8-weeks. Repeat assessments using the three instruments took place at 6, 12 and 24 weeks.

The findings for the patients treated with rivastigmine ($n = 17$) were compared to findings of DS persons with DAD treated with placebo previously ($n = 13$; see Prasher *et al.*, 2002), called 'the untreated group' in this study. There was no statistically significant difference for age (53.2 years rivastigmine group *vs* 54.9 years untreated group), gender, severity of LD, residence and severity of AD.

There was deterioration on the global assessment for both groups over 24 weeks (see Table 1). The percentage change was less for the rivastigmine group (7.8%) compared to the untreated group (10.7%), but there was no statistically significant difference in the rate of decline ($F_{1,116} = 0.11$, $p = 0.74$). There was a greater than five-point decline in DMR scores in 53% of the untreated group compared to 35% of the

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Table 1. Baseline and study endpoint results for primary and secondary efficacy variables

Efficacy variable	Baseline total score		Endpoint total score		Change (%)
	Mean	SD	Mean	SD	
DMR-rivastigmine group	47.5	16.3	51.2	15.4	3.7 (7.8%)
-untreated group	58.2	16.9	64.4	14.2	6.2 (10.7%)
NPI-rivastigmine group	14.5	12.1	12.9	10.6	−1.6 (11.0%)
-untreated group	8.0	7.6	3.6	5.0	−4.4 (55.0%)
ABS-rivastigmine group	109.8	27.2	102.0	33.7	−7.8 (7.1%)
-untreated group	93.0	19.2	84.5	22.4	−8.5 (9.1%)

rivastigmine group. This suggests that fewer of the treated group had a clinically significant decline in global functioning. Both groups improved on NPI scores and there was no statistically significant difference in the rate of change ($F_{1,116} = 0.67, p = 0.4$). The rate of deterioration in adaptive behaviour in the untreated group (9.1%) compared to the rivastigmine group (7.1%) was greater, but this was not statistically significant ($F_{1,116} < 0.001, p = 0.98$). The commonest side-effects reported with rivastigmine were diarrhoea, fatigue, insomnia, nausea and vomiting.

Treatment of DAD in individuals with DS remains in its infancy stage. Rivastigmine is an anticholinesterase and butylcholinesterase inhibitor developed for the treatment of DAD. This study investigates the use of rivastigmine in adults with DS. In this study individuals treated with rivastigmine had less of a decline over 24 weeks in global functioning and adaptive behaviour compared to the untreated group. Although non-significant at the 5% level, this may be due to small sample size, rather than rivastigmine not being significantly effective. Evidence from randomized control trials in the general population and findings from this study would suggest that rivastigmine can be effective in people with DS who have DAD. Further research is required to investigate the long-term efficacy of rivastigmine, its efficacy compared to other anti-dementia drugs and its role in prevention of intellectual decline in well older adults.

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