BEST in Mental Health
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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

How effective are anti-dementia medications in treating patients with Down Syndrome suffering with Dementia?*

Clarification of question using *PICO* structure

Patients:	Patients with Down Syndrome suffering with dementia
Intervention:	Anti-dementia medications
Comparator:	Other or no intervention
Outcome:	All patient outcomes

*with particular interest in bradycardia, which can be caused by both Down Syndrome and anti-dementia medication

Plain language Summary

There is very little research evidence to say whether medications are successful for treating dementia in people with Down syndrome. More research should be completed to provide more information.

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Clinical and research implications

No definite clinical implications may be made based on the evidence presented in this BEST summary. There is very little evidence on pharmacological treatments for people with Down's syndrome and dementia. One good quality study found that memantine is not effective for this group of patients. The authors of this study stated that therapies that are beneficial for those with Alzheimer's disease may not be effective for those with Down's syndrome.

What does the evidence say?

Number of included studies/reviews (number of participants)

One systematic review (SR) (Mohan et al. 2009) and two randomised controlled trials (RCTs) (Hanney et al. 2012; Prasher et al. 2002) met the inclusion criteria for this BEST summary.

Main findings

The SR aimed to determine the effectiveness and safety of rivastigmine compared with placebo for people with Down's syndrome who develop Alzheimer's disease (Mohan et al. 2009). The authors searched for relevant randomised controlled trials up to October 2008, but no studies were identified that met the inclusion criteria for their review.

The RCT by Hanney et al. (2012) compared 10 mg memantine with placebo on cognition and function in 173 people older than 40 years' of age with Down's syndrome. After one year, there were no significant differences between the groups for any of the outcomes. Both groups showed a decline in cognition and function by 52 weeks. Eleven percent of participants in the memantine group and 7% in the control group experienced serious adverse events (p=0.33).

The pilot RCT by Prasher et al. (2002) compared 10 mg donepezil with placebo in 30 patients with Down's syndrome and Alzheimer's disease. After 24 weeks, there were no significant differences between the groups for cognition and functioning. Behavioural problems measured using the Neuropsychiatric Inventory showed less improvement in the donepezil group compared with the placebo group (p=0.03), but no significant differences were found when the Adaptive Behavior Scale was used. Fifty percent of participants in the donepezil group 20% in the control group experienced serious adverse events (p value not reported).

Authors' conclusions

Mohan et al. (2009) stated that they could not make recommendations, but that well-designed adequately powered studies are required.

Hanney et al. (2012) concluded that memantine is not an effective treatment for people older than 40 years with Down's syndrome.

Prasher et al. (2002) concluded that "there is some possible efficacy in the treatment of mild to moderate Alzheimer's disease…although the sample size of this study was too small for statistical significance. It is recommended that donepezil, with the appropriate precautions, should be considered for the treatment of AD in adults with DS as deemed by a specialist".

Reliability of conclusions/Strength of evidence
The search strategy and data collection methods in the SR by Mohan et al. (2009) were well-conducted.

The RCT by Hanney et al. (2012) was considered to have a low risk of bias so that the results from this study are likely to be reliable.

The RCT by Prasher et al. (2002) was considered to have a high risk of bias. The evidence presented does not appear to support the author's conclusion and recommendations.

What do guidelines say?

Neither National Institute for Health and Care Excellence (NICE) nor Searching of Scottish Intercollegiate Guidelines Network (SIGN) guidelines comment on the effectiveness of anti-dementia medications in treating patients with Down Syndrome suffering with Dementia.

Date searches conducted: 25/03/2015
Date answer completed: 10/11/2016

References

Systematic reviews
Mohan, M., Bennett, C., & Carpenter, P. K. (2009). Rivastigmine for dementia in people with Down syndrome. *The Cochrane Library*.

Randomised controlled trials
Hanney, M., Prasher, V., Williams, N., Jones, E. L., Aarsland, D., Corbett, A., ... & Ballard, C. (2012). Memantine for dementia in adults older than 40 years with Down's syndrome (MEADOWS): a randomised, double-blind, placebo-controlled trial. *The Lancet*, *379*(9815), 528-536.

Prasher, V., Huxley, A., & Haque, M. S. (2002). A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Down syndrome and Alzheimer's disease—pilot study. *International Journal of Geriatric Psychiatry*, *17*(3), 270-278.

Results

Systematic reviews

Author (year)	Search date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Mohan et al. (2009)	April 2015	*Participants*: People with Down Syndrome (DS) diagnosed with dementia using standardised measures. *Intervention*: Any dose of oral Rivastigmine. *Comparator*: Placebo *Outcome*: -Primary outcomes: (i) Global functioning and cognition; (ii) behavioural problems (both outcomes measured by validated scales); (iii) daily functioning, measured by carer feedback; (iv) adverse events (e.g. side-effect from medication); (v) Hospitalisation/institutionalisation. -Secondary measures: (i) Reduction in carer's stress; (ii) economic outcomes. *Study design*: Systematic review of randomised controlled trials.	0	No studies met the inclusion criteria for this review.	Low

Randomised controlled trials

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Prasher	*Participants*: Individuals with DS and mild-	31	Over the 24 week study period, there was no statistical	High (due to low

et al. (2002)	moderate Alzheimer's Disease (AD), as measured by the Diagnostic Research Criteria (DCR-10), and the International Classification of Disease (ICD). Medical records and physical, haematological, biochemical examinations and thyroid status screening were reviewed to exclude other possible causes of cognitive decline. *Intervention*: Donepezil over 24 weeks; 5mg/day for weeks 1-4, then 10mg/day for weeks 5-24 (minus 3 patients who remained on 5mg/day due to adverse side effects). *Comparator*: Placebo over 24 weeks (equal dosage to Donepezil). *Outcome*: -Primary outcome: Global functioning (intellectual, social and behavioural), as measured by the Dementia Questionnaire for Mentally Retarded Persons (DMR). -Secondary outcomes: (i) Cognitive function, as measured by the Severe Impairment Battery (SIB); (ii) behavioural problems measured by the Neuropsychiatric Inventory (NIP); and (iii) adaptive functioning as measured by the Adaptive Behavior Scale (ABS).	randomised (27 included in the analysis)	difference between change in DMR scores between the intervention and control group (change in score in the donepezil group was 0.8 and 6.2 in the placebo group, p=0.22). Cognitive function as measured using the SIB was also not statistically significant between the groups (change in score in the donepezil group was -5.2 and -16.0 in the placebo group, p=0.06). Behavioural problems measured using the NIP showed less improvement in the donepezil group compared with the placebo group (change in mean total score in the donepezil group was -2.2 and -4.4 in the placebo group [decline in scores equates to a clinical improvement], p=0.03), but was not statistically significant when measured using the ABS (change in score in the donepezil group was -0.9 and -8.5 in the placebo group, p=0.51). Fifty percent of participants in the donepezil group 20% in the control group experienced serious adverse events (p value not reported).	power and small sample size)
Hanney et al. (2012)	*Participants*: Adults aged over 40 with DS, or of any age but with DS and diagnosed with dementia (by ICD-10). *Intervention*: Memantine 10mg/day over 52	173 randomised (88 to memantine	There were no significant differences between the groups for any of the outcomes evaluated. Both groups showed a decline in cognition and function by 52 weeks. Mean change in DAMES at 52 weeks (ITT analysis): memantine: -	Low

	weeks (with dosage increased over the first 8 weeks from 5mg/day). *Comparator*: Placebo (with equal dosage to Memantine). *Outcome*: -Primary outcome: Cognition and functioning, measured by the Down's Syndrome attention, memory and executive function scales (DAMES) and the ABS. -Secondary outcomes: (i) Overall improvement, measured by the Clinical Global Impression of Change Scale; (ii) Adverse events.	group and 85 to placebo group) (146 with data at 52 weeks)	4.9 (SD 32.9); placebo: -1.1 (SD 19.3). Mean change in ABS part I at 52 weeks: memantine: -10.7 (SD 37.1); placebo: -1.7 (SD 35.1). Mean change in ABS part II at 52 weeks: memantine: 1.0 (IQR -19 to 15); placebo: 0.0 (IQR -13 to 11). Mean global impression of change p value at 52 weeks was 0.21. 10 (11%) of participants in the memantine group and 6 (7%) in the control group experienced serious adverse events (p=0.33).	

Risk of bias

Systematic reviews

Author (year)	RISK OF BIAS				
	Inclusion criteria	Searches	Review process	Quality assessment	Synthesis
Mohan et al. (2009)	☺	☺	☺	NA	NA

Randomised controlled trials

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Prasher et al. (2002)	☺	☺	☺	☺	☺	☺
Hanney et al. (2012)	☺	☺	☺	?	☺	☺

☺ Low risk ☹ High risk ? Unclear risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
Guidelines			
NICE	down syndrome dementia	15	0
Systematic Reviews			
CDSR	#1 MeSH descriptor: [Dementia] explode all trees 3897 #2 MeSH descriptor: [Down Syndrome] explode all trees 316 #3 #1 and #2 15	15	0
Primary Studies			
EMBASE	12. EMBASE; DOWN'S SYNDROME/; 26756 results. 13. EMBASE; "Down* syndrome".ti,ab; 20993 results. 14. EMBASE; 12 OR 13; 29316 results. 15. EMBASE; memantine.ti,ab; 3479 results. 16. EMBASE; donepezil.ti,ab; 3552 results. 17. EMBASE; GALANTHAMINE/; 5679 results. 18. EMBASE; galantamine.ti,ab; 1603 results. 19. EMBASE; rivastigmine.ti,ab; 1867 results. 20. EMBASE; antidementia.ti,ab; 467 results. 21. EMBASE; 15 OR 16 OR 17 OR 18 OR 19 OR 20; 12347 results. 22. EMBASE; 14 AND 21; 106 results. 23. EMBASE; 22 [Limit to: (Clinical Trials Clinical Trial or Randomized Controlled Trial)]; 40 results.	40	2
PsycINFO	1. PsycInfo; DOWN'S SYNDROME/; 5261 results. 2. PsycInfo; "Down* syndrome".ti,ab; 3812 results. 3. PsycInfo; 1 OR 2; 5886 results. 4. PsycInfo; memantine.ti,ab; 1038 results.	28	1

	5. PsycInfo; donepezil.ti,ab; 1206 results. 6. PsycInfo; GALANTHAMINE/; 258 results. 7. PsycInfo; galantamine.ti,ab; 511 results. 8. PsycInfo; rivastigmine.ti,ab; 571 results. 9. PsycInfo; antidementia.ti,ab; 182 results. 10. PsycInfo; 4 OR 5 OR 6 OR 7 OR 8 OR 9; 2840 results. 11. PsycInfo; 3 AND 10; 28 results.		
CENTRAL	#1 MeSH descriptor: [Dementia] explode all trees 3897 #2 MeSH descriptor: [Down Syndrome] explode all trees 316 #3 #1 and #2 15	15	0

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