Review: hydergine leads to greater global improvement and greater improvement on comprehensive rating scales in dementia

Olin J, Schneider L, Novit A, et al. *Efficacy of hydergine for dementia*. (Cochrane Review, latest version 27 May 1998). In: *Cochrane Library*. Oxford: Update Software.

Question

In patients with possible dementia, is hydergine effective and what are the potential moderators of an effect?

Data sources

Studies were identified by searching the Cochrane Trials Register using the terms hydergine, ergoloids, ergoloid mesylates, dihydroergocristine, dihydroergocryptine, dihydroergotoxine, and dihydroergocornine; searching ELITE, SAMD, Medline, and EMBASE/Excerpta Medica using similar search terms; reviewing the bibliographies of published reviews; and by consulting with Sandoz Pharmaceutical Corporation.

Study selection

Studies were selected if they were randomised, double blind, placebo controlled trials evaluating the effectiveness of hydergine for >1 week treatment duration in patients with dementia or patients who had symptoms consistent with dementia. Additional selection criteria included specification of sample selection criteria, absence of other psychiatric disorders, specification outcome instruments, and sufficient statistical information to calculate an effect size between drug and placebo treatment groups using Cochrane Review Manager Software.

Data extraction

Data were extracted independently by 2 reviewers on study design, patient characteristics, intervention dose and duration, and outcome measures.

Main results

19 trials met the selection criteria. 12 trials provided data on global improvement and pooled results showed statistically signifi-

cant improvement in patients in the hydergine group (table). 9 trials provided data on change in scores on comprehensive rating scales and pooled results showed statistically significant improvement in those receiving hydergine (weighted mean difference 0.96, 95% CI 0.54 to 1.37). Hydergine was well tolerated by all patients in all trials. Subgroup analyses were done to determine the potential moderators of the effect of hydergine (age, sex, diagnosis, dose response, duration, and inpatient status). All subgroup analyses were statistically non-significant, except for possibly a greater effect size on global ratings associated with younger age (65–75 y).

Conclusion

In patients with possible dementia, hydergine leads to greater global improvement and greater improvement on comprehensive rating scales.

*Hydergine v placebo in patients with possible dementia (treatment lasted from 9 weeks to 15 months)**

Outcome	Weighted event rates		RBI (95% CI)	NNT (CI)
	Hydergine	Placebo		
Global improvement	60%	23%	103% (48 to 178)	3 (2 to 5)

*Abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.

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Commentary

This review by Olin *et al* was a brave undertaking. Hydergine studies span 40 years and number 142, eventually covering the period of development of trial design methodology. To find 19 studies of sufficient quality was a feat in itself, and the results are as valid as they could be (a good example of the way such reviews can be helpful).

The bottom line is that hydergine has some global effect, although the effect size is small and the number needed to treat is 3. We have heard this before. Donepezil data are remarkably similar—the difference now is that dementia studies use robust common designs with better measurement tools. Perhaps meta-analysis of newer drug studies will prove easier.

However, questions similar to those asked in older studies still remain. What does this small effect with large confidence intervals really mean? The answer is that we are not sure. Trials of drugs in dementia often show an effect in some patients. The situation will become clearer as we learn more about what to measure and which symptoms respond to treatment. The hydergine studies are not disease specific and use old outcome measures, but they suggest that hydergine has an effect in all dementias, implying a nootropic action. These drugs are licensed in some countries (eg, memantine in Germany) and used with good effect. It is therefore surprising that this drug has never really been used in the UK, where it has been licensed for years.

One explanation is that clinicians looking after these patients may not have been ready to use these treatment options 10 years ago. Those that were may have been unconvinced by the available evidence—a situation comparable to that of today?

Better outcome measures now exist. We need to use licensed products and do proper clinical research to evaluate the effect of the drugs on clinically meaningful outcomes. This review provides evidence that further research on hydergine is warranted. With the advent of biological markers outcomes will be clearer, but trial design and methodology may alter once again.

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