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SHORT REPORT

TREATMENT OF SENILE DEMENTIA WITH THYROTROPHIN RELEASING HORMONE AND CLOMIPHENE

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In a review article by Bloom (1982), neurotransmitters are seen to hold the key in future advancement in neurological disease. In senile dementia of Alzheimer type (SDAT), several neurotransmitter deficiencies have been identified and one of these (Oram *et al.*, 1982) showed diminished levels of thyrotrophin releasing hormone (TRH), gonadotrophin releasing hormone (LHRH) and somatostatin in the lumbar CSF of patients suffering from SDAT.

It was decided to give patients TRH and clomiphene (to raise cerebral levels of LHRH) to see if this improved mental function. Patients were selected with a moderate degree of memory impairment as judged by a score of between 4 and 7 out of 10 on the Modified Northwick Park test (Quereshi and Hodkinson, 1974). These patients had the typical progressive history and features of SDAT, displayed none of the typical traits associated with multi-infarct dementia, and obvious secondary causes such as myxoedema and low B12 were excluded. Permission was obtained from the patient and his closest relative, ethical approval from St George's Hospital and clinical trials exemption certificates were also obtained. Patients were required to come into hospital four days prior to the trial starting so that they could settle into the hospital and a pretrial mental test score could be obtained.

The different drug regimes were given over four weeks and then one week later a post-trial test score was performed. The drug regimes were given on a daily basis at 9.30 each morning from Monday to Friday and psychological testing occurred on the fifth day of each regime at 10.15 am. The weekly drug regimes were as follows:

1. Placebo tablet and i.v. injections (5 ml N/saline)
2. Clomiphene tablet (50 mg) and i.v. placebo injection
3. Placebo tablet and i.v. TRH (500 μg)
4. Clomiphene tablet (50 mg) and i.v. TRH (500 μg)

Only one patient could be included in the trial at any one time, since it required five and a half weeks' hospitalization. The high-pressure service commitment of the unit meant that the washout periods between regimes had to be very short (two days) and the post-trial score carried out only one week after all treatment had ceased. For this reason the number of participants was limited to 10.

The psychological tests were drawn from a standard battery of cognitive tests (Ravens matrices, Inglis, Wais and an orientation test). The mean cognitive scores for the 10 patients on the four different regimes are shown in Fig. 1.

Because of the skewed distribution of the data, it was decided to use non-parametric tests (Wilcoxon matched pairs signed-rank test) in the statistical analysis. There appears to be a weak (though not statistically significant) effect of treatment on cognitive scores when the double

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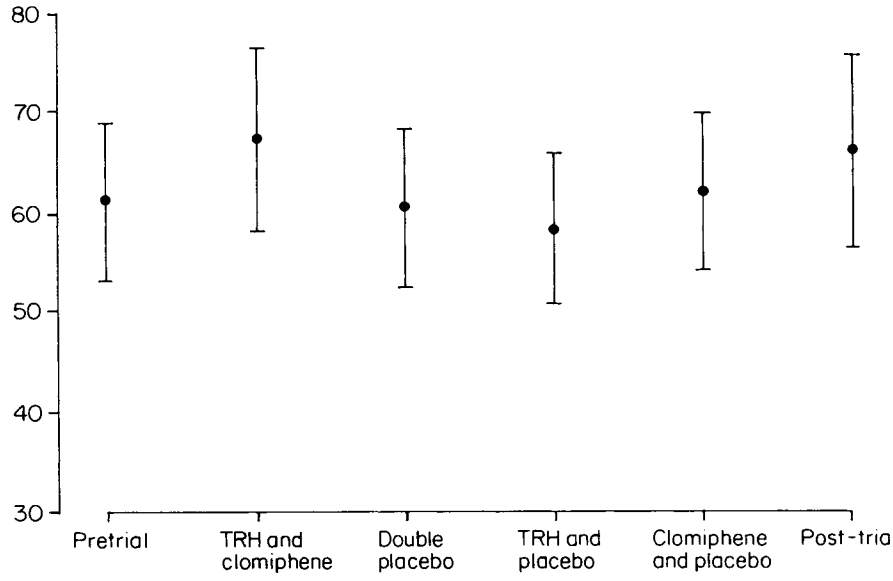

Fig. 1. Mean cognitive scores (and SEM) in 10 senile dementia patients in the neuropeptide treatment trial

active regime (mean ± SEM) 67·3 ± 9·2 is compared to the pretrial score 61·1 ± 7·9 ($p < 0{\cdot}069$) and double placebo regimes 60·7 ± 8·3 ($p < 0{\cdot}067$). A carryover effect could not be tested since treatment order needs to be taken into account, and in this trial it was completely random.

Treatment with this double active drug regime of TRH and clomiphene had no untoward side-effects and we feel the positive trend in cognitive function found in this trial merits further investigation. This would involve comparing only the one drug regime of TRH and clomiphene against placebo and using far greater numbers.

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