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A Validation Study of Nealbarbitone

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A preliminary study (Robin *et al.*, 1961) of twenty out-patients showed nealbarbitone to be a therapeutically useful drug. The following study was undertaken to validate this trial.

Method

Fifty consecutive out-patients suffering from anxiety states were treated in random order in a "double blind" trial with either nealbarbitone or amylobarbitone for a period of a month. An initial dose of 60 mg. t.i.d. of either drug was prescribed and this was increased to 120 mg. t.i.d., if clinically desirable, after two weeks. Seven patients on nealbarbitone and five on amylobarbitone received the higher dosage. The patients were interviewed and rated on an anxiety scale before commencing treatment, after two weeks, and after a month. Standardized actuarial data was collected on all patients admitted to the trial. The symptomatic picture of the patients treated resembled that of patients with anxiety reactions studied in two previous trials (Robin, 1959; Robin *et al.*, 1961) (Table I).

Table I

Distribution of Symptoms in Anxiety States

	Trial 1 (Robin, 1959)	Trial 2 (Robin *et al.*, 1961)	Trial 3
Total patients	21	20	50
	Percentage of Patients Affected		
Tremor	62	40	50
Fidgety	96	65	78
Muscle twitching	38	35	30
Headache	67	65	62
Muzziness or pressure	72	60	64
Tension, strung up, anxious, unrelaxed	100	100	100
Could scream or smash	77	70	56
Could cry	96	80	74
Can't get off to sleep	62	55	40
Sleep broken or restless	72	45	44
Dreaming more	53	20	34
Poor concentration	77	85	72
Loss of interest	67	65	62
Loss of pleasure	77	65	68
Fatigue: lassitude	77	80	72
Irritable or excitable	82	85	88
Worrying about trivialities	86	75	84
Ideas of reference	67	35	30
Phobias: insanity	53	40	30
Dry mouth	67	70	50
Loss of libido	57	80	60
Dyspepsia	53	35	64
Sweating	62	55	64

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Group Matching

Twenty-four patients were treated with amylobarbitone and twenty-six with nealbarbitone. The two groups of patients were shown to be comparable in sex, age, civil state, diagnostic subgroup, types of precipitant, duration of illness, clinical assessment of intelligence and personality type, previous history of illness and prognosis rating. The pre-treatment ratings on twenty-nine symptoms of anxiety scored on a three-point scale were comparable except in so far as four symptoms were concerned: tension, loss of interest, fatigue, loss of libido (Table II). Similar numbers of patients in the two groups were affected by these symptoms, but the amylobarbitone treated group showed higher scores.

Results

After two weeks' treatment the amylobarbitone group showed significantly more improvement in three symptoms: tremor, muscle twitching, inability to get off to sleep at night. No differences were found as far as the rest of the ratings were concerned. After four weeks' treatment the degree of improvement in all twenty-nine symptoms was similar in the two treatment groups (Table III). The number

Table II

Pre-treatment Scores of Patients Treated with Amylobarbitone and Nealbarbitone

	Number of Patients Affected								Significant Differences
	Amylobarbitone				Nealbarbitone				
Score	0	1	2	Total	0	1	2	Total	
1 Tremor	11	6	7	24	14	7	5	26	–
2 Fidgety	8	9	7	24	3	16	7	26	–
3 Muscle twitching	15	5	4	24	20	6	–	26	–
4 Headache	9	7	8	24	10	9	7	26	–
5 Muzziness or pressure	7	5	12	24	11	9	6	26	–
6 Tension, strung up, anxious unrelaxed	0	0	24	24	0	10	16	26	*
7 Could scream or smash	11	4	9	24	11	6	9	26	–
8 Could cry	6	8	10	24	7	8	11	26	–
9 Can't get off to sleep	14	7	3	24	16	6	4	26	–
10 Sleep broken or restless	10	9	5	24	18	5	3	26	–
11 Wakes early	17	4	3	24	14	6	6	26	-
12 Dreaming more	15	1	8	24	18	4	4	26	–
13 Poor concentration	4	11	9	24	10	11	5	26	–
14 Loss of interest	5	11	8	24	14	7	5	26	*
15 Loss of pleasure	6	11	7	24	10	9	7	26	–
16 Fatigue: lassitude	6	3	15	24	8	11	7	26	*
17 Irritable or excitable	3	9	12	24	3	9	14	26	–
18 Worrying about trivialities	3	8	13	24	5	9	12	26	–
19 Ideas of reference	17	4	3	24	18	6	2	26	–
20 Phobias: Insanity	14	3	7	24	21	1	4	26	–
21 Disease	13	5	6	24	13	5	8	26	–
22 Crowds	14	4	6	24	18	3	5	26	–
23 Enclosures	19	2	3	24	18	3	5	26	–
24 Spaces	22	0	2	24	23	1	2	26	–
25 Others	20	0	4	24	21	2	3	26	–
26 Sweating	7	8	9	24	11	12	3	26	–
27 Dry mouth	14	5	5	24	11	10	5	26	–
28 Dyspepsia	11	7	6	24	7	10	9	26	–
29 Loss of libido	10	4	10	24	10	13	3	26	*

* $P = <0{\cdot}05$

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of new symptoms reported was 18 in the amylobarbitone group and 22 in the nealbarbitone group.

Discussion

Amylobarbitone can be used as a standard of comparison in the treatment of anxiety states, as it has already been shown to be effective in the symptomatic treatment of neurotic anxiety in a number of controlled trials (Raymond *et al.*, 1957; Scott, 1955; Robin, 1959).

The preliminary trial of nealbarbitone (Robin *et al.*, 1961) used a crossover design and showed this drug to have similar therapeutic effects to amylobarbitone in out-patients suffering from anxiety states and treated for a period of a week. A comparative trial with EEG control showed nealbarbitone to be less hypnotic than amylobarbitone or pentobarbitone.

Subsequently, Rickels *et al.* (1963) in a "double blind" controlled study have shown nealbarbitone to produce significant improvement, as compared with placebo, in anxious neurotic out-patients, using the Clyde Mood Scale for their measurements; while Hinton (1963) has shown the drug to be weak in hypnotic action.

The study reported here once again shows that nealbarbitone and amylobarbitone are

Table III

Difference in Scores of Patients Treated with Amylobarbitone and Nealbarbitone for One Month

	Number of Patients Affected											
	Amylobarbitone						Nealbarbitone					
(Difference in score—Week 1 minus Week 3)	−2	−1	0	+1	+2	Total	−2	−1	0	+1	+2	Total
1 Tremor	–	2	13	6	3	24	1	1	14	8	2	26
2 Fidgety	–	2	13	8	1	24	–	–	12	11	3	26
3 Muscle twitching	–	1	16	3	4	24	–	–	23	3	–	26
4 Headache	1	2	11	8	2	24	–	–	16	8	2	26
5 Muzziness or pressure	–	1	10	9	4	24	–	–	17	7	2	26
6 Tension, strung up, anxious, unrelaxed	–	1	10	8	5	24	–	–	11	8	7	26
7 Could scream or smash	–	1	12	7	4	24	–	1	12	7	6	26
8 Could cry	–	3	11	6	4	24	–	1	11	8	6	26
9 Can't get off to sleep	1	2	12	7	2	24	1	–	17	5	3	26
10 Sleep broken or restless	–	1	14	7	2	24	–	2	18	6	–	26
11 Wakes early	1	4	13	5	1	24	–	–	18	3	5	26
12 Dreaming more	1	2	18	–	3	24	–	–	19	5	2	26
13 Poor concentration	–	2	7	11	4	24	–	1	17	8	–	26
14 Loss of interest	–	3	10	6	5	24	1	–	18	5	2	26
15 Loss of pleasure	1	1	12	9	1	24	1	–	15	7	3	26
16 Fatigue: lassitude	–	2	12	8	2	24	–	1	16	7	2	26
17 Irritable or excitable	–	2	11	7	4	24	–	–	10	11	5	26
18 Worrying about trivialities	–	3	12	6	3	24	–	2	11	8	5	26
19 Ideas of reference	–	1	18	5	–	24	–	–	19	6	1	26
20 Phobias: Insanity	1	–	16	1	6	24	–	–	22	1	3	26
21 Disease	–	2	15	6	1	24	–	–	18	5	3	26
22 Crowds	–	–	16	4	4	24	1	1	17	2	5	26
23 Enclosures	–	1	18	3	2	24	–	–	18	4	4	26
24 Spaces	–	–	23	–	1	24	–	–	24	1	1	26
25 Others	–	–	22	1	1	24	–	–	23	1	2	26
26 Sweating	–	–	17	6	1	24	–	1	15	10	–	26
27 Dry mouth	–	1	17	5	1	24	–	–	15	10	1	26
28 Dyspepsia	2	1	15	5	1	24	–	2	12	6	6	26
29 Loss of libido	1	–	16	4	3	24	–	2	15	8	1	26

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essentially similar in therapeutic effect. Once again no major side-effects were observed, while the incidence of new symptoms (possible side-effects) encountered after the drugs was similar.

The weaker hypnotic effect of nealbarbitone should make the drug very suitable for use as a daytime sedative and also reduce the danger from accidental or deliberate overdosage.

Summary

A validation study confirms that in the treatment of matched groups of patients with anxiety reactions, nealbarbitone and amylobarbitone have similar therapeutic properties.

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