A CONTROLLED TRIAL OF RESERPINE IN CHRONIC SCHIZOPHRENIA

By

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Uncontrolled Trials

SINCE the introduction of reserpine by Kline in 1954 there have been relatively few studies of its use in schizophrenia and most of these have been uncontrolled. It is characteristic of these uncontrolled trials that when the results are assessed, they are described in glowing terms, and the percentage of patients reported as showing "moderate" or "marked" improvement is high.

For early investigators the figures are:

	Marked or Moderate Improvement
Noce, Williams, and Rapaport (1955)	64%
Barsa and Kline (1955) (total)	62%
Hollister *et al.* (1955)	46%
Kinross-Wright (1955)	70%
Tasher and Chermak (1955)	64%

More recently Moore and Martin (1957) reports a similarly uncontrolled study. Out of 22 chronic deteriorated schizophrenics they find "improvement" in 12; while out of 21 acute schizophrenics they find "much improvement" in 18.

Controlled Trials

When trials are controlled a quite different picture emerges. Outstanding among the early investigators, Campden-Main and Wegielsky (1955) found no difference between patients having reserpine and patients on placebo tablets. Finn *et al.* (1955) reached a similar conclusion. Shepherd and Watt (1956) found that reserpine gave results which were even worse than those given by the placebo.

The only optimistic report in a controlled trial has been that of Naidoo (1956). He investigated the effect of reserpine and E.C.T., in the same trial, either separately or combined, and with a placebo control.

He found that reserpine alone produced:

25 per cent. marked improvements;

50 per cent. moderate or mild improvements;

25 per cent. not improved but easier to nurse;

with no improvements in the placebo group.

He thought that E.C.T. given with the reserpine gave a more rapid improvement at first, but that the final results were little better than without it. E.C.T. alone in this group gave only a mild degree of improvement.

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It was therefore proposed to repeat Naidoo's work, expressing the results as a week-by-week variable, but using a more carefully designed rating-scale.

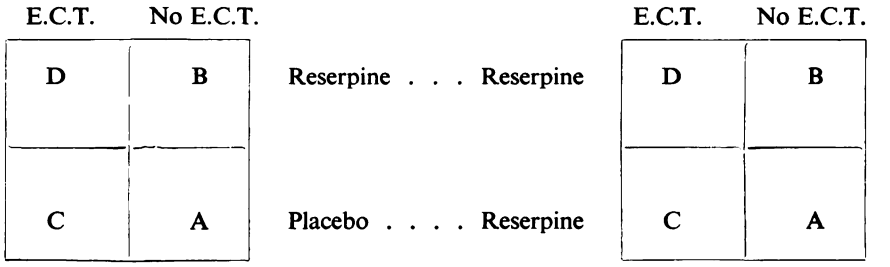
Materials and Methods

All patients in the trial were females, from a chronic (but not refractory) ward. Those patients who were being treated currently, in any way, were not considered for the trial. Patients over seventy years of age were excluded. This gave thirty-two patients who were having no treatment at the time and in fact had had very little treatment in the past. They were divided into four groups matched as far as possible for age, length of illness and stay in hospital.

By random methods of allocation, two of these groups were put on reserpine and the other two on placebo tablets. One of the reserpine groups and one of the placebo groups was given E.C.T. from beginning to end of the trial.

The trial lasted eighteen weeks, and halfway through, i.e. at the beginning of Week 10, the patients then on placebo were changed to reserpine. Patients having reserpine were left unchanged.

In diagram:



First nine weeks of trial *Second nine weeks of trial*

Dosage of reserpine was: In the first two weeks 6 mg. orally and 2·5 mg. intramuscularly per day; thereafter 6 mg. or less orally per day and nothing intramuscularly. If side-effects were troublesome the oral dose was cut down as necessary and resumed later. *Dosage of E.C.T.* was twice a week at first and then less, depending on its effects. Patients who showed confusion and forgetfulness, or excessive euphoria, had their dose reduced.

Each group, A, B, C or D, originally had eight members, but three patients dropped out during the trial for reasons unrelated to it, making the groups uneven.

Group	No. in Group	Average Age in Years	Average Length Illness Years	Average Stay in Hospital Years
A	7	57	26	21
B	8	55	28	25
C	8	55	25	18
D	6	57	29	24
All groups	..	56	27	22

System of Rating

Each patient was seen once a week and rated for six aspects of her condition by myself and the nursing staff jointly. The first rating was done before the trial started. Also, when the trial was started a "note" was written (i.e. a statement

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of the patient's clinical condition) and this was compared with a similar note written at the end of the trial.

The six aspects rated weekly were:

Coherence of thinking
Communicativeness
Affect
} The "Medical" aspect of the patient.

General helpfulness
Suitability for different wards
Suitability for various degrees of parole and discharge
} The "Nursing" aspect of the patient.

In each category the lowest weekly score was 0 and the highest 4, giving a total maximum obtainable of 24. The scale for rating is appended below. It will be seen that the lowest score, 0, represents a patient who is about as mad as can be, whereas the highest, 24, is barely distinguishable from complete sanity.

Rating Scale

The numbers appended represent the value given to each rating, as a weekly mark.

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Coherence	Communicativeness	Affect	Helpfulness	Warding	Dischargeability
0. Entirely incoherent. Blocks freely. Very deluded.	0. Entirely uncommunicative.	0. Absent or entirely incongruous.	0. Needs all nursing care and attention.	0. Suitable for refractory ward.	0. Not reliable outside hospital.
1. Much incoherence, blocking and delusions.	1. Usually withdrawn but communicative occasionally.	1. Much reduced or mostly ingruous.	1. Needs some supervision.	1. Suitable for ordinary ward.	1. Fit for occasional leaves.
2. Moderately incoherent, etc.	2. As often communicative as withdrawn.	2. Moderately reduced or moderately incongruous.	2. No special trouble. Can look after self.	2. Suitable for quiet closed ward.	2. Fit to go often on leave.
3. Slightly incoherent, etc.	3. Usually communicative, but occasionally withdrawn.	3. Slightly reduced or slightly incongruous.	3. Looks after self and is partly helpful to others.	3. Suitable for open ward.	3. Suitable for trial out of hospital.
4. Entirely coherent. No blocking. Not deluded.	4. Always communicates freely.	4. Normal.	4. Entirely helpful socially.	4. Can be left to self entirely. Entirely reliable.	4. Suitable for outright discharge.

It will be seen that each patient in the trial therefore got a weekly mark representing their clinical condition on a theoretically absolute scale. This made it all the easier to assess progress on the conventional scale of "slight", "moderate" and "much" improvement.

The table which follows shows this.

Groups not having E.C.T.

	First nine weeks	Second nine weeks
Group A	*Placebo*	*Reserpine*
Patient No. 1	No change	No change
2	,, ,,	,, ,,
3	,, ,,	Slightly improved
4	,, ,,	No change
5	,, ,,	,, ,,
6	,, ,,	,, ,,
7	,, ,,	,, ,,

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Group B		*Reserpine*	*Reserpine*
Patient No.	1	No change	No change
	2	,, ,,	,, ,,
	3	,, ,,	Slightly improved
	4	Slightly improved	,, ,,
	5	,, ,,	Moderately improved
	6	,, ,,	Slightly improved
	7	No change	No change
	8	Slightly improved	Slightly improved

Groups having E.C.T.

		First nine weeks	Second nine weeks
Group C		*Placebo*	*Reserpine*
Patient No.	1	No change	Much improved
	2	,, ,,	No change
	3	,, ,,	Slightly improved
	4	,, ,,	No change
	5	,, ,,	,, ,,
	6	,, ,,	,, ,,
	7	,, ,,	,, ,,
	8	,, ,,	Much improved

Group D		*Reserpine*	*Reserpine*
Patient No.	1	No change	No change
	2	Much improved	Much improved
	3	No change	No change
	4	,, ,,	Moderately improved
	5	,, ,,	No change
	6	,, ,,	,, ,,

RESULTS

1. In general the improvement in all patients is slight. At the end of the trial, out of 29 patients all having had at least nine weeks' reserpine, of whom 14 had E.C.T. in addition, the figures are:

No change	Slight Improvement	Moderate Improvement	Much Improvement	Total
18	6	2	3	29

2. If we take the figures for E.C.T. groups and non-E.C.T. groups separately we have:

	No Change	Slight Improvement	Moderate Improvement	Much Improvement	Total
Groups A & B (no E.C.T.)	9	5	1	—	15
Groups C & D (E.C.T.) ..	9	1	1	3	14

This difference is not significant at the 0·1 level. ($\chi^2 = 5{\cdot}7$)

3. If we take the figures for reserpine and placebo groups, during the first nine weeks, for which they are comparable, we have:

	No Change	Slight Improvement	Moderate Improvement	Much Improvement	Total
Groups A & C (placebo)	15	—	—	—	15
Groups B & D (reserpine)	9	4	—	1	14

This difference is again not significant at the 0·1 level. ($\chi^2 = 6{\cdot}07$)

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Conclusions

1. The effect of reserpine, as measured during the first nine weeks of the trial, is not significantly better than that of placebo.

2. Groups which are given E.C.T. in addition to reserpine are not significantly better than those without E.C.T.

Summary

Thirty-nine female chronic schizophrenic patients were treated variously with placebo, E.C.T. and reserpine.

The results provide no evidence that reserpine has any great place in the treatment of chronic schizophrenia.

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