THE USE OF TOFRANIL IN MENTAL HOSPITAL PRACTICE

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Over the last few years there has been an appreciable increase in the admission rate to hospitals of patients suffering from depressive conditions. Until now only electric convulsive therapy (ECT), together with psychotherapy, have provided any degree of success in the treatment of these depressive states. As a result of the overcrowding of mental hospitals, the shortage of medical staff, and the limited facilities for treating these conditions in general hospitals and private practice, these methods of treatment have not been exploited fully. Moreover, ECT is sometimes contra-indicated by some concomitant organic disease.

Up to this stage the results obtained with psychopharmacological drugs in the treatment of the depressive conditions have been most disappointing; their action being slight or indeed completely absent. However, these drugs often have a beneficial effect on anxiety and restlessness, producing tranquillity and relaxation (chlorpromazine, reserpine, meprobamate); or they have an excitatory effect promoting increased activity (amphetamines).

Tofranil

Recently, several reports have been published on the use of a new antidepressive drug, imipramine (G22355 or Tofranil).† Tofranil (N-(3-dimethylaminopropyl) iminodibenzyl hydrochloride) belongs to the new group of iminodibenzyl derivatives. The clinical effect of Tofranil resembles an 'unblocking' and brightening of the fixed depressive mood. Although no specific pharmacological basis for its action has yet been established, it is thought that Tofranil acts on the pathological mechanism characteristic of depression and interrupts its further progress.

† These reports are briefly discussed in an article by Dr. M. Russell Clarke, which is published on page 990 of this issue of the *Journal*.

TABLE I. RESULTS OF TREATMENT

Case	*Sex*	*Age*	*Diagnosis*	*Previous treatment*	*Daily dosage*	*Results*	*Side-effects*
1	M	45	Manic-depressive (depressed)	ECT	See below	Recovery	Nil
2	M	40	Manic-depressive (depressed)	ECT	See below	Poor	Nil
3	M	45	Manic-depressive (depressed)	ECT	See below	Recovery	Nil
4	M	54	Manic-depressive (depressed)	ECT	See below	No change	Nil
5	M	50	Manic-depressive (depressed)	ECT	See below	Treatment stopped	Agitation
6	M	48	Manic-depressive (depressed)	ECT	See below	Improvement	Nil
7	M	44	Reactive depression	ECT	*See below	Recovery	Nil
8	M	46	Reactive depression	ECT	See below	Marked improvement	Nil
9	M	58	Senile psychosis (depressed)	ECT	See below	Marked improvement	Nil
10	M	66	Senile psychosis (depressed)	ECT	See below	Marked improvement	Nil
11	M	67	Senile psychosis (depressed)	ECT	See below	Treatment stopped	Nil
12	M	47	Involutional melancholia	ECT	See below	No change	Nil
13	M	53	Involutional melancholia	ECT	See below	No change	Nil
14	M	59	Involutional melancholia	ECT	See below	No change	Nil
15	M	46	Involutional melancholia	ECT	See below	Treatment stopped	Nil
16	F	61	Reactive depression	Nil	See below	Marked improvement	Nil
17	F	54	Manic-depressive (depressed)	ECT and Largactil with amphetamine	See below	Recovered	Dizziness
18	F	48	Reactive depression	ECT	See below	Recovered	Restlessness
19	F	47	Reactive depression	Nil	See below	Recovered	Nil
20	F	56	Reactive depression	ECT	See below	Recovered	Restlessness
21	F	53	Reactive depression	Nil	See below	Recovered	Nil

Dosage = 100 mg. daily, increasing to a maximum of 250 mg. daily, thereafter decreasing until maintenance dose of 100 - 150 mg. attained, given orally.
* = The mg. dosage given in this case was the same as in all other cases with the exception that a combination of tablets and ampoules were used.

CLINICAL EXPERIENCE

My observations on G22355 (Tofranil) were carried out on 21 patients in Valkenberg Hospital. Fourteen patients were chronic cases over the age of 40, and 7 patients were recent admissions. The dosage schedule was as follows: 100 mg. daily, increased to 250 mg. daily, thereafter decreasing to maintenance dose of 100 - 150 mg. daily. The time taken for improvement varied between 4 days and 3 weeks.

Side-effects were minimal. One patient complained of dizziness. A manic-depressive (depressed) patient became highly agitated and actively suicidal, probably due to the fact that Tofranil cleared the psychomotor inhibition.

In 2 patients (recent admissions with reactive depression), the original symptoms became accentuated and they complained of a feeling of fear. However, on continuation of therapy these patients improved markedly and were discharged. In 3 cases therapy was discontinued because of coincidental physical illness, the patients being removed to a clinic. No allergic reactions developed. The drug did not interfere with sleep. Photosensitivity and visual disturbances due to its atropine-like action have been reported, but the general toxicity is claimed to be low.

A summary of the results of the cases treated in a trial series are given in Table I.

RESULTS

Of the 21 cases treated (Table I), 8 recovered, 5 showed a marked improvement, in 3 treatment was stopped because of physical reasons, and in 5 there was no change. Excluding the 3 patients in whom treatment was stopped, this represents a recovery and marked improvement rate of 72%. The following are examples of the results of treatment in a case of recent onset of symptoms, and in a chronic case:

Case 1

This male patient, a recent admission, aged 44 years, presented himself at the Cape Mental Health Clinic, Cape Town, complaining of gross depression coupled with numerous hypochondriacal symptoms. It was obvious that he was basically a neurotic person and that he was suffering from a reactive depression. He was admitted to Valkenberg Hospital as a voluntary patient and after only 4 days began to show a marked improvement. The gross depression lifted and his other complaints became minimal. After a further week's treatment he requested to go and was discharged. He has been seen at an out-patients' clinic since his discharge, and he has maintained his improvement.

Case 2

A man, aged 54, who has been an inmate of Valkenberg Hospital for the past 10 years. He was originally admitted in a state of gross depression associated with hallucinations and persecutory delusions. Despite numerous courses of ECT, little or no improvement was noted.

Before treatment with Tofranil he was dull, dejected, inhibited in all his actions, full of petty complaints and had always to be coaxed to eat. After some 3 weeks of treatment he became brighter and generally more active. He began to help in routine ward work and ate without prompting. He has maintained his improvement on a maintenance dose.

DISCUSSION

The results obtained in treating this small series of cases have proved most gratifying. The best results were obtained in recent admissions although satisfying results were also obtained in long-standing chronic cases.

Recently we have combined Tofranil with ECT for the treatment of severely depressed cases with the most encouraging results. Moreover, we encountered no unpleasant side-effects. Kielholtz and Battegay[1] state that when the action of Tofranil is insufficient, its combination with ECT is recommended since Tofranil reduces the number of treatments required. It is interesting to note that in the trial series many cases responded remarkably well to Tofranil alone after ECT had failed. Azima[2] states that about 80% of patients formerly requiring ECT may no longer require this treatment as the result of the introduction of Tofranil.

From the above observation it would appear that Tofranil has a place in the treatment of hospitalized cases of depression, and that it is useful in out-patient and office practice, especially in treating cases of reactive depression where facilities for psychotherapy and ECT are limited.

SUMMARY

1. Tofranil has a definite place in the treatment of depressive states.

2. It will undoubtedly prove useful in out-patient clinics, especially in the treatment of cases of reactive depression.

3. It has been successfully used in combination with ECT for the treatment of severely depressed cases.

4. In combination with promazine derivatives it will be of use to counteract depressions caused by these derivatives in certain cases.

5. The side-effects are minimal. Special attention should, however, be given to the danger of suicide, which is potentially present in every case of depression, since Tofranil may remove psychomotor retardation.

6. In the present series the recovery/improvement rate was 72%.

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REFERENCES

1. Kielholtz, P. and Battegay, R. (1958: Schweiz. med. Wschr., **88**, 763.
2. Azima, H. (1959): Canad. Med. Assoc). J., **80**, 535.