offer some orientation for a more systematic approach in studying prognoses of schizophrenia. It is reasonable to follow the demand of Renton et al. (1963) that a special follow-up clinic for discharged schizophrenic patients should be created to provide an adequate service and to facilitate proper research.

SUMMARY

In the International Pilot Study of Schizophrenia, 127 psychotics and 10 neurotics were included at the Taipei Field Research Center. Although 87 schizophrenics were registered at the initial examination, 89 cases were diagnosed as schizophrenic at the time of the second-year follow-up. Except for 4 cases, dead or missing before the follow-up, 85 schizophrenics were evaluated in terms of their initial social and clinical data and the treatment course during the two-year follow-up period.

The following findings emerged from this study:

1) Among 85 schizophrenics alive, 11 cases showed no abnormal mental symptoms, 23 cases were neurotic, 19 cases mildly psychotic, 21 moderately psychotic, and 11 markedly psychotic at the time of the second-year follow-up.
2) The schizophrenic patients who displayed derealization or obsessive-compulsive traits at the initial examination showed better improvement than the ones having no such symptoms.
3) The cost of treatment during the follow-up period related significantly to treatment status and clinical outcome at the time of the follow-up.
4) Three subgroups of schizophrenia are derived in relation to neuroleptic medication: a) the improved cases with short-term treatment; b) the improved cases with long-term medication, and c) the non-improved cases even with continuous drug therapy. Further elaboration of these subgroups will contribute to the prediction of clinical outcome of schizophrenia with neuroleptic medication.

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TRIAL OF LEPONEX (CLOZAPINE) IN SCHIZOPHRENIA

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INTRODUCTION

Leponex (generic name clozapine), a piperazine derivative of dibenzodiazepine, has been reported to have an antipsychotic effect (de Maio, 1968; Gross and Langner, 1969) but without the cataleptic activity or inhibition of apomorphine-induced

stereotyped behaviour in rats characteristic of neuroloptics (Stille and Hippius, 1971). So far as we are aware, no controlled study of its efficacy has been reported. We, therefore, undertook such a study on schizophrenic patients.

METHOD

The study involved 33 adult in-patients of both sexes, diagnosed schizophrenia with acute symptomatology. It was double-blind and compared Leponex with Placebo. Treatment duration was 11 weeks made up of the following successive periods: 1. dosage adaptation – 1 week; 2. Leponex treatment – 4 weeks; 3. Placebo treatment – 2 weeks; 4. Leponex treatment – 4 weeks. At the start of the trial, the patient was put on Leponex (tablets of 100 mg each, 2 – 4 times daily); during the period of dosage adaptation on optimum dose was arrived at, and thereafter he continued on the same number of tablets of Leponex or Placebo. Clinical assessments during the trial (there were 8) were made by the examining doctor with the help of the nursing staff, all of whom were kept unaware of the change from one therapy to another. Other psychiatric medication and ECT were withheld from two weeks before the trial. Laboratory investigations included complete blood picture and liver function tests in all cases. Data obtained were subjected to computer analysis.

FINDINGS

Of 33 patients selected, 2 dropped out of the trial because they became unmanageable, and one was omitted because his muteness made assessment with the BPRS difficult. The average dosage of Leponex was 442 (± 85.5) mg daily (range 200 – 600 mg).

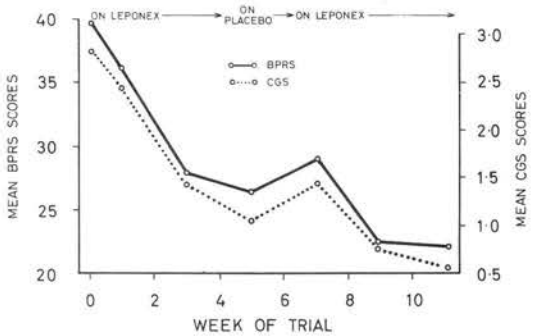
Patient Characteristics

All were Chinese – 22 males and 8 females. Age distribution by decades was: 2nd = 3, 3rd = 8, 4th = 11; 5th = 5; 6th = 3. (Mean 34.4 ± 11.4 years). There were 21 paranoid schizophrenics and 9 hebephrenics: 22 were relapses after symptom-free (or almost) intervals; 6 were first breakdowns and 2 had a chronic-productive course. The illness was rated as severe in 17 and moderate in 13. Mean duration of illness was 4.0 years (±3.3), of previous episodes 3.6 (±3.3) months, of present illness 3 (±4.5) months and of present hospitalisation 11.4 (±7.8) days. Mean number of previous episodes was 1.6 (± 1.3)

Scores

Patients were rated on a Clinical Global Scale (CGS) which scored illness from 0 = asymptomatic to 3 = severely ill, and the Brief Psychiatric Rating Scale (BPRS), which rated 28 symptom parameters, from 1= not present to 7 = extremely severe. It will be seen (Figure) that in terms of both the BPRS and the CGS patients steadily

Figure



and consistently improved on Leponex but deteriorated on Placebo. A similar pattern of response was found in most of the items of the BPRS: somatic concern, anxiety, tension, emotional withdrawal, conceptual disorganization, mannerisms and posturing, depressive mood, hostility, suspiciousness, motor retardation, un-cooperativeness, blunted affect and excitement. As regards the remaining items, there was improvement during both Leponex and Placebo periods in respect of grandiosity, hallucinatory behaviour, and unusual thought content, while there was little response to either Leponex or Placebo in respect of guilt feelings and disorientation. The items that showed the greatest improvement at the end of the trial were hallucinatory behaviour, suspiciousness and unusual thought content.

Clinical impression during and after the trial was that sedative action was more rapid and effective, and control of patients who showed continued aggressive and impulsive behaviour more effective than with the use of chlorpromazine or trifluoperazine.

Side-effects

These were noted only if the patient spoke of them or the doctor or nursing staff observed them, and were as follows: CNS – drowsiness (63%), headache (20%); autonomic – hypersalivation (87%); dry mouth (40%); disturbed visual accommodation (40%); sweating (13%); extrapyramidal – tremor (83%); rigidity (3%); circula-

tory – hypotension with collapse (13%); gastro-intestinal – constipation (53%), nausea or vomiting (23%). Most side-effects were mild and transitory but drowsiness tended to be prolonged, probably because of the high dosage used. A serious side-effect however was hypotension with collapse (13%) which occurred at onset of therapy but could be prevented by starting with low dosage and gradual increase. Some reduction of blood pressure – mainly systolic – and tachycardia (hitherto unreported) occurred in the majority of cases and persisted unabated throughout the trial (statistics supplied on request). Tremor was mild but only partially responsive to antiparkinsonic drugs given after the trial. There were no changes in blood picture and liver function.

CONCLUSION

Leponex appeared effective for control of the florid features of schizophrenia, particularly paranoid manifestations. Clinical impression during and after the trial was that onset of sedative action was more rapid, and control of aggressive patients often more effective than with say chlorpromazine, but Leponex caused more drowsiness. Extrapyramidal signs, apart from mild tremor, were virtually absent; hypotension however required caution at start of treatment. Tentatively at this stage the drug may be recommended for use in aggressive and impulsive patients who have not responded to the usual phenothiazines. The drug however needs to be further evaluated as regards its cardiovascular side-effects, and its efficacy in the long-term and in comparison with the established phenothiazines. The average daily dosage of 422 mg. in this trial was probably on the high side.

SUMMARY

33 Chinese in-patients in Hong Kong, diagnosed schizophrenia with acute symptomatology were involved in a double-blind cross-over trial comparing Leponex (clozapine) with Placebo. Leponex was found to be effective particularly in the control of paranoid manifestations and excited and aggressive behaviour, with rapid onset of action. The drug should however be used with some caution at this stage because of its hypotensive effects, which led to collapse in 13% of cases in the initial stages of treatment. The side-effect could be avoided by starting on low dosage.

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WITHDRAWAL OF MEDICATION AS A CAUSE OF RELAPSED SCHIZOPHRENIA: SOCIO-CULTURAL PERSPECTIVES

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INTRODUCTION

One of the most significant breakthroughs in the management of schizophrenia was the discovery and the introduction of a phenothiazine drug, namely, chlorpromazine, in 1952. However, despite the introduction of numerous other psychoactive agents in the management of schizophrenia, over the last twenty years, treatment has been essentially on an empirical and symptomatic level. Frequently, patients relapsed when the drug was removed, and re-admission to hospital was necessary. It appears then, that the most effective method of counteracting frequent relapses of schizophrenia, is continuous maintenance on phenothiazines at sufficient therapeutic doses.

Few experienced psychiatrists would deny the