resistant and unresponsive to psychotherapy and had good results. He used from 10 to 30 mg Valium and added 20 mg methylamphetamine to induce talkativeness. All the patients were alert throughout the interview.

The purpose of using intravenous Valium in this study is to induce a more productive interview or to recall Amnesia. If funtional amnesia is the result of a repressive force because of threat of anxiety and Valium reduces anxiety, then the patients should be better able to recall their repressed memories. This was not the case in the three patients with amnesia. Valium did not appear to be able to assist patients to recall amnesia if they do not wish to do so. (3 cases accused of murder, denied during narcoanalysis), On the other hand for a number of patients (5 patients), their mental state improved after the experience of interview under Valium injection. e.g. one patient who remained mute during the interview confessed that he was malingering. A similar result was also noticed in another case (not in the series) who was interviewed under sodium amylobarbitone.

Side effects

These were characterised by their absence. Only 2 patients felt drowsy and somnolent. The blood pressure remained unchanged or dropped only by 10 mm. Hg. systolic and diastolic. In one case, the systolic rose by about 20 mm. Hg.

CONCLUSION

As a method of treatment, Narcoanalysis does not seem to have much of a place in Psychiatry. This could partly be due to the dangers inherent in the treatment – which in some cases is equivalent to administering an anaesthetic. Intravenous Valium appears to have overcome this obstacle in that it can be given in the office or in the medical ward without any pre-operative preparation.

The author feels that there is room for a more extensive trial of this procedure, as it is not more difficult than giving an intravenous injection and is almost without danger. Valium should replace amylobarbitone for general use.

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A TWO-YEAR FOLLOW-UP STUDY OF 85 SCHIZOPHRENICS

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In the investigation of prognoses of mental disorders, most previous reports have focused on follow-up studies of schizophrenia. However, they have used so many different methods and criteria that their resuits have hardly been comparable with each other. In order to collect a comparable sample, diagnostic tools applied should be clearly defined. To evaluate individual features in their relationship to a course of a certain illness, a treatment method or some social factors should be controlled. The International Pilot Study of Schizophrenia (IPSS) has been carried out in nine field research centres, located: Aarhus, Agra, Cali, Ibadan, London, Moscow, Prague, Taipei, and Washington, to meet the former conditions. This project has been under the sponsorship of the World Health Organization, which will publish the first report in 1973.

I am going to present a part of this research, a two-year follow-up study, relating mainly to neuroleptic medication which is the main theme, and also our concern in this Seminar; although this study has not been well controlled in terms of treatment methods and social environment.

Methods

As one of nine participating centres in the IPSS, we examined 127 psychotics and 10 neurotics between April 1968 and June 1969. We used the standarized methods with Present State Examination (PSE) originally developed by Dr. J. K. Wing and modified by IPSS collaborating investigators; also, Psychiatric History (PH), Social Description (SD), Physical and Neurological Examination (PNE), and Diagnostic Assessment (DA) schedules.

These cases should have resided in the catchment area for more than 6 months before the inclusion in this study. They should all be between ages 15 and 44, have suffered from mental illness without any organic manifestation for less than 3 years, and not have been admitted to a mental hospital for more than 2 years totally during the past 5 years. These 137 patients were followed up at the time of 2 years plus or minus 1 month after the initial examination, with the follow-up PH and SD schedules in addition to other forms used at the time of inclusion.

Results

1) *Diagnostic Classification*

The psychiatric diagnoses of each case were re-evaluated at the time of follow-up. There were 87 cases diagnosed as schizophrenic at the beginning, but two years later two of them were transferred to the category of reactive psychoses. On the other hand, three cases diagnosed as reactive psychoses and one case of depressive neurosis at the initial examination turned out to be schizophrenic. Therefore, at the time of the second-year follow-up, there were 89 schizophrenics all of whom we were fortunately able to locate and examine. Among five major diagnostic categories, the diagnosis of those suffering a paranoid state seemed to be most unchanged and the diagnoses of reactive psychoses were most changeable, 6 out of 21 cases (28.6%). There were altogether 10 of 137 cases (7.3%) that had changed their major diagnostic category at the time of follow-up.

Among 85 schizophrenics that had maintained the same diagnoses, some cases had changed their subtype classification. 72 schizophrenics did not shift their subtypes, but 13 of 85 (15.3%) were categorized in different subtypes. The subtype of acute schizophrenic episode seemed to be the most variable 3 out of 4; hebephrenics being the next closest with 5 out of 30. Five other subtypes had one each out of their categories.

2) *Patient Status at the Time of Follow-Up*

So far as the results of the second-year follow-up are concerned, there were 89 cases of schizophrenia, 10 affective psychoses, 11 paranoid state, 18 reactive psychoses and 9 depressive neuroses. In this report, clinical outcome at follow-up will be taken into consideration in relation to neuroleptic medication. The clinical outcome at follow-up is divided into the following five levels: i) not mentally abnormal, ii) mildly or moderately neurotic, iii) mildly psychotic or severely neurotic, iv) moderately psychotic, and v) markedly psychotic. The first three groups are regarded as improved and the last two groups as not improved. Treatment status is determined mainly by regularity of medication. If a patient had taken medication regularly during the two-month period prior to the time of follow-up, he would be considered on medication.

Of 89 schizophrenics, 4 cases were dead or missing: two died of suicide; one in a traffic accident, and another was missing on the front line. This paper will concentrate on the analysis of data obtained from the other 85 cases, mainly by comparing information gathered at the initial and follow up examinations.

Among 47 patients without medication, 17 cases (36.17%) still showed moderate or marked psychotic impairment. Among 38 patients with medication, 15 cases (39.47%) revealed the moderate or marked degree of psychotic impairment. Therefore, altogether 32 of 85 (37.65%) of the schizophrenics were regarded as not improved, in contrast with 7 of 48 (14.68%) of other psychiatric cases. The former is about two and a half times as many as the latter.

3) *Social Data at the Initial Examination*

The number of male patients was almost the same as females (43:42). However, while most of male patients were single, female patients were evenly distributed in the single and married classes. The sex and marital status did not relate significantly with treatment results. Neither age, education, nor social class of patients affected treatment results, though younger or single patients had received higher education than older or married ones.

4) *PSE Ratings at the Initial Examination*

In order to find out if there was any relationship between initial symptomatic manifestation and treatment results, 61 out of 367 PSE ratings at the initial examination were compared with four groups of treatment results. In regard to

"derealization", 27 of 32 cases who showed mild impairment eventually improved significantly. The only other symptom which indicates statistically significant improvement was obsessive-compulsive traits.

5) *Subtypes at the Time of Follow-Up*

Other subtypes than hebephrenic and paranoid showed the most favorable treatment results, the hebephrenic type was most unfavorable, and the paranoid was in the middle. These differences reveal statistical significance.

6) *Cost of Treatment*

During the two-year follow-up period, these schizophrenics received various kinds of treatment in different settings and for different lengths of time with different sequences followed. In order to evaluate this complicated treatment course, the weighting scale for cost of treatment is arranged. Psychiatric treatments are weighted according to: treatment status, drug therapy, electric convulsive therapy, psychotherapy, and frequency of outpatient visits. By adding weights of each treatment multiplied by treatment days, cost of treatment can be calculated. The group which improved without medication needed the least cost of treatment. The groups of the improved and not-improved, both with medication, had the most expensive treatment cost, while the group of the not-improved without medication had the middle cost of treatment. These differences are statistically significant. An interesting relationship between married status and cost of treatment indicated that single patients needed more cost of treatment than married cases which showed statistically significant difference.

7) *Correlation Coefficients*

Initial examination data such as 34 symptom units, 27 symptom groups and 9 clinical and social factors are correlated with each other and also with 5 items of follow-up data such as degree of impairment, number of relapses, number of readmissions, and cost of treatment. The correlation coefficients beyond ±0.25 are significant. Four out of these 5 correlations relate with cost of treatment. Age, suspiciousness and poor rapport correlate negatively, and previous treatment positively, with cost of treatment. Ideas of reference seem to correlate negatively with the number of readmissions.

DISCUSSION

1) *Change of Diagnoses*

The detailed examination such as a PSE interview and collection of information on PH and SD were given to each patient in the follow-up study as well as in the initial investigation. The final diagnoses established from all information are definitely more reliable than the initial diagnoses. Therefore, this report was based on the final diagnoses instead of using initial diagnoses which was the usual procedure of other previous studies. By utilizing the final diagnoses, predictors of prognosis can be derived meaningfully from careful analysis of the data obtained.

2) *Predictors of Prognosis*

The patients who displayed "derealization" or "obsessive-compulsive traits" showed better improvement than the ones having no such symptoms. Chapman (1966) enumerated some early symptoms of schizophrenia and emphasized the disturbance of visual perception which can be measured by ratings of derealization in our sample. Although Chapman found disturbances of visual perception to be associated with poor prognosis, Varsamis and Adamson (1971) reported these with good prognosis. Both derealization and obsessive-compulsive traits may be considered as early manifestations of schizophrenia, so that patients with these symptoms seem to be more responsive to psychiatric treatment than those with more advanced symptoms. Ideas of reference show negative correlation with readmission, and on the other hand, suspiciousness and poor rapport correlate negatively with cost of treatment. However, we need to accumulate more cases to formulate any explanation for these findings. Younger patients needed more intensive treatment which is reflected in higher costs of treatment and can be easily understood by our clinical experiences. The patients who had received psychiatric treatment previously may be rather intractable, so that they needed larger cost of treatment.

3) *Improvement Rate*

The percentage of the subcategory 1, 2, 3, 4, and 5 according to the level of impairment mentioned above was 12.4, 25.8, 21.3, 23.6, and 12.4 respectively, while 4.5% died. These numbers are similar to the recent study of Niskanen and Achte (1972) who used a five-way breakdown somewhat different from ours in assessing the patient's psychic condition. At the two-year follow-up study of 100 schizophrenic and paranoid

patients drawn from their sample of the year 1965, they found 14, 21, 27, 27 and 8 cases in each of the five groups from normality to severe abnormality, while 3 cases were dead. However, they did not mention the direct effects of therapeutic intervention prior to the follow-up time on prognosis of mental disorders.

Twenty-five of 85 schizophrenic (29.4%) relapsed and 28 (32.9%) were readmitted to mental hospitals during our two-year follow-up period. No comparison can be made with other studies which were carried out with different research methods in different treatment settings. It should be emphasized that research methodology had better be integrated for international comparison.

4) *Treatment Course*

As mentioned above, the drug-treated group and the non-treated group in our study showed almost the same improvement rate, 63.83% and 60.53% respectively. We have to discuss why the drug-treated group did not show better results than the non-treated group.

Firstly, we may suspect that patients with medication were not actually taking drugs. Parks et al. (1962) and Willcox et al. (1965) reported the well-known possibility of patients not taking their drugs. Hogarty and Goldberg (1973) also described that relapses in the placebo group were twice that of the drug group, but one half of all relapsers (drug and placebo) cease medication prior to relapse. Therefore, we should consider how to motivate patients to take drugs regularly and how to adjust adequate doses for patients in order to promote drug effects. This is the most important problem in the community care of mental disorders and we can succeed only by the team work of mental health personnel.

Secondly, we may speculate that we are dealing with different types of schizophrenia. The detailed analysis of the treatment course discloses the following findings:

i) The improved patients without medication needed the shortest treatment period and showed the best prognosis among the four groups. They received drug treatment for the average length of 4.9 months and discontinued their medication when they felt their symptoms were steadily improving. Full remission took place about 4 months later and had remained thereafter. We have to study these cases in more detail in order to detect any possibility that these are cases of "reactive schizophrenia."

ii) The improved patients with medication had taken drugs for the longest period among the four groups. These patients experienced exacerbation of their mental symptoms soon after they discontinued medication and realized that they would be better off as long as they continued their drug therapy. These cases should continue medication on a maintenance dose under psychiatric supervision.

iii) Most of the non-improved patients without medication would not accept psychiatric treatment because of lack of their insight and the family could not force them to be admitted to a mental hospital. Some patients of this group could not be given adequate psychiatric treatment because of their family's financial difficulty. Therefore, these patients will be given the privilege of receiving more intensive psychiatric treatment only after the establishment of a Mental Health Act and Social Security or Welfare System.

iv) Most of the non-improved patients with medication showed the worst prognosis among the four groups. The readmission rate was also highest; 6 of the 15 cases under in-patient care at the time of follow-up. These patients may be labelled as "process schizophrenia." A more intensive rehabilitation programme should be organized for these cases instead of merely giving drug treatment.

From these findings, the following three subgroups of schizophrenia may be 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 with neuroleptic medication.

Hoenig (1967) pointed out that nothing definite was known about the important question of how long neuroleptic drugs should be continued. Based on the above-mentioned results of our study, we may suggest that neuroleptic medication should be continued for about 5 months, and then if mental condition remits steadily, clinical check-up should be maintained for 4 or 5 more months to make sure if psychiatric improvement is well accomplished. In case that a definite improvement cannot be achieved at one-year follow-up, more intensive treatment and rehabilitation should be planned.

Although the present report is handicapped by uncontrolled treatment variables, our findings will

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