TREATMENT OF AMBULATORY NEUROTIC PATIENTS WITH RO 5–3350 IN JAKARTA

(A Preliminary Report)

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I. A new minor tranquillizer developed by ROCHE LABORATORIES was recently introduced to the medical profession. The drug, a benzodiazepine derivative (experimental code number RO 5–3350) is indicated for the treatment of severe neurotic conditions (obsessions, compulsions, obsessive compulsives, phobias). Basically it has the same indications as Diazepam (Valium) with the exception of epilepsy.

One hundred and ninety-five ambulatory neurotic patients were treated between October 1970 – and June 1971. Actually seventy-five more patients were treated in these series, but considered as "drop-outs" since less than the five weekly required evaluations were available.

The drug was given to – "new" (male as well as female), patients of ages 16–69 and to "old" patients as well if they had not taken psychotropic medication for 3–4 weeks.

Pregnant women were excluded from this study. The trial is a "straight, uncomplicated or open study" and carried out at the Out-Patient Service, Department of Psychiatry, University of Indonesia, Jakarta, and the Out-Patient Service, Dharmawangsa Sanitarium, Kebayoran-Baru, Jakarta, a private psychiatric facility.

II. *Method and Material*

The trial is open trial. All ambulatory neurotics coming to the Out-Patient Service, University of Indonesia, Department of Psychiatry and Dharmawangsa Mental Health Clinic were treated with the drug.

They were seen once weekly and followed up for at least six weeks. Some of these patients remained under therapy up to 2 months or even longer.

Dosages were changed according to the development of symptomatology and aimed at producing optimal improvement of the patient's condition. No or only very superficial psychotherapy was carried out. Concomitant drug therapy was not done.

Of the 195 ("recordable") patients, 120 were males and 75 females. The prominent ages were 20–29 years followed by the 30–39 years age group.

Laboratory tests were done if indicated.

III. *Rating*

Symptoms reported by the patients were rated according to a four-point numerical scale grading: 0 standing for absent, 1 for minimal, 2 for moderate and 3 for marked. Target symptoms for measurement are: anxiety, irritability, phobias, compulsive ideas and impulses, compulsive acts, loss of drive and interest, tension, restlessness, depression, trouble of onset of sleep, trouble of continuity of sleep, palpitation, sweating, gastro intestinal disturbances, vasomotor lability and some other symptoms.

IV. *Dosages*

Two forms of RO 5–3350 tablets are available for this study: 10 mg and 12 mg tablets.

Initial dosages are usually 6–10 mg per day, divided in 2–3 dosages, and maintained for one week.

In the second and following weeks dosages are either maintained or increased (up to higher than 32 mg per day) depending on the development of symptomatology.

V. *Drug responses.*

These are recorded according to the following categories:

- very good, if most of the target symptoms disappeared, subjectively as well as objectively;
- good, if most target symptoms are reduced in intensity and personality functioning is satisfactory.
- moderate, if symptoms are somewhat decreased while patient feels relieved subjectively and personality functioning is considered more or less reasonable;
- no effect, if symptoms remain as they were before treatment;

worse, if symptoms are increased in intensity and personality functioning has deteriorated.

VI. *Treatment results*

In general, it can be said that treatment results can be seen during the second week after the institution of treatment, to gradually stabilize the third and fourth week (table VI).

Most prominent dosages were between 18–20 mg, followed by dosages of 24–30 mg per day (table II).

Responses are very good in 20% of the patients, 38% good and 32% moderate, so that 90% showed improvement while under treatment, while 10% did not improve (table III). Diagnostic categories are listed in table IV with most patients showing anxiety neurosis (71) psychophysiologic reactions (47) and obsessive-compulsive reactions (26) as the largest groups.

Other diagnosis are personality disorders (16), depressive reaction (18), unspecified neurosis (7) transient situational disorders (6), phobic reactions (3) and conversion reaction (1).

In the anxiety group more than 75% improved markedly. The improvements obtained in transient situational disorder (67%), psychophysiologic disorders (more than 60%) and obsessive compulsive reactions (40%) was somewhat less. Neurotic depressions, personality disorders, conversion reaction and phobic reactions do benefit from the drug although their numbers as well as improvement rates are less impressive.

In general, it can be said that the treatment results are most satisfactory especially if we keep in mind the variety of conditions in which the drug proved beneficial.

VII. *Side effects*

Side effects consisted of fatigue, drowsiness, dizziness, disturbance of motoric coordination, gastrointestinal disturbances, cephalalgia, insomnia (very seldom), loss of appetite, general weakness, and sometimes excitement. It is our impression that side effects generally are not severe and have the tendency to diminish or disappear spontaneously afterwards, with or without reducing the dosage.

Usually side effects tend to appear in the first or second week of treatment both with low, as well as high dosages.

In our clinical study 13% (26) of the 195 patients developed side effects, 10 of them experienced one sort of side effect, 5 of the patients 2; 7 of them 3; and 4 patients 4 kinds of side effects.

Usually side effects are transient. Tolerance towards the drug is good.

VIII. *Conclusion*

A simple and open drug study was done with RO 5–3350 on 195 ambulatory patients suffering from a variety of neurotic conditions. The effectiveness of the drug was assessed and established based on clinical experiences. It is our impression that RO 5–3350 although at present not yet available commercially on the Indonesian market, can be listed as a highly effective anti-neurotic drug. It is well tolerated by the majority of patients.

Based on experiences with the drug further studies with this compound are suggested especially in diagnostic categories which are, so far very resistent to drug-therapy, such as obsessive-compulsive neurosis and psychopathic conditions, since RO 5–3350 seems to give new hope in the treatment for these conditions.

Table I

AGE AND SEX OF PATIENTS

Age	Number of male patients	Number of female patients	Totals
10–19	16	7	23
20–29	55	28	83
30–39	24	21	45
40–49	15	12	27
50–59	9	4	13
60–69	1	3	4
Totals	120	75	195

Table: II

DOSAGE PER DAY

Amount	Percentage
5 – 6 mg	6%
9 – 10 mg	20%
12 – 15 mg	19%
18 – 20 mg	38%
24 – 30 mg	29%
32 mg and higher	21%

Table: III

IMPROVEMENT RATES

Result of treatment	Number of Patients	Percentage	
Very good	39	20%	
Good	74	38%	90%
Moderate	63	32%	
No effect	19	10%	
Totals	195	100%	

Table: IV

DIAGNOSTIC CATEGORIES, NUMBER OF PATIENTS AND IMPROVEMENT RATES

Diagnosis	Number of Patients			Rating of Effectiveness			
	Men	Women	Totals	Very good	Good	Moderate	No Effect
Anxiety neurosis	50	21	71	20	34	14	3
Psychophysiologic - reaction	28	19	47	10	20	15	2
Obsessive Compulsive - reaction	15	11	26	5	8	8	5
Reaction/neurotic- depression	8	10	18	–	5	10	3
Phobic reaction	2	1	3	–	–	1	2
Conversion reaction	–	1	1	–	–	1	–
Transient situational disorder	3	3	6	3	1	1	1
Personality disorder	10	6	16	1	2	11	2
Unspecified neurosis	5	2	7	–	4	2	1
Totals	120	75	195	39	74	63	19

Table: V

RATING IN PERCENTAGES OF EFFECTIVENESS

Diagnosis	Very good	Good	Moderate	No effect
Psychophysiologic reaction	21%	42.5%	32 %	4.5%
Anxiety neurosis	28%	48 %	19.5%	4.5%
Obsessive-Compulsive reaction	19%	31 %	31 %	19. %
Reactive/Neurotic depression	–	28 %	55.5%	16.5%
Conversion reaction	–	–	100 %	–
Phobic reaction	–	—	33 %	67 %
Transient situational disorder	50%	17 %	17 %	17 %
Personality disorder	6%	12.5%	69 %	12.5%
Unspecified neurosis	–	57 %	28.5%	14.5%
Totals	20%	38 %	32 %	10. %

Table: VI

IMPROVEMENTS

First week	5%
Second week	55%
Third week	47%
Fourth week	8%

INTRODUCING VALIUM IN NARCOANALYSIS

(A preliminary report of 10 cases)

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Narcoanalysis is a well-known method of interviewing a person by putting him under the influence of a drug which acts by disinhibiting higher cerebral functions. Its introduction probably arose out of the observation that certain chemicals like alcohol could make a normally reserved person more talkative and willing to divulge secret information or exert a disinhibiting influence on the person's behaviour.

Psychophysiologically this could be explained by the tranquillizing effect to the drug on the person's higher cerebral activities, allowing shameful or embarrassing materials to be released from the subconscious (normally suppressed or repressed).

Alcohol as an agent, though effective, is difficult to administer and measure. A variety of substances have been tried as a substitute for this purpose amongst which are amylobarbitone, methylamphetamine, ether, nitrous oxide, carbon dioxide and even LSD.

Barbiturates had been used by Sargant & Slater (1940) in the treatment of war neurosis with success. It was found to bring relaxation and