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RESOCIALIZING EFFECT OF PIMOZIDE ON CHRONIC INSTITUTIONALIZED SCHIZOPHRENIC PATIENTS

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INTRODUCTION

Pimozide, chemically designated as 1-(4.4 bis (p. fluorophenyl) butyl)-4-piperidyl)-2 benzimedazolone, with the trade name of ORAP, is a psychotropic drug of the diphenylbutylpiperidine category. In animal experiments and in early chemical trials it was noted that pimozide was effective in a single, daily oral dose (Pöldinger, 1971). This would be an important factor in the ease of administration, since a single dosage regimen promotes regular and continued use of the drug in maintenance therapy of chronic schizophrenic patients, both in hospital and on an outpatient basis as well.

Interesting for us was the report that pimozide would promote social contact, interest and initiative, and also increase the work capacity of chronic schizophrenics, which would be beneficial for the resocializing ability of the patients. The drug would be even effective in defective schizophrenics in whom the disease is fixed and accompanied by inertia, and who, moreover, have become incapable of self-criticism (Wauters, 1969).

An interesting point is further the report that extrapyramidal side-effects would occur less frequently than other potent neuroleptics and virtually no hypnosedative action which would facilitate the social integration of patients.

To check the above mentioned report, a clinical trial with pimozide has been conducted on chronic patients in the State Mental Hospital of Pakem, Yogyakarta, during about six months from January 1976 until June 1976.

AIM OF THE TRIAL

The aim of the trial was to investigate the actual effect of pimozide on chronic patients of the State Mental Hospital of Pakem, Yogyakarta, where most inhabitants consist of chronic schizophrenics who would stay in the hospital for their whole lives.

In this connection it would be very important if indeed we could increase their work-performance, productivity and social adaption, which would be very beneficial for the patients themselves and for the maintenance and the development of the hospital as well.

MATERIAL AND METHODS

1. Patient selection

The material of patients available for the trial was determined by the Director of the Hospital. Our sample consisted of twenty chronic schizophrenic patients of at least 3 years hospitalization, who did not get any neuroleptic drug for at least one year. They were all from a low social class, Javanese and have had a low formal education, ranging from elementary to primary high school education. Their age varied between 20 and 40 years.

Their mental status was checked by the usual psychiatric interview using the questionaire of the modified brief psychiatric rating scale comprising the following points:

1. communication ability
2. somatic concern
3. anxiety
4. emotional withdrawal
5. conceptional disorganization
6. guilt feelings
7. tension
8. mannerism and posturing
9. grandiosity
10. depressed mood
11. hostility
12. suspiciousness
13. hallucination behaviour
14. motor retardation
15. incooperativeness
16. unusual thought content
17. blunted affect
18. excitement
19. disorientation
20. interest
21. work performance

The psychiatric examination was supplemented by the oral report of the nurse and the ward attendant about the general behaviour and attitude of the patients, in particular concerning the work performance and social integration.

Possible side-effects which were considered during the trial included the following items:

1. extrapyramidal hypokinesia
2. muscular rigidity
3. muscular tremor
4. akathisia
5. insomnia
6. transpiration
7. dry mouth
8. blurred vision
9. Hypertension
10. vomiting

It appeared that all patients were chronic schizophrenics with some communication ability, very autistic with social and emotional withdrawal, blunted affect and low work performance.

At the beginning and at the end of each trial (stage) all patients were also physically and neurologically examined, including routine laboratory examination and liver function test. They did not show any remarkable deviation. The population was devided at random in 2 groups of samples, consisting of ten patients each, namely group A and group B. Group A consisted of 4 males and 6 females; group B consisted of 5 males and 5 females.

2. Trial design and description

The whole trial proceeded in two stages, each stage lasted for about 6 weeks. Between stage I and stage II was inserted a relaps period of 8 weeks.

In stage I group A was the trial group, group B was the control group. In stage II the groups were crossed over, so group A became the control group and group B the trial group.

The trial was conducted by a team consisting of the author as coordinator and responsible person, assisted by a clinical psychologist, a nurse/supervisor and the ward attendant in charge. The drug was taken orally by the patients of the trial group as a single dose in the morning before breakfast. The control group did not get any neuroleptic drug.

We began with a low dose of 2 mg a day and increased the dose gradually until the optimum dose was reached, which appeared to be about 6 mg a day for our patients. The optimum dose found in stage I was administered unchanged for the remaining trial. The task of the daily drug supply and administration was carried on by the nurse/supervisor assisted by the ward attendant in charge.

The weekly assessment was done by the psychiatric resident with the assistance of the nurse and supplemented by her observation report concerning the progress and development of the trial.

At the end of each stage a final assessment was conducted by the team. To obtain objective data concerning the resocializing effect of pimozide on the patients a special psychotest was matched and used, namely some parts of the modified Wechsler adult intelligence test.

Three items were considered relevant to the work performance and social cooperativeness of the patients, namely:

A — test for obedience and cooperation to do a task
B — test for work endurance
C — test for work effectivity

To obtain quantitative data a 4 point scoring scala was made.

For test A (obedience and cooperation to do a task).
score 4: means the task was spontaneously done
score 3: some work was done after some persuasion
score 2: some work done after some pressure
score 1: very small performance in spite of pressure
score 0: no performance at all.

For test B (work endurance)
score 4: endurance until the task was finished
score 3: endurance until the task was nearly finished
score 2: endurance until half of the task was finished
score 1: working for a while and than stopped
score 0: no work at all.

For test C (work effectively)
score 4: the task finished within a definite time

score 3: the task nearly finished
score 2: half of the task finished
score 1: a small part of the task finished
score 0: no performance at all.

The test was conducted to the trial group as well as to the control group at the end of each stage before and after the crossing over. So we used in this trial the experimental pattern the "same subject design". By this method we would minimize the impact of the variables such as education, intelligence, experience, culture and so on.

We would only to know the effect of the drug; this would say: was there any significant improvement in the work performance and social adaptability of the patients after taking pimozide for about 6 weeks. For that purpose we used the technic of the "null hypothesis", which we could state that there was no significant difference between the groups after taking the drug and without treatment at all. If we could reject the null hypothesis, so we might draw the conclusion, that indeed the drug had a real and significant effect.

STATISTICAL DATA

By combining the experimental data obtained in stage I and stage II, we got the following Table.

	Name	Gender	Trial Score			Control Score		
			A	B	C	A	B	C
1.	M	m	4	3	3	2	1	1
2.	B	fm	2	1	1	0	0	0
3.	M	fm	4	4	4	3	3	2
4.	M	fm	3	2	2	0	0	0
5.	S	fm	3	2	1	0	0	0
6.	S	fm	4	3	2	0	0	0
7.	S	fm	2	1	0	0	0	0
8.	S	fm	4	4	3	3	3	3
9.	S	fm	4	4	4	2	2	2
10	S	fm	0	0	0	0	0	0
11.	L	fm	4	4	4	0	0	0
12.	J	fm	4	3	3	2	2	2
13.	D	m	4	4	4	2	2	2
14.	S	m	4	4	4	4	4	4
15.	P	m	4	4	4	3	3	3
16.	S	m	3	2	1	0	0	0
17.	M	m	2	1	1	0	0	0
18.	S	m	0	0	0	0	0	0
19.	G	m	2	1	1	0	0	0
20.	J	m	0	0	0	0	0	0

About further statistical operation see Appendix.

RESULT

By applying the t-test (formula) for small samples we obtained the following result:

For test A: $t = 3{,}48$; so $p < 0{,}05$
,, ,, B: $t = 3{,}00$ $p < 0{,}05$
,, ,, C: $t = 2{,}77$ $p < 0{,}05$

With above mentioned result, the null hypothese was rejected. Thus, we might say, that there was indeed a significant difference between the groups treated compared with the same groups when not treated. The result of the test was supplemented by the qualitative evaluation of the team during the trial.

It appeared that the evaluation of the team concerning the improvement of the communication ability, work capacity and social adaptability of the treated patients was also positive.

Concerning the side effects, we could not observe remarkable side effects except, two patients who showed slight tremor and rigidity which could be controled by some extrapyramidal drug.

It appeared further, that the effect of pimozide became remarkable after at least two weeks of treatment.

All in all we may regard the resocializing effect of pimozide on chronic institutionalized schizophrenic patients as positive and significant.

COMMENT AND CONCLUSION

Although the trial was positive, nevertheless we may not draw any general or far reaching conclusion from the trial. We admid, that there were some weaknesses in our experiment, namely the sample was not drawn randomly, but determined by the Director of the Hospital. And further the trial was not conducted as a double blind trial.

Whatever it might be, there was some satisfaction that our results were supported by earlier international trials concerning the resocializing effect of pimozide on chronic schizophrenic patients, among others Kristjansen (1971) and van Wijk (1972).

However, it is a pity, that we could not confirm the statement of Wauters, that even on defective patients pimozide would be effective, when we considered the absolute failure of pimozide on some patients in our trial (patients no. 10, 18 & 20). Finally, the practical use of pimozide for the patients in the state mental hospitals in Indonesia is small in our opinion, because of the expensive price at present.

SUMMARY

A clinical trial of pimoxide has been conducted on 20 chronic institutionalized schizophrenic patients, using the "same subject design". The aim was to check the resocializing effect of pimozide such as reported in same papers.

A psychotest was constructed to obtain quantitative data concerning obedience and cooperativeness to do a task, work and work capacity. The quantitative data obtained were supplemented with the data observed qualitatively by the experimenting team.

The effect of pimozide appeared to be positive and significant with minimal side effect.

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APPENDIX: Statistical analysis

Test A	Trial				Control			
	x	f	fx	fx^2	y	f	fy	fy^2
	4	10	40	160	4	1	4	16
	3	3	9	27	3	3	9	27
	2	4	8	16	2	4	8	16
	1	0	0	0	1	0	0	0
	0	3	0	0	0	12	0	0
	—	20	57	203	—	20	21	59
		N Σ	fx Σ	fx^2		N Σ	fy Σ	fy^2

1. $M_x = \frac{fx}{N} = \frac{57}{20} = 2{,}85$

2. $SD_x^2 = \frac{\Sigma fx^2}{N} - (m_x)^2$

$= \frac{203}{20} - (2{,}85)^2$

$= 10{,}15 - 8{,}12$

$= 2{,}03$

3. $SD_{M_x}^2 = \frac{SD_x^2}{N-1}$

1. $M_y = \frac{fy}{N} = \frac{21}{20} = 1{,}05$

2. $SD_y^2 = \frac{\Sigma fy^2}{N} - (M_y)^2$

$= \frac{59}{20} - (1{,}05)^2$

$= 2{,}95 - 1{,}10$

$= 1{,}85$

3. $SD_{My}^2 = \frac{SD_y^2}{N-1}$

$= \frac{2,03}{20-1} = 0,168$ $= \frac{1,85}{20-1} = 0,09$

4. $SD_{bM} = \sqrt{(SD_{Mx}^2 + SD_{My}^2)}$

$= \sqrt{(0,168 + 0,09)}$

$= \sqrt{0,258} = 0,52$

5. $t = \frac{M_x - M_y}{SD_{bM}} = \frac{2,85 - 1,05}{0,52} = \frac{1,80}{0,52} = 3,48$ $p < 0,05$

Test B	Trial			Control			
x	f	fx	fx^2	y	f	fy	fy^2
4	7	28	112	4	1	2	16
3	3	9	27	3	3	9	27
2	3	6	12	2	3	6	12
1	4	4	4	1	1	1	1
0	3	0	0	0	12	0	0
	20	47	155		20	20	56
	$N\Sigma$	$fx\Sigma$	fx^2		$N\Sigma$	$fy\Sigma$	fy^2

1. $M_x = \frac{fx}{N} = \frac{47}{20} = 2,35$

1. $M_y = \frac{fy}{N} = \frac{20}{20} = 1$

2. $SD_x^2 = \frac{\Sigma fx^2}{N} - (M_x)^2$

$= \frac{155}{20} - (2,35)^2$

$= 7,75 - 5,52 = 2,23$

2. $SD_y^2 = \frac{\Sigma fy^2}{N} - (N_y)^2$

$= \frac{56}{20} - (1)^2$

$= 2,80 - 1 = 1,80$

3. $SD_{Mx}^2 = \frac{SD_x^2}{N-1}$

$= \frac{2,23}{20-1}$

$= 0,117$

3. $SD_{My}^2 = \frac{SD_y^2}{N-1}$

$= \frac{1,80}{20-1}$

$= 0,09$

4. $SD_{bM} = \sqrt{(SD_{Mx}^2 + SD_{My}^2)}$

$= \sqrt{(0,117 + 0,09)}$

$= \sqrt{0,207}$

$= 0,45$

5. $t = \frac{M_x - M_y}{SD_{bM}} = \frac{2,35 - 1}{0,45} = \frac{1,35}{0,45} = 3,00$ $p < 0,05$

Test C	Trial			Control			
x	f	fx	fx^2	y	f	fy	fy^2
4	6	24	96	4	1	4	16
3	3	9	27	3	2	6	18
2	2	4	8	2	4	8	16
1	4	0	0	0	1	1	1
0	4	0	0	0	12	0	0
	20	42	136		20	19	51
	$N\Sigma$	$fx\Sigma$	fx^2		$N\Sigma$	$fy\Sigma$	fy^2

1. $M_x = \frac{fx}{N} = \frac{42}{20} = 2,10$

1. $M_y = \frac{fy}{N} = \frac{19}{20} = 0,95$

2. $SD_x^2 = \frac{\Sigma fx^2}{N} - (M_x)^2$

$= \frac{136}{20} - (2,1)^2$

$= 6,8 - 4,41 = 2,39$

2. $SD_y^2 = \frac{\Sigma fx^2}{N} - (M_y)^2$

$= \frac{51}{20} - (0,95)^2$

$= 2,55 - 0,90 = 1,65$

3. $SD_{Mx}^2 = \frac{SD_x^2}{N-1}$

$= \frac{2,39}{19} = 0,13$

3. $SD_{My}^2 = \frac{SD_y^2}{N-1}$

$= \frac{1,65}{19} = 0,076$

4. $SD_{bM} = \sqrt{(SD_{Mx}^2 + SD_{My}^2)}$

$= \sqrt{(0,13 + 0,076)}$

$= \sqrt{0,206} = 0,45$

5. $t = \frac{M_x - M_y}{SD_{bM}} = \frac{2,10 - 0,95}{0,45} = 2,777.$ $p < 0,05$