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Psychiatric Complications of Propranolol Therapy in Essential Hypertensives

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ABSTRACT

Thirty patients, 25–57 years old, subjects of uncomplicated essential hypertension were chosen from Fayoum General Hospital out-patients. Propranolol was used as 40 mg t.d.s. for one week then 80 mg t.d.s. for 2 weeks. Half of the subjects started on propranolol for 3 weeks and shifted to placebo for another 3 weeks. The other half started by the placebo for 3 weeks then shifted to propranolol. The Brief Psychiatric Rating Scale of Overall and Gorham (1962) was used to assess the subjects before and after treatment on 11 psychiatric variables. The design was a double blind cross over one. Under propranolol there was definite improvement in somatic concern, anxiety, tension and emotional withdrawal. and there was deterioration of depressive mood, guilt feelings, motor retardation and psychological impotence. All patients showing depression and psychological impotence showed type B behavior of Friedman & Rosenman.

The implications of these results in the fields of theory and practice are discussed.

INTRODUCTION

Essential hypertension is a very important public health problem all over the world with a marked variance in prevalence and incidence

between different populations. Current (1976) estimated a prevalence of 9.2% in males and 4.5% in females between ages of 25 and 34 years. It is a multicausal disorder of homeostasis resulting from environmental stress, social factors and emotional factors.

Psychopathologically hypertension occurs when the normal mechanisms are exaggerated by continual stress or trauma. Dynamically hypertension occurs when an active aggression response is inhibited. Certain personalities and acts will make a person more liable to hypertension. Psychophysiologically the tension is channelled through the hypothalamic vasomotor center and leads to sympathetic activity. Long term stresses raise the general adaptation syndrome responses of the pituitary – adrenal system. However testosterone and oestrogen levels also affect the blood pressure (Price, 1982).

There is some evidence for a relationship between type A and hypertension. Friedman and Rosenman (1959) reported a Type A pattern in 34.8% of hypertensives and 4.5% Type B. Type B behavior is less prevalent in hypertensives than coronary heart disease patients.

Management of essential hypertension involves early detection, early and consistent treatment with hypotensive drugs, support of the patient's motivation for continued treatment, psychotherapy, and psychotropic drugs during periods of excessive emotional arousal.

B-Blockers are widely used nowadays as hypotensives alone or combined with other drugs and usually tried early and administered for a long time. B-Blockers main mode of hypotensive action is still uncertain; of the known mechanisms are reduction in cardiac output, resetting of baroceptors or other long term adaptation, reduction in plasma renin and reduction in plasma volume. Site of action is B-adrenoceptors, Renin-Angiotensin system and probably an unidentified mid brain antihypertensive action. Recommended daily hypotensive dose of Propranolol is 30 – 960 mg. (Lund-Johansen

and Ohm, 1976; Buhler et al., 1972; Rand et al., 1976; Stumpe et al., 1976).

Propranolol is a non selective B1 + B2 blocker. It antagonizes competitively the effects of catecholamines released from adrenerigic nerves or from adrenal medulla on all B-receptors (Groth, 1981). During B-blocking the plasma nor-adrenaline clearance is markedly reduced. Reduction of adrenergic activity involving B-adrenoceptors can be beneficial whether peripheral sympathetic, adrenal medullary secretion or C.N.S. adrenergic activity (Laurence and Bennett, 1980).

B-adrenergic blocking agents may block the autonomic signals of anxiety, i.e. improve anxiety symptoms but not insomnia. Because of its blocking effects on catecholamine receptors, propranolol was tried on acute schizophrenics with some success. 640 mg. per day for three months did not improve schizophrenic symptoms in chronic schizophrenics (Peet et al., 1981). 160 mg. propranolol causes E.E.G. change and suggests a direct action on the brain in the corticothalamic and deeper subcortical area. This action on the brain is fast and confirms the ability of the drug to pass the blood brain barrier (Roubicek, 1980).

The psychiatric complications of B-blockers include lack of concentration, loss of ambition, depression, sexual side effects, confusion, blurring of vision, visual hallucinations and catatonia. Disturbance of sleep patterns and troublesome dreams are not infrequent in patients taking large doses.

Petrie et al (1982) reported three cases out of 34 patients had depressive episodes after administration of propranolol for medical illness. Other authors who documented the propranolol's psychiatric complications are Anne-Gremone (1983), Schuckit and Russel (1982) and Schildkraut et al. (1968).

MATERIAL AND METHOD

Subjects were 30 male hypertensive patients aged 25 – 57 years and outpatients. They were selected from a population of 57 users of the Fayoum General Hospital. Criteria for inclusion as subjects were a mild to moderate state of uncomplicated essential hypertension and suitability for propranolol therapy. Criteria for exclusion were diabetes, cardiac or urinary abnormalities, bronchial asthma, depression and poor cooperativeness. They were divided into 2 subgroups (16 subjects and 14 subjects) almost similar as regards age, social standard, physical status and prevalence of type A behavior. Design of experiment was a double blind crossover administration of propranolol or placebo. The first group went for 21 days on placebo then 21 days on propranolol (40 mg t.d.s. for one week then 80 mg t.d.s. for two weeks). The second group started the experiment by the drug then followed the placebo.

Before introduction to the experiment, the subjects underwent a basic clinical and standard laboratory evaluation including full urine picture and blood urea estimation. A psychiatric interview was used to exclude cases of psychiatric disorder or severe symptoms. All subjects were assessed as regards Type B behavior according to the method of Friedman and Rosenman (1959). Also their profile as regards Type A and Type B patterns according to Jenkins et al. (1968) was drawn.

Throughout the experiment the physical clinical evaluation was done every week. The Brief Psychiatric Rating Scale of Overall and Gorham (1962) was the main tool to assess psychiatric effects of the drug and placebo. It was applied before and after the drug or the placebo. An Arabic version of the original English scale was used.

Statistical analysis of the results included :

1. Determining the statistical significance of differences between means with the threshold of 5% as the acceptable.

2. Pie-charts and scatter diagrams to indicate the relation between score before and after different phases of the experiment.

RESULTS

A – Table I shows the effects of either propranolol or placebo on the 11 psychiatric variables measured by the Brief Psychiatric Rating Scale. The effect due to spontaneous change over time is also taken in consideration.

B – The Salient results of the statistical analysis are :

1. Somatic Concern :

   a – Placebo does not seem to have an effect on somatic concern.

   b – After propranolol all patients had lower grades of somatic concern,to a highly statistically significant degree.

2. Tension :

   There was a tendency towards decrease in tension under propranolol. Differences did not reach statistical significance.

3. Anxiety :

   After propranolol all patients tended to have lesser degrees of anxiety. Differences did not reach statistical significance.

4. Motor Retardation :

   There was no evidence for a relationship between motor retardation and propranolol in this study.

5. Depressive Mood :

   a – There was a tendency to increase in depressive mood under propranolol therapy that was very close to the threshold of statistical significance.

   b – There was a tendency to decrease to the initial level after placebo.

TABLE I

Summarizing the Trend Direction of Change of Different Symptoms in the Different Phases of Each Experiment.

SYMPTOM	No. of Patients	After 21 days on placebo				After 21 days on placebo + 21 days on propranolol.				After 21 days on Propranolol.			After 21 days on propranolol + 21 days on placebo.				
		Absent	No change	Increase	Decrease	Absent	No change	Increase	Decrease	Absent	No change	Increase	Decrease	Absent	No change	Increase	Decrease
Somatic concern	30	—	6	6	4	7	—	1	8	6	—	—	8	—	3	10	1
Anxiety	12	—	3	2	2	3	—	1	3	2	—	1	2	—	3	1	1
Tension	12	2	2	1	—	3	2	—	—	3	1	3	—	3	2	1	1
Motor Retardation	8	—	5	—	—	1	—	3	1	2	—	1	—	1	—	2	—
Guilt Feelings	7	—	3	—	—	1	—	2	—	2	—	2	—	2	2	—	—
Depressive Mood	6	—	3	—	—	—	—	2	1	—	—	3	—	2	—	—	1
Uncooperativeness	5	—	1	—	1	2	—	—	—	1	—	—	2	2	1	—	—
Emotional Withdrawal	3	—	1	—	1	2	—	—	—	1	—	—	—	—	1	—	—
Psychological Impotence	3	—	—	—	—	—	—	—	—	—	—	3	—	—	—	—	3
Blunted Affect	2	—	1	1	—	2	—	—	—	—	—	—	—	—	—	—	—
Hallucinatory Behaviour	1	—	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—

6. **Guilt Feelings :**

The relation between guilt feelings and propranolol cannot be proved by these results.

7. Uncooperativeness :

There is no marked effect on uncooperativeness by propranolol .

8. **Emotional withdrawal :**

Numbers are too small to draw a definite conclusion.

9. **Psychological Impotence :**

There is no evidence of a marked relationship between this symptom and propranolol.

10. Blunted Affect :

The number of patients is too small to detect any relationship.

11 Hallucinatory Behavior :

One patient developed hallucinatory behavior up to grade three after propranolol therapy, that disappeared on withdrawal of the drug.

C – The profile of the 30 hypertensive Egyptian patients as regards Type A and Type B behavior went on a continuum as follows :

Type A=8, more towards type A = 10, mixed A & B =4,more towards B=6, and Type B=2.

There was a 26.6% prevalence of Type A Behavior and 6.6% prevalence of Type B Behavior.

DISCUSSION

I – Variables that improved under propranolol therapy were somatic concern, anxiety, tension and emotional withdrawal. The mechanism of action of propranolol on these psychiatric symptoms is largely unknown and could be on central or peripheral nervous system. Also it is relevant here to remember that propranolol has pharmacological effects other than beta-adrenergic blockade including membrane stabilizing activity (quinidine like or local anaesthetic action with large doses, and a sedative and anti-convulsant central nervous effect (Heiser and Derancisco, 1976). Propranolol blocks peripheral autonomic events including the autonomic signals of anxiety. Propranolol reduces tachycardia, palpitation, tremor and vascular headache but not insomnia, and it does not work by inducing sedation (Kelly, 1981).

II – Variables that deteriorated under propranolol were depressive mood, guilt feelings, motor retardation, and psychological impotence. In this area it is easier to find mechanisms of action. Propranolol deterioration may result from central beta blockade and is consistent with catecholaminergic theories of depression which relate such illness to a decrease in central norepinephrine activity. More recent theories of affective illness have postulated a defect of B - adrenergic regulation of post-synaptic receptor sensitivity, rather than altered availability of neurotransmitters at receptor sites (Petrie **et al.,** 1982).

IV – Our findings cross validate many published reports that propranolol induces significant side-actions in the psychiatric variables of patients, e.g. Stephens (1966), Greenblatt and Shader (1972) and Peters **et al.** (1978).

V – 26.6% Type A and 6.6% Type B behavior prevalence in our Egyptian hypertensives is not quite concordant with the

rates of Rosenman and Friedman (1959) on their hypertensive patients (34.8% type A and 4.5% type B). Explanation of this is to be sought in variance as regards sex, culture, environment and social factors.

VI – All patients who were affected by depression and psychological impotence were of Type B behaviour. Other psychological disorders were not related to the type of behavior. This is just one of the insights into the relation between behavior type and psychopathology in this study. We may come to more in a separate publication.

VII – We can safely state the following advice for users of propranolol in hypertension:

a – Propranolol in the 120 – 240 mg daily doses for as short a time as one to two weeks can cause insomnia, nightmarse, depression, visual hallucinations and toxic psychosis.

b – We suggest that you avoid late evening dosage for the sleep disturbances.

For depression, visual hallucinations or toxic psychosis, stop the drug and change to other drugs excluding also methyldopa, reserpine and clonidine.

c – Special care should be given to patients showing type B behavior for their greater susceptibility to show depressive mood under propranolol.

c – We recommend the combined hypotensive drug therapy that minimizes the dose of any one drug and decreases its side effects.

VIII – We recommend a wider and longer clinical trial of propranolol for its psychiatric side effects in Egypt.

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الموجـــــــز

الآثار النفسية لعقار البروبرانولول فى مرضى ارتفـــاع ضغط الدم الأســـاسى

موضوع الدراسة ثلاثون مريضا بارتفاع ضغط الدم الأســـــاسى تم اختيارهم من العيادة الخارجية لمستشفى الفيوم العام على أساس عمرى بين ٢٥ ـــ ٤٢ ومن الذكور فقط وخلوهم من المضاعفات الجسمية والنفسية.

تم تصنيفهم من حيث سيادة السلوك « الف » أو « باء » حســـــب تقسيم فريدمان وروزنمان .

تمت تجربة الدواء بروبرانولول على جميع المرضى لمدة ثلاثة أسابيع (أسبوع بـ ٤٠ ملجم ٣ مرات يوميا واسبوعين بـ ٨٠ ملجم ٣ مرات يوميا)

فى مقابل مدة ضابطة تناول فيها نفس المرضى مادة خاملة (بلاسيبو) لمدة ثلاثة أسابيع كذلك . ابتدأ نصف المرضى بالعقار النشـــــط وابتدأ النصف الثانى بالمادة الخاملة وروعى فى تنفيذ التجربة جهل الباحث والمريض كلاهما بطبيعة المادة موضوع التجربة (تكنيك الدوبل بليند) .

تم تقويم الحالات قبل وبعد تناول العقارين النشط والخامل باستخدام أداة « مقياس الطب النفسى القصير » لأوفراول وجورهام ويشـــــمل ١١ متغيرا .

ظهر من الدراســـة تحســـــين حالة المرضى على أربع متغيرات هى الانشغال بالحالة الجسمية ، التوتر ، الانسحاب العاطفى ، وكذلك تدهور حالة المرضى على أربع متغيرات هى المزاج المكتئب ، مشـــــاعر الذنب ، التأخير الحركى ، العنة النفسية .

أظهر المصابون بالمزاج المكتئب والعنة النفسية سيادة للســـــلوك « باء » .

تناقش الدراســـــة انعكاس هذه النتائج على الجوانب النظـــــرية والعملية .

ABSTRAIT

Complications Psychiatriques Du Traitemeut Au Propranolol Dans L'Hypertention Essentielle

Nous avons choisis 30 malades, agés de 25 – 57 ans, atteints d'hypertention essentielle sans complications, de la clinique de l'hôpital genéral de Fayoum. La dose de propranolol était de 40 mg trois fois par jour, pour une durée d'une semaine, suivit de 80 mg trois fois par jour pour deux autres semaines.

La moitié des malades commencèrent par le propranolol pour une durée de 3 semaines puis continuèrent avec un "placebo" pour 3 autres semaines, l'autre moitié suivirent le regime contraire, 3 semaines avec un "placebo" suivit de 3 semaines sur propranolol.

Le B.P.R.S. (Brief psychiatric rating scale) a été utilisé pour évaluer les malades avant et après le traitement, à propos de 11 variables psychiatriques.

Sous traitement avec le propranolol, une amélioration a été clairement remarquée en ce qui concerne les préoccupations somatiques, l'anxiété, la tension, et l'isolement affectif. Par contre aggravation s'est produite en ce qui concerne l'humeur depressive, les sentiments de culpabilité, l'inhibition motrice, et l'impuissance psychologique.

Les implications pratiques et théoriques de ces résultats sont discutées dans cette étude.