Pharmacopsychiatry
Main Editor: B. Saletu (Vienna)

Neuropsychobiology

Original Paper

Neuropsychobiology 1996;33:186–188

L. Rampello[a], *R. Raffaele*[a]
G. Nicoletti[b], *F. Le Pira*[a]
M. Malaguarnera[c], *F. Drago*[d]

Institutes of
[a] Neurological Sciences,
[b] Neurosurgery,
[c] Internal Medicine, and
[d] Pharmacology, University of Catania, Italy

Hysterical Neurosis of the Conversion Type: Therapeutic Activity of Neuroleptics with Different Hyperprolactinemic Potency

Key Words
Hysterical neurosis
Prolactin
Sulpiride
Haloperidol

Abstract
To show a possible correlation between drug-induced hyperprolactinemia and improvement of hysterical neurosis of the conversion type, we followed 18 patients monitoring clinical somatic and psychic symptoms as well as serum prolactin levels. Six patients were treated with haloperidol and 12 with sulpiride; after 2 months sulpiride was administered at half the daily dose to 6 patients previously treated with the same drug. Clinical evaluation showed that sulpiride treatment led to a greater improvement compared to the haloperidol group. The different effectiveness of treatment could be explained by the different hyperprolactinemic potency. The therapeutic efficacy of neuroleptics suggests also that hyperactivity of dopaminergic transmission is involved in the pathophysiology of hysterical neurotic symptoms.

Introduction

An incidence of hysterical neurosis among neurological patients ranging between 1 and 9% has been reported [1]. Although this matter has been the subject of extensive investigation, little is known about its pathophysiology in terms of neurochemical abnormalities. In this study we have addressed this problem by comparing the therapeutic efficacy of haloperidol with that of sulpiride, a D2-receptor antagonist with marked hyperprolactinemic effects, in patients affected by hysterical neurosis of the conversion type.

Materials and Methods

We have studied 18 patients (13 females and 5 males; age range: 24–64 years) suffering from recurrent hysterical neurosis of the conversion type, according to the Diagnostic and Statistical Manual of Mental Disorder-III-R criteria (n. 300.11) [2]. The most common symptoms observed were: paralysis, anesthesia, pseudoseizures, ataxia, aphonia, amnesia and agraphia (table 1). The psychological factors of their etiology were mostly (70%) related to family, occupation, relationship problems and to a smaller extent, to intrapsychic conflicts. Most (n = 12) patients had been unsuccessfully treated with antidepressants (desipramine, clomipramine or amitryptiline) and/or benzodiazepines (bromazepam, diazepam or lorazepam). All patients were hospitalized before inclusion in the study and subjected to routine laboratory and X-ray analysis, EEG recording, computed tomography or magnetic resonance imaging. Patients suffering from severe somatic illness, brain damage, myelinopathy or a psychotic disorder were excluded. After a washout period of at least 1 week, two groups sex- and age-matched were randomly treated with haloperidol (n = 6) and sulpiride (n = 12). Haloperidol was administered orally in a dose of 1 mg b.i.d. for the 1st week and increased to 2 mg t.i.d. in the 2nd week of treatment (a large dose of haloperidol impairs compliance in these patients). Sulpiride was administered orally at an initial dose of 100 mg per day. The daily dose was gradually increased to 400 mg b.i.d. from the 4th day of administration. After 2 months the drug was administered at half the daily dose to 6 patients of the last group while the treatment with haloperidol was discontinued. Our study lasted 4 months. The severity of symptoms was evaluated before and every month after the treatment by 2 physicians unaware of the medication, using the clinical evaluation of somatic symptoms (paralysis, anesthesia, pseudoseizures), the 8

KARGER
E-Mail karger@karger.ch
Fax + 41 61 306 12 34
http://www.karger.ch

0302–282X/96/0334–0186$10.00/0

Prof. Liborio Rampello
Istituto di Scienze Neurologiche
Policlinico dell'Università di Catania
V.le A. Doria, 6
I–95125 Catania (Italy)

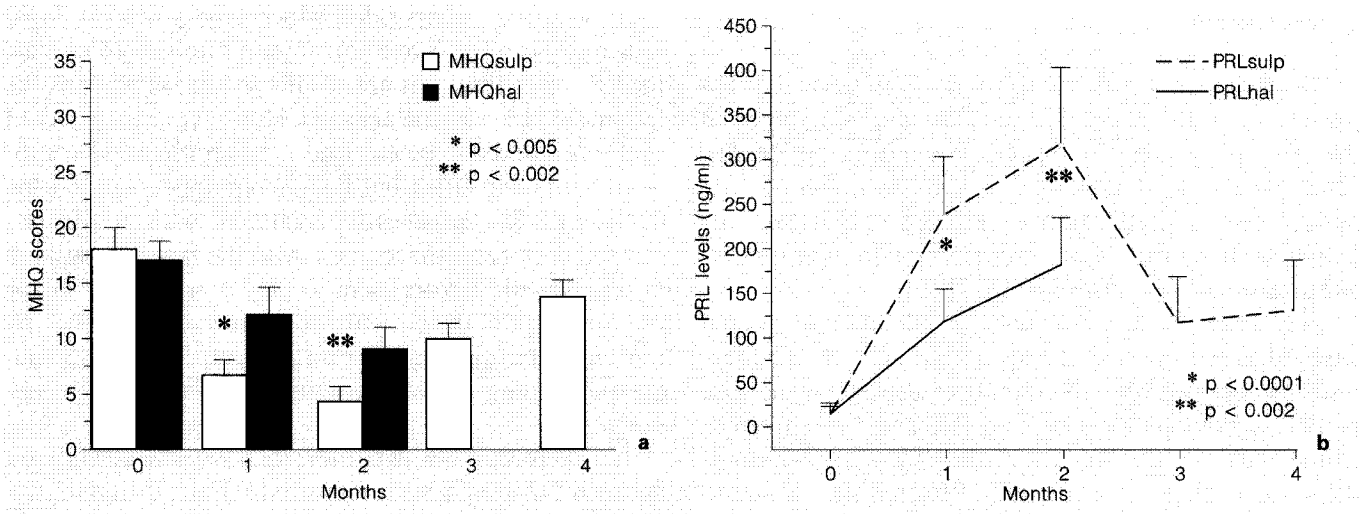

Fig. 1. Severity score of neurotic symptoms (**a**) and PRL levels (**b**) in patients treated with sulpiride (sulp) and haloperidol (hal) for 4 months. A score ranging from 0 to 3 was given to each of the 8 items of the subtest specific for hysterical traits and symptoms in the MHQ. A comparison is made between the two treatments after 1 and 2 months. **a** * $p < 0.005$; ** $p < 0.002$. **b** * $p < 0.0001$; ** $p < 0.002$.

items of the subtest of the Middlesex Hospital Questionnaire (MHQ) specific for hysterical traits and symptoms (MHQ) [3] and the Hamilton Depression and Anxiety Rating Scale (HDRS and HARS) [4, 5]. Blood samples for prolactin (PRL) determination were collected every month at the same time. All blood samples were collected in heparin, rapidly centrifuged, and stored at −20 °C until assayed. PRL was measured by RIA (Amersham). The sensitivity of the PRL assay was 1 ng/ml and intra- and interassay coefficients of variation were 4.5 and 6%, respectively. Student's test, analysis of variance and correlation coefficient determination were used in the statistical analysis to determine the differences between means and the correlation between the various parameters.

Table 1. Symptoms exhibited by 18 patients (some complained of more than one symptom)

Symptoms	Patients
Paralysis	9
Anesthesia	5
Pseudoseizures	4
Ataxia	2
Aphonia	2
Amnesia	1
Agraphia	1

Results

The results showed that both HDRS and HARS scores exhibited slight variations from normal values for depression and anxiety without significant differences, measured by the analysis of variance, during the treatment with the two drugs. Although other authors [6, 7] have observed the presence of depression in convension phenomena, our patients showed neither important depressive symptomatology nor anxiety. Clinical evaluation and the MHQ showed that sulpiride treatment led to a greater improvement in neurotic symptoms compared to the haloperidol group, inducing a slow but progressive motor and/or sensory recovery, decrease or disappearance of pseudoseizures. Patients treated with haloperidol also improved, albeit to a smaller extent. In the sulpiride group 8 patients remarkably improved, 2 partially improved and 2 did not improve while in the haloperidol group 1 remarkedly improved, 3 partially improved and 2 did not improve.

In both groups we found significant differences ($p \leq 0.0001$), measured by the analysis of variance, in MHQ scores. As expected, repeated sulpiride and haloperidol administration induced a marked increase in plasma PRL levels with significant differences compared with basal levels. In the next 2 months, the reduction of the sulpiride dose induced a relevant decrease of PRL plasma levels in 6 patients which paralleled a decrease in clinical improvement (fig. 1). The regression analysis showed a significant negative correlation between clinical data and PRL levels ($r = -0.795$; $p \leq 0.0001$).

Discussion

The therapeutic efficacy of sulpiride suggests that hyperactivity of dopaminergic transmission is involved in the pathophysiology of hysterical neurotic symptoms. This hypothesis is supported by the impairment of the clinical picture that we have observed [11] in patients treated with amineptine, a drug reported to increase central dopaminergic transmission [12].

The action of sulpiride both in clinical and animal studies has been ascribed to the inhibition of the D2 dopamine receptor subtype which induces also a large increase in PRL secretion [8]. The drug-induced hyperprolactinemia could, at least in part, explain the effectiveness of sulpiride in our neurotic patients. PRL has been found to act as a modulator of central dopaminergic transmission in experimental animals [9, 10]. It is consistent with this hypothesis that haloperidol, which blocks central dopamine receptors but is less potent than sulpiride in increasing PRL secretion, was not as effective as sulpiride in the treatment of hysterical neurosis. However, the activity of sulpiride could also be ascribed to its antidepressant and/or tranquilizing effect but this theory appears untenable because of the unsuccessful treatment with antidepressants and/or benzodiazepines. Also the possible changes in psychogenic factors seem to play a minor role in the improvement of the patients' condition since the therapy was only pharmacological. Furthermore during the washout period only slight nonsignificant changes were observed.

In conclusion, our data indicate a positive correlation between D2-dopamine receptor inhibition, drug-induced plasma PRL levels and the improvement of patients affected by hysterical neurosis of the conversion type.

References

1 Lempert T, Dieterich M, Huppert D, Brandt T: Psychogenic disorders in neurology: Frequency and clinical spectrum. Acta Neurol Scand 1990;82:335–340.

2 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 3. Washington, APA, 1987.

3 Crow NS, Crisp AH: A follow-up of patients suffering from hysteria. Br J Psychiatry 1966; 112:917.

4 Hamilton M: Development of a rating scale for primary depressive illness. Br J Clin Psychol 1967;6:278–296.

5 Hamilton M: The assessment of anxiety states by rating. Br J Med Psychol 1959;32:50–55.

6 Purtell JJ, Robin E, Cohen ME: Observation on clinical aspects of hysteria. A quantitative study of patients and 156 control subjects. JAMA 1951;146:902–909.

7 Zeigler FJ, Imboden JB, Mejer E: Conversion reactions: a clinical study. Am J Psychiatry 1960;116:901–910.

8 Aparicio NJ: Effects of sulpiride on serum prolactin levels in humans. J Clin Endocrinol Metab 1976;42:181–184.

9 Drago F, Bohus B, Canonico PL, Scapagnini U: Prolactin induces grooming behavior in the rat: Possible involvement of nigrostriatal dopaminergic system. Pharmacol Biochem Behav 1981; 15:61–63.

10 Drago F, Genazzani AA: Prolactin affects adaptation and dysfunction to stress in the rat. Proc Int Congr Stress Related Disord, Modena 1990, pp 151–156.

11 Rampello L, Nicoletti G, Drago F: The dopaminergic hypothesis for hysterical neurosis of the conversion type: A study with sulpiride, haloperidol and amineptine. Acta Ther 1991; 17:195–202.

12 Garattini S, Mennini T: Pharmacology of amineptine: Synthesis and updating. Clin Neuropharmacol 1989;12(suppl 2):S13–S18.