Levodopa-Nicotinic Acid Interaction in Psychiatric Patients

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Introduction

The use of nicotinic acid for treatment in schizophrenia was and remains a controversial issue.[1, 2] The rationale for nicotinic acid therapy is based upon its capacity to accept methyl groups, thereby preventing the formation of an abnormal methylated compound with psychotomimetic properties.

Reports that the administration of levodopa causes psychiatric symptoms in Parkinson patients[3] and aggravates schizophrenic patients[4] has prompted us to theorize that levodopa might be a biochemical link in the formation of a pathological metabolite that could cause some forms of mental illness. If this aberrant metabolite requires a methyl group for its formation, it would be of interest to observe if nicotinic acid and L-Dopa have any antagonistic effect when administered to schizophrenic patients. Therefore, we initiated this study in our research facilities and the following is our preliminary report.

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Methodology

Nine male psychotic patients were selected for this study. The experimental design is shown in Table 1. Nicotinic acid was administered in tablets of 500 mg., three times daily in doses up to 2,000 mg. each. Levodopa was administered in capsules with gradual increases until 3 gm. daily was established within a two week period. Placebo constituted lactose in both tablet and capsule forms.

Blood chemistries, electroencephalograms and electrocardiograms were performed at regular intervals. Psychiatric Ratings and tests included the Brief Psychiatric Rating Scale, Clinical Global Impressions, Nurses' Observation Scale for Inpatient Evaluation, Treatment Emergent Symptoms and the Bender Gestalt test. Picture tests for recall, judgment, sensorium and reasoning were administered for each drug stage. Clinical psychiatric interviews were performed at more frequent intervals.

Results

One patient was discontinued from the project due to excessive nausea and vomiting when receiving L-Dopa. Seven patients sustained a weight loss with a minimum of five pounds and a maximum of ten pounds ($x = 7.7$).

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A decrease in blood pressure values were recorded in seven patients while receiving either nicotinic acid or L-Dopa; conversely, these readings returned to baseline values when both drugs were combined. Clinical observations indicated that nicotinic acid (4.5 gm. daily) when given alone had tran-quilizing effects in two patients.

When L-Dopa was administered alone an alerting effect and an increase of verbalization, besides the aggravation of their mental symptoms, was noticed. During the combined administration, the exacerbation of symptoms were not controlled in two patients. The alerting effect and increased verbalization at low doses of L-Dopa disappeared with the addition of nicotinic acid, and three patients became depressed.

Severe paranoid symptoms at low and high doses of levodopa discontinued when 6 gm. of nicotinic acid was added. The same response was noticed in one patient who had auditory hallucinations.

Table II shows the findings of the psychological tests. Positive or negative changes are recorded, with blank areas representing no changes. Patient R.K. was uncooperative and refused to perform psychological tests; therefore he was not included in Table II.

Discussion

Although the hypotensive action of nicotinic acid and levodopa are known to exist, we are not able to explain the return to basal levels when drugs were combined.

Another interesting finding is the weight loss experienced by patients throughout the study, without the presence of anorexia. Before the onset of this study our patients were receiving phenothiazine medication,

TABLE I

RESEARCH DESIGN

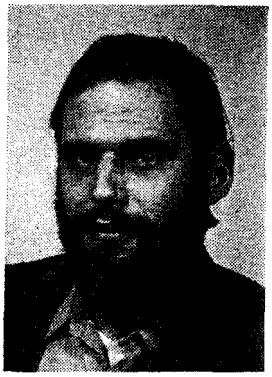
Patient	*Stage I Experimental Drug Alone (low dose)*	*Stage II Experimental Drug Alone (high dose)*	*Stage III Combined Drugs (low dose)*	*Stage IV Combined Drugs (high dose)*
C.E.	1 gm. L-dopa	3 gm. L-dopa	3 gm. L-dopa + 3 gm. Nicotinic Acid	3 gm. L-dopa + 6 gm. Nicotinic Acid
R.G.	1 gm. L-dopa	3 gm. L-dopa	3 gm. L-dopa + 3 gm. Nicotinic Acid	3 gm. L-dopa + 6 gm. Nicotinic Acid
R.K.	1 gm. L-dopa	3 gm. L-dopa	3 gm. L-dopa + 3 gm. Nicotinic Acid	3 gm. L-dopa + 6 gm. Nicotinic Acid
T.O.	1 gm. L-dopa	3 gm. L-dopa	3 gm. L-dopa + 4.5 gm. Nicotinic Acid	3 gm. L-dopa + 6 gm. Nicotinic Acid
A.B.	3 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid + 1 gm. L-dopa	4.5 gm. Nicotinic Acid + 3 gm. L-dopa
M.G.	3 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid + 1 gm. L-dopa	4.5 gm. Nicotinic Acid + 3 gm. L-dopa
N.L.	3 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid + 1 gm. L-dopa	4.5 gm. Nicotinic Acid + 3 gm. L-dopa
R.W.	3 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid	4.5 gm. Nicotinic Acid + 900 mg. L-dopa	4.5 gm. Nicotinic Acid + 2 gm. L-dopa

which usually causes weight increase. Therefore, the discontinuation would account for the loss of weight. In addition, levodopa is known to increase metabolic activities, thus augmenting caloric con-sumtion.

All patients experienced changes on the Bender Gestalt test. Hains suggests that this test does not pick up impairment associated with small localized lesions in the brain, but is sensitive to diffuse cortical damage.[5] An improvement in the Bender Gestalt test in five patients receiving levodopa alone or combined, corroborated previous psychophysiological evidence depict-ting L-dopa as having a cortical action.[6]

Our clinical findings somewhat support previous reports where nicotinic acid was shown to have antipsychotic properties[1] and levodopa or its metabolites to be a psychomimetic agent.[4] In this regard there is some evidence that 6-hydroxydopamine can be a psychotomimetic agent.[7]-[8] If this is the pathological metabolite that produces mental symptoms, it has yet to be determined.

On the other hand, a transmethylation disorder in catecholamine synthesis for the etiology of schizophrenia has been offered by various investigators.[9, 10] Nicotinic acid, as a methyl acceptor, would have a therapeutic effect with these patients.



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It should be considered that schizophrenia as defined today, may be more than one disease. Thus, selecting samples of patients becomes quite complex, and uniformity of response to drug action cannot always be expected. This could account for the various responses seen during this study, including the complete lack of interaction in two cases.

At the present time we continue to investigate levodopa-nicotinic acid interaction.

TABLE II

PATIENT CHANGES ON PSYCHOLOGICAL TESTS

Patient	**Recall** Improve	Worse	**Judgment** Improve	Worse	**Sensorium** Improve	Worse	**Reasoning** Improve	Worse	**Bender-Gestalt** Improve	Worse
C.E.	II, IV	I, III	IV				IV	II	III, IV	
R.G.		IV	II	III				III	IV	
T.O.			II, IV	III			I, III	II	I	
A.B.	IV		IV		IV		III, IV		III, IV	
M.G.	IV	III	I, III	II, IV	III	II, IV	III, IV	I, II	IV	I, II, III
N.L.			IV	II		IV		IV		
R.W.			I	II			I	III	III	II

Code: Stage I = Experimental Drug alone—low dose; Stage II = Experimental Drug alone—high dose; Stage III = Combined drugs—low dose; Stage IV = Combined drugs—high dose.

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References pertaining to Article on pages 177 to 179 entitled "Levodopa-Nicotinic Acid Interaction in Psychiatric Patients"

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