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POST-TRAUMATIC CEREBELLAR SYNDROME

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About 25-30% of severe brain injury showed a post-traumatic cerebellar syndrome. The symptomatology can appear in the first remission phase or after variable lenght of latency.

The complete expression of the syndrome can be observed at the time of the reacquisition of finalized motility.

The most frequent symptoms of post-traumatic cerebellar syndromes are static and dynamic ataxia, as well as dysarthria, accompanied by cranic nerves disfunctions, such as disturbances in oculomotricity, vestibular systems and peripheric facial paresis.

Moreover bilateral lesions of pyramidal traits are often observed. An extrapyramidal symptomatology consisting of tonus increase, dyskinesias and myoclonus, can also appear as brainstem disorder (1).

Rodineau considered the duration of coma as an important predictive factor of severity of the cerebellar symptomatology (2).

In fact cerebellar disorders seem to appear with disturbances of conscioussness of at least 30 days.

Postural and intentional tremor are the symptoms most difficult to modify pharmacologically.

Sabra described a therapeutic trial with Isonicotinic acid hydrazide (I.N.H.) in patients with multiple sclerosis, showing, cerebellar symptomatology. This drug acts as competitive GABA agonist at receptorial level or as an inhibitor of GABA catabolism.

A significant amelioration was observed particularly in the intentional tremor, although Morrow referred weakness at lower limbs as side effect of the same treatment (4).

Hallet confirmed, in a controlled trial, a good efficacy of I.N.H. versus placebo, in patients with cerebellar tremor (5).

On the contrary, Koller could not demonstrate, in a double blind study I.N.H. versus hydrocloride propranolol, any appreciable amelioration in patients with cerebellar tremor (6).

This drug, which was also utilized in patients with Huntington chorea, increases GABA concentration in C.S.F. (7).

METHODS

Nine patients (mean age 20.5 years, ranging 14 to 27 years) with post-traumatic cerebellar syndrome appearing after prolonged mesencephalic and apallic syndromes were studied.

Admission criteria were severity of intentional tremor and the presence of cerebellar dysarthria.

4 examinations at different times were performed:

T0 = first basal time without therapy
T1 = after one month of I.N.H. treatment
T2 = second basal time after two weeks wash-out
T3 = after one month of propranolol treatment

The initial dose of I.N.H. was of 600 mg daily. B6 Vitamin was also administered (150 mg daily) with weekly controls of liver function.

The propranolol dosage was 60 mg daily with regular blood pressure controls.

Three different timed tests at each hand were performed during every examination (T0, T1, T2, T3).

A reduction of two of the three timed tests performed, of at least 1/4 of the initial time, was defined as criterium of amelioration.

Speech tests for dysarthria consisted in 3 different key words, in which the patients had to repeat 15 times the first word, 10 times the second and 5 times the third ones. Also in these tests, times were measured and compared.

RESULTS

Of 9 patients which were included, 7 completed the study. One patient was excluded after the first phase of the trial (I.N.H. month), although she showed a significant amelioration in one of the three timed tests performed. She refused to continue the trial with propranolol because of the frequent controls needed.

Another patient stopped the administration of I.N.H. after three days of treatment because of appearing of ataxia, asthenia at lower limbs and drowsiness.

Four out of 6 patients showed a significant amelioration of tremor during the treatment with I.N.H., 3 of them during propranolol (Tab. I).

The speech tests with repetition of the three key words showed a tendency of amelioration with both I.N.H. and propranolol.

As regards the incidence of side effects, three patients after administration of I.N.H. complained of severe worsening of static and dynamic ataxia. In two patients a moderate increase of liver enzymes was evidenciated but did not determine the interruption of the trial.

In one patient, during treatment with propranolol 60 mg daily, hypotension without clinical relevance was observed.

DISCUSSION

The positive results obtained with I.N.H. in multiple sclerosis suggested this study in post-traumatic cerebellar syndrome. I.N.H. inhibits GABA aminotransferase, the most important enzyme in GABA catabolism.

Perry showed that, at the dosage of 1200 mg daily, I.N.H. determined a 3-5 fold increase in GABA CSF concentration (7).

The clinical amelioration, obtained in 4 out of 6 patients, during I.N.H. therapy, seems to suggest the efficacy of this drug in the treatment of post-traumatic cerebellar tremor, as well as in multiple sclerosis. The improvement observed in three patients during

Table I

Pat.	Age	Sex	Duration of the cerebellar symptomatology (in months)	Lateralisation (side prevalence)	Response to the therapy IHN	Response to the therapy Propranolol	Side effects INH	Side effects Propranolol
1	17	M	24	RI	*	*	-	-
2	21	M	11	RI	*	*	-	-
3	27	F	20	RI	*	*	ATAXIA	L.B.P. #
4	25	F	16	RI	N.S.	*	INCREASED LIVER ENZYMES TESTS	L.B.P.
5	14	F	34	RI	N.S.	N.S.	ATAXIA	-
6	22	F	72	RI	*	N.S.	ATAXIA	-
7	18	F	30	RI	N.S.	-	-	L.B.P.

* Amelioration of at least 1/4 of the basal time of at least 2 tests

\# Low Blood Pressure

N.S. = Not Significant

therapy with propranolol confirmed the well known effects of this drug in tremor of different genesis.

As a whole, I.N.H. does not seem to be a drug of first choice in the treatment of post-traumatic cerebellar tremor, because of side effects such as ataxia, progressive asthenia at lower limbs, as well as impairment of liver functions.

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