A TRIAL OF UCB 6215 (PIRACETAM) 
IN INFANTILE NEURO-PSYCHIATRY 

by 

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Registered name : Nootropyl\textsuperscript{(R)} - Nootropil\textsuperscript{(R)} 
Generic name : Piracetam 
Code number : UCB 6215 
Chemical name : 2-pyrrolidone acetamide 

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1. DESCRIPTION OF THE DRUG

PIRACETAM has a chemical formula which is closely related to gamma-aminobutyric acid.

It is a water-soluble powder. The chemical investigations effected have shown that it is very slightly toxic, that it is rapidly absorbed by the parenteral as well as by the oral route, that it passes the blood-brain barrier and that it is rapidly excreted with the urine.

The animal experiments have shown that the drug:

a) reduces the labyrinthic excitability.

b) inhibits the cortical spreading of the epileptic discharges induced by a local irritation [strychnine] while it does not alter the basic EEG-tracing or the polysynaptic, evoked potentials;

c) facilitates the learning process by reducing its duration in situations of operational conditioning [maze-tests] as well as in situations of Pavlovian, conditioned reflexes or of pain-conditioning;

d) finally, and it is mainly from here that the clinical indications will be derived, the latter performances are altered in animals by anoxia, senescence, electroshock or various intoxications [alcohol...]

Now, PIRACETAM reduces very significantly those untoward effects.

A number of neuropharmacological investigations suggest that these actions of PIRACETAM are in relation with an increase of the energetic potential of the cortical cells. This is mainly accounted for by an activation of the synthesis of ATP and a decrease of the oxidoreduction potential. Such an acceleration of the metabolism has been constantly evidenced, especially in the course of several types of cerebral hypoxia.

Eventually, further investigations have shown that the drug has no spasmolytic, vasopressor, bronchodilatant or peripheral, neurovegetative action.
After these preliminary studies, one is led to consider the use of PIRACETAM in all the syndromes where the cerebral cell-metabolism is altered, although irreversible, histological lesions are not necessarily present. Therefore, the use of the drug is directed toward the following indications:

- hypoxia of respiratory or hematological origin;
- certain toxi-infectious or endotoxic disorders (mental confusion as a result of acute or subacute alcoholism, for instance);
- disturbances of the brain-vascularization that may result:
  a) either from acute, ischaemic or even haemorrhagic damages - in such cases the drug may improve the metabolism in the perilaesional areas -
  b) or from chronic manifestations of cerebral atherosclerosis with its twofold, neurological or psychiatric symptoms.

This led us to think that an action of the drug might be expected in children with mental insufficiency.

2. HOW THE EXPERIMENT WAS CONDUCTED

UCB 6215 was investigated in the following conditions:

1) The patients:

The children treated belonged either to a department for mentally deficient or psychotic children at the Psychiatric Hospital at Font-d'Aurelle, attached to the department for infantile neuropsychiatry at the University Hospital Centre of Montpellier (26), or to a department for infantile neuropsychiatry at the Psychiatric Hospital of Uzès (12), so that the whole group included in total 38 cases.

The cases of prepsychosis or psychosis which were not associated with a primary mental insufficiency were discarded.

2) The staff:

In one of these departments, the staff included in addition to the attending doctors and consultants, a small number of psychiatric hospital attendants and agents of the hospital services;
in the other one, in addition to the attending physicians and consultants, it included only psychiatric hospital attendants.

3) Dosage:

The doses used were three capsules a day in three intakes of one capsule, which represents a daily dosage of 1,200 mg.

The treatment was initiated on November 1st, 1971 and has been continued without any interruption till March 31st, 1972 when the follow-up examinations were performed. It is still running now.

Combined medications were used in a few cases only. In fact, only the antiepileptic drugs were maintained.

On the other hand, the psychotherapeutic treatments, the mothering, the psychomotor, orthophonic or kinesitherapic rehabilitation were not discontinued.

The children did not experience any change in their daily life and were not submitted to any distinction or diet.

4) The investigational conditions:

An attempt has been made to standardize the experiment to every possible extent and to retain those evaluation parameters that were at the same time simple and easy and left but little room for interpretation.

Before the institution of the treatment with UCB 6215, a balance was struck for each patient at three levels: behaviour, medical examination (including those additional examinations that were deemed to be useful) and psychological status. For the latter we used mainly the tests of BOREL-MAISONNY and BRUNET-LEZINE.

After the treatment, the same balance was struck again and in order to avoid to every possible extent the easily too enthusiastic, subjective impressions of the environment, several synthesis meetings were held to define the answers to the various, rather simple criteria that had been retained as the following ones:
- contact,
- food consumption,
- sphincter control,
- sleep,
- spontaneous behaviour,
- behaviour toward the objects,
- behaviour toward water,
- behaviour toward other children,
- behaviour toward adults,
- behaviour toward mirrors,
- speech,
- miscellaneous.

The medical examination was as complete as possible and was directed toward the detection of damages to the large ways as well as of balance disorders, walking difficulties, coordination disturbances and disorders of epileptic origin. The psychological examination was performed with the tests of BOREL-MAISONNY and BRUNET-LEZINE.

On the whole, however, on account of the fact that they had to effect regular observations, the nurses and the attendants were perhaps induced to take care more extensively of these children.

The treatment was continued after the follow-up psychological and medical examinations and, in all cases where it occurred, the improvement has been maintained.

Age:

The age-distribution was as follows:

- 5 years = 1
- 7 years = 1
- 9 years = 5
- 10 years = 1
- 11 years = 2
- 12 years = 7
- 13 years = 6
- 14 years = 6
- 15 years = 5
- 16 years = 3
- 17 years = 1
One may be surprised by the fact that our investigation was extended to the age of 17 years. These patients were adolescents whose stature and morphology corresponded to those of much younger children.

3. INCIDENTS AND ACCIDENTS

Two cases of motor excitation were observed; both of them regressed rapidly under a treatment with small doses of Valium.

No sleep disturbances or changes in the appetite were noticed. No distress or faint was observed.

In the epileptic patients, the number or the frequency of the seizures were not increased and no seizures were induced by the treatment.

No incident occurred.

4. COMMENT

The three directions in which our study was conducted call for the following comment:

1) Medical criterion:

No change in the reflexes of the locomotor system was observed. No balance disturbances occurred. The reflexes were not altered. The EEG's of the epileptic patients failed to evidence any additional disturbance.

2) Psychometric criterion:

The performances in the objective tests remained unchanged. This has perhaps to be ascribed to a lack of sensitivity of the tests used, but these tests are not usually blamed for that.

The various tests where the children had failed before the treatment were not performed successfully after the treatment. On the whole, the children showed an increased interest and alertness as if their spontaneous attention were more active. On the other hand, the opposition and aggressivity are more freely expressed.
3) **Behaviour criterion** :

It is here that the best results appear to have been achieved.

If the appetite and sleep were but slightly modified, the threshold of consciousness was, on the reverse, increased and permitted an accelerated learning, for instance, for the use of a spoon or of a fork in the autonomous feeding. The incontinentiae alvi or urinae diminished or disappeared. The same applied for self-mutilation, a syndrome that is so distressing for the children as well as for the attending staff. The understanding was improved and an approach to speech became possible.

The deep retardation states drew but little benefit from the treatment.

The states of deep mental debility, plain or associated with a discrete psychotic component, were improved to a significant extent. These favourable results were noticed irrespective of the origin of the mental insufficiency (trisomia 21 - Bourneville's sclerosis - encephalitis).

Whenever the psychotic component was predominant, the results were poor.

This is a confirmation of what we had been told by the manufacturer: the drug is not intended for psychotic patients.

The site of action appears to be rather located at the level of the consciousness.

**5. GENERAL CONCLUSIONS**

Our investigation had a duration of four months from November 1st, 1971 till March 31st, 1972. It was conducted on 38 mentally debile children.

Except for epileptic patients, no combined medication was used.

More often than not, the dosage used was three capsules a day. These are rather small doses. The treatment has been continued without any interruption.
The few incidents (states of agitation or excitation) that were noticed, occurred in the early part of the study and disappeared rather rapidly although the treatment was not discontinued; they subsided spontaneously in most cases or, in a few cases, after the intake of a tranquilizer for a few days.

In general the good results were achieved within the first fifteen days and, at the latest, within the first month. It is apparently useless to continue the treatment further when no result has been achieved by that time. We proceeded unnecessarily.

In the dosages used the compound had no toxic effect. No sign of intolerance has been noticed.

The indications appear to be rather extensive since the results achieved in mentally insufficient children have been supported by those obtained in the course of another investigation in mentally insufficient adults as well as in cases of dementia.

The action does not appear to be profound and seems to have its main impact on the level of consciousness and attention.

A better learning is thus possible; the performances as well as the memory are improved.

The mood is frequently improved although the action of the drug does not appear to be specific. The state of well-being or, in some cases, even of euphoria might be a consequence of the gratification resulting from the better performance.

This improvement in the field of learning might be an explanation for the failures in the cases of predominating infantile psychosis.

In psychotic conditions the therapeutic courses based upon the rehabilitation are, indeed, those which have the most mutilating and the least certain effects.

As a conclusion, UCB 6215 has a place in the infantile therapy.

It facilitates the resumption of the individual contact, the sociability and the learning. It is completely harmless; it can be safely used in epileptic patients and its side-effects are unfrequent and minor.