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CLINICAL EVALUATION OF CDP-CHOLINE (STARTONYL) IN PATIENTS WITH PARKINSON'S DISEASE

(Untersuchung zur wirksamkeit von CDP-Cholin (Startonyl) bei patienten mit Parkinson' scher krankheit)

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SUMMARY

The effect of CDP-choline in patients with Parkinson's syndrome was investigated in a clinical study. After a short washout period, 5 patients received the first 10 days 500 mg of CDP-choline infusion daily and during 20 days 1000 mg daily by intravenous route.

The second group received during the first 20 days 1000 mg CDP-choline by intravenous route and then for 10 days in addition to CDP-choline daily 100 mg L-dopa intravenously. Analysing the results obtained by the 10 patients treated with CDP-choline, we can conclude that 60% of the patients showed an improvement concerning the symptoms rigor and/or akinesia. The effect on tremor was moderate. 60% of the patients showed an improvement of behaviour and of their general mood. After L-dopa was added, 4 of 5 patients improved over the stage after CDP-choline treatment. When the study was concluded the patients were treated with an adjusted dose of L-dopa. We found an improvement in 70% of the patients with a dose which was lower than that administered before this treatment with CDP-choline. No side effect were observed in the patients treated with 1,000 mg CDP-choline i.v. daily.

Key words: CDP-choline, L-dopa, parkinsonism, therapy, rigor, akinesia, tremor.

Introduction

L-dopa has shown to be very successful in therapy of Parkinson's syndrome (1, 3). The therapeutic principle of L-dopa therapy is based on a re-concentration of the extrapyramidal system with dopamine which is formed from L-dopa by decarboxylation following passage through the cerebral blood barrier. With a view to the required high therapeutic doses of L-dopa a number of untoward reactions such as nausea, vomiting, disorders of the circulatory system as well as psychical disturbances cannot be excluded in substitution therapy of Parkinson's disease.

The advantages of a combination therapy of L-dopa with other drugs (2, 5, 18) lie in a better tolerance as well as in the possibility to reduce doses of L-dopa.

In the present study the effect of CDP-choline alone and in combination with L-dopa had been investigated in patients suffering from Parkinson's disease. It is known from biochemical investigations that CDP-choline influences the dopamine metabolism.

CDP-choline is a coenzyme which plays an important role in the biosynthesis of the phospholipids (6, 17). Its function on the central nervous system consists in an organization of the structure of the cellular membrane, particularly in a regulation of the selective permeability. Animal experiments by Manaka et al. (8) in 1974 showed that an experimental degeneration of nerve cells of the pars compacta in the substantia nigra of cats leads to an evident decrease of the dopamine concentration in the nucleus caudatus. Experimental animals receiving CDP-choline showed on the other hand a markedly reduced loss of nerve cells in the substantia nigra as compared to the control group without CDP-choline. The results showed that CDP-choline significantly reduces the decrease of the dopamine concentration in the nucleus caudatus which occurs as a consequence of an experimentally induced cell degeneration in the ipsilateral substantia nigra. According to the Authors this observation can be explained by an improvement of the metabolism of the phospholipids in the degeneratively altered cells of the substantia nigra but also in the nigrostriated tract by CDP-choline. They are of the opinion that CDP-choline produces an increased dopamine production and enhances the transportation activity of dopamine.

Various investigations (7, 11, 12, 13, 15) have demonstrated that after parenteral application, CDP-choline produces a normalization of the phospholipid level in patients with cranial and cerebral traumatic conditions resulting in an improvement of the cerebral blood flow and utilization of glucose.

Since 1970 several Authors had described results of clinical investigations indicating that CDP-choline is useful in the therapy of Parkinson's disease (1, 4, 9, 10, 14, 19, 20). These investigations did in general show positive results of CDP-choline in the therapy of Parkinson patients but there were partly conflicting statements as to the effectiveness in the various symptoms of Parkinson's disease. The purpose of our study was to obtain an objective picture on the effectiveness of CDP-choline in patients suffering from Parkinson's disease.

Patients and method

Five male and five female in-patients (aged between 50 and 72 years) suffering from various types of Parkinson's disease (9 suffering from idiopathic and one from post-encephalitic Parkinson's disease), of various severity (5 with slight, 2 with medium and 3 with severe symptomatology) were divided into two groups. After a short washout period, Group I received during the first 10 days 500 mgs CDP-choline

daily (i.v. infusion) and over a subsequent period of 20 days 1000 mgs daily (i.v. injection). The second group was treated during the initial 20 days with 1000 mgs CDP-choline i.v. daily and during a subsequent period of 10 days with an additional dose of 100 mgs L-dopa daily administered by i.v. route. Both groups were treated for a period of 30 days. During this period no other anti-Parkinson drug was given. Prior to initiation of the treatment and after completion of therapy all appropriate laboratory controls have been performed.

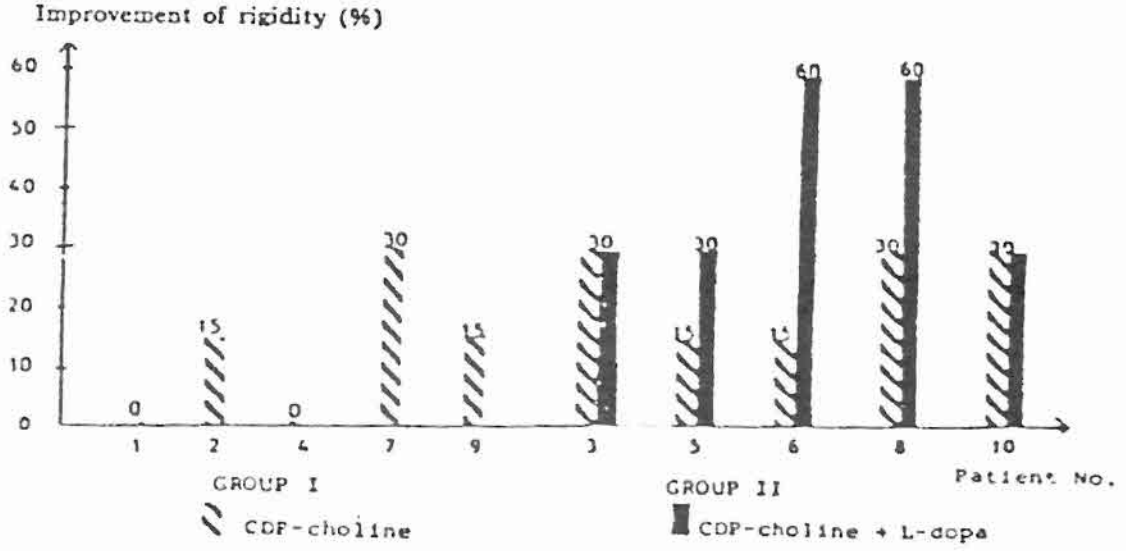
For evaluating the effectiveness of CDP-choline the symptoms rigor, tremor, bradykinesia, general mood and vegetative symptomatology have been observed throughout therapy using various testing methods:

- Physician's diagnosis
- Observation by nursing personnel: hygiene, eating and drinking, talking, raising from chair.
- A 10-graduated rating scale was used for evaluation. In addition a walking test (the time required for walking a certain distance was measured) and a capability test (time required by the patient to button up a shirt with 10 buttons) was performed.
- Drawing and writing test
- Motor test according to Grünberger-Gerstenbrand
- Cross-out test according to Brickenkamp (2d-Test)
- Pressure counting test according to Kozma
- 100 mm - Test for evaluation of general state of patient
- Laboratory controls have been made for each patient prior to and after completion of therapy.

Results

The effect observed in the total status of rigor is evident from Figure 1.

Figure 1 - Effect of CDP-choline on status of rigor.



Evaluation of the total effects of treatment yielded an improvement of rigor for 3 patients of Group I (CDP-choline monotherapy). 5 patients of Group II showed an improvement of rigor after 20 days of treatment with 1000 mgs CDP-choline i.v. Supplementary administration of 100 mgs L-dopa produced an additional marked improvement of symptoms of rigidity in 3 patients.

Figure 2 shows the effect of CDP-choline on the total status of akinesis.

In 3 patients of Group I a success for the symptom akinesis was only seen at a dose of 1000 mgs. Of the Patients in Group II four showed an improvement after 20 days of monotherapy. The additional administration of L-dopa produced a further improvement in 4 of 5 patients.

Figure 3 shows the effect of CDP-choline on the total status of tremor.

In only one patient of Group I tremor could be positively influenced by the 1000 mg dose. In Group II in two cases a marked effect could be seen after 20 days of monotherapy. After addition of L-dopa 3 of 5 patients showed an improvement of the symptom tremor.

A marked improvement of the general condition (considering the sum of all controls performed) could be noted in 6 patients. 4 patients showed no alteration as compared with the condition at the beginning of treatment. After addition of L-dopa two patients of Group II showed a deterioration of the depressive disorder which was prevailing in all 5 subjects.

As a total result of the present clinical study it could be shown that in 60% of the 10 patients suffering from various degrees of

Figure 2 - Effect of CDP-choline on status of akinesis.

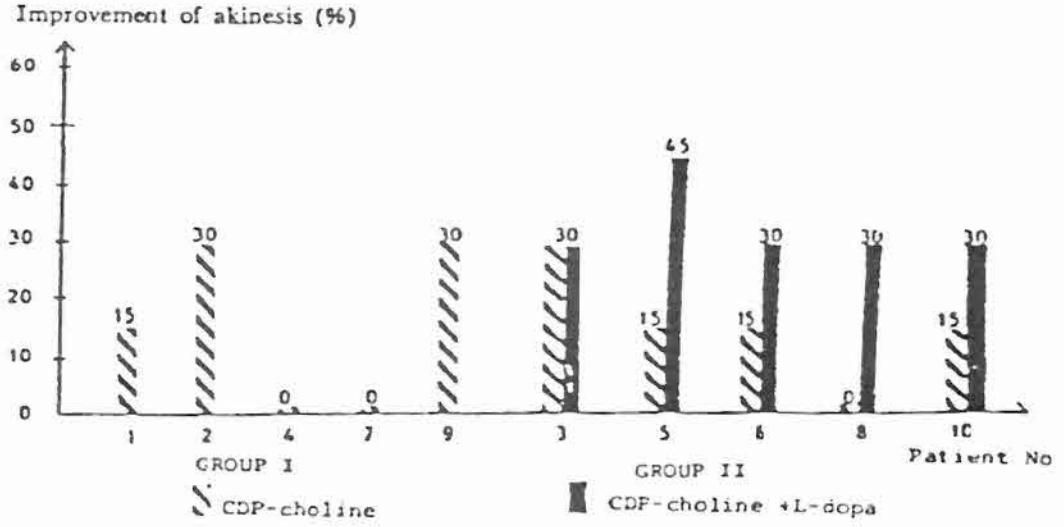


Figure 3 - Effect of CDP-choline on status of tremor.

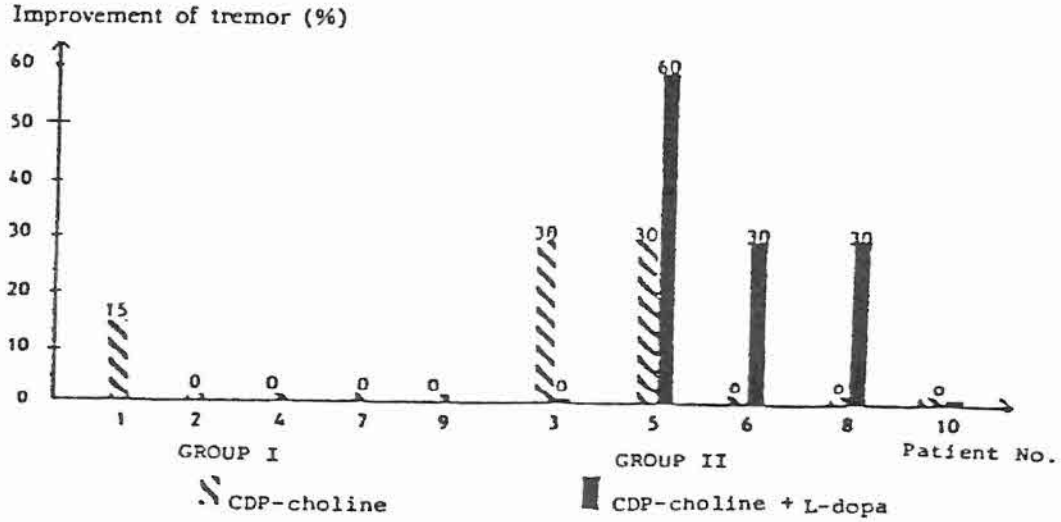
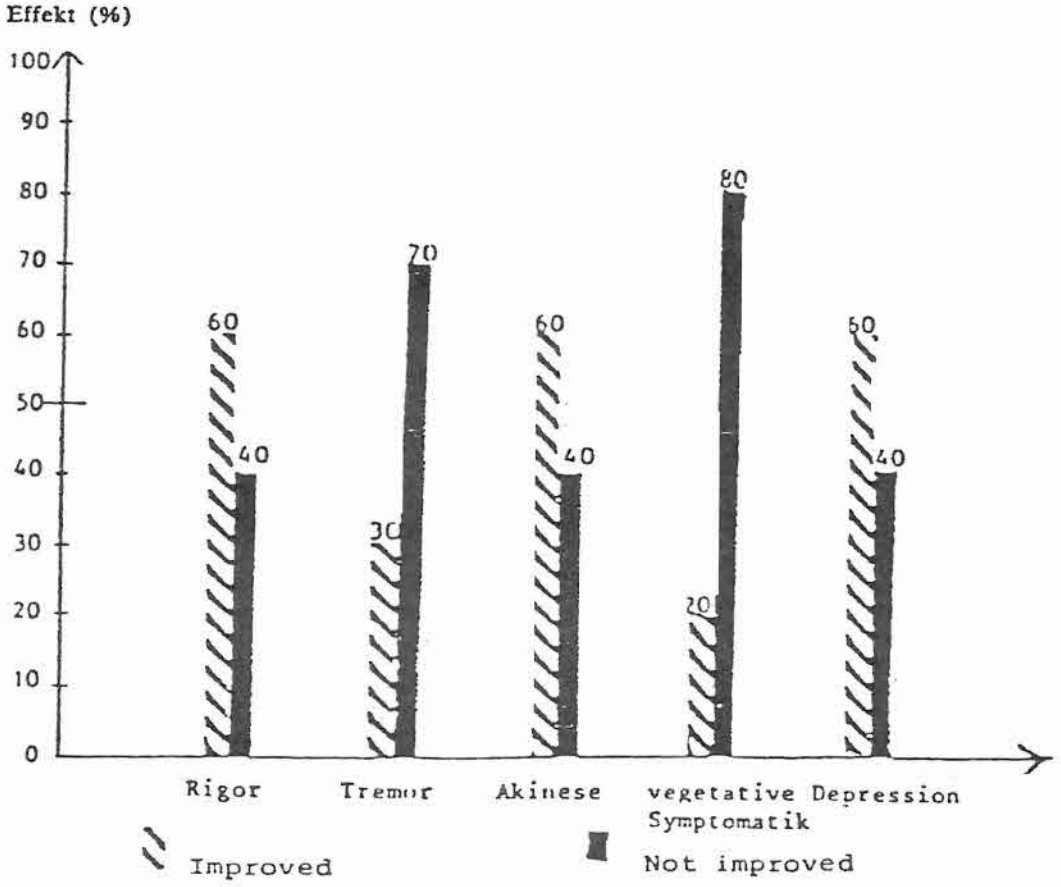


Figure 4 - Results of therapy with CDP-choline in 10 patients suffering from Parkinson's disease in respect of the symptoms rigor, tremor, akinesis, depression as well as vegetative symptomatology (10 patients ≙ 100%).



Parkinson's disease a positive effect of monotherapy with CDP-choline could be found. Particularly the symptoms rigor and akinesis could be improved to a varying degree, whereas tremor and the vegetative symptomatology have in general not been substantially influenced.

Figure IV shows a summary on the results of treatment of 10 patients suffering from Parkinson's disease by administration of CDP-choline.

As a result of subject study it can be stated that CDP-choline alone possesses an effect on the Parkinson's syndrome. In combination with L-dopa the total effect can be enhanced. The possibility of reducing the dose of L-dopa by administration of CDP-choline is subject of further study.

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