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Infusion Therapy with MIF (Melanocyte Inhibiting Factor) in Parkinson's Disease

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A few years ago, several studies were published about MSH (melanocyte stimulating hormone) and its efficacy in the central nervous system and, among other things, deterioration of parkinsonian syndrome[1,7,8,9]. Subsequently it was attempted to improve the symptoms of parkinsonism by using the inhibiting factor MIF (melanocyte inhibiting factor) produced in the hypothalamus[10,11]. Different experimental papers about MIF evidence an oxotremorine and deserpidine antagonism as well as a potentiation of the L-dopa effect[13,14,15]. Although there are few clinical observations about MIF in tablets and i.v. application[4,5,6,12], it could be demonstrated that the tablets were without and the i.v. form with a mean therapeutic effect. Nevertheless, in our opinion the i.v. dosis was too low. However, there was a high effectiveness in a combination of L-dopa and MIF.

Unsatisfied of these results, we investigated a parkinsonian therapy with i.v. application of MIF alone, but in a higher dosage as yet known. First results were published recently[2].

Materials and Methods

In total, ten patients with Parkinson's disease of mild (3 cases), moderate (5 cases) and severe (2 cases) degree have been treated. In one case, treatment was interrupted for reasons not connected with the substance. None of the patients was receiving any other anti-parkinsonian therapy at the time of MIF treatment.

The dosage of MIF was determined at 400 mg daily, administered as a continuous i.v. infusion over 10 days. In order to evaluate efficacy, an extended Webster rating scale, a nurse's rating scale and a handwriting test were employed. A psychological test battery (PDT) according to Gerstenbrand et al.[3], which gives information about fine motoric, visomotoric, concentration and amnestic ability, was performed before and after treatment. The results were evaluated statistically.

After the 10-day infusion period the patients were seen as out-patients at weekly intervals for four weeks for evaluation of the Parkinson's disease manifestations. Some of the patients who showed deterioration in condition during this follow-up period were given an i.v. injection, 200 mg twice daily, until such a time they returned to the same improvement achieved under infusion therapy or for a maximum of 10 days. One patient received a second course of infusion therapy.

As is to be seen in Table 1, in all nine patients who finished MIF infusion therapy, we were able to observe an effect upon all the symptoms of Parkinson's disease, including akinesia, rigidity and tremor. This effect was first seen approximately three days after the beginning of

Table 1 Evaluation of treatment with MIF i.v. of 10 patients with parkinsonian syndrome. Effect of MIF in Parkinson's disease (400 mg daily).

No. of patient	Initials	Age	Sex	Diagnosis	Degree pre A	R	T	post A	R	T	Global clinical improvement %	Psychol. state pre	post	Depot effect	Remarks
1	F.R.	47	M	P.a.	3	3	0	1	1	0	75	D	N	+	—
2	J.F.	67	M	P.a.	3	3	3	1	2	2	50	D	N	±	—
3	J.K.	61	M	P.a./T	1	1	3	0	0	2	75	D	Hm	±	A 2nd course of treatment produced the same effect
4	E.W.	70	M	P.a.	1	3	2	0	2	1	50	N	N	+	An i.v. injection course produced the same effect
5	J.D.	66	M	P.a.	4	4	1	3	3	1	25	D	N	—	—
6	P.K.	62	F	P.a.	3	3	0	1	2	0	75	N	N	+	—
7	M.S.	67	F	P.a./T	2	2	3	2	2	3	0	D	D	—	Interruption of study. Patient declined further treatment
8	L.H.	64	M	P.a.	1	2	1	0	1	0	75	N	N	+	—
9	Th.Z.	60	M	P.a.	2	2	2	1	1	1	75	D	N	+	—
10	B.S.	68	F	P.a./T	2	1	4	1	1	3	25	D	D	±	Rapid deterioration of tremor after cessation of treatment

Psychological state: D = depressed, N = normal, Hm = hypermanic.
P.a. = paralysis agitans A = akinesia M = male
T = tremor R = rigidity F = female

treatment. In five of the nine patients a significant general clinical improvement was observed, in two patients a moderate improvement and in two patients a mild improvement. The latter two patients (Nos. 5 and 10) had severe manifestations of Parkinson's disease at the outset. In general, a better effect was obtained in mild to moderate cases than in severe cases of Parkinson's disease.

There was an effect of MIF therapy on akinesia in all ten patients (Figure 1). A significant improvement was obtained in three patients, a moderate improvement in four patients and a mild improvement in two patients. Also an effect of MIF therapy on rigidity could be seen in all ten patients (Figure 2). A significant improvement was observed in one patient, a moderate improvement in three patients and a mild improvement in four patients. Rigidity in one patient remained unchanged. Significant improvements of tremor were not observed (Figure 3). A moderate improvement was observed in two patients, a mild improvement in four patients, and tremor in one patient remained unchanged. Two patients had no symptoms of tremor at the outset.

Remarkable in almost every case was the occurrence of elevated mood which continued during treatment and throughout the four-week observation period. Seven of the ten patients showed depressed symptoms at the beginning of the study (Table 1). Of these, four achieved a normal psychological state, one became hypomanic, one remained depressed and the patient whose treatment was interrupted also remained depressed. In all patients, clearer and definitely improved, well-ordered thinking was observed.

Particularly worthy of emphasis is the continuing effect of MIF for up to four weeks after discontinuation of the infusion series without any other anti-parkinsonian therapy. A depot

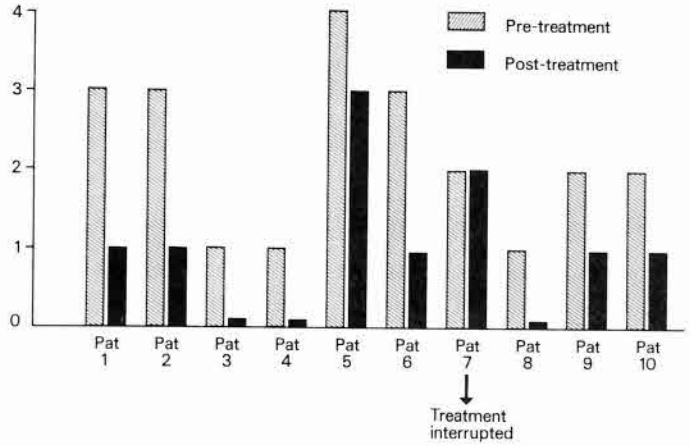


Figure 1 Effect of MIF i.v. (400 mg daily through 10 days) on akinesia of 10 patients with parkinsonian syndrome.

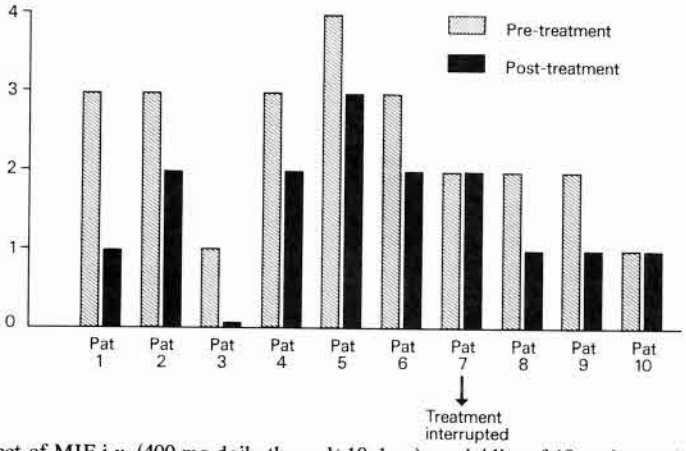


Figure 2 Effect of MIF i.v. (400 mg daily through 10 days) on rigidity of 10 patients with parkinsonian syndrome.

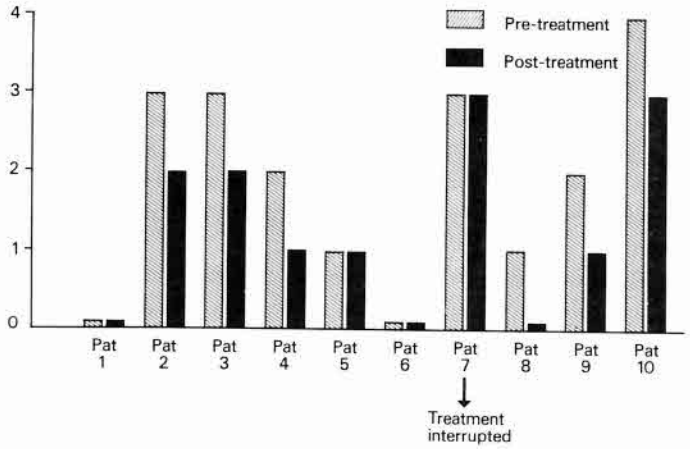


Figure 3 Effect of MIF i.v. (400 mg daily through 10 days) on tremor of 10 patients with parkinsonian syndrome.

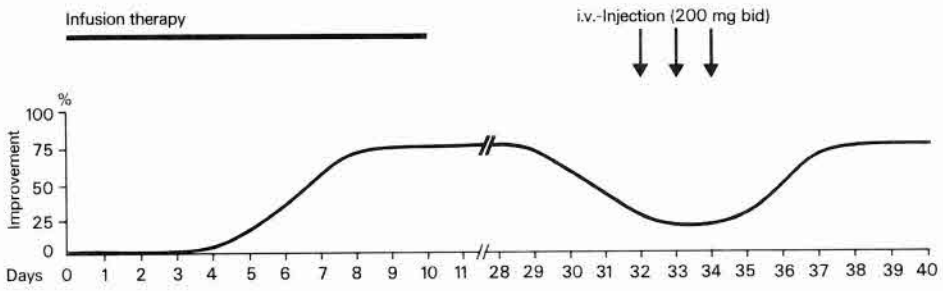


Figure 4 Course of treatment with MIF i.v., patient F. R., 47 years, male, paralysis agitans, 400 mg daily through 10 days with following i.v. application. Improvement in percentage.

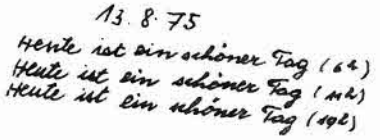
effect was observed in eight patients, continuing in five patients for up to four weeks. In one patient, deterioration of condition was evident two days after cessation of treatment. Three patients received an i.v. injection of MIF, 200 mg twice daily, when deterioration became evident which was approximately two-and-a-half weeks after termination of the infusion therapy. The substance was administered for a period of 3 to 5 days. These patients achieved a similar improvement in condition to that which was observed during the infusion therapy (Figure 4).

An improvement was also observed in the patients' ability to walk, eat, dress and write, the latter being particularly obvious. Without exception there is in every case a marked improvement in the handwriting of patients after treatment with MIF (Figures 5 and 6).

After evaluation of the test batteries performed by patients before and after treatment, it can be stated that:

1. In the AD test (for concentration and alertness) a definite improvement was seen in six of the nine patients.

2. In the d2 test (also for concentration and alertness) a definite improvement was seen in six patients while three remained unchanged.



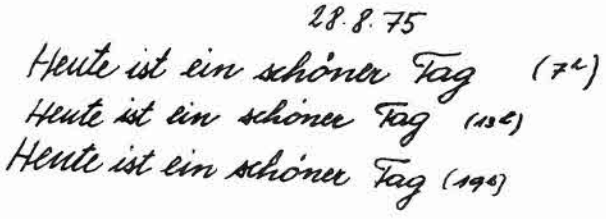


Figure 5 Pattern of handwriting, patient J. F., 67 years, male, paralysis agitans, comparison before treatment and five days after infusion therapy with MIF (400 mg daily through 10 days).

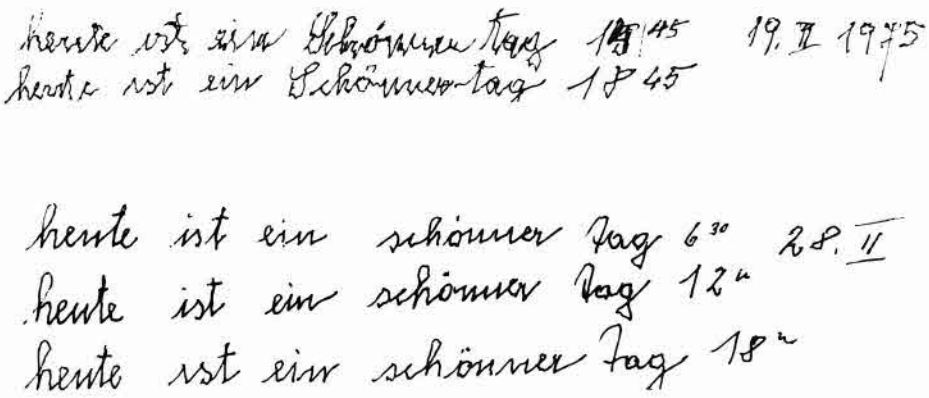


Figure 6 Pattern of handwriting, patient J. K., 61 years, male, paralysis agitans, comparison of handwriting before treatment and after 9 days of infusion therapy (400 mg daily).

3. The letter check test (for completion of movement, speed and mobility) showed that eight patients had definitely improved.

4. In the number symbol test (for intellectual abilities) six of the nine patients had definitely improved; one had deteriorated.

5. The motor function test measured by the respective test was in eight cases definitely improved, in one case worse.

6. The number memory test had in six patients definitely increased and remained in three patients unchanged.

In analysing the results from the test batteries, the nine patients showed an overall improvement of approximately 67%.

Summary

To summarise, it can be concluded that there is an overall obvious improvement in patients with Parkinson's disease treated with MIF (melanocyte inhibiting factor) by intravenous administration. Remarkable is the depot effect up to 4 weeks. Additional effects were the elevated mood, an improvement of concentration, alertness and of the highest brain functions. No side-effects were observed.

On the basis of recent publications and of our own experience, MIF would appear to be a very promising anti-parkinsonian agent. In addition to the theoretical considerations of the biochemical-pathophysiological sphere, the question of the correct dosage for practical use seems to us to be of particular interest. We are of the opinion that more studies have to be carried out in order to obtain a dosage with maximum effect.

At present, we are investigating a new series with i.v. injection of MIF alone as well as a combination of MIF and L-dopa.

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