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MEĐUNARODNI SIMPOZIJUM

O EKSPERIMENTALNOM TREMORU

1 — 3. APRIL 1971. GODINE

Urednik
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OUR EXPERIENCES WITH L-DOPA IN THE TREATMENT OF PARKINSON'S SYNDROME

Basal ganglia and similar structures of normal human brain contain the greatest quantity of dopamin (2). However, in patients with Parkinson's disease dopamine is found in very low concentrations in nuclei of extrapyramidal system (nucleus caudatus, putamen, substantia nigra) (6, 8, 1). Biochemical examinations showed that dopamine does not cross the blood-brain barriere but its precursor dihydroxyphenylalanine (DOPA) has this property. Taking this fact in consideration, DOPA was tried in the therapy of Parkinson's disease (5, 9, 4, 3, 7), and most reports show the efficiency of such a treatment. L-DOPA in higher oral doses and with effective results in patients with these extrapyramidal disorders, was used for the first time by Cotzias et al. (4, 5). Similar results were got by Yahr et al. (9). The investigations till now show that this drug gives a great promise in the treatment of this chronic disease of nervous system.

MATERIAL AND METHODS

Our intention was to examine the effects of L-DOPA preparation of the firm »Hoffmann — La Roche AG« Grenzach Baden (caps. à 500 mg) in patients with Parkinson's syndrome.

Our material were the patients with Parkinson's syndrome who were hospitalized at Sarajevo, Neuropsychiatric clinic in 1970. Before the treatment decision the patients were the subjects to adequate clinical (neurological, ophatalmological and internal examination) and laboratory (haemoglobin, red blood picture, reticulocites, white blood picture, thrombocites, Heinz-bodies, Coombs'test, ECG, EEG, transaminases, alkaline phosphatase, serum bilirubin, BSP, protrombine time, urine, urea clearance) examinations. Patients with lesions of parenhimatose organs (heart, liver, kidney) were excluded from L-DOPA treatment

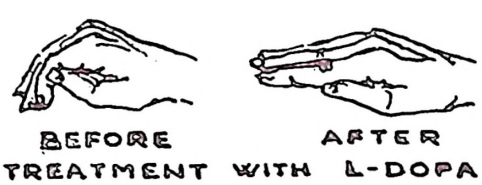
The average duration of the treatment was 90 days. Daily doses were 3—9 g. The beginning was with small doses which successively increased. Clinical and laboratory examinations (as at the beginning)

were performed at the end of the treatment and they were also done during the treatment if it was necessary. The values of pulse, blood pressure and the number of respirations were measured every day.

The evaluation of therapeutic effects was done on the basis of the following parameters: rigidity, tremor, gait and posture, hypomimia, vegetative symptoms (facies oleosa and hypersalivation), handwriting, psychical condition. The results were esteemed as improvement, without effects and decline. The side effects in each patient were observed (nauzea, vomiting, hyperkineziae, insomnia, restlessness, depression and complications on parenhimatose organs).

RESULTS

Thirty patients with Parkinson's syndrome were hospitalized. L-DOPA treatment could not be applied in 18 patients because of contraindications (lesions of cardiovascular system, liver and kidney) and so the clasic antiparkinson therapy was used. Twelve patients were treated with L-DOPA, five of them with essential Parkinson's disease, six with arteriosclerotic, and one with postencephalitic Parkinsonism.



The results of our examinations are shown in the following tables 1, 2, 3.

T A B L E 1

CASE NR	INITIALS	AGE	AETIOLOGY	SEX	DURATION (YR)	STEREOTAC. OPER.		RIGIDITY	TREMOR	GAIT AND POSTURE	HYPOKINESIA	VEGET. SYMPT.	HAND-WRITING	BRADY-PSYCHIA	SUBJECTIVE FEELING	SIDE-EFFECTS	MAXIMAL DOSE L-DOPA	FINAL THERAPEUTIC EFFECT
1	A M	46	ES	M	8	+	B	+++	++	++	+++	+++	++	++	GOOD	HYPERKIN.	9 g	IMPROVEMENT
							A	+	++	+	+	+	+	++				
2	I H	51	ES	M	5	–	B	++	+++	++	++	++	++	++	VERY GOOD	—	6 g	IMPROVEMENT
							A	+	–	+	+	+	–	+				
3	J K	48	ES	M	2	+	B	+++	++	+++	+++	+++	++	+++	VERY GOOD	—	6 g	IMPROVEMENT
							A	+	+	+	+	+	+	+				
4	S F	55	ES	M	6	+	B	++	+++	++	+	++	++	++	GOOD	INSOMNIA	7,5 g	IMPROVEMENT
							A	+	++	+	+	+	+	+				
5	S C	52	ES	F	5	–	B	++	++	++	+	++	++	++	VERY GOOD	NAUZEA	3 g	IMPROVEMENT
							A	+	++	+	+	+	+	+				
6	P R	76	ART	M	10	–	B	+++	++	+++	++	+++	+++	++	BAD	NAUZEA, VOMITING, COR DECOMP., RESTLESSNESS	3 g	DECLINE
							A	+++	++	+++	++	+++	+++	++				
7	H V	63	ART	M	3	–	B	++	+++	++	++	+	++	++	MODERATE	—	3 g	WITHOUT EFFECT
							A	++	+++	++	+	+	++	++				
8	H N	61	ART	M	2	–	B	+++	+++	++	+	+	+++	++	MODERATE	NAUZEA, VOMITING, INSOMNIA	3 g	WITHOUT EFFECT
							A	+++	+++	++	+	+	+++	++				
9	P G	75	ART	M	7	–	B	+++	+++	+++	++	++	++	++	VERY GOOD	NAUZEA, VOMITING	6 g	IMPROVEMENT
							A	+	++	+	+	+	+	–				
10	E K	68	ART	M	7	–	B	+++	+++	+++	++	+++	+++	+++	VERY GOOD	—	4 g	IMPROVEMENT
							A	+	++	+	+	+	+	+				
11	M M	80	ART	F	2	–	B	++	++	++	++	+	++	++	VERY GOOD	—	7,5 g	IMPROVEMENT
							A	+	+	+	+	+	+	+				
12	J O	61	PE	F	18	–	B	+++	+++	+++	+++	+++	+++	+++	BAD	RESTLESSNESS, COR DECOMP., VOMITING, DEPRESSIO, INSOMNIA	3 g	DECLINE
							A	+++	+++	+++	+++	+++	+++	+++				

LEGEND

B = BEFORE
A = AFTER
+++ = COMPLETE EXPRESSION OF SYMPTOM
++ = MODERATE -"- -"- -"-
+ = MILD -"- -"- -"-
– = WITHOUT SYMPTOM
ES = ESSENTIAL PARKINSONISM
ART = ARTERIOSCLEROTIC PARKINSONISM
PE = POSTENCEPHALITIC -"-

Table 2.

	NUMBER OF CASES		
	VERY GOOD IMPROVEMENT	GOOD IMPROVEMENT	WITHOUT EFFECT
RIGIDITY	4	4	4
TREMOR	1	5	6
GAIT AND POSTURE	3	4	5
HANDWRITING	2	6	4
VEGETATIVE SYMPTOMS	3	4	5
PSYCHICAL STATE	2	4	6
HYPOMIMIA	2	5	5
COMPLETE FINAL RESULT	4	4	4

Table 3.

SIDE-EFFECTS	NUMBER OF CASES
1. NAUZEA	5
2. VOMITING	4
3. INSOMNIA	3
4. RESTLESSNESS	2
5. HYPERKINEZIAE	1
6. DEPRESSION	1
7. COR. DECOMP	2

SUMMARY

Thirty patients were admitted at the Neuropsychiatric clinic for the treatment with L-DOPA. All of them suffered from Parkinson's syndrome of different ethyology. After carefull selection (excluding heart diseases, liver damages and lesions of other organs), only 12 patients could underwent prolonged treatment with L-DOPA. Daily dose was 3—9 g. Duration of the treatment was three months.

Results showed good improvement which consists of the decrease of rigidity, salivation, the feeling of bether-being, the improvement of gait and the facial expression. The disappearance of tremor was noticed only at one patient, but the others did not exibit significant improvement of tremor.

As side-effects are noticed — nauzea and vomiting in five patients, and a few patients exibited insomnia and restlessness, as well as hyper-

kineziae of temporarily character. The cardiac failure was noticed in two patients, suffering previously of heart disease. Two patients showed increased sexual activity.

We would like to point out the necessity of carefull selection of patients, as well as beginning of the treatment in the hospital conditions.

Unfortunately, we did not dispose cocarboxylase inhibitor (MK 485) which decrease significantly the therapeutical doses and in this way makes possible wider use of L-DOPA.

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NAŠA ISKUSTVA U TERAPIJI PARKINSONOVOG SINDROMA L-DOPOM

KRATAK SADRŽAJ

U toku 1970. godine hospitalizovano je 30 bolesnika sa Parkinsonovim sindromom na Neuropsihijatrijskoj klinici u Sarajevu radi tretmana preparatom L-DOPA- Kod 18 bolesnika ovaj vid liječenja nije se mogao primijeniti zbog različitih kontraindikacija. L-DOPA je primijenjena kod 12 bolesnika u trajanju od tri mjeseca. Doze su se kretale od 3—9 gr dnevno. Kod 10 bolesnika nastupilo je poboljšanje, a kod 2 pogoršanje. Poboljšanje se sastojalo kod svih u smanjenju rigiditeta muskulature, smanjenju salivacije, opštem popravljanju stajanja, hodanja i izrazu lica. Tremor je potpuno iščezao samo kod jednog bolesnika, a kod drugih nastupilo je neznatno njegovo smanjenje. Prethodno ugašena seksualna potencija vratila se kod dva bolesnika. Pored toga, bolesnici su pokazivali i porast psihičkog energetskog potencijala.

Od sporednih efekata zapazili smo: nauzea i povremeno povraćanje kod 5 bolesnika, kratkotrajna nesanica i uznemirenost kod dva bolesnika, a prolazne hiperkinezije kod jednog bolesnika. Kod 2 bolesnika primijećeni su znaci popuštanja kardiovaskularnog sistema.

Prema našim skromnim iskustvima možemo zaključiti da L-DOPA predstavlja novi veliki napredak u tretmanu parkinsonizma, ali uz prethodnu brižljivu selekciju bolesnika, s obzirom na diferentnost lijeka.

Moramo naglasiti da nismo primjenjivali inhibitor kokarbiksilaze (MK 485), da bismo na taj način smanjili terapeutsku dozu.

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DISCUSSION

Barbeau: I am puzzled by your selection of only 12 patients out of 30 for treatment. This is probably besause you are very prudent. The treatment should not be limited by questions of age or previous surgery. The only limiting factor are severe arteriosclerosis (carebral) and active liver, kidney or heart disease.

Kantardžić: I must say that our patients, who could not underwent the therapy with L-DOPA, were very old almost all of them generalised arteriosclerosis, some of them with hypertension of the second and third degree, some with clear liver and kidney damages. They were in seventh or eight decade of life. The majority of those patients could not walk without help, some couldn't turn from one side to another in bed. There existed social reasons, not only medical, in their hospitalisation. So these were the reasons we did not give L-DOPA to such patients.

We thank to prof Barbeau on these very interesting remarks which we are going to take into consideration in our further investigations with L-DOPA.

Barbeau: One last point about the effect of L-DOPA upon tremor is worth mentioning: the best effect is observed after weeks or even month of administration and is mainly upon the slow 3—5 sec. type of rest tremor. The more rapid attitude or fast tremor occasionaly seen in Parkinson disease is often made worse.

Kantardžić: Only one patient showed good improvement of tremor after the treatment with L-DOPA, but we have to point out five patients showed good improvement. Thus means that six out of twelve patients showed a certain degree of improvement of tremor and this is almost equaly with results from literature (about fifty per cent).

Dimitrijević: Could I ask you whether the dravings you shoved represent your patient-artist himself or another patient.

Kantardžić: The artist made these paintings to show himself, his own good improvement after the treatment with L-DOPA.