Effects of L-DOPA Treatment on Indole Metabolism in Parkinson's Disease

Large doses of L-dopa are used in the treatment of Parkinson's disease for the relief of akinesa, rigor and tremor[1]. This report describes effects of this treatment on urinary indoles.

Methods. 24 h urinary excretion of 5-hydroxyindole-acetic acid (5-HIAA), total indole-3-acetic acid (total IAA) and tryptamine were determined by quantitative methods[2-4] in parkinsonian patients on 2 to 3 successive days before (1st period) and at least 4 weeks after onset of L-dopa therapy (2nd period). In all patients the initial dose of L-dopa was 0.5 g/day and was increased to 3 g/day within 4 weeks. At the time of the 2nd investigation period in this group of patients the daily L-dopa dosis varied from 3 to 4.5 g/day. In both investigation periods the patients received 1-bicyclo-heptenyl-1-phenyl-3-piperidino-propanol-(1) (Akineton®, 3 × 2 mg/day). In addition to the chemical analyses described above 5-hydroxyindole-acetic acid was determined by thin layer chromatography in 2 patients using chloroform, methanol, acetic acid (75/20/5) as solvent and Ehrlich's reagent as spray.

Results. The results are summarized in the Table. They show a significant reduction in the urinary excretion of 5-hydroxyindole-acetic acid during L-dopa administration, while at the same time urinary total indole-3-acetic acid and tryptamine were not affected by the treatment ($p > 0.2$). Thin layer chromatography confirmed the decrease of 5-hydroxy-acetic acid during L-dopa administration.

Discussion. EVERETT and BORCHERDING[5] investigated the effects of L-dopa on brain amines in mice and reported a remarkable decrease of serotonin 30 min after i.p. injection of the drug. Because of a simultaneous increase of brain 5-hydroxyindole-acetic acid, these authors interpreted the results in terms of an increase in the release and metabolism of serotonin due to displacement by dopamine. Our findings of decreased urinary excretions of 5-hydroxyindole-acetic acid during longterm L-dopa treatment indicate that release and displacement of serotonin from its storage sites apparently do not represent the only effects of L-dopa on serotonin metabolism, but additional mechanismus must be considered. The unchanged urinary excretions of total indole-3-acetic acid and tryptamine suggest that absorption of tryptophan is not impaired. In addition, the observed normal excretions of urinary tryptamine give no evidence of decreased decarboxylase or monoamine oxidase activities. Although the biochemical mechanisms responsible for the decreased excretions of 5-hydroxyindole-acetic acid during L-dopa treatment are not clear as yet, it might be speculated that they are due either to decreased activity of tryptophan-5-hydroxylase or to increased activity of tryptophan pyrrolase diverting tryptophan metabolism away from the 5-hydroxytryptophan pathway.

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Investigation-periods	5 HIAA (mg/day)	Total IAA (mg/day)	Tryptamine (μg/day)
1. Control-period	6.4 ± 2.13 (20)	6.5 ± 1.83 (23)	64 ± 39.2 (15)
2. L-dopa (3–4.5 g/day)	1.7 ± 1.19[a] (18)	7.1 ± 2.92 (18)	81 ± 30.2 (10)

24 h urinary excretions of 5 HIAA and Total IAA were determined in 8 patients, tryptamine in 5 patients. Total number of 24 h urinary samples analyzed are shown in parentheses. [a] Different from control $p < 0.005$.

Zusammenfassung. Orale L-Dopa-Behandlung bewirkt bei Patienten mit Parkinsonismus eine signifikante Minderung der Harnausscheidungen von 5-Hydroxyindolessigsäure.

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Length Measurement of Gut Segments for Mucosal Transport Studies

In studies on absorption or transport functions of gut segments in vivo and in vitro it is necessary to standardize transport to some reference quantity of the gut segment in order to compare results in several pieces of gut. Ideally the reference quantity should be some direct measure of the mucosal layer itself and length measurement of gut segments is the simplest direct estimate which can be made although it is apparently often considered too imprecise to be useful. Various workers have used protein content or wet or dry tissue weight as reference quantities in calcium transport studies but some difficulties with these have been noted[1] and it has been reported[2] that standardization according to simple length measurements can, under some conditions at least, give more meaningful results. In this laboratory calcium transport in rat gut segments has been referred to length measurements done