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TREATMENT OF MOTOR FLUCTUATIONS IN PARKINSON'S DISEASE WITH SUBCUTANEOUS APOMORPHINE

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14 patients with idiopathic Parkinson's disease and response oscillations to sustained oral levodopa therapy were treated with additional subcutaneous apomorphine for periods up to 35 months (8 to 35, mean 20,6). Apomorphine was given as continuous 24 hour infusion via mini pumps.

Mean doses of apomorphine were 160 mg/d on a 24 hour infusion regimen, the daily dose of levodopa could be reduced in all patients, from mean daily doses of 1260 mg/d (500-2400) before to 280 mg levodopa / d (0-750) with treatment of apomorphine and some cases no longer required oral drugs at all. There was a significant and sometimes dramatic reduction in the sum of daily "off"-hours from a mean of 5,7 (3-10) to 2,4 hours / d (0-5). Coincidencing with reduction of oral levodopa there was a decrease of peak dose dyskinesias from 3 to 1, using an intensity score ranging from 0 to 3.

Tolerability of apomorphine was good with no signs of nephrotoxicity or drug induced psychosis. Treatment details and results will be presented and the role of subcutaneous apomorphine in the treatment of fluctuating Parkinson's disease will be discussed.

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RECTAL APOMORPHINE IN PARKINSONIAN "ON-OFF" FLUCTUATIONS

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Since 1989 apomorphine has been introduced as an effective treatment of response-fluctuations in Parkinson's Disease. Firstly by subcutaneous administration and recently also by intranasal and sublingual administration. More recently the first promising experiences with rectal application of apomorphine are published. We report a pilot-study with 5 patients. All patients had "on-off" fluctuations and had already experienced subcutaneous and/or intranasal apomorphine, with a good clinical response. Before starting the clinical part of this study, we did in-vitro release-studies with 5 different apomorphine-suppositories: enema, witepsol, H15 base, P.E.G. (poly-ethyleneglycol base) and gelatine base, with apomorphine partially or totally in solution. All suppositories showed a good in-vitro release of apomorphine, with exception of the P.E.G.base. This one therefore was excluded from further clinical research. Before study-entry each patient underwent a rectoscopy to exclude rectal pathology which might have possible influence on absorption. All patients were given Domperidon 20mg t.i.d. and anti-Parkinsonian medication was stopped each evening before testing one type suppository. One hour before testing they received a phosphate enema. Every 10 min. a blood-sample was taken and clinical efficacy was measured by tapping-scores, walking-time and scoring of dyskinesia and tremor. This was done for one hour or until base-line assessments were reached. The plasma levels of apomorphine were measured by a high pressure liquor chromatography-method (HPLC). Our results show a good clinical response of every tested suppository. The differences in optimal doses and pharmacokinetic profiles of the different suppositories will be presented. No evident adverse affects were seen. Our results suggest an important role for rectal apomorphine administration in relieving "on-off" fluctuations by their possible long-lasting clinical efficacy, dependent of dose and type suppository. Another advantage is that patients who had adverse effects of subcutaneous and intranasal apomorphine, now have another possibility to use apomorphine.

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PATHOPHYSIOLOGICALLY DETERMINED SURGICAL THERAPY OF THE PARKINSON'S SYNDROME AND INTRAOPERATIONAL PREDICTION OF THE LONG-TERM FOLLOW-UP RESULTS

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Achievement of positive effect of surgical treatment of parkinsonism is provided by intraoperational (IO) morpho-physiological control (CT, EMG, microelectrode investigation of neuronal activity). Attampts have been made to apply the method of IO EMG for determination of minimal volume of coagulodestruction (CD) in case of parkinsonism (38 operations of 36 patients). EMG was made before and after inserting criocannula into the target, as well as after performing CD. Calibration of criocannula, i.e. volume of CD focus, was performed before each operation and was expressed in the volume of ice sphere, formed 30-60-90-120s earlier (≈60-100-150-200mm^3 respectively). It was determined that in case of availability of one symptom (tremor) CD volume ≈60mm^3 is sufficient, in case of mixed form, for liquidation of disease symptoms 100-150mm^3 CD volume is necessary. Sufficiency of CD volume was determined by disappearance of EMG-symptoms of the disease in the process of CD and non-restoration of them within 4-5 min. Absence of restoration of EMG symptoms during the noted time is a reliable criterion of steadfast positive effect of the operation. Selective approach to determination of targets for treatment of separate components in parkinson's syndrome (tremor, rigidity) will be discussed from the point of view of their pathological mechanisms.

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