WHAT IS THE BEST TREATMENT IN ADVANCED PD? - APOMORPHINE INFUSION

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The management of parkinsonian patients is frequently complicated by sometimes unpredictable or drug-resistant akinetic periods and abnormal involuntary movements. These alterations in l-dopa responsiveness manifested by motor fluctuations and dyskinesias is one of the most limiting factor in the long term treatment of Parkinson's disease. Evidence suggests that many of these phenomena directly reflect oscillations in l-dopa plasma levels and the rate of l-dopa transport to the brain.

The use of standard oral formulations of l-dopa does not allow maintaining adequate plasma levels throughout the day, and also slow release preparations have not been successful in severely complicated patients. Many studies have shown that fluctuations in motor performance occur when l-dopa is administered intermittently but not when it is administered continuously. Unfortunately, l-dopa is not suitable for chronic parenteral therapy in outpatients, as it requires high volumes of solution to be administered intravenously.

Apomorphine is a potent dopamine receptor agonist water-soluble that have been shown to successfully control motor fluctuation when subcutaneously infused in complicated parkinsonian patients.

Apomorphine is infused subcutaneously by a modified insulin pump programmable for varying infusion rates according to the patients' individual daytime requirements. These pumps are able to hold between 0.1 to 5 ml of solution in a hour (1-50 mg of apomorphine), therefore the ampoule had to be refilled every 1-2 days. Catheters of different length could be used to ensure the patient's maximum comfort. The needle is placed subcutaneously into the abdominal wall, and could be changed every 2-3 days but the majority of the patients preferred to remove the needle at night and re-insert it the following morning. The initial infusion rate is determined on basis of previous intravenous apomorphine infusions in the same patients and adjusted according to therapeutic requirements on following days. Subcutaneous apomorphine is administered without any additional antiparkinsonian medication between 8.00 am and 8 pm and discontinued overnight. This regime is maintained for about one week increasing the dose to obtain the best clinical response. In those patients not completely mobile or still fluctuating during apomorphine infusions, oral levodopa plus a peripheral decarboxylase inhibitor is added starting with a single morning dose. The mean dosage of apomorphine necessary to control optimally the parkinsonian symptoms is 4-10 mg/hour. All the patients received oral domperidone (60 mg/daily) pre-treatment to prevent systemic side effects. Moreover, it is possible to administer a bolus of apomorphine by pushing a button: it shows very useful to solve unpredictable "off" periods.

In summary, apomorphine infusion reduces levodopa dosage, reduces time spent "off" and improves dyskinesias in complicated parkinsonian patients. The technique is demanding, but could be managed relatively easily, also if the patients must be hospitalized for the initial clinical evaluation and administration.

Apomorphine infusion has the advantage of an easy subcutaneous infusion, do not require any surgical intervention, can be infused using small and programmable pumps, is well tolerated and reduce OFF time and dysinesias.