

to facilitate communication about such phenomena. No single term is entirely satisfactory but unless subtypes are adequately delineated, requiring further elaboration of the terminology, emotionalism seems to be the best choice.

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Sublingual apomorphine and Parkinson's disease

Sir: Subcutaneous injection of the dopamine receptor agonist apomorphine combined with oral domperidone is a safe, effective therapy for otherwise refractory disabling "off period" disabilities in patients with Parkinson's disease receiving long term l-dopa treatment.^{1–4} After a therapeutic suprathreshold injection "unblocking"

occurs after 5–10 minutes and lasts for 30–90 minutes. Although apomorphine can produce anti-parkinsonian effects when administered orally, very large doses (500 mg per day) are needed, the speed of action is much slower and unacceptable elevations in blood urea and plasma creatinine can occur.⁵ We have therefore investigated the alternative possibility of administering the drug by the sublingual route.

Nine patients with idiopathic Parkinson's disease and severe refractory motor fluctuations agreed to participate after giving their informed consent. Their median age was 64 years, mean duration of disease 12 years (4–20 years), mean duration of l-dopa therapy 11 years (4–17 years), mean dose of l-dopa 600 mg, mean stage of Hoehn and Yahr when "off" 3.9. All the patients were known to respond to subcutaneous injections of apomorphine, mean dose 3 mg (1–5 mg). After pilot studies it was decided to give all the patients a standard 30 mg sublingual dose (10, 3 mg tablets), when fasting, after 48 hours of oral domperidone pre-treatment (20 mg tds) to ensure a maximum therapeutic response.

Anti-parkinsonian drugs were stopped for 12 hours before each study. Baseline assessments, tapping test and timed walking tests were carried out and were repeated every 10 minutes after the administration of sublingual apomorphine. A modified Webster scale (to include rising from a chair and balance) was carried out at baseline and then again at the time of maximum therapeutic response.⁶

All patients switched "on" with sublingual apomorphine with a therapeutic effect approximately comparable to that seen after subcutaneous apomorphine. Five of the patients were asked to let the tablets dissolve under the tongue whereas in the other four, the tablets were crushed up first. The mean time for dissolution was 33 minutes (20–45 minutes) and the mean time from complete dissolution to full switch on was a further 10 minutes. The therapeutic response lasted for a mean 73 minutes (30–110 minutes), the mean increase in tapping score was 16 per 30 seconds (from 26–42), the mean reduction in walking time was 15 seconds (from 30–15 seconds), tremor was abolished in all seven cases where it was present and drug induced dyskinesias were seen in six patients. Adverse reactions were mild sedation (six patients), slight nausea (two patients), and yawning (two patients). One patient whose tablets dissolved extremely rapidly almost fainted, with a significant drop in blood pressure.

These results confirm that sublingual apomorphine is an effective anti-parkinsonian preparation producing therapeutic

responses qualitatively similar to those seen with oral levodopa. Although the latent period between therapeutic effects was longer than that seen after subcutaneous apomorphine injection, this was largely due to the time taken for the tablets to dissolve. We believe that this delay can be overcome by more efficient formulation. Preliminary work with liquid apomorphine administered sublingually suggests that only two or three times the dose of sublingual apomorphine would be necessary to produce comparable effects to those seen following parenteral administration. Sublingual apomorphine is likely to provide a viable alternative to intermittent injections of apomorphine in the treatment of "off period" disabilities in Parkinson's disease.

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