Apomorphine

Apomorphine (brand names Apokyn, Ixense, Spontane, Uprima) is a type of aporphine having activity as a non-selective dopamine agonist which activates both D2-like and, to a much lesser extent, D1-like receptors.

It also acts as an antagonist of 5-HT2 and α-adrenergic receptors with high affinity. The compound is historically a morphine decomposition product made by boiling morphine with concentrated acid, hence the -morphine suffix. Apomorphine does not actually contain morphine or its skeleton, nor does it bind to opioid receptors. The apo- prefix relates to it being a morphine derivative ("[comes] from morphine").

Currently, apomorphine is used in the treatment of Parkinson's disease. It is a potent emetic and should not be administered without an antiemetic such as domperidone. The emetic properties of apomorphine are exploited in veterinary medicine to induce therapeutic emesis in canines that have recently ingested toxic or foreign substances.

Apomorphine was also used as a private treatment of heroin addiction, a purpose for which it was championed by the author William S. Burroughs. Burroughs and others claimed that it was a "metabolic regulator" with a restorative dimension to a damaged or dysfunctional dopaminergic system. There is more than enough anecdotal evidence to suggest that this offers a plausible route to an abstinence based model; however, no clinical trials have ever tested this hypothesis. A recent study indicates that apomorphine might be a suitable marker for assessing central dopamine system alterations associated with chronic heroin consumption.

There is, however, no clinical evidence that apomorphine is an effective and safe treatment regimen for opiate addiction.

Subcutaneous apomorphine infusion is a clinically established therapy for patients with Parkinson's disease with motor fluctuations not optimally controlled by oral medication. Open-label studies have shown that apomorphine infusion is effective in reducing off time (periods when antiparkinsonian drugs have no effect), dyskinesias, and levodopa dose, but confirmatory evidence from double-blind, controlled studies is lacking.

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Britannia Pharmaceuticals, Reading, UK.Sigma Statistical Services, Balmullo, UK. University College London Institute of Neurology, London, UK, aimed to investigate the efficacy and safety of apomorphine infusion compared with placebo in patients with Parkinson's disease with persistent motor fluctuations despite optimised oral or transdermal treatment.

In a randomised, placebo-controlled, double-blind, multicentre trial, Katzenschlager et al., enrolled patients at 23 European hospitals who had been diagnosed with Parkinson's disease more than 3 years previously and had motor fluctuations not adequately controlled by medical treatment. Patients were randomly assigned (1:1) with a computer-generated randomisation code, stratified by site, to receive 3-8 mg/h apomorphine or placebo saline infusion during waking hours (16 h a day [range 14-18 was acceptable]) for 12 weeks. The flow rate of the study drug and other oral medications could be adjusted during the first 4 weeks on the basis of individual efficacy and tolerability, after which patients entered an 8-week maintenance period. The primary endpoint was the absolute change in daily off time based on patient's diaries, and was assessed in the full analysis set, which was defined as all patients who received at least one dose of allocated study drug and had efficacy data available at any timepoint post-baseline. Safety was assessed in all patients who received at least one dose of apomorphine or placebo. All study participants and investigators were masked to treatment assignment. Both the 12-week double-blind phase and the 52-week open-label phase of this study are now complete; this paper reports results for the double-blind phase only. This study is registered with ClinicalTrials.gov (NCT02006121).

Between March 3, 2014, and March 1, 2016, 128 patients were screened for eligibility and 107 were randomly assigned, of whom 106 were included in the full analysis set (n=53 in both groups). Apomorphine infusion (mean final dose 4·68 mg/h [SD 1·50]) significantly reduced off time compared with placebo (-2·47 h per day [SD 3·70] in the apomorphine group vs -0·58 h per day [2·80] in the placebo group; difference -1·89 h per day, 95% CI -3·16 to -0·62; p=0·0025). Apomorphine was well tolerated without any unexpected safety signals. Six patients in the apomorphine group withdrew from the study because of treatment-related adverse events.

Apomorphine infusion results in a clinically meaningful reduction in off time in patients with Parkinson's disease with persistent motor fluctuations despite optimised oral or transdermal therapy [1)].

1)
Katzenschlager R, Poewe W, Rascol O, Trenkwalder C, Deuschl G, Chaudhuri KR, Henriksen T, van Laar T, Spivey K, Vel S, Staines H, Lees A. Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial. Lancet Neurol. 2018 Jul 25. pii: S1474-4422(18)30239-4. doi: 10.1016/S1474-4422(18)30239-4. [Epub ahead of print] PubMed PMID: 30055903.