

Apomorphine: A Promising New Oral Treatment for Erectile Dysfunction

Apomorphine is a fast-acting, sublingual agent for the treatment of erectile dysfunction that is widely available outside North America. According to Peter J. Pommerville, MD, the drug could be an important addition to American and Canadian physicians' armamentariums.

Pommerville is Principal Investigator and Urology Consultant at Can-Med Clinical Research Inc. in Victoria, British Columbia, Canada. He is also a practicing urologist on staff at the Vancouver Island Health Authority. He presented the clinical profile of apomorphine at the 10th annual World Congress of the International Society for Sexual and Impotence Research (ISSIR), which took place from September 22 to 26, 2002 in Montreal, Canada.

Erectile Dysfunction and its Treatment

Erectile dysfunction, or ED, is a complex condition that has several mechanisms and etiologies and occurs in a variety of psychosocial contexts. Current therapies for ED are not satisfactory for all sufferers. In particular, many patients are not comfortable with the injection administration required by some therapies or find that the slow onset of action of other treatments limits the natural spontaneity of the sexual encounter.

According to Pommerville, the ideal ED treatment would elicit reliable, consistent erections, have a short onset of action, restore the spontaneity of sexual intercourse, and be free of unwanted side effects. None of the ED therapies currently available in North America approach this ideal. As a result, additional options for the treatment of ED are required.

“Drugs with different modes of action offer some diversity for the patient,” said Pommerville. “It offers the patient a choice. We can tailor these new medications to the patients’ needs, and I think the future of erectile dysfunction treatment is very bright and encouraging because we might be able to manage patients often in the same way that family doctors have managed patients with hypertension.”

Clinical Trials with Apomorphine

To date, more than 30 clinical trials involving 3,183 patients have been conducted with apomorphine, which acts directly on the paraventricular nucleus in the hypothalamus of the brain. Patients involved in these trials were, on average, aged 56 years and had been suffering from ED for 5.7 years. With respect to comorbidities, 14% suffered from coronary artery disease (CAD), 20% from benign prostatic hyperplasia (BPH), 35% from hypertension, 18% from diabetes, and 20% from dyslipidemia.

Most trials for other ED treatments have focused on patients with mild to moderate ED. However, in apomorphine efficacy studies, fully 68% had moderate to severe ED.

The primary endpoint of clinical studies with apomorphine was attempts resulting in erections firm enough for sexual intercourse. Secondary endpoints included rates of intercourse, time to develop an erection, IIEF overall scores, IIEF domain scores, and partner responses.

Efficacy of Apomorphine

Patients taking 2 or 3 mg of apomorphine experienced a significantly greater percentage of erections firm enough for intercourse compared to placebo ($p < 0.001$). Specifically, there was a 66% improvement over baseline for patients taking 2 mg of the drug, compared to 23% for those taking placebo, and there was a 120% improvement for those taking 3 mg of the drug, compared to 47% for those on placebo. Patients with mild to moderate ED who took 3 mg of apomorphine experienced a twofold improvement in attempts to have erections firm enough for intercourse.

Patients taking apomorphine enjoyed a statistically significant improvement in all areas of measurement of erectile functioning compared to placebo, including total IIEF scores, EF domain scores, and patient satisfaction with both the treatment and their sexual functioning. These results were corroborated by partner impressions, as documented by diaries and a sexual functioning questionnaire.

In terms of IIEF scores, patients taking 2 mg of apomorphine had an improvement of just over three points compared to placebo, and patients taking 3 mg of the drug had an improvement of almost four points compared to placebo. Both these differences were highly statistically significant. With respect to the EF domain of the IIEF, over 70% of those taking 2 mg and almost 78% of patients taking 3 mg had improved scores.

Partners of patients taking apomorphine reported a 48% improvement in success with attempts at erections firm enough for intercourse, compared to 34% for partners of patients taking a placebo ($p < 0.001$.)

Patients' ability to achieve an erection firm enough for intercourse increased with continued use of the drug. Among those taking 3 mg, 53% were able to achieve such an erection with the first attempt, but this increased to 70% by the fourth attempt. In patients with mild to moderate ED, 67% were successful with the first attempt, and 86% were successful by the fourth.

Onset of Action and Long-Term Efficacy of Apomorphine

The onset of action of apomorphine is very quick. Most patients (71%) achieve an erection within 20 minutes of administration, and 34% achieve one within ten minutes. Time to erection was not affected by patients' age or food intake. This fast onset of action mirrors the timing of the natural erectile response and helps restore the naturalness and spontaneity to the sexual experience.

Importantly, apomorphine is effective over the long term. Among patients taking a 2 mg dose of the drug, 37% of their attempts to have an erection firm enough for intercourse were successful. This rose to 93% within a month and remained in this range through to six, 12, and 18 months.

Safety and Tolerability of Apomorphine

Safety and tolerability studies with apomorphine have been promising. During clinical trials and post-marketing surveillance of over 4.5 million patients who have taken apomorphine at least once, there have been no drug-related deaths, MIs, cerebrovascular accidents, priapism, or inappropriate erections. There have only been 19 reports of side effects that meet International Conference on Harmonisation (ICH) criteria.

Dose escalation studies from 2 to 3 mg reveal that 12.5 to 13.3% of patients experienced side effects, the most common of which were nausea (3.0-4.2%), headache (2.4-3.0%), and dizziness (2.4-1.8%). Less than 2% of patients taking 2 mg of apomorphine and 0.1% taking 3 mg experienced syncope, which was not cardiac in nature but simply a sympathetic vasovagal reaction. In over 90% of cases, there were prodromal symptoms warning of impending syncope.

Adverse events were generally mild and self-limiting. Patient reports of side effects diminished by the fourth dose and almost disappeared by the eighth dose. Only 3% of patients discontinued the drug because of side effects, usually because of nausea, headache, or dizziness.

Apomorphine Safe in Combination with Other Medical Conditions and Drugs

Apomorphine appears to be safe in patients with CAD, depression, and hypertension as well as in those taking antihypertensives and nitrates. Patients with these comorbid conditions and/or taking these medications concomitantly did not experience an increase in adverse events.

Patients who drank alcohol, often more than two units, immediately before using apomorphine did not experience an increased incidence of side effects.

“Apomorphine appears to be well-tolerated,” said Dr. Pommerville. “The side effects are mild to moderate in most instances. They appear to be very transient and as well self-limiting. ... Apomorphine has a very safe profile in patients with cardiac disease. In patients taking nitrates, this medication does not appear to interact with it. There’s no dose adjustment or avoidance of alcohol. There doesn’t appear to be any cytochrome 450 drugs interaction, and there’s no need to alter the dose in older patients.”