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(54) Title: DROPERIDOL COMPOSITIONS AND METHOD FOR USING SAME

(57) Abstract

Oral, sublingual, buccal, nasal and injectable dosage forms of droperidol are provided and a method for treating migraine using such formulations. The dosage forms include oral tablets, capsules, powders, effervescent formulations and syrups, sublingual tablets and solutions, buccal tablets, nasal solutions, suspensions, gels and injectable solutions.

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DROPERIDOL COMPOSITIONS AND METHOD FOR USING SAME

FIELD OF THE INVENTION

This invention relates to the field of migraine treatment.

BACKGROUND OF THE INVENTION

The prevalence of migraine is said to be approximately 6% of the male population and 18% of the female population. Treatment for many patients having the occasional migraine usually involves simple analgesics, non-steroidal anti-inflammatory agents, or specific agents such as ergotamines or triptans. Approximately 10% of migraine sufferers have three or more attacks per month and warrant prophylactic treatment. Preventative agents such as beta-blockers, tricyclic antidepressants and divalproex sodium can reduce but not eliminate migraine attacks in some patients. Thus, there remains a need for migraine specific medications such as sumatriptan. In the remaining population of migraine sufferers, and in those with intolerable side-effects from available drugs, there is a lack of conventional pharmaceutical preparations that exhibit therapeutic effect, without severe side-effects.

Droperidol presently is marketed by Akorn, Inc. under the trademark Inapsine, as an injectable formulation used in anesthesia for preoperative surgery. It has never been approved for use in the treatment or management of migraine attacks.

The concentration of droperidol in the Inapsine is 2.5 mg/ml. That is the only concentration of droperidol that has been approved for human injection. Further, droperidol is present as the lactate salt in Inapsine. No droperidol salt, other than the lactate, has been used for human injection.

A limited, uncontrolled, non-blinded, use of droperidol lactate (2.5 mg/ml droperidol) to treat migraine attacks was attempted and the results published in *Headache,* April 1996, p.280. In that publication it was reported that 20 patients received from 2.5 to 7.5 mg droperidol intravenously, in increments of 2.5 mg every 30 minutes until the patient was headache free or until a total of three doses had been administered. All of the patients received prior treatment with migraine therapies. Eighteen of the patients reported to be headache-free by the last dose. Although the article reports on apparently encouraging results in treating migraine attacks with droperidol, no definitive conclusions can be reached from the results reported in that article as the number of patients treated was small, the study was not blinded, all patients received other agents to treat the migraine episode prior to receiving droperidol, and there was no placebo control. Also, there was no attempt to repeat the results with the patients. Further, no attempt was made to prolong therapy beyond the initial treatment to a headache-free state and most patients had continuing symptoms to some degree within 24 hours after the last droperidol treatment.

The study used multiple treatments of droperidol, with many patients receiving more than 2.5 mg of droperidol to reduce the migraine symptoms. The problem with administering droperidol at such a concentration is that the patient receives a significant volume of fluid in order to achieve a therapeutically effective amount of droperidol. This is of particular concern if the patient is receiving the droperidol through intramuscularly (I.M.) injection. Muscle pain and irritation and other problems may be associated with such large fluid injections.

Additionally, the aforementioned study and article only used intravenous droperidol. Others also have used intramuscular droperidol in uncontrolled studies for treatment of migraine. The use of droperidol by injection raises several issues, not the least of which is inconvenience to the patient, caused by the need to have the droperidol administered by a health care professional.

Accordingly, a need exists for a means to treat patients who suffer from, or are at risk of, a migraine episode, that does not require the use of injections of droperidol.

SUMMARY OF THE INVENTION

In accordance with the present invention, droperidol is supplied in a dosage form that provides better patient tolerance and improved ease of administration. The present injectable dosage forms provide a higher concentration of droperidol than has been available previously. In particular, the dosage forms contain from 2.75 to 10.0 mg/ml of droperidol.

The injectable dosage forms of the present invention may be used to treat migraine episodes, by administration intravenously ("I.V."), intramuscularly ("I.M."), or subcutaneously to a patient during a migraine attack, in an amount that is effective to treat symptoms of migraine.

In another embodiment, the present invention relates to the use of oral dosage forms of droperidol. The oral dosage forms of the present invention comprise tablets, capsules, powders, syrups and effervescent compositions.

In a further embodiment, the present invention relates to the use of sublingual and buccal dosage forms of droperidol. Such dosage forms comprise sublingual tablets and solution compositions that are administered

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