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Review Article

Hydromorphone Hydrochloride

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Abstract

Hydromorphone hydrochloride is a hydrogenated semisynthetic ketone derivative molecule of morphine. It is 5-7 times more potent than morphine and 4 times more potent than oxycodone. It is a morphine-like opioid agonist that has been used in the treatment of acute and chronic pain for about 80 years, and is an excellent alternative, especially in elderly patients with impaired renal function. The development of slow-release formulations of opioids has added versatility to the available options. While there are more than 80 powerful forms and types of opioids in European and American countries, the fact that there is only one option in our country made opioid rotation impossible in some naive opioid patients. Thanks to the Oros push-pulsation mechanism, higher bioavailability can be achieved as the drug is released more in the distal intestinal regions and the first pass metabolism from the liver is reduced. jurnista oros uses the push-pull osmotic pump transmission system.

Key words: paın; therapy; oros-pull opioid

Introduction

Hydromorphone hydrochloride is a hydrogenated semisynthetic ketone derivative molecule of morphine. It is 5-7 times more potent than morphine and 4 times more potent than oxycodone. It is a morphine-like opioid agonist that has been used in the treatment of acute and chronic pain for about 80 years, and is an excellent alternative, especially in elderly patients with impaired renal function [1]. Similar to morphine, it mainly exerts its effects on the mu opioid receptor. Hydromorphone also acts on the delta receptor to a lesser extent. Its pharmacological profile is similar to that of morphine. However, its use causes less itching, nausea, vomiting, sedation and cognitive impairment. Although the exact mechanisms of action of opioids such as hydromorphone are unknown, they are thought to be related to opioid receptors in the central nervous system. Orally administered hydromorphone is more potent than many commonly used opioid agonists. Different formulations containing hydromorphone are available today: immediate-release tablets, controlled-release capsules, oral liquid, rectal suppositories, powder, cough syrup, intravenous, subcutaneous, and intramuscular injection solutions.

The development of slow-release formulations of opioids has added versatility to the available options. While there are more than 80 powerful forms and types of opioids in European and American countries, the fact that there is only one option in our country made opioid rotation impossible in some naive opioid patients. There have been major problems with the misuse of some slow-release opioid preparations, obscuring the true benefits and therapeutic choice of these drugs. It can meet the analgesic needs of adult patients with chronic pain in a short time, whether they have used opioids before or not. Convenience in patients using multiple drugs meets an important need for patients who cannot use transdermally due to cachexia.

There are two types of hydromorphone with rapid release and slow release. There is no rapid release form in our country. The immediate-release form reaches a measurable plasma concentration in the 15th minute following oral ingestion, and the maximum concentration in 1 hour, and shows its effect within 30 minutes[2].

Immediate-release hydromorphone exhibits lower peak concentrations and less variation throughout the day, while jurnista provides more consistent hydromorphone release with constant plasma concentrations. Peak plasma concentrations of jurnistan are reached at 12-16 hours, while 50% of peak levels are reached in about 5-6 hours. After steady-state concentrations of jurnistan are reached within 2 days, plasma level fluctuations over time decrease compared to immediate-release hydromorphone [3].

The pharmacokinetics of Juristan differ markedly from immediate-release hydromorphone and are in line with expectations in the long-term treatment of chronic pain. Jurnista provides a constant drug release for 24 hours, minimizing valley-peak fluctuations. With Jurnista, the valley-to-peak fluctuations in plasma levels are reduced by 40% compared to immediate release hydromorphone.

Thanks to the Oros push-pulsation mechanism, higher bioavailability can be achieved as the drug is released more in the distal intestinal regions and the first pass metabolism from the liver is reduced.

jurnista oros uses the push-pull osmotic pump transmission system. If we explain this system technology;

Oros push-pull technology: Oros technology has been used for the last 20 years to provide controlled release of various drugs and can be adapted to obtain a stable, shaped or rapid drug release.

The push-pull osmotic delivery system uses a two-layer technology, which provides us with constant release and consistent therapeutic drug levels. The pull layer (pull or drug layer) contains the hydrophilic osmotically active substance together with hydromorphone hydrochloride. The second layer, the push layer, contains a high molecular weight osmotically active expansion polymer, a complementary osmotic agent (sodium chloride) and a coloring agent to distinguish the layers during laser piercing. The layers are shaped and bonded together to form a single, round shaped tablet by tablet compression. In 8, and 16mg forms, the filler target is 8.72mg and 16.35mg, respectively, to achieve a targeted hydromorphone release over 24 hours.

In the gastrointestinal tract, hydromorphone becomes suspended due to the passage of fluid through the semipermeable membrane at a controlled rate, and the osmotic layer swells. As the expanding osmotic layer compresses the drug layer, the hydrated hydromorphone is expelled from the release hole at the same rate as the liquid inlet. There is a fluid loading period of approximately 2 hours before drug release from the Oros system begins. The empty drug shell is insoluble and is excreted unchanged by the system faeces.

The jurnista oros push-pull osmotic pump used in this study uses the transfer system. If we explain this system technology; 2.3.8.1 Oros push-pull technology: Oros technology has been used for the last 20 years to provide controlled release of various drugs and can be adapted to obtain a stable, shaped or rapid drug release. The push-pull osmotic delivery system uses a two-layer technology, which provides us with constant release and consistent therapeutic drug levels. The pull layer (pull or drug layer) contains the hydrophilic osmotically active substance together with hydromorphone hydrochloride. The second layer, the push layer, contains a high molecular weight osmotically active expansion polymer, a complementary osmotic agent (sodium chloride) and a coloring agent to distinguish the layers during laser piercing. The layers are shaped and bonded together to form a single, round shaped tablet by tablet compression. To achieve a targeted release of hydromorphone for 24 hours in 8, and 16mg forms, the filler target is 8.72mg and 16.35mg, respectively (cross-section of the OROS Push-pull drug delivery system). In the gastrointestinal tract, hydromorphone becomes suspended due to the passage of fluid through the semipermeable membrane at a controlled rate, and the osmotic layer swells. As the expanding osmotic layer compresses the drug layer, the hydrated hydromorphone is expelled from the release hole at the same rate as the liquid inlet. There is a fluid loading period of approximately 2 hours before drug release from the Oros system begins. The empty drug shell is insoluble and the system is excreted unchanged with faeces .

Pharcokinetics:

Hydromorphone can be measured within 15 minutes after oral administration. It is rapidly absorbed, reaching plasma concentrations and a maximum plasma concentration in approximately 1 hour. Thanks to these properties, its effect starts in about 30 minutes. Its half-life is 2-3 hours. Therefore, immediate release formulations should be used every 4-6 hours to maintain therapeutic concentration.

Hydromorphone is primarily metabolized by gluronidation in the liver and excreted in the urine. The main compounds found in urine are hydromorphone 3 glucuronide (H3G) compound (40%), unchanged drug (6%), and dihydroisomorphine (<0.1%). Unlike morphine, hydromorphone does not have an analgesic 6-glucuronide metabolite, which can accumulate in the event of renal failure and contribute to the occurrence of side effects such as respiratory depression.

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Peak hydromorphone peak concentrations are achieved with Jurnista later than with immediate release hydromorphone (8, 16, 12-16 hours after 32 mg jurnista administrations versus <1 hour after 8mg immediate release hydromorphone administration). However, 80% of peak hydromorphone plasma concentrations after jurnista administration It is reached after 6 to 8 hours and the concentration remains high for approximately 24 hours after administration.

In a study conducted in 30 healthy volunteers, it was shown that Jurnistan was affected by food at a minimum level [4]. Participants were randomized to receive a single dose of jurnista 16 mg on an empty stomach, a single dose of jurnista 16 mg on a full stomach, and a single dose of naltrexone 50 mg and a jurnista 16 mg on a full stomach. At the end of the study, 27 subjects completed the study and it was stated that the effect of food on the rate and degree of absorption of jurnista was minimal [4].

Tolerability

Hydromorphone is an agent with proven safety and torability. Side effects are similar to those observed with morphine. Known dose-related side effects include nausea, vomiting, and rarely respiratory depression. The most frequently reported adverse events in Jurnista clinical studies were constipation, nausea, and vomiting. These side effects can usually be addressed with dose reduction, appropriate use of laxatives or antiemetics. It is stated that the incidence of sedation, itching, nausea-vomiting is less than morphine.

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Nausea, vomiting, and respiratory depression are dose-related side effects. Side effects can be managed with dose reduction, laxatives, and appropriate use of antiemetics. Side effect profile of hydromorphone. The long-term safety and tolerability profile of Jordan in chronic pain patients was evaluated in a US study that included 388 patients and had a mean duration of treatment of 274 days. The most frequently reported adverse events by patients treated with Jurnista were gastrointestinal and central nervous system, while no patient developed respiratory depression. It is

stated that most of these side effects are mild or moderate and can be easily managed [5].

Use in elderly patients

Physiological changes with age affect the pharmacokinetic and pharmacodynamic properties of drugs. For example, increased visceral and intermuscular fat ratio in the elderly may cause accumulation of fat-soluble analgesics. Hydromorphone prevents its accumulation in the body due to its slower lipophilicity and 303 liters of distribution volume compared to morphine. [5].

The prevalence of pain increases with age. However, pain management in elderly patients becomes difficult due to concomitant diseases. Unlike morphine, hydromorphone can be used as an alternative to morphine in elderly patients with renal insufficiency, since it does not have an analgesically active 6-glucuronide metabolite. Since moderate to severe renal insufficiency may be seen more frequently in elderly patients, hydromorphone therapy should be started at a low dose in these patients. The protein binding rate of hydromorphone is low. It is not metabolized by the Cyp enzyme system, undergoes glucuronidation in the liver, and has a low potential to interact with the metabolism of other drugs. There are no drug interactions such as oxycodone and codeing, and due to these pharmacokinetic properties, hydromorphone is a safe option for elderly patients using multiple drugs. Thanks to its once-daily use feature, it provides an advantage in increasing the compliance of elderly patients who use multiple drugs to treatment.

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