The Role of Hydromorphone in the Management of Chronic Pain

Essay submitted for M.Sc. Degree Anaesthesia

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abstract

OROS Hydromorphone is an effective opiate drug in the management of chronic pain that requires round-the-clock analgesia compared to other long acting opiate drugs available in our country namely: MST 30, Duragesic patch and Oxycontin.

Kay word ; hydromorphone - management - chronic

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Introduction

Opiates are essential for relieving chronic pain and particularly cancer pain. Long acting opiates have a major role in improving the quality of life in cancer patients.

Morphine although the standard opiate reference yet it produces active metabolites.

Fentanyl is void of active metabolites yet it has a significant drug interaction mainly because it is a protein bound drug.

Hydromorphone is a relatively new opioid drug that voids having active metabolites or having a major drug interaction but is of short acting duration.

The development of a long acting Hydromorphone (OROS Hydromorphone) is of immense practical benefit in the management of chronic pain and worth evaluation.

The aim of this study is to evaluate OROS Hydromorphone as an effective opiate drug in the

management of chronic pain that requires round-the-clock analgesia and to compare it with other long acting opiate drugs available in our country namely: MST 30, Duragesic patch and Oxycontin.

This study includes:

1- Hydromorphone pharmacokinetics and pharmacodynamics.

2- Long acting Hydromorphone system.

3- An effort will be given to compare and contrast OROS Hydromorphone to MST, Duragesic patch and Oxycontin in all aspects.

4- Opioid rotation and equianalgesic ratios.

Chapter 1

Basic Pharmacology

History

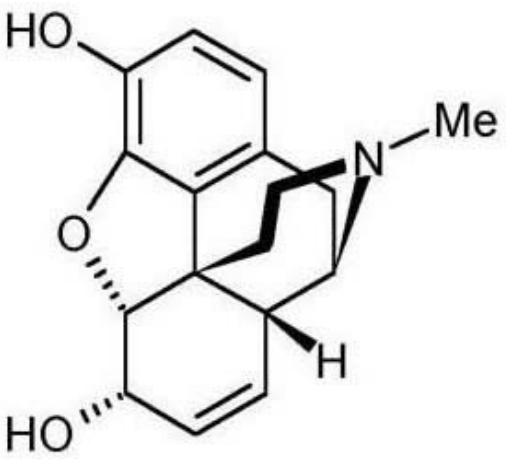
Hydromorphone is a semi-synthetic opioid agonist and a hydrogenated ketone of morphine.[1] It was first synthesized in Germany in 1921 and was introduced into clinical practice by 1926. Although there were over 200 publications supporting its pain relieving qualities within ten years of its introduction to clinical medicine, hydromorphone has commonly been viewed as a second-line drug to morphine in the treatment of both acute and chronic pain.[1] Oral morphine is the drug of first choice for chronic cancer pain as recommended by the World Health Organization,[2] because of its global availability and the extensive clinical experience and pharmacokinetic and pharmacodynamic data available.[3] Despite this recommendation, a significant proportion of patients do not achieve adequate pain relief with morphine, commonly because of unmanageable adverse effects such as

nausea, delirium, or myoclonus. It has been shown that rotating from one opioid to another can improve pain control as well as reduce opioid-related toxicity, although the mechanisms are unclear.[4–7] Therefore, hydromorphone has a key role in the area of chronic and acute pain relief as an alternative to morphine. It is included in clinical practice guidelines for the management of pain secondary to cancer [2,8] and has been well studied as an analgesic for post-operative pain.[9–11] Raymond W. Houde and Ada Rogers started an informal group called the New York Pain Group in the early 1960s and went on to cofound the American Pain Society in the late 1970s. Houde is professor emeritus at Memorial Sloan Kettering Cancer Institute and has written numerous articles on pain, its physiology, and treatment. He was involved in studies during the 1980s which elucidated the equianalgesic ratio between oral and potential hydromorphone, as well as the potency of hydromorphone compared to morphine.[12] However, to this day

further research is ongoing to add to understanding of this drug and it clinical applications.

Chemistry

Hydromorphone



Morphine

Hydromorphone is structurally very similar to morphine; it differs from morphine by the presence of a 6-keto group and the hydrogenation of the double bond at the 7-8 position of the molecule.[13] Like morphine, it acts primarily on μ opioid receptors, and to a lesser degree on delta receptors. Hydromorphone does not effect kappa, sigma, or epsilon receptors.[14] μ receptors mediate the pain relieving properties of opioids but also mediate unwanted

side effects, such as constipation, nausea, and respiratory depression.

Pharmacokinetics

Oral

Hydromorphone is available in the following oral preparations: powder, solution, immediate release tablet, and modified-release tablet. It is absorbed in the upper small intestine, is extensively metabolized by the liver, and has a variety of renally excreted, water-soluble metabolites. Approximately 62% of the oral dose is eliminated by the liver on first pass, partly accounting for oral bioavailability in the range of 1:2 to 1:8.[15] For orally-administered, immediate release preparations, the onset of action is approximately 30 minutes with a duration of action of about 4 hours. For modified-release preparations, the bioavailability is similar to immediate-release preparations, with a duration of

action of either 12 or 24 hours depending on the particular formulation.[16–18]

Parenteral

Hydromorphone can be administered parenterally by intravenous, intramuscular, and subcutaneous routes. The oral to parenteral equianalgesic ratio has been estimated as 5:1,although a range has been described and clearly there is a great deal of interindividual variablility.[15] Subcutaneous administration has been found to have 78% of the bioavailability of intravenous dosing.[19] Onset of action of hydromorphone after intravenous dosing is approximately 5 minutes, although maximum effect is not achieved for as long as 20 minutes due to the hysteresis (compartment) effect of a partially lipid soluble agent and the delayed penetration of the blood–brain barrier.[20] Because it is more fat soluble than morphine, its onset of action is correspondingly faster than that of

morphine, but is slower than highly lipid soluble drugs such as fentanyl. Hydromorphone can be prepared in highly concentrated solutions (up to 100 mg/mL) and because of the smaller volumes, can be easier to administer as a subcutaneous infusion than morphine in the setting of very high dose opioid administration, such as in opioid-resistant cancer pain.[21] However, hydromorphone administered subcutaneously in high concentrations can result in a painful local reaction,[22] although many patients do not experience this toxicity.[23]

Spinal

Hydromorphone can be given via the epidural route. The epidural to parenteral equianalgesic ratio is approximately 1:2.[24] Duration of action after a single epidural dose of hydromorphone has been