Efficacy and Safety Profile of a Single Dose of Hydromorphone Compared with Morphine in Older Adults with Acute, Severe Pain: A Prospective, Randomized, Double-Blind Clinical Trial

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ABSTRACT

Background: Older adults (ie, those aged ≥65 years) are the fastest growing segment of the US population, with an estimated ~71 million expected by 2030. Over the past 10 years, there has been an 11% increase in the number of emergency department (ED) visits by older adults, and pain is their most common chief complaint.

Objective: The goal of this study was to compare weight-based IV hydromorphone and IV morphine in adults aged ≥65 years presenting to the ED with acute, severe pain.

Methods: This was a prospective, randomized, double-blind clinical trial of older adults with acute, severe pain at an adult, urban academic ED. Patients were randomly allocated to receive a single dose of 0.0075-mg/kg IV hydromorphone or 0.05-mg/kg IV morphine. The primary outcome was the between-group difference in decrease in pain from baseline to 30 minutes after the medications were infused. Patients' degree of pain was measured on a numerical rating scale (NRS) where "0" was defined as "no pain" and "10" was defined as "the worst pain possible." Adverse effects, pain reduction at 10 minutes and 2 hours postbaseline, patient evaluations of satisfaction and pain relief at 30 minutes postbaseline, and use of additional analgesics and antiemetics were tracked as secondary outcomes.

Results: A total of 194 patients were randomized to treatment; 183 patients (hydromorphone group, n = 93; morphine group, n = 90 [overall mean (SD) age, 75 (8) years]) had sufficient data for analysis at the primary end point of 30 minutes postbaseline. The mean decrease in pain from baseline to 30 minutes in patients allocated to IV hydromorphone was 3.8 versus 3.3 NRS units in patients allocated to IV morphine. This difference of 0.5 NRS unit (95% CI, –0.2 to 1.3) was neither clinically nor statistically significant. A majority of patients in both groups (57.0% randomized to hydromorphone and 58.9% randomized to morphine) failed to achieve a ≥50% reduction in pain within 30 minutes of treatment. The incidence of adverse effects from baseline to 30 minutes was not statistically different in the 2 groups.

Conclusions: A single dose of IV hydromorphone at 0.0075 mg/kg was neither clinically nor statistically different from IV morphine at 0.05 mg/kg for the treatment of acute, severe pain at 30 minutes postbaseline in these older adults in the ED. The incidence of adverse effects was not statistically different. Our data suggest that hydromorphone and morphine in the doses given had similar efficacy and safety profiles in these older adults. Neither regimen provided ≥50% pain relief for the majority of patients. Future investigations of acute pain management in older adults should examine the efficacy and safety of higher initial (loading) doses of opioids titrated at frequent intervals until adequate analgesia is achieved. (*Am J Geriatr Pharmacother.* 2009;7:1–10) © 2009 Excerpta Medica Inc.

Key words: elderly, older adults, pain, acute, emergency department, morphine, hydromorphone.

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INTRODUCTION

Older adults (ie, those aged ≥65 years) are the fastest growing segment of the US population, with an estimated ~71 million expected by 2030.[1] Over the past 10 years, there has been an 11% increase in the number of emergency department (ED) visits by older adults, and pain is their most common chief complaint.[2]

Numerous physiologic changes are associated with the aging process. Many of these changes can affect responses to pharmacotherapy, medication tolerance, and the threshold for toxicity. Both the pharmacokinetic and pharmacodynamic responses of drugs are influenced. Age itself may also affect pain perception, as the number of myelinated and unmyelinated sensory fibers in the skin appears to decline with age.[3] This may mean that older adults have less warning when an acute painful stimulus is becoming injurious.[3] Older adults also appear to be more prone to prolongation of hyperalgesia after exposure to persistent noxious stimuli.[3] In all age groups, inadequate treatment of acute pain has been shown to contribute to the development of chronic pain and prolonged disability.[4–6]

Older adults are at risk for oligoanalgesia; these patients commonly receive inadequate doses of pain medication, especially in EDs.[7–11] As crowding in EDs becomes more widespread, the potential for delivery of poorer quality care in older adults will only increase.[12] It has been recommended that older persons with most types of acute, severe pain in the ED should be treated with IV opioids because oral medications are unlikely to act quickly or provide adequate analgesia.[3] Medications given by the IM route are difficult to titrate because peak absorption may be delayed by hours.[3]

In the ED setting, available parenteral opioids include morphine, hydromorphone, fentanyl, and meperidine, although the latter is no longer stocked in many EDs due to its neurotoxicity.[13] Hydromorphone is an opioid with ~7 times the potency of morphine.[14] Although morphine is generally the first-line parenteral opioid used in treating severe pain, a significant minority of patients suffer either intolerable adverse effects, inadequate pain relief, or both.[15] It is partly for these reasons that switching to an alternative opioid, such as hydromorphone, is becoming increasingly common in clinical practice despite the lack of evidence for such a strategy.[15]

Our previous research in younger adults (age range, 21–65 years) suggests that those who received IV hydromorphone had a clinically and statistically significantly greater decrease (difference, 1.3 numerical rating scale [NRS] units; 95% CI, 0.5–2.2) in pain than those given an equianalgesic dose of IV morphine.[16] Because it is unknown whether older adults respond differently from younger adults to these 2 opioids, the goal of the current study was to compare weight-based IV hydromorphone and IV morphine in adults aged ≥65 years presenting to the ED with acute, severe pain.

PATIENTS AND METHODS

Study Design

This was a prospective, randomized, double-blind clinical trial. The study was approved by the institutional review board of the Montefiore Medical Center (Bronx, New York). It was conducted in an adult, urban academic ED that has an annual volume of ~89,000 patients.

Selection of Participants

The study population consisted of adults aged ≥65 years who presented to the ED with acute pain (defined as pain <7 days in duration) of sufficient severity, in the judgment of the ED attending physician, to warrant use of IV opioids. Exclusion criteria included previous allergy to hydromorphone or morphine, systolic blood pressure (SBP) <90 mm Hg, alcohol or other drug intoxication as judged by the attending physician, use of other opioids or methadone within the past 7 days, use of a monoamine oxidase inhibitor, chronic pain syndromes (eg, sickle cell disease, fibromyalgia), and abnormal mental status as judged by the attending physician (ie, unable to sign consent form). Patient weight was obtained by asking patients directly. Patients weighing >220 lb (100 kg) were excluded because appropriate weight-based dosing of these individuals would exceed the predetermined maximum initial dose of 0.75-mg hydromorphone or 5-mg morphine used in this study.

Trained, bilingual research assistants (RAs) enrolled patients from July 2005 to March 2007.

Interventions

After written informed consent was obtained (in either English or Spanish), enrolled patients were randomly allocated to receive a single IV dose of hydromorphone (0.0075 mg/kg) or morphine (0.05 mg/kg) administered in a double-blind fashion. The equianalgesic dose ratio of 6.67:1 (morphine to hydromorphone) was chosen based on the most recent information available at the time from *Goodman & Gilman's The Pharmacological Basis of Therapeutics*.[14] Although this equianalgesic ratio varies substantially depending on the source used, we believed this publication would be widely regarded as a reasonably authoritative source.