

Incidence of hydromorphone associated opioid-induced neurotoxicity

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Purpose

Morphine is commonly utilized for pain management in hospice patients. However, accumulation of its toxic metabolite (morphine-3-glucuronide) could lead to opioid-induced neurotoxicity, especially when used in high doses and in patients with renal insufficiency. Hydromorphone is a semi-synthetic opioid with similar metabolism. Accumulation of the toxic metabolite hydromorphone-3-glucuronide could potentially cause this rare opioid-induced neurotoxicity as well, yet there are small clinical studies that have shown hydromorphone to be safe and effective in patients with renal insufficiency. The purpose of this study was to determine the incidence of opioid-induced neurotoxicity in hospice patients whose pain is managed with hydromorphone.

Method

This was an observational, prospective study, included all inpatient hospice patients who had been initiated on scheduled hydromorphone for pain management. Physician assessment of each enrolled patient was performed daily for neurotoxicity symptoms of hyperalgesia, allodynia, myoclonus, and seizures. Data collection was performed by the study investigators using a standard data tracking form, including hospice diagnosis, comorbidities, hydromorphone regimen, and whether or not the patient experienced any of the aforementioned symptoms. Dose and duration of therapy were compared between patients with vs without symptoms. Patients' current medical conditions and past medical history were also analyzed.

Results

A total of 156 patients were enrolled and analyzed in this study. Age range was between 36 and 95 years of age, with the mean of 70 years. Ten patients (6.4%) developed symptoms of hydromorphone-induced neurotoxicity (HINT). The mean age of those that developed HINT was 73 years vs a mean of 70 years in the group that did not. All patients experienced hyperalgesia, allodynia, myoclonus, or a combination of these symptoms, though none had seizures. Of those that experienced HINT, the average dose and duration was 2.152 mg/hr continuously for 6 days compared to 0.87 mg/hr continuously for 5.48 days in the group that did not. Two of the ten patients in the HINT group had renal failure and one had chronic kidney insufficiency. The mean serum creatinine in the HINT group was 3.2 mg/dL in contrast to 1.3 mg/dL.

Conclusions

Based on the data from this study, it appears that HINT in hospice patients is related to kidney function and dose and duration of therapy. This study established a dose and duration that increases the likelihood of developing this adverse event in hospice patients. As seen from the results, the likelihood of developing HINT could potentially develop with a hydromorphone regimen greater than 2 mg/hr continuously for at least 6 days. It also appears that increased serum creatinine increases the likelihood of developing HINT in hospice patients. Patients that developed HINT were opioid rotated to either parenteral fentanyl or methadone.