



DELIRIUM RISK ASSOCIATED WITH VARIOUS OPIOID MEDICATIONS

Delirium is a state of confusion that can occur in hospitalized elderly patients who have several confounding factors (e.g., infections, new medications, environmental changes). Approximately 10-30% of patients admitted to the hospital develop delirium and these patients have poor recovery, increased morbidity, mortality, and healthcare costs. Several factors may be associated with delirium; however, several studies have shown that opioids may be a precipitating factor for delirium. This issue of *CLIPs* reviews a systematic review that evaluated if delirium risk differs between the various opioids. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Swart LM, van der Zanden V, Spies PE, de Rooij SE, van Munster BC. The comparative risk of delirium with different opioids: a systematic review. 2017; *Drugs Aging*. (doi:10.1007/s40266-017-0455-9)

Introduction

- Patients with delirium have approximately 5.2 predisposing factors and 3 precipitating factors for delirium.
- Pain and opioids are associated with being a precipitating factor for delirium.
- The cause of delirium has not been elucidated; however, inflammation is believed to play an essential role.
- Drug-induced delirium may be due to an over-activity of the dopaminergic system and underactivity of the cholinergic system.
- In general, the larger the anticholinergic activity, the greater the risk for delirium.
- Different opioid products may be associated with variable risks for delirium.
- Some opioids (e.g., meperidine and tramadol) have metabolites with a high anticholinergic property.

Methods

- A Medline search was combined with a geriatric search filter from 1946 to December 2014 to locate relevant articles.
- A bibliographic search of the relevant literature was conducted.
- Studies included in the review were written in English or Dutch, randomized controlled trials, prospective/retrospective cohort studies, case-control studies in hospital, long-term, or palliative care, with delirium as an outcome measure was included.
- All opioids were included.
- Studies were scored as high, moderate or low quality.
- Odds ratios (OR), hazard ratio (HR), or relative risks (RR) were included in the review.

Results

- A total of 966 articles were located and 924 were excluded based on information from the title and abstract. A total of 6 articles were included in the final review.
- The six studies included evaluated eight different opioids: morphine, meperidine, fentanyl, tramadol, oxycodone, codeine, hydromorphone, and hydrocodone.
- No study was considered of high quality, one study was moderate quality, and 5 were low quality.
- Two retrospective cohort studies, prospective cohort studies, and nested case control studies were included.
- Two studies used a matched case-control design and one study evaluated 7 perioperative factors.
- All studies were performed in surgery departments. The number of patients in each study ranged from 92 to 541.

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Results (continued)

- Three studies found a significant risk of delirium with meperidine compared with other opioids (RR, 2.4; 95% CI, 1.3-4.5), no opioid (OR, 2.7; 95% CI, 1.3-5.5), or morphine (OR 2.5; 95% CI, 1.15-4.17).
- Results documented in the other studies included the following: increased risk of delirium with tramadol compared with no opioid (HR, 7.1%; 95% CI, 2.2-22.5), decreased risk from hydromorphone compared to other opioids (OR, 0.3; 95% CI, 0.14-0.65); and decreased risk from fentanyl compared with morphine (OR 0.22; 95% CI, 0.07-0.69).
- Combined use of morphine and oxycodone was associated with a significant increase in the risk of delirium.
- Several characteristics could not be located in some of the studies (e.g., delirium definition, opioid dose, timing of administration) were not available.

Discussion

- An increased delirium was observed from the use of meperidine.
- Tramadol's association with delirium was observed with only one, low quality study. Several case reports did indicate an increased risk with tramadol.
- Hydromorphone and fentanyl did not appear to have a negative effect on delirium.
- Several limitations were associated with the review due to selection bias, lack of definition of delirium, cognitive impairment, and comorbidity; and lack of details about opioid use.

Conclusion

- There is no conclusive evidence that the risk of delirium in elderly patients is dependent on the type of opioid.
- Many of the studies were low to moderate quality.
- Meperidine may increase the risk of delirium in elderly patients.
- Additional studies are needed to assess the role of opioids in the development of delirium.

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