JOURNAL WATCH

Immediate- or sustained-release morphine for dose finding during start of morphine to cancer patients: a randomized, double-blind trial.
P.Klepstad, Stein Kaasa, Åse Jystad, Bjørn Hval, Petter C.Borchgrevink. *Pain 101:193-198, 2003.*

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Abstract:

A titration procedure using immediate-release morphine given 4-hourly is recommended during start of oral morphine for cancer pain. This recommendation is not based on evidence from controlled studies, and many physicians start morphine treatment with controlled-release morphine. We included 40 patients with malignant disease and pain despite treatment with opioids for mild to moderate pain in a randomized, double-blind, double-dummy, parallel-group study comparing titration with immediate-release morphine given 4-hourly with titration with sustained-release morphine given once daily. The primary end point was the time needed to achieve adequate pain relief. Secondary end points were other symptoms (nausea, tiredness, lack of sleep, vertigo, appetite and constipation), health related quality of life and patient satisfaction. The mean times needed for titration were 2.1 (95% CI; 1.4–2.7) days using immediate-release morphine and 1.7 (95% CI; 1.1–2.3) days using sustained-release morphine. Patients titrated with immediate-release reported statistically significant more tiredness at the end of titration. We observed no other differences in adverse effects or health related quality of life functions between the two treatments. Similar global satisfactions with the morphine treatments were reported. In conclusion, a simplified titration using sustained-release morphine once daily is equally effective as immediate-release morphine given 4-hourly.

Author Keywords: Pain; Cancer; Morphine; Start; Sustained-release morphine; Immediate-release morphine

Comments:

Strengths/uniqueness:
A randomized, double-blind, double-dummy, parallel group design was applied. Results are based on a strict design following recommendations for randomized controlled trials. The authors looked at relevant outcomes other than pain such as nausea, loss of sleep, tiredness, loss of appetite, constipation, vertigo, Karnofsky performance status and health-related quality of life and a global satisfaction with the pain treatment. The authors try to question accepted guidelines for management of cancer pain.

Weaknesses:
No characteristics of the pain, such as the Edmonton Staging System, were provided. Patients received a two-day baseline treatment, which influenced pain control even before they received the study drugs. During the study different treatments were allowed (chemotherapy,

radiotherapy, NSAIDS) and the distribution of patients receiving different treatments in two groups was not similar. The starting dose of 10mg q4h or 60mg q daily may be high for some opioid naive patients and the method of opioid titration (60-90-120-180-270-360mg morphine daily) is not based on any established guidelines. The costs of the different treatments were not compared.

Relevance to Palliative Care:

Opioids are widely used in palliative care. Although this study does not fully answer the question of which method of opioid initiation is preferable, it is important to continue to conduct well-designed research to improve pain control and quality of life for this patient population.