Original Article

Should the Rate of Opioid Dose Escalation Be Included as a Feature in a Cancer Pain Classification System?

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Abstract

The purpose of this study was to assess the need for opioid dose escalation as a feature of a pain classification system for advanced cancer patients. Opioid dose escalation was included as a prognostic feature in the original Edmonton Staging System (ESS) for pain classification, but was not included among the five features of the revised ESS (rESS): pain mechanism, incident pain, psychological distress, addictive behavior, and cognitive function. Mercadante et al.'s definition of opioid escalation index percentage (OEI%) has been used as a surrogate marker for opioid responsiveness. Our hypothesis was that younger age (< 60 years), neuropathic pain, incident pain, psychological distress, and addictive behavior would be associated with an OEI% > 5%. Using data from a recent multicenter validation study of the rESS, a secondary analysis of a subsample of 532 advanced cancer patients with a pain syndrome was conducted. Approximately 44% (n = 232) of the patients had an OEI% > 5%. There were no significant associations between OEI% and age, neuropathic pain, incident pain, psychological distress, or addictive behavior. As originally proposed as a clinical marker, the OEI% may oversimplify the complexity of pain management in advanced cancer patients. Future studies are required to better elucidate the need for opioid dose escalation as a feature of a cancer pain classification system. J Pain Symptom Manage 2008;35:51–57.

Key Words

Opioid escalation index, cancer pain, pain classification

Introduction

The need for opioid dose escalation is a complex phenomenon of cancer pain management in palliative care.[1] In cancer pain, the titration of opioid dose reaches an endpoint determined by either unacceptable side effects or acceptable pain control. The need for opioid dose escalation incorporates clinical factors and pharmacodynamic changes that reflect potential mechanisms for opioid-related

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tolerance.[2] In advanced cancer patients, increasing pain may be more likely attributed to worsening disease progression or psychological processes, rather than true pharmacodynamic changes.[3] Rapid opioid dose escalation has been identified as a significant predictor due to difficulty in achieving stable pain control.[4]

The use of opioid dose escalation as a clinical marker has historically evolved over time. Opioid dose escalation was initially included as a prognostic feature in the original Edmonton Staging System (ESS) for pain classification in advanced cancer patients.[4] In a pilot study of the ESS, Bruera et al. designated the average percentage daily increase of opioid dose, adjusted for number of days of treatment, as a surrogate marker of opioid tolerance. Bruera et al. hypothesized that an average daily increase of opioid dose >5% would reflect a significant pain management problem. In Bruera et al.'s study, this need for opioid dose escalation was identified as a significant prognostic factor for achieving pain control ($P = 0.0001$). In a subsequent prospective multicenter study of the ESS, the average daily percentage increase of opioid dose was again used as a surrogate marker for opioid tolerance, and was identified as a significant prognostic feature in cancer pain management.[5]

Difficulties with prognostic interpretations and feature definitions have limited the international acceptance of the ESS. The ESS was further refined, resulting in the development and initial validation of the revised Edmonton Staging System (rESS).[6] Further construct validation resulted in a name change to the Edmonton Classification System for Cancer Pain (ECS-CP).[7] The rESS consists of five features, which are assessed at the bedside by palliative care specialists—pain mechanism, incident pain, psychological distress, addictive behavior, and cognitive function. These five features have demonstrated value in predicting pain management complexity. The need for opioid dose escalation was not included in the rESS, however, due to difficulty in defining and clinically interpreting this phenomenon.[6]

The concept of opioid dose escalation was further refined by Mercadante et al., using a surrogate marker known as the opioid escalation index percentage (OEI%) as a measure of opioid responsiveness.[8] Mercadante et al.'s OEI% reflected the mean percentage daily increase in opioid dose from initiation of opioid treatment, thus comparing the opioid starting dose with the maximum opioid dose during a four-week period. In a prospective study of advanced cancer patients, Mercadante et al. used the OEI% and a pain intensity score to categorize degrees of opioid responsiveness, with OEI% ≥5% and pain score ≥4 on a 0–10 scale being considered "poor responders." Opioid responsiveness is defined as the level of analgesia achieved with an opioid titrated to balance acceptable pain relief with unacceptable side effects.[9] Thus, Mercadante et al.'s concept of opioid dose escalation evolved as a surrogate marker for opioid responsiveness, in contrast to Bruera et al.'s concept of opioid dose escalation as a surrogate marker for opioid tolerance.

Given that Bruera et al.'s original ESS has also evolved, the need for opioid dose escalation as an outcome measure was identified as a key area of future research in the development of this cancer pain classification system.[6] In Fainsinger et al.'s multicenter validation study of the rESS, younger age (<60 years), neuropathic pain, incident pain, psychological distress, and addictive behavior were significantly associated with longer time to achieve stable pain control, in a univariate analysis ($P < 0.05$). On the basis of the length of time to achieve stable pain control, therefore, we hypothesized that younger age (<60 years), neuropathic pain, incident pain, psychological distress, or addictive behavior would be significantly associated with an OEI% >5%.

Methods

The findings in this article are based on a secondary analysis of a subsample of 532 advanced cancer patients with a pain syndrome, derived from a multicenter validation study of the rESS. The design and methods for this multicenter study have been described in detail elsewhere.[6] We initially identified advanced cancer patients through referral to a palliative care service. Consecutive patients were admitted to a tertiary palliative care unit in a teaching hospital, an acute care palliative consultation service in a second teaching