Opioids for the management of breakthrough (episodic) pain in cancer patients.

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Abstract
Background: Breakthrough pain is a transient increase in pain intensity over background pain. It is a common and distinct component of cancer pain that can have a negative impact for both patient and carers' quality of life. Breakthrough pain's usually related to background pain and is typically of rapid onset, severe in intensity, and generally self-limiting with an average duration of 30 minutes. At present current management to breakthrough pain is using supplemental analgesia (also known as rescue medication) at a dose proportional to the total around-the-clock (ATC) opioid dose. Objectives: To explore and assess evidence for the use of opioids in the management of breakthrough pain in patients with cancer. Methods: Selection criteria: Randomized controlled trials (RCTs) of opioids used as rescue medication against active or placebo comparator in patients with cancer pain were included. Outcome measures sought were reduction in pain intensity measured by an appropriate scale, adverse effects, attrition, patient satisfaction and quality of life. There were no language restrictions. Data collection and analysis: Eligible studies were selected and examined independently by the two reviewers. Full text was retrieved if any uncertainty about eligibility remained. Non-English texts were screened. Quality assessment and data extraction were conducted using standardized data forms. Drug and placebo dose, titration, route and formulation were compared and detail of all outcome measures (if available) recorded. Results: Four studies (393 participants) met the inclusion criteria, all were concerned with the use of oral transmucosal fentanyl citrate (OTFC) in the management of breakthrough pain. Two studies examined the titration of OTFC, one study compared OTFC to normal release morphine and one study compared OTFC to placebo. OTFC was shown to be an effective treatment for breakthrough pain. When compared to placebo and morphine, participants gave lower pain intensity scores and higher pain relief scores for OTFC at all time points. Global assessment scores also favored OTFC. Conclusions: The only studies identified in this review related to the use of OTFC, a drug specifically developed for the management of breakthrough pain. All studies included similar outcome measures and all had high quality scores. There is evidence that OTFC is an effective treatment in the management of breakthrough pain. The randomized trial literature for the management of breakthrough pain is small and no trials were found for other opioids. Given the importance of this subject, more trials need to be undertaken.
**Strengths/Uniqueness:**
In this Cochrane reviews of literatures, all randomized controlled trials, blinded and non-blinded, published and unpublished, which assess the management of breakthrough pain, were included.

**Weakness:**
The practice of delivering a fixed proportion of the ATC dose as rescue medication is not supported by this review. All four included studies found no meaningful relationship between the successful dose of OTFC and ATC oral or transdermal opioid medication.

A number of alternative opioids are now available for the management of breakthrough pain and these opioids could be delivered by different routes. However, the evidence exists only for the use of OTFC. Other opioids such as morphine, oxycodone, hydromorphone, and oxycodone need to be compared perhaps using the studies with OTFC as a template.