Clinical Note

Fentanyl Buccal Tablets for Breakthrough Pain in Highly Tolerant Cancer Patients: Preliminary Data on the Proportionality Between Breakthrough Pain Dose and Background Dose

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Abstract

Context. Cancer patients receiving high doses of opioids as background medication are challenging, and it would be useful clinically to know whether a rapid-onset opioid (ROO) for breakthrough cancer pain (BTcP) may be started at a dose proportional to the background opioid dose.

Objectives. The aim of this study was to assess the efficacy and safety of the fentanyl buccal tablet (FBT) in doses proportional to the opioid dose administered for background analgesia in a sample of patients with BTcP who were receiving high doses of opioids.

Methods. Twelve patients who were receiving opioids for background analgesia at doses equivalent to more than 500 mg of oral morphine and had adequately controlled pain were prospectively recruited. BTcP was treated with proportional doses of FBT: patients receiving 600 mg of oral morphine equivalents were administered 1000 μg of FBT, patients receiving 900 mg of oral morphine equivalents were administered 1500 μg of FBT, and so on. For each episode of BTcP, trained nurses collected pain intensity (on a 0−10 numerical rating scale) and emerging problems when called for increases in pain considered to be severe in intensity by patients (T0) and 15 minutes after FBT administration (T15).

Results. Patients were receiving mean doses of oral morphine equivalents of 1340 mg (±585; range 720−2400). Seventy-nine events were treated with FBT (6.6 ± 4.9 for each patient). The median pain intensity of BTcP events was 8 (range 7−10), and the mean dose of FBT administered was 2233 μg (±975; range 1200−4000). In most events, a decrease in pain intensity >33% and >50% was observed ($n = 14$ and $n = 48$, respectively) 15 minutes after the administration of

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FBT. Data on 11 episodes were missed. Only six events were unsuccessfully treated. In all the patients, the level of adverse effects after FBT administration was mild and indistinguishable from that associated with the background opioid analgesia.

Conclusion. FBT in doses proportional to the high doses of opioids used for background analgesia was efficacious and well tolerated when administered for BTcP. Controlled studies with a specific design and a large number of patients should confirm such preliminary results. J Pain Symptom Manage 2011;42:464–469.

Key Words
Cancer pain, breakthrough pain, opioids, fentanyl buccal tablets

Introduction

In the cancer population, breakthrough cancer pain (BTcP) is a transitory exacerbation of pain superimposed on an otherwise stable pain pattern in patients treated with opioids.[1] BTcP is normally severe in intensity and has a rapid onset. The presence of BTcP has been considered as a negative prognostic factor for adequate pain control and interferes with the quality of life of these patients.[2] The availability of supplemental doses of opioids in addition to the continuous analgesic medication is the main treatment suggested to manage these pain flares, either during dose titration or when basal pain is under control. The use of rapid-onset opioids (ROOs) has been shown to provide pain relief that occurs more quickly than that achieved with an orally administered drug.[3]

The opioid dose to be administered for BTcP is controversial. All the trials with ROOs, including oral transmucosal fentanyl citrate (OTFC) and the fentanyl buccal tablet (FBT), suggest a lack of relationship between the effective the fentanyl dose and a fixed-schedule opioid regimen, regardless of the opioid used.[3] However, in these studies, a substantial proportion of patients failed dose titration of OTFC or FBT,[4] and observations from data pooled from trials of OTFC showed a statistically significant relationship between the breakthrough dose and around-the-clock dose, despite enormous interindividual variability in patients' dose requirements for BTcP.[5] Moreover, an unclear distinction between the basal pain of mild-moderate intensity and BTcP of moderate-severe intensity makes the interpretation of data provided by these studies difficult. The use of proportional doses has been shown to be promptly effective without producing relevant adverse effects in an acute palliative care unit setting.[6–9] A predictable dose may favor an easy prescription, resulting in better patient compliance.

The findings of these studies suggest that patients receiving opioids for chronic cancer pain may not sustain more risk from the administration of a ROO dose that is proportional to the basal opioid regimen, especially if the background opioid dose is relatively high. This can be explained by the protective effect offered by opioid tolerance in patients chronically receiving relevant opioid doses for the management of cancer pain.

It would be useful clinically to know whether a ROO may be started at a dose proportional to the background opioid dose. If the ROO is initiated at too low a dose, in an attempt to titrate the doses individually, this could result in unnecessary suffering, lowered clinical compliance, and refusal to continue the treatment. Patients receiving high doses of opioids as background medication are challenging and have never been the subject of clinical studies. The aim of this study was to prospectively assess the efficacy and safety of FBT in doses proportional to opioid doses for background analgesia given chronically for the treatment of BTcP in cancer patients receiving high doses of opioids.

Patients and Methods

Patients receiving opioids at doses equivalent to more than 500 mg of oral morphine as background analgesia and having pain under control for most daily hours (pain intensity $\leq 4/10$ on a numerical scale of 0–10) were prospectively recruited for this study for a period of eight months. Other medications, including