PEER REVIEWED

Managing breakthrough cancer pain

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Cancer pain is common and can manifest both as a continuous symptom and as distinct limited exacerbations. Breakthrough pain originates from a wide variety of causes and situations, with great individual variation in presentation and severity. Engaging the GP as part of the patient's care team is important to maintain an individualised and interdisciplinary approach to successful management.

Key points

- **Breakthrough cancer pain is a significant distinct pain state that needs to be addressed together with continuous cancer pain.**
- **Most people rate breakthrough pain as severe or moderately severe.**
- **Poorly controlled breakthrough pain is associated with increased morbidity and diminished quality of life.**
- **Immediate-release opioid rescue dosing and continuous opioid dose titration remain the cornerstones of pharmacological treatment of breakthrough cancer pain.**

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In clinical practice, the term 'breakthrough pain' is used to describe a heterogeneous mix of distinct, episodic pain exacerbations that patients with cancer may experience throughout their illness. The pain is usually sudden, acute and intense, being categorised as 'spontaneous' for unexpected pain occurrences, or 'incidental' when precipitated by a trigger or an intervention such as a therapeutic procedure.[1]

Prevalence and character of breakthrough pain

It has been estimated that more than half of all patients with cancer experience significant breakthrough pain. Although the prevalence varies from the time of cancer diagnosis, during remission and maintenance, and with advancing disease, over 80% of hospice inpatients have been observed to experience breakthrough pain.[2]

Even though most people experience a specific pain as either an incidental or a spontaneous event, both can occur at the same time. Almost all patients rate their breakthrough pain as severe or moderately severe, and on average three breakthrough episodes occur per day, with a peak in intensity at around 10 minutes, lasting up to 60 minutes if no pain-modifying medications are taken. Most patients have stated that the pain significantly affects their daily lives, resulting in poor sleep, inability to work, shop or prepare meals, compromised ability to care for their families, more psychological distress and feeling more socially isolated.[3]

What to enquire about

Clinical presentations vary within and between individuals and by episode, cause and over time, and may represent more than one issue. Encouraging patients to effectively communicate the description of their pain is an important consideration and is also helpful in characterising each pain episode and guiding ongoing assessment, investigation and management. This may involve understanding the:

- location of the pain, which is often (but not always) the same as the background pain
- severity of the pain
- temporal relationships of the pain as episodes per day, timing of onset and duration
- precipitating factors, with or without any predictability
- possible pathophysiology of the pain – nociceptive, neuropathic or a mixed pain

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1. Key recommendations for managing breakthrough cancer pain[6]

- An established algorithm should be used for patient assessment.
- Management should be individualised and involve several interventions tailored to each individual patient.
- Scheduled analgesia and use of supplemental analgesia should be optimised.
- Successful management should include adequate reassessment of the patient.

- likely aetiology of the pain, whether it is from cancer, cancer treatments or unrelated to the cancer.[4]

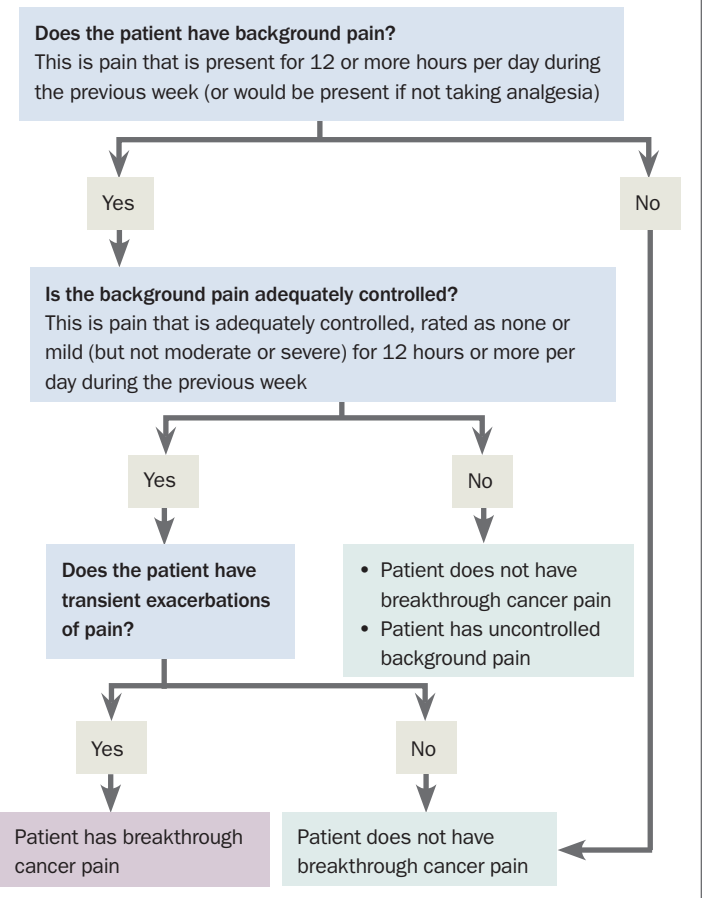
Algorithms can also be useful to clarify the type and nature of the pain (see the flowchart).[5] The first step aims to establish whether the patient has background pain and whether it is adequately controlled. The next step is to determine whether the patient has breakthrough exacerbations of this same pain. If so, does the dose of the long-acting opioid analgesia need to be increased to reduce the frequency and possibly the intensity of breakthrough pain? Is the patient taking the background around-the-clock opioid medication as prescribed? Is there an adjuvant medication that can treat an aspect of the pain that is not being optimally targeted by the patient's current medication? If there is no adjuvant medication, it is necessary to reassess and understand the alternative aetiology of the pain(s) and whether the precipitants are cancer-related. This leads to use of more standard pain questions, which include:

- What is the onset, frequency, site and radiation of the pain?
- What is the character, intensity and duration of the pain?
- Are there exacerbating or relieving factors?
- What is the response to analgesics or other interventions?
- Are there any other associated symptoms?
- Does the pain interfere with activities of daily life?[6]

Management plans

Better assessment and understanding of the nature of the breakthrough pain and the use of oncology, pain and palliative care specialist review has greatly assisted in the development of more effective, but flexible individualised treatment plans. Although the management plans may not be able to reduce the frequency of the pain, particularly with pain precipitated by incidental anticipated activity, the aim of treatment is to reduce the intensity, severity and effect of each episode of pain and to lessen the impact on the patient's quality of life. An interdisciplinary approach, for example an immediate call for advice from a palliative care team or palliative medicine clinician, with a possible review at a cancer tumour stream meeting, can help GPs better treat and manage escalating or poorly controlled pain. Key recommendations for managing breakthrough cancer pain are shown in Box 1.[6]

Diagnosing patients with breakthrough cancer pain[5]



Adapted from Davies, et al. Eur J Pain 2009; 13: 331-338.[5]

To effectively manage patients with breakthrough cancer pain, the following questions can be asked:

- Are there lifestyle changes that would help avoid the pain or triggers that might be minimised?
- Can any reversible causes be managed?
- Can the pain's pathological processes be modified?
- What pharmacological, nonpharmacological and interventional techniques could best manage this pain?

Medication management

Currently, there are no 'gold standard' medications for the pharmacological management of breakthrough cancer pain. Although less intense, mild to moderate breakthrough pain can be treated with immediate-release nonopioid paracetamol or NSAIDs, the use of immediate-release rescue opioids, with titration of the regular background opioid in response to the daily rescue opioid, has proven to be a useful approach. Moderate to severe breakthrough pain requires opioid rescue doses upfront and at higher doses as described below, without any trial of immediate-release nonopioids. A good balance between dose of analgesia and potential adverse events is required.

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2. Example: continuous opioid dose titration and adjustment of the breakthrough dose[7]

Example: A patient is taking morphine 10 mg orally four-hourly and requires three breakthrough doses of morphine 10 mg.

What dose should the regular dose of morphine be increased to?
Answer: 15 mg four-hourly.
This is calculated as follows:
10 mg taken every four hours = 60 mg in 24 hours
Three breakthrough doses of 10 mg = 30 mg
Total dose in 24 hours = 90 mg
For the next 24 hours, divide 90 mg by 6 to make four-hourly doses = 15 mg four-hourly
The breakthrough dose must also be increased to remain at 1/12 to 1/6 of the total daily dose = 7.5 to 15 mg as necessary

It is important to continue to reassess and use patient self-reporting, often through pain diaries. This can help us to better understand the relationship between a pain episode and the administration of medications, assist with monitoring of how the treatment is tolerated and reveal any changes in the nature of the pain.

Opioid treatment titration

Immediate-release rescue opioids should be prescribed in combination with the around-the-clock opioid regimen and taken as needed, either at the onset of the pain or in anticipation of an expected pain precipitant. According to the Palliative Care Therapeutic Guidelines, breakthrough doses between 1/12 and 1/6 of the total daily dose should be ordered.[7] Adjustments for elderly patients or patients with renal impairment, using the lower dose or slower titration, should be considered. Doses should not be given more frequently than every 30 minutes, to allow for absorption. The regular continuous dose of opioid should always be taken at its scheduled time. Red flags for the clinical review of an episode of breakthrough pain need to be considered if the pain remains uncontrolled after three or more breakthroughs over a 24-hour period. This review may, with advice, trigger a dose titration of the continuous opioid, adding the total breakthrough amount to the continuous 24-hour dose. This increase in the dose of background opioid depends on the clinical situation, previous dose escalations and whether the pain appears to be opioid sensitive. Subsequently, the breakthrough dose needs to be adjusted to remain either at 1/6 or 1/12 of the new total 24-hour dose (see Box 2).[7]

If the pain has been assessed as incident-related, precipitated by known specific movement or activities such as sitting to standing transfers, showering or toileting, then a breakthrough dose should be given 15 to 20 minutes before the activity. Breakthrough doses for incident-related pain may be used with or without continuous background opioids and higher than the 1/12 to 1/6 of a total continuous background dosing. Dose titration of the continuous opioid should still be considered.

Opioid medication

Morphine, oxycodone and hydromorphone are often prescribed in their specific continuous and immediate-release forms for managing breakthrough pain. The same type of opioid is used for managing both the continuous and breakthrough pain. Patients should be referred to a palliative care team or palliative medicine clinician if a GP is unfamiliar with opioid medications. Adverse effects of either type of preparation may necessitate the use of different opioids for the continuous pain and the breakthrough pain.

Although a typical breakthrough pain episode is of rapid onset and short duration, most opioids have a delayed onset of effect and long duration of action, which can result in unacceptable adverse effects of immediate-release opioids, especially if used frequently in response to severe episodes. To overcome this issue, transmucosal and intranasal fentanyl opioid formulations, such as buccal tablets, lozenges and drops, have been developed to specifically treat breakthrough cancer pain, but the use of fentanyl remains limited by lack of clinician familiarity, restricted availability and patient preference for oral preparations.[8] Titration of the dosing for breakthrough fentanyl buccally does not follow a predictable formula such as that used for oral immediate-release breakthrough opioids. The current recommendation is to start low and titrate upwards to effect.

Nonpharmacological adjuncts

Physiotherapy and occupational therapy approaches that limit pain triggers or provide adaptations to patients' surroundings should be used in conjunction with medication. Massage, application of heat or cold, acupuncture, distraction, relaxation techniques and cognitive behavioural strategies have been reported to be helpful in an effective pain management plan. Palliative care team staff or local support groups may assist in accessing help in this area. In some patients, despite thorough assessment and comprehensive treatment, breakthrough pain persists or management creates significant adverse effects. These patients may benefit from referral to palliative medicine specialists and chronic pain specialists for consideration of interventional techniques through anaesthesia, radiology or neurosurgery, trigger-point injection, vertebroplasty, neural blockade, neuroablation or intrathecal drug infusion as available. These techniques may be available locally or regionally through palliative care advice, or referral to more specialised hospital-based services may be required.[7]

Conclusion

Breakthrough cancer pain is common and can be associated with significant morbidity and impaired quality of life. It is a heterogeneous condition that requires individualised management. Although a variety of pain management strategies are in use today, the mainstay continues to be the use of rescue opioid medication. However, by taking an interdisciplinary approach to the patient's pain issues, GPs have more options to treat and manage escalating or poorly controlled breakthrough pain. PMT

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: None.

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