Breakthrough cancer pain guidelines 2013

European Oncology Nursing Society guidelines

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Introduction

Breakthrough cancer pain (BTCP) has been recognised as a burdensome, psychologically distressing, symptom that is inadequately treated and often unresolved in many cancer patients.[1,2] The scope of these guidelines, developed by EONS, is to describe and explain BTCP as an independent phenomenon with distinct clinical symptoms, and to provide guidance on the assessment, identification, and management of BTCP.

Overall goal

The overall goal of the guidelines is to help oncology nurses understand and recognise BTCP and to improve the management of BTCP for patients. These guidelines may also offer assistance to any health professional involved in treating cancer patients who are experiencing breakthrough pain.

Specific targets and aims

The targets and aims of these guidelines are to:

- Increase nurses' (and other healthcare professionals') knowledge of specific elements of BTCP
  - Causes/precipitants
  - Features and symptoms
  - Distinction from end-of-dose pain and from pain during initiation/titration of background opioid analgesics
  - Consequences
  - Treatment measures
- Enable nurses to assess and identify BTCP
- Encourage successful management of BTCP
- Facilitate nurses in the successful implementation of guidelines in their local setting.

Appendix 1 presents real-life case studies which illustrate the different types of BTCP patients experience, and shows how BTCP is recognised and assessed in clinical practice. These case studies also illustrate different management strategies for BTCP according to the nature of the breakthrough pain.

Appendix 2 provides information to aid with the implementation of these guidelines into practice.

The nurse's role

Oncology nurses have consistently identified pain relief and the provision of comfort to their patients as a major priority for their clinical practice. In the clinical and home-based settings, the nurse is one of the core professionals within a multidisciplinary team who is well positioned to identify problems and plan care accordingly.

Oncology nurses have a key role to play in identifying, assessing, and managing BTCP, which should be conducted for each patient on an individual basis.[3] Frequent contact with patients allows nurses to observe these individuals and actively communicate with them about their pain, potentially resulting in a more accurate diagnosis, better management of BTCP, and improved patient satisfaction with treatment.

Moreover, good collaboration between health professionals, patients, and carers represents an essential component for the provision of optimal care for cancer patients.[4] Cancer pain has many dimensions, including psychological, physical, and social aspects, which must be addressed in order to improve quality of life and functional ability.[4] Spirituality is another aspect of pain, which must be considered as a component of comprehensive pain assessment and treatment.[5] It is important that nurses assessing a patient's pain should consider how each of these components may influence the patient's perception and understanding of pain. To overcome one of the nurse's greatest challenges – providing effective pain management – a thorough assessment of the patient, and their experience of pain, is required.[6]

The nurse's role requires good communication and listening skills, in order to gain an accurate description of the patient's pain and to identify factors that aggravate and relieve the pain. The nurse is then able to advise on different management strategies and tailor treatments to the patient's specific needs. An important aspect of the role is the ability to differentiate between BTCP and poorly-controlled background pain.

What is BTCP?

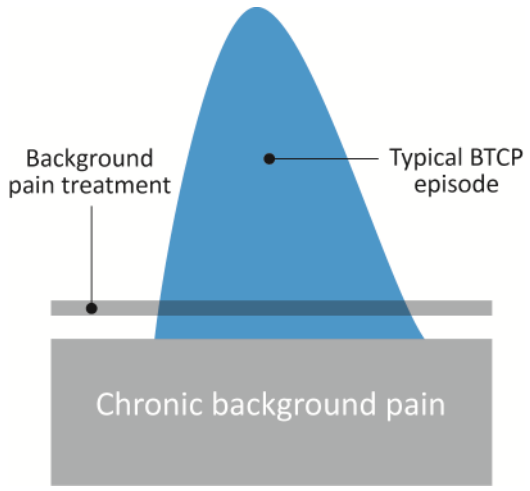
Although several definitions of BTCP exist, as yet, there is no universally accepted definition, or agreed-upon term, to describe BTCP.[7] For the purpose of these guidelines, we support one of the more cited definitions, suggested by an expert group in 2009:

"A transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain"

Task group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland[7]

BTCP is differentiated from background pain by being transient or episodic and breaking through the stable, controlled chronic background pain (see Figure 1). Consequently, the treatment of BTCP demands a different management strategy. The term 'breakthrough cancer pain' is used in practice, however, as the term 'breakthrough' has no literal translation or cognate in many other languages, other terms such as 'episodic' or 'transient' pain have been used to describe BTCP.[8,9]

Figure 1. A 'typical' episode of BTCP



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Characteristics of BTCP

BTCP is a heterogeneous pain symptom.[7] The two widely identified and accepted categories of BTCP are spontaneous pain and incident pain:[7]

- Spontaneous pain ('idiopathic pain') – these episodes are not related to an identifiable precipitant and so, are unpredictable in nature.
- Incident pain ('precipitated pain') – these episodes are related to an identifiable precipitant, and can be generally predictable in nature. Incident pain is usually sub-classified into one of three categories:
  - Volitional incident pain – brought on by a voluntary act (e.g., walking)
  - Non-volitional incident pain – brought on by an involuntary act (e.g., coughing)
  - Procedural pain – related to a therapeutic intervention (e.g., wound dressing).

BTCP is not to be mistaken for episodes of pain that occur in situations where the patient does not have controlled background pain. One example of such a situation is where episodes of pain occur during initiation or titration of opioid analgesics for the treatment of background pain – such episodes should be termed either a 'background pain flare', or simply an 'exacerbation of background pain'.[7] Another example is where episodes of pain occur before the administration of opioid analgesics (i.e., 'end-of-dose failure').[7] It should be noted, however, that end-of-dose failure is regarded as a subtype of breakthrough pain by some experts in the field.[7]

The clinical features of BTCP vary from individual to individual, episode to episode, and may vary within an individual over time.[10] Usually, BTCP is characterised by the following features:[10,11]

- Location (usually the same as background pain)
- Severity (usually more severe than the background pain – e.g., considered 'severe' or 'excruciating')
- Temporal characteristics (number of episodes per day, onset, duration)
- Precipitating factors (incident or spontaneous)
- Predictability (predictable, unpredictable)
- Pathophysiology (nociceptive, neuropathic, or mixed)
- Aetiology (cancer, cancer treatment, or unrelated to cancer)
- Palliative factors (e.g., relieved by the use of analgesia or by restricting movement).

Although the presentation of BTCP episodes can be temporally heterogeneous in nature, a typical episode of BTCP is characterised by a fast onset of severe to excruciating pain (reaching a maximum severity within 5 minutes), with a short duration (subsiding within 30–60 minutes), and which occurs 3–4 times per day.[10–15]

Prevalence of BTCP

Breakthrough pain is common in patients with cancer. The reported prevalence rates vary widely – up to 95% of patients[16] – depending on the definition of BTCP, the methods used to assess BTCP, and the populations studied.[9,17] Inconsistency in the assessment of BTCP by pain specialists from different countries,[18] potentially results in instances of unsatisfactory and inadequate treatment. The clinical picture may also vary greatly between patients and is often more prevalent in the later stages of cancer.[2,19,20] Variations in duration and intensity of BTCP episodes, as well as differences in the time between episodes, occur among patients.[2,19,11] Furthermore, the occurrence of BTCP has been shown to vary over the course of a day, e.g., in one study of 22 hospice patients experiencing some degree of pain, 86% of patients experienced BTCP episodes during the day and 45% experienced this pain during the night.[20]

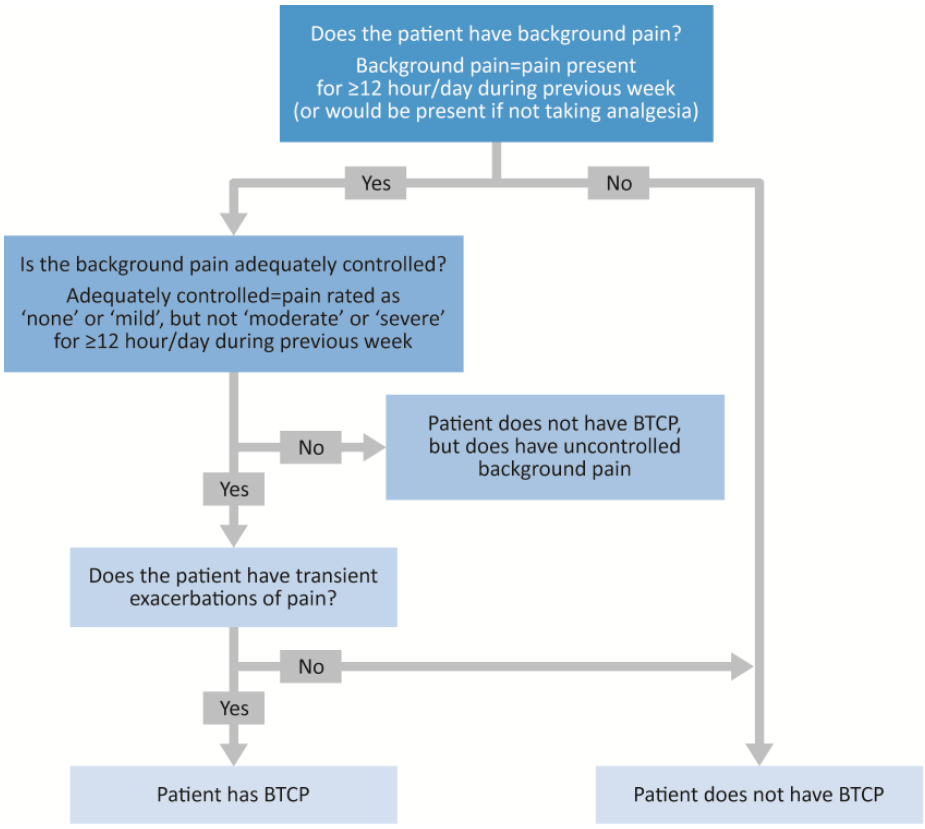
How is BTCP recognised and assessed?

A comprehensive assessment of the cancer patient's pain is an essential component of recognising and managing BTCP and, subsequently, improving daily life for the patient. In addition to considering BTCP, the assessment should identify the presence of background pain and determine if it is adequately controlled. Such assessments can increase the nurse's awareness of the patient's pain and prompt initiation of a treatment action plan.

BTCP versus uncontrolled background pain

According to the definition of BTCP applied in these guidelines, it is important to distinguish BTCP pain from uncontrolled background pain, since the two types of pain are distinct and require individual assessment and therapy.[7,9,21] In 1999, Portenoy *et al.* developed a diagnostic algorithm for BTCP, which required the presence of controlled background pain for BTCP to be identified.[2] Later, Davies *et al.* (2009) adapted this diagnostic algorithm to include stricter criteria for controlled background pain[7] – in fact, using this new algorithm can help to distinguish between BTCP and uncontrolled background pain (see Figure 2).

Figure 2. Algorithm for diagnosing patients with BTCP[18,22,23]



Algorithm as described by the Science Committee of the Association of Palliative Medicine (APM) of Great Britain and Ireland,[7] adapted from Portenoy, Payne & Jacobsen (1999)[2] and Portenoy, Payne, Coluzzi, *et al.* (1999)[24]
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Answering the following questions could be helpful in optimising the management of BTCP:

- Is further investigation (e.g., x-rays, magnetic resonance imaging [MRI], venous Doppler ultrasound tests), consultation (e.g., radiation oncology for palliative radiation, interventional radiology for kyphoplasty), or immediate intervention (e.g., paracentesis, intra-articular joint injection, treatment of herpes zoster) indicated? The intervention could even be as simple as treating constipation.[1]
- Does the dose of the patient's opioid regimen for background pain need to be increased to reduce the frequency, and possibly the intensity, of BTCP?
- Is the patient taking the analgesics for background pain as prescribed, including at the required intervals (to rule out end-of-dose failure)?
- Is there an adjuvant medication that can treat an aspect of the pain that is not being optimally targeted by the patient's current regimen (e.g., steroids, non-steroidal anti-inflammatory drugs [NSAIDs], bisphosphonates for pain related to bone metastases, or a tricyclic antidepressant to treat a neuropathic pain component)?

Assessment of BTCP

Once it has been decided that the patient's background pain is appropriately controlled and that the patient is experiencing BTCP, a more in-depth assessment of the breakthrough pain should be performed. Successful assessment involves determining the aetiology (e.g., cancer-related, non cancer-related) and pathophysiology (e.g., nociceptive, neuropathic, mixed) of the BTCP, as well as any pain- or patient-related factors that would indicate or contra-indicate specific interventions.[7,10]

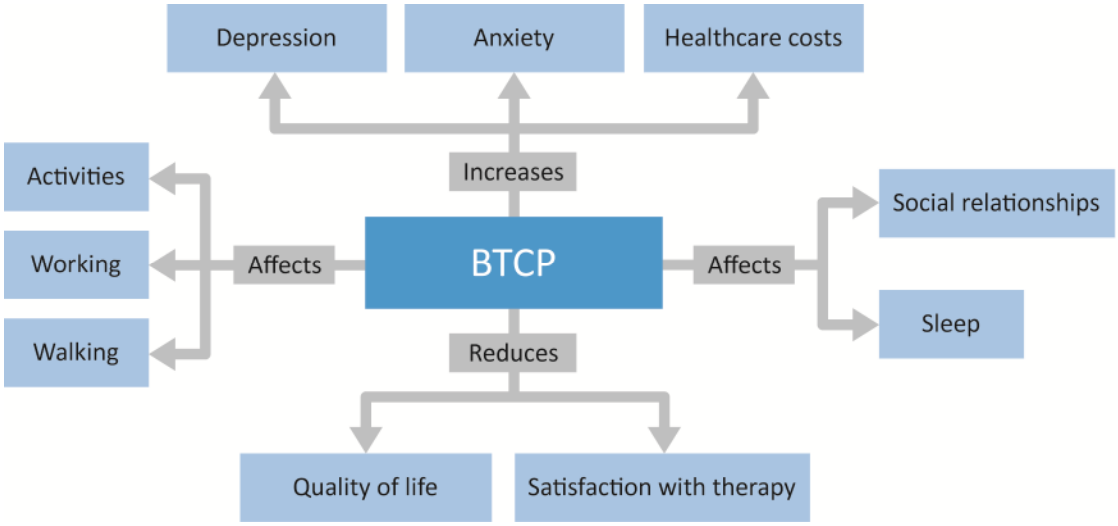
To date, no validated assessment tool for BTCP has been developed for clinical use.[7] Therefore, Davies *et al.* (2009) recommend using the following standard pain questions to examine the patient:[7]

- Onset of pain?
- Frequency of pain?
- Site of pain?
- Radiation of pain?
- Quality (character) of pain?
- Intensity (severity) of pain?
- Duration of pain?
- Exacerbating factors?
- Relieving factors?
- Response to analgesics?
- Response to other interventions?
- Associated symptoms?
- Interference with activities of daily living?

What are the implications of BTCP?

BTCP is a challenging aspect of cancer. Despite its self-limiting nature, the presence of BTCP can have a significant, negative, impact on the quality of life of patients and caregivers.[13,15] BTCP may result in a number of complications – physical (e.g., related to reduced activity and movement),[25] psychological (e.g., presence of anxiety and depression),[2] social (e.g., decreased levels of working and social interaction),[2,26] and economic (e.g., increased healthcare costs)[27,28] – as shown in Figure 3. Spirituality is another aspect of pain, which can an affect individual's perception of pain, the significance of the meaning of the pain, and the acceptance of a medical treatment plan.[5]

Figure 3. Implications of BTCP[15]



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Physical and social impact

BTCP may have a major impact on patients by interfering with their activities of daily living.[14,29] Additionally, BTCP may cause marked disability, resulting in decreased function and the loss of social activities.[2,13]

Davies *et al.* (2011) questioned more than 300 adult patients experiencing BTCP, from four Northern European countries, on their perceptions of this pain.[14] Of 320 patients, 261 stated that the BTCP prevented them from participating in different activities, with only 33 patients stating that BTCP did not interfere with their daily activities.[14] Interference with daily activities (as measured using an 11-point Numeric Rating Scale [NRS]) was highest for certain aspects, such as general activity, normal work, and relations with other people.[14] Other elements influenced by BTCP were mood, walking ability, sleep, and enjoyment of life.[14]

In a survey of 1,241 European nurses, 78% reported that BTCP had a significant impact on their patients' quality of life.[30] They believed that enjoyment of life was the most affected element, followed by work, mood, sleep, and movement.[30] General activity and relations with other people were the elements least affected by BTCP, in the opinion of the nurses.[30]

Another survey assessed 573 adult cancer patients from 11 European countries and Israel.[31] All patients had experienced pain of at least moderate intensity occurring several times a week for the last month; 281 patients were considered to have BTCP.[31] A good quality of life was reported by 48% of all patients, with 51% reporting that pain affected their ability to concentrate and think, and 69% reporting that pain impacted negatively on performing normal activities of daily life.[31] A good proportion of patients (43%) reported that the pain made them an increased burden to others, and in those patients still working, pain was reported to have an impact on work performance.[31]

Psychological impact

Patients with BTCP may experience psychological consequences, such as anxiety and depression.[2] Such consequences can result from a number of factors. For example, the BTCP can be a constant reminder of the presence of cancer, or the resulting lifestyle changes may create feelings of a 'loss of role'.[29] Furthermore, patients may feel that they have a lack of control over their own body due to unpredictable episodes of BTCP.[2,29] However, it is important to note that patients may find it difficult to differentiate the impact of BTCP from other effects of cancer (e.g., weakness, tiredness, etc.).[29]

Patients with BTCP are often less satisfied with their analgesic therapy than those who do not suffer from such pain.[11] BTCP can be a poor prognostic indicator for the overall effectiveness of opioid therapy, and can also result in the increased reliance on healthcare professionals and medication.[13,32,33] Therefore, it is important for healthcare professionals to ensure that patients gain a clear understanding of the underlying cause of their BTCP, as this can lead to improvements in the treatment of the pain. It is well known that patients who adopt active coping strategies may have better outcomes overall.[11] Specific interventions to encourage this are relatively inexpensive, and may empower patients to accept responsibility for their own pain management and be more involved in their treatment.[11]

Economic impact

BTCP can have significant economic implications, not only for the patient and their relatives, but also for the healthcare system and society. Patients with BTCP are more likely to incur higher direct costs (e.g., costs of medical visits, analgesic prescription charges) and indirect costs (e.g., transportation costs, over-the-counter medicine charges) than patients without BTCP.[27] Furthermore, patients with BTCP may require additional healthcare resources through an increase in emergency and medical visits and hospital admissions, with longer hospital stays, than patients who are not experiencing BTCP.[28]

A study of cancer patients in the USA found that the total costs for pain-related hospitalisations, emergency visits, and physician office visits for patients with BTCP was US$ 12,000 (€10,914 based on conversion rates as of 1st January 1998)[34] per patient per year, compared with US$ 2,400 (€2,183 based on conversion rates as of 1st January 1998)[34] for cancer patients without BTCP.[27]

How is BTCP managed?

The aim of BTCP management is to reduce the intensity, severity, and effect of each pain episode, and to lessen the impact of BTCP on patients' quality of life.[15,35] The management of BTCP should be individualised to each patient, with the optimal approaches depending on a variety of pain- and patient-related factors.[7,36]

Pain-related factors include:[7,36]

- Aetiology of the pain (cancer-related, treatment-related, concomitant illness)
- Pathophysiology of the pain (nociceptive, neuropathic, mixed)
- Clinical features of the pain.

Patient-related factors include:[7,36]

- Stage of the disease (early, advanced)
- Performance status of the patient (good, poor)
- Personal preferences of the patient.

BTCP management requires a comprehensive, multidisciplinary approach and a combination of management strategies, which may include pharmacological and non-pharmacological treatment modalities.[37] The following strategies should be considered:[15]

- Lifestyle changes
- Management of reversible causes
- Modification of pathological processes
- Non-pharmacological management
- Pharmacological management
- Interventional techniques.

Lifestyle changes

Many patients have to change their lifestyle in order to ameliorate the frequency and/or severity of their BTCP – the association between movement and the onset of pain is often a key driver in the need for such changes.[29] While some changes can be extreme (e.g., giving up work), others are less so (e.g., missing a social event). Specific interventions that encourage lifestyle changes are relatively inexpensive and can encourage patients to accept responsibility for, and be more involved in, their own pain management.[15] Examples include: pacing techniques to reduce activities that precipitate BTCP; the use of specific aides for activities of daily living (e.g., washing, dressing, and cooking); performing specific exercises; or utilising the assistance provided by family, to maximum benefit.[15]

Management of reversible causes

BTCP may be precipitated by numerous processes, some of which are amenable to either pharmacological or non-pharmacological therapy.[15,19] Management of BTCP should, therefore, take into account the importance of avoiding, or treating, the precipitating factors in patients with incident-type BTCP.[7] For example, bone metastases are well known to be the cause of movement-related volitional incident pain.[38] In some cases, this may be addressed by appliances (orthotics and/or physical therapy) that limit the mobility of the joint, or by creating strategies to minimise the amount of movement required, such as provision of simple adaptations to patients' surroundings and additional practical support.[7,13,15,38] Other examples relate to the BTCP. For example, where BTCP is being triggered by a cough, this could, potentially, be ameliorated by an antitussive, and where BTCP is being triggered by constipation, the use of a laxative could be considered.[15] Thus, the assessment of patients with BTCP should identify all potential precipitants in the hope that primary interventions against the precipitating process can be implemented and, thereby, reduce reliance on symptomatic therapy.[13]

Modification of the pathological processes

Consideration should be given to treating the underlying cause of the pain as interventions that modify pathological processes may result in an improvement in background pain and in BTCP.[7,15] In most cases (65–76%), the underlying cause of the pain is a direct effect of the cancer.[39] The options for treatment are potentially numerous, with new treatments emerging all the time, and so it is important to ensure a close cooperation with the relevant oncology team.[7] Possible interventions include systemic therapies (e.g., chemotherapy, biological therapies, and hormonal therapies), radiation therapy, and surgery, which can be used either singly or in combination.[13,15] Since infection can be a cause of pain, its treatment is another primary intervention that has the potential to improve BTCP.[13] Although infection is usually obvious, some clinical scenarios are challenging, and suggest the value of empirical therapy.[13] For example, worsening BTCP in a previously irradiated region or a region adjacent to a pressure ulcer may be related to a concomitant infection that is difficult to diagnose.[13]

Non-pharmacological management

Despite a lack of evidence from appropriately designed clinical trials, non-pharmacological approaches should be considered in the management of BTCP.[7,15] For example, an orthotic to brace a painful limb may be used to reduce or even prevent BTCP, or imagery may be used as part of cognitive therapy.[13] Rubbing/massage, application of heat or cold, distraction techniques, and relaxation techniques are also possibilities.[7,10,15,20,40,41] Related cognitive behavioural strategies might also be considered, as can other complementary strategies, such as therapeutic exercise and acupuncture.[13] Indeed, patients have reported a number of these techniques to be helpful.[15] Non-pharmacological strategies can be used prior to, or alongside, pharmacological therapy.[15]

Pharmacological management

Currently, there is no 'gold standard' for the pharmacological treatment of BTCP.[15] Treatment options include optimising the scheduled background analgesia (around-the-clock medication) and supplementing with additional analgesia when BTCP occurs (also known as rescue medication).[13,15]

Optimising around-the-clock medication

When deciding on the best course of action for the management of BTCP, modification of the background analgesic regimen (around-the-clock medication) should be considered.[7] The World Health Organization (WHO) guidelines provide a framework for the pharmacological management of cancer-related pain.[42] These guidelines recommend that analgesics should be selected according to the severity of the pain and not the severity of the disease, and that they should be administered sequentially (according to an 'analgesic ladder') until adequate pain relief is obtained.[42] Usually, fixed-schedule oral opioid therapy is the first-line treatment of moderate-to-severe pain in patients with cancer.[13] It is important to optimise this background analgesia by considering a number of strategies, such as an appropriate opioid titration (to obtain the best balance between analgesia and adverse effects), the addition of adjuvant analgesics/other adjuvant drugs and non-opioid analgesics, and also being prepared to switch opioids if adequate pain relief is still not obtained.[7,10,21,26] Adjusting the existing opioid regimen (e.g., increasing the dose) is appropriate for patients experiencing end-of-dose failure. However, if a dose increase leads to adverse effects, the original regimen should be reinstated.[13] Thereafter, a patient's pain may be reassessed and the management of BTCP changed accordingly, if necessary.

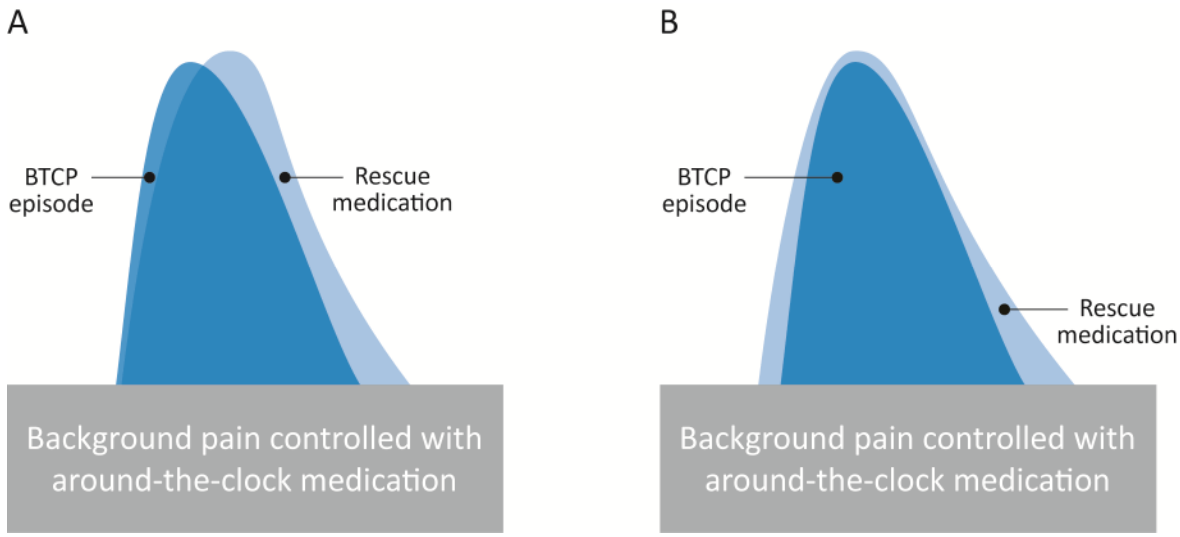
Optimising the background analgesic regimen can play an important role in the management of BTCP and should be considered at all stages of the patient's illness, as well as at each step of the WHO analgesic ladder.[15] Paracetamol and NSAIDs are widely used in the management of mild BTCP,[14] with evidence that intermittent use of NSAIDs may actually prevent or limit the occurrence of BTCP.[13,21]

It should be noted that neuropathic cancer pain is evident in approximately one third of cancer pain cases.[43] Adjuvant analgesics are well integrated into cancer pain-management strategies, and are often used as first-line options for the treatment of neuropathic cancer pain.[43,44] Some of these drugs, including certain antidepressants and anticonvulsants, are recommended by evidence-based guidelines for the treatment of various conditions.[43] Other drugs, such as lidocaine patches, are supported by randomised, controlled, clinical trial data and are included in guidelines for the treatment of specific conditions.[43] In general, an important recommendation for initiating pharmacological therapy for neuropathic cancer pain is to introduce one drug at a time, with gradual upward titration according to patient's response.[43]

Rescue medication

Rescue medication refers to the use of a symptomatic medication that is prescribed in combination with the background analgesic regimen, and is taken for BTCP as required rather than on a regular basis.[7,13] In the case of spontaneous pain or non-volitional incident pain, the treatment should be taken at the onset of the BTCP (see Figure 4A).[7] In the case of volitional incident pain or procedural pain, the treatment should be taken in anticipation of the relevant precipitant of the pain (see Figure 4B).[7]

Figure 4. (A) Rescue medication delivered reactively at the onset of spontaneous or non-volitional incident pain, and (B) rescue medication delivered pre-emptively before a procedural or volitional incident pain, such as walking, washing or wound dressing.[15]



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In addition to treating background pain, opioids are the rescue medication of choice in the management of BTCP episodes.[7] Traditionally, the most common form of rescue medication has been the oral normal-release ('immediate-release') formulations of morphine and other relevant opioid analgesics.[7] The European Association for Palliative Care recommends treating BTCP with a fixed-proportion of the daily background opioid dose,[45] However, these recommendations are based entirely on anecdotal experience,[21] resulting in the Association of Palliative Medicine (APM) recommendation to determine the dose of rescue medication by individual titration.[7] Also, in many cases, oral opioids are no longer considered the most appropriate treatment for BTCP.[21]

Although the oral route is often preferred for rescue medication, the pharmacokinetic and pharmacodynamic profiles of oral opioids (slow onset, long duration of action) do not tend to mirror the temporal characteristics of most BTCP episodes (rapid onset, short duration).[7,11,13,46] This can result in only partially effective treatment and/or troublesome adverse events.[15] Nevertheless, oral opioids do have a role in the management of certain types of BTCP, i.e., they may be useful in the management of episodes lasting longer than 60 minutes and may be considered in the pre-emptive management of volitional incident pain or procedural pain.[7] However, if oral opioids are used pre-emptively, they must be taken at least 30 minutes in anticipation of the relevant precipitant of the pain.[7]

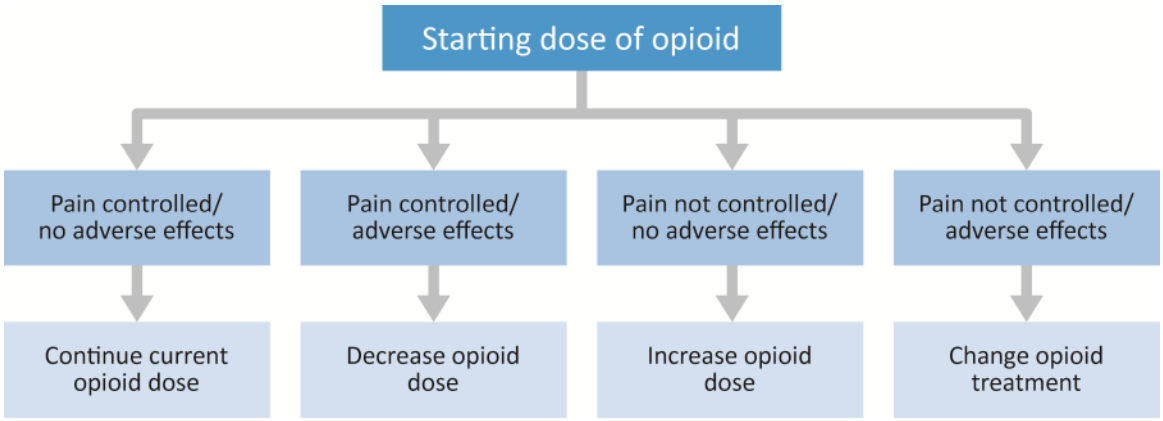
Rectal administration has been used for many years and a number of short-acting opioids are commercially available in rectal formulations.[13] For example, morphine and hydromorphone are available as a rectal suppository formulation; solutions of methadone, oxycodone, codeine and tramadol can also be administered through the rectum.[47]

The ***ideal treatment*** for most BTCP episodes is a rescue dose of a medication with the following features:[15,35,37]

- It is effective (a strong opioid)
- It has pharmacokinetic properties that closely match the temporal characteristics of a BTCP episode, i.e., has rapid onset of action with a relatively short duration of action
- It is patient-friendly – non-invasive, simple to administer
- It has minimal adverse effects
- It is cost-effective.

Since pain relief is usually required urgently, routes of administration designed to deliver drugs rapidly are often chosen.[21] The decision to use a specific opioid preparation should be based on a combination of the BTCP characteristics (onset, duration), the product characteristics (pharmacokinetics, pharmacodynamics), the patient's previous response to opioids (efficacy, tolerability) and, in particular, the patient's preference.[7] It is extremely unlikely that any one opioid preparation will be suitable for all patients with BTCP.[7] The dose of opioid 'rescue medication' should be determined by individual titration, as shown in Figure 5.[7,19,48]

Figure 5. Dose titration scheme for opioid 'rescue medication'[7]



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Rapid-onset opioids

Rapid-onset medications have been developed, specifically, for the treatment of BTCP. Fentanyl has been the opioid of choice for the development of BTCP medications that use the oral transmucosal and intranasal routes of administration. This is due to the small molecular size and high lipophilicity of fentanyl, which allow it to pass easily through highly vascularised compartments and be rapidly absorbed across mucosal membranes.[21,49] Consequently, fentanyl has a rapid onset and short duration of effect.[21]

Transmucosal administration of lipophilic substances has gained popularity in recent years due to the rapid, clinically observable, effect occurring 10–15 minutes after drug administration,[21] and the association with

high levels of acceptability and familiarity to patients.[15] The oral and nasal mucosae are easily accessible and convenient sites for drug delivery, since they allow for a non-invasive, less threatening approach to patients than other routes of administration, such as intravenous or intramuscular.[15] Furthermore, delivery of oral and nasal medication often requires minimal technical equipment, expertise, preparation, and supervision.[15] Oral transmucosal administration of these medications consists of absorption via the oral cavity and, as such, these drugs are not swallowed. Fentanyl delivered by the nasal route is absorbed locally within the nasal cavity.

As there are a number of rapid-onset fentanyl products for the treatment of BTCP on the market – each with diverse features, delivery profiles, and efficacy in the treatment of BTCP – it is important to highlight the differences between these products.

- ***Oral transmucosal fentanyl citrate (OTFC):*** OTFC was the first rapid-onset opioid for the treatment of BTCP. It is a fentanyl-impregnated lozenge applied to, and absorbed across, the buccal mucosa.[15,21] The lozenge normally dissolves within 10–15 minutes and analgesic effects occur within 20–30 minutes after initiating administration.[15] OTFC has been shown to produce a much faster onset, and a greater degree, of pain relief than placebo and oral morphine/other oral opioids in the treatment of BTCP.[24,48,50,51]

- ***Fentanyl buccal tablet (FBT):*** FBT is a sugar-free tablet formulation that provides rapid penetration of fentanyl through the buccal mucosa, by using a fast dissolving, effervescent formulation.[15,21,52] Fentanyl is more rapidly absorbed, and bioavailability is higher, with FBT than with OTFC.[21] The onset of analgesia for BTCP is seen as early as 10 minutes after administration of FBT.[53]

- ***Fentanyl sublingual tablet (SLF):*** Composed of micronised fentanyl citrate adhered to water soluble carrier particles in an ordered mixture, SLF is a rapidly disintegrating tablet formulation that must be placed under the tongue.[15,54] While held under the tongue, the released fentanyl is absorbed through the mucosa.[15] Two studies assessed the clinical efficacy of SLF in comparison with placebo and reported that SLF produces a significant reduction in the intensity of BTCP.[55,56]

- ***Fentanyl buccal soluble film (FBSF):*** FBSF uses dissolvable film technology, consisting of a small, bio-erodible polymer film for application to the buccal mucosa.[57] The film is designed to adhere to the oral mucosa in less than 5 seconds and bio-erodes within 15–30 minutes, delivering fentanyl to the mucous membrane.[57] The efficacy of FBSF in reducing the intensity of breakthrough pain in cancer patients has been shown in double-blind, placebo-controlled studies.[15,58]

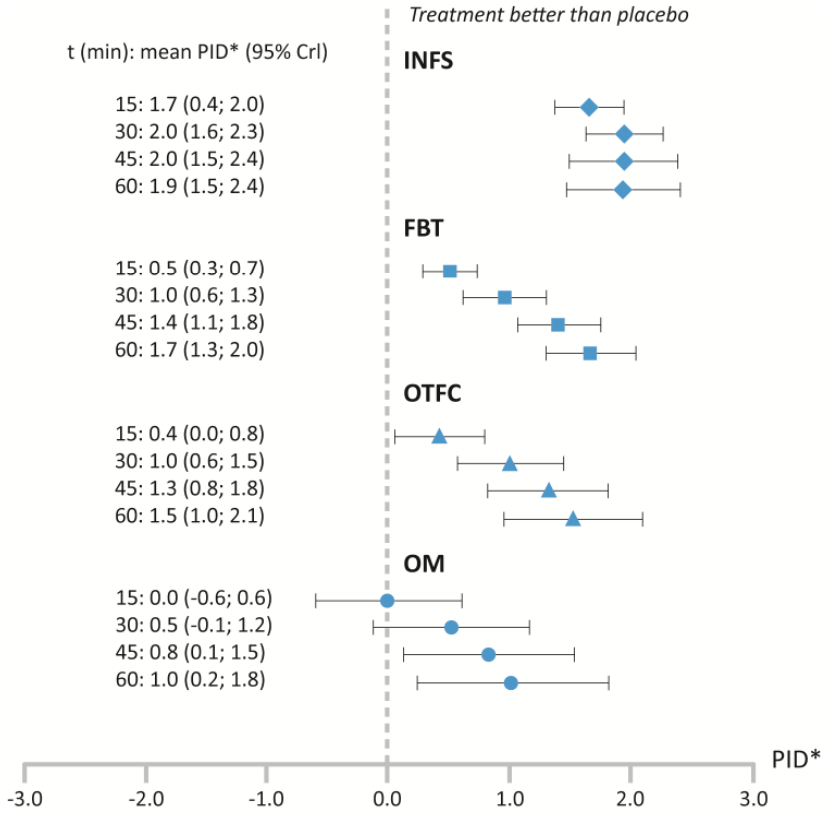
- ***Intranasal fentanyl spray (INFS):*** INFS was the first intranasally administered BTCP medication to be marketed. It is a nasal spray containing fentanyl citrate solution,[59] which is absorbed very rapidly across the nasal mucosa.[60] Efficacy in reducing pain intensity has been shown in a randomised, double-blind, placebo-controlled study in patients with BTCP.[61] Furthermore, INFS has shown a faster 'meaningful' pain relief (as judged by the patient) than OTFC (11 minutes for INFS vs 16 minutes for OTFC) in the only head-to-head clinical study among BTCP medications to date.[62]

- ***Fentanyl pectin nasal spray (FPNS):*** FPNS is an aqueous nasal spray of fentanyl using a pectin-based transmucosal delivery system.[15,63] An adhesive gel is formed upon contact with the nasal epithelium,[15] which may facilitate a slow and controlled delivery of fentanyl across the mucosa. A randomised, double-blind, placebo-controlled efficacy study showed a clinically meaningful pain reduction (≥2-point reduction in pain intensity score) from 10 minutes onward in the treatment of BTCP.[63,64]

It is difficult to make a direct comparison between the different studies of rapid-onset opioids. Therefore, Vissers *et al.* (2010) indirectly compared the efficacy of FBT, OTFC, INFS, and oral morphine in BTCP treatment using a 'mixed treatment comparison' (MTC) analytical method.[65] MTC is an extension of a traditional meta-analysis that allows indirect comparisons of relative efficacy in the absence of head-to-head trials.[65] According to the MTC inclusion criteria, eligible studies were randomised, controlled trials of FBT, OTFC, INFS, and oral morphine for the treatment of adult cancer patients with BTCP.[65] Outcomes were pain intensity difference (PID) between the start of a BTCP episode and different time points for up to 60 minutes thereafter, as measured using an 11-point NRS.[65]

All fentanyl treatments were more effective than placebo in treating BTCP from 15 minutes after the onset of pain and at each subsequent time point assessed.[65] However, oral morphine did not produce superior pain relief relative to placebo until 45 minutes after pain onset (see Figure 6).[65] INFS provided a greater reduction in pain intensity relative to oral morphine at all time points assessed, a greater reduction relative to OTFC at time points before 60 minutes, and a greater reduction to FBT at time points before 45 minutes.[65] The MTC has recently been updated to include FPNS, FBSF, and SLF – similar trends were reported.[66,67]

Figure 6. Pain intensity difference following opioid treatment for BTCP relative to placebo – results of a mixed treatment comparison[65]



*PID=pain intensity difference (a positive value reflects an improvement); INFS=intranasal fentanyl spray; FBT=fentanyl buccal tablet; OTFC=oral transmucosal fentanyl citrate; OM=oral morphine.
Reproduced from Vissers *et al*. Efficacy of intranasal fentanyl spray versus other opioids for breakthrough pain in cancer. Curr Med Res Opin 2010; 26 (5): 10371045, with kind permission from Informa Healthcare.

The choice of dose of a rapid-onset opioid remains controversial.[21] The need for titrating opioid doses, and individualising to patient's BTCP needs, has been commonly recommended for all studies of OTFC and FBT.[21] This is because there is little correlation between a patient's background medication requirements and their BTCP therapy needs.[7] The Summaries of Product Characteristics for the BTCP medications advise titrating from the smallest available dose.[59,68–72] If a single administration at this dose is not effective after a short time (e.g., after 15–30 minutes) a second administration of the same dose should be given (except in the case of FBSF, which should only be used once during a BTCP episode).[59,68–72] If adequate analgesia is still not obtained, the dose should, subsequently, be increased to the next available strength.[59,68–72] Dose escalation should continue in a stepwise manner until adequate analgesia is obtained, whilst maintaining acceptable levels of side effects.[59,68–72] There are limitations on how many doses should be administered in a 24-hour period, usually only up to four times a day – the focus being on BTCP and not background pain.[59,68,70–72]

The choice of optimal BTCP medication for a given patient should be made, based on a number of factors. In particular, the heterogeneity between BTCP profiles (between patients and for different episodes in the same patient) should be considered.[7,21] BTCP with different precipitants, times of onset, intensity, and duration may be treated by different medications.[21] Another factor for consideration is the availability of rapid-onset opioids,[14] which is very diverse among European countries. Furthermore, patient-related factors, such as their reasons for taking/not taking their medication and their opinions on important features and acceptable routes of administration for the medication, should be considered.[14, 73] It is imperative that nurses routinely assess adherence to medication and explore patient concerns where issues with compliance may be evident.

Interventional techniques

Despite comprehensive assessment and the careful use of systemic pharmacological therapy, some patients fail to gain adequate analgesia.[13] These patients may benefit from interventional anaesthetic techniques to manage certain clinical problems associated with BTCP.[7,13] A variety of different techniques are available, including trigger-point injection, neuraxial (epidural or intrathecal) drug infusion, neural blockade, neuromodulation (e.g., transcutaneous nerve stimulation), and neuroablation.[7,13,17,38,74–76] Interventional radiological techniques may also be useful to manage certain clinical problems associated with BTCP.[7] These procedures are usually not considered unless invasive strategies are ineffective, and the goals of care support such an intervention.[13] In such cases, a consultation with a specialist is required.[13]

Reassessment of the management of BTCP

In addition to making appropriate initial decisions regarding BTCP management strategies, successful management depends on adequate reassessment of the patient and their pain.[77]

The objectives of reassessment are to determine the efficacy and tolerability of the BTCP treatment and whether or not there has been any change in the nature of the BTCP.[7] Methods used to reassess BTCP include (among others) evaluations of pain intensity, pain relief, and improvements in daily function. Due to the lack of a clinically validated assessment tool for BTCP, standard pain scales (verbal and numeric rating scales) should be used to determine the response to treatment.[7] The choice of pain scale should be individualised to each patient, since patients vary in their ability to complete different types of pain scales.[7]

Inadequate reassessment of BTCP may lead to the continuation of ineffective and/or inappropriate treatment.[7]

Summary

Managing BTCP in accordance with the latest scientific understanding and medical consensus allows optimal treatment to be delivered to patients. Following the examples set out in these guidelines, which include the latest information on assessment, implications, management and reassessment, can help raise the standard of care in BTCP, and patients' pain outcomes in general.

Nurses have a key role to play in implementing these improvements into practice. As outlined in these guidelines, nurses have a unique interaction with the patient, and play a large part in identifying, assessing and managing BTCP in a timely fashion. The frequent contact between patients and their carers provides a platform for observation and active communication. Such an approach can result in a more accurate diagnosis and optimal management of BTCP, including improvements in patient satisfaction with treatment.

By helping to broaden the understanding and management of BTCP across the nursing and other healthcare professions, these educational EONS guidelines will, hopefully, improve assessment and overall management of breakthrough pain in cancer patients by utilising the latest available evidence.

Appendices

Appendix 1: How does a patient with BTCP present?

Four case studies of patients with BTCP, and one case study of a cancer patient without BTCP, are presented below. Each of them exemplifies the complexities surrounding the identification of BTCP and how it manifests across patients. A review of these cases reveals the heterogeneity and potential sources of difficulty in diagnosing BTCP and how this can impact on patients' daily life. For effective pain management, nurses should pay attention to all aspects of pain presentation when considering BTCP as a possible symptom.

The case studies assessment is outlined according to the Association of Palliative Medicine (APM) of Great Britain and Ireland's algorithm for diagnosing patients with BTCP,[7] and the standard pain questions described in the section of these EONS guidelines entitled, 'How is BTCP recognised and assessed?'. The case studies management is outlined as described in the section entitled, 'How is BTCP managed?'.

Case study 1: Non-volitional incident pain

BASIC PATIENT DATA

Patient demographics: 58-year-old man who lives alone. He is divorced and his son lives with his ex-wife.
Patient history: Nine months ago, the patient was diagnosed with a T3 N1 M0 squamous-cell carcinoma of the oesophagus and was treated with brachytherapy. A recent gastroscopy showed no visible tumour or stenosis.
Pain presentation: Over the past three weeks, the patient visited the accident and emergency departments of different hospitals, suffering from severe retrosternal pain. For this reason, he is now hospitalised.

ASSESSMENT OF PRESENCE OF BTCP

Q1: Does the patient have background pain?
- **A1:** Yes, he has a continuing, grumbling pain.

Q2: Is the background pain adequately controlled?
- **A2:** Yes, with a fentanyl patch of 100 µg per hour the pain is bearable (NRS 4).

Q3: Does the patient have transient exacerbations of pain?
- **A3:** Yes, the patient has severe exacerbations of pain.

IN-DEPTH ASSESSMENT OF BTCP

Q4: **Describe the onset of pain?**
- **A4:** The exacerbations of pain have a very rapid onset of only a few minutes.

Q5: What is the frequency of pain?
- **A5:** The frequency varies from 2–5 episodes a day.

Q6: Where is the site of pain?
- **A6:** The oesophagus.

Q7: What is the radiation of pain?
- **A7:** There is no radiation of the pain.

Q8: What is the quality or character of pain?

- **A8:** The patient describes his pain as cramping.

Q9: What is the intensity or severity of the pain?

- **A9:** The exacerbations of pain are very severe (NRS 10).

Q10: What is the duration of pain?

- **A10:** The exacerbations of pain last 30–60 minutes.

Q11: What are the exacerbating factors?

- **A11:** Hiccups, belching, and swallowing food.

Q12: What are the relieving factors?

- **A12:** The pain is a little less severe if the patient lies on his left side.

Q13: What is the response to analgesics?

- **A13:** The pain does not respond to orally, subcutaneously, or intravenously administered opioids.

Q14: What is the response to other interventions?

- **A14:** No other interventions have been offered at this time.

Q15: What are the associated symptoms?

- **A15:** The patient is depressed because the pain does not respond to any treatment.

Q16: What is the interference with activities of daily living?

- **A16:** The patient has trouble sleeping because of his pain and he is afraid to eat.

MANAGEMENT OF BTCP

Lifestyle changes: The patient can take liquid food to avoid exacerbations of pain.
Management of reversible causes: The exacerbations of pain are most likely caused by spasms of the oesophagus (cf. their cramping character, and non-response to opioid treatment). The treatment is administration of a spasmolytic medicine.
Modification of pathological processes: No interventions using modification of pathological processes have been used, since the gastroscopy showed no visible tumour or stenosis.
Non-pharmacological management: The patient can influence his pain by adopting a comfortable posture (lie on his left side).
Pharmacological management: The spasms of the oesophagus are being treated with spasmolytic medicine. In this case, scopolamine butyl has been administered.

Evaluation: The scopolamine butyl resulted in decreased pain (from NRS 10 to NRS 5). After four days, the scopolamine butyl treatment had to be stopped because of severe adverse effects. The patient has been successfully switched to baclofen, another spasmolytic medicine.

Case study 2: Procedural pain

BASIC PATIENT DATA

Patient demographics: 70-year-old woman.
Patient history: The patient has a locally advanced carcinoma of the breast with bone metastases. The tumour has broken through the skin and the patient has a cancer wound. The patient refuses chemotherapy and receives hormonal therapy.
Pain presentation: The patient experiences severe pain every time the wound is treated.

ASSESSMENT OF PRESENCE OF BTCP

Q1: Does the patient have background pain?
- **A1:** Yes, pain from the bone metastases and pain in the wound.

Q2: Is the background pain adequately controlled?
- **A2:** Yes, this pain is successfully treated with slow-release morphine and paracetamol in combination with an NSAID, and with morphine gel in the wound (NRS 3–4).

Q3: Does the patient have transient exacerbations of pain?
- **A3:** Yes, the patient has BTCP, which presents every time the wound is treated.

IN-DEPTH ASSESSMENT OF BTCP

Q4: **Describe the onset of pain?**
- **A4:** Immediately after the wound is touched, during wound treatment.

Q5: What is the frequency of pain?
- **A5:** Once a day (when the wound is treated).

Q6: Where is the site of pain?
- **A6:** In the wound, especially at the edge of the wound where the skin turns into tumour.

Q7: What is the radiation of pain?
- **A7:** There is no radiation of the pain.

Q8: What is the quality or character of pain?
- **A8:** The pain feels dull in the wound (background pain). At the edges, the pain is more cutting, stinging, and burning.

Q9: What is the intensity or severity of the pain?
- **A9:** The pain at the edges is very severe (NRS 10).

Q10: What is the duration of pain?
- **A10:** During wound treatment the pain is constant.

Q11: What are the exacerbating factors?
- **A11:** Every time someone touches the wound while treating.

Q12: What are the relieving factors?
- **A12:** A thick string of lidocaine and prilocaine gel on the edges relieves the pain after 15–30 minutes. Sometimes it takes up to an hour before the pain is gone.

Q13: What is the response to analgesics?
- **A13:** The response is almost complete, but it takes time.

Q14: What is the response to other interventions?
- **A14:** Radiotherapy has been discussed, which would be a good option in this case.

Q15: What are the associated symptoms?
- **A15:** There is also a lot of fluid in the wound and an awful smell, which in this case are symptoms of an anaerobe infection.

Q16: What is the interference with activities of daily living?
- **A16:** The patient is uncomfortable with the smell and is anxious that the dressing will leak. She rarely goes out and feels restricted due to the daily wound care. She is also scared every time the dressing is due to be changed because of the pain.

MANAGEMENT OF BTCP

Lifestyle changes: At this time, she stays at home to avoid embarrassing situations (bad odour, leaking wound). Hopefully, this will not be necessary with a good approach.
Management of reversible causes: The infection can be treated with antibiotics, locally or systemically.

Modification of pathological processes: Radiotherapy has been initiated in order to reduce the wound size and, subsequently, alleviate the pain. She is also treated with hormonal therapy.
Non-pharmacological management: Proper dressing materials to avoid pain during removal the dressing and to prevent odour and leaking; relaxation with music during the treatment of the wound.
Pharmacological management: The morphine gel and the lidocaine and prilocaine gel alleviate the pain, but take too long. A rapid-onset opioid just before treating the wound is added.

Evaluation: Wound treatment was bearable with a rapid-onset opioid (NRS 5). The change of dressing materials and treatment with antibiotics reduced the odour and leaking, which improved her quality of life.

Case study 3: Volitional incident pain

BASIC PATIENT DATA

Patient demographics: 60-year-old widowed man who lives alone. His son lives 100 miles away and his daughter lives 20 miles away – they are both married with young children.
Patient history: Diagnosed with cancer of the prostate three years ago. The patient developed metastatic bone disease in the spine and, more recently, in the femur.
Pain presentation: Throughout the day, his pain score is NRS 2, which he tolerates. The pain increases to NRS 8 upon weight bearing.

ASSESSMENT OF PRESENCE OF BTCP

Q1: Does the patient have background pain?
- **A1:** Yes.

Q2: Is the background pain adequately controlled?
- **A2:** Yes, he takes 60 mgs slow release oral morphine twice daily for the last month, with immediate release oral morphine 20 mgs as required.

Q3: Does the patient have transient exacerbations of pain?
- **A3:** Yes.

IN-DEPTH ASSESSMENT OF BTCP

Q4: Describe the onset of pain?
- **A4:** When walking, the pain increases even with the use of a walking stick to help reduce the pressure through the leg.

Q5: What is the frequency of pain?
- **A5:** The frequency varies, but usually up to 6 episodes a day.

Q6: Where is the site of pain?
- **A6:** Right femur.

Q7: What is the radiation of pain?
- **A7:** Along the top of the femur.

Q8: What is the quality or character of pain?
- **A8:** Deep ache.

Q9: What is the intensity or severity of pain?
- **A9:** The exacerbations of pain are severe (NRS 7–9).

Q10: What is the duration of pain?
- **A10:** The exacerbations of pain last 45–60 minutes.

Q11: What are the exacerbating factors?

- **A11:** Weight bearing when having to move short distances.

Q12: What are the relieving factors?

- **A12:** Sitting or lying down.

Q13: What is the response to analgesics?

- **A13:** He takes immediate release oral morphine, but finds he sleeps for a couple of hours afterwards, limiting his quality of life.

Q14: What is the response to other interventions?

- **A14:** Radiotherapy to the femur. Intravenous biphosphonates monthly. The pain decreased in the first few weeks following radiotherapy; the effect of the radiotherapy can last for the next four weeks.

Q15: What are the associated symptoms?

- **A15:** Loss of appetite; constipation; low mood.

Q16: What is the interference with activities of daily living?

- **A16:** The patient is not as interested in eating as he needs to walk to the kitchen to prepare food. Dressing takes time. Cleaning the house is difficult, which affects his pride and limits visits from friends. He liked to go out to the local pub to socialise, but this has not been possible.

MANAGEMENT OF BTCP

Lifestyle changes: The patient has acknowledged the rationale for the pain and identifies with the improvement, which in turn has empowered him to allow his friends to come and take him out. He takes fentanyl with him and administers as required.
Management of reversible causes: Referred to physiotherapy to assist with exercise and aids.
Modification of pathological processes: Radiotherapy and referral to the orthopaedic surgeon for consideration of prophylactic surgery to prevent a fracture.
Non-pharmacological management: Rests if pain increases; use of a walking stick.
Pharmacological management: Changed to sublingual fentanyl which he takes just prior to moving – this reduces the pain and although he may rest afterwards, he does not need to sleep.

Evaluation: The patient recognises that his quality of life is improving. He is not sleeping following medication. He is finding his appetite has improved as he has changed his routine and adapted the kitchen so he can sit down when preparing foods. He attends a palliative care exercise class where he meets other people living with cancer. The radiotherapy has reduced the pain. He is receiving the bisphosphonate, zoledronic acid, which has reduced the pain further. The patient accepts that consideration for surgery is a positive way forward to further improve his quality of life.

Case study 4: Spontaneous pain

BASIC PATIENT DATA

Patient demographics: 45-year-old woman.
Patient history: History of cervical carcinoma and treated with hysterectomy, adnexectomy, and radiotherapy. The patient was admitted to the hospital because of diarrhoea and vomiting, dehydration, hypovolaemic shock symptoms, abdominal pain, and incipient mechanic ileus.
Pain presentation: Pain in the abdomen. An accumulation of the pain at certain times of the day or after activities was not noticed.

ASSESSMENT OF PRESENCE OF BTCP

Q1: Does the patient have background pain?

- **A1:** Yes.

Q2: Is the background pain adequately controlled?

- **A2:** The patient had uncontrolled background pain at the time of admission, but after a titration phase, the background pain is well controlled with stable intravenous doses via a patient-controlled analgesia (PCA) pump filled with opioids and non-opioid agents, neuroleptic agents, and a corticosteroid.

Q3: Does the patient have transient exacerbations of pain?

- **A3:** Yes, the patient experiences spontaneous BTCP, probably due to the progressive abdominal cancer disease.

IN-DEPTH ASSESSMENT OF BTCP

Q4: Describe the onset of pain?

- **A4:** The BTCP is spontaneous.

Q5: What is the frequency of pain?

- **A5:** Approximately 1–2 times per day, independent of activities.

Q6: Where is the site of pain?

- **A6:** The pain is present locally in the patient's abdomen, mainly in the epigastrium.

Q7: What is the radiation of pain?

- **A7:** There is no radiation of the pain.

Q8: What is the quality or character of pain?

- **A8:** The pain feels dull.

Q9: What is the intensity or severity of pain?

- **A9:** The pain is described as an NRS 8.

Q10: What is the duration of the pain?

- **A10:** The severe pain often lasts for approximately 25–40 minutes.

Q11: What are the exacerbating factors?

- **A11:** There were no exacerbating factors identified.

Q12: What are the relieving factors?

- **A12:** A warm abdomen pack and/or a lavender-belt sleeve are convenient.

Q13: What is the response to analgesics?

- **A13:** The background pain is well-controlled. The BTCP is alleviated with the PCA pump. The PCA pump is also filled with neuroleptic agents, and a corticosteroid. This medication extends the pain therapy.

Q14: What is the response to other interventions?

- **A14:** The pain is less intense following the use of a warm abdomen pack and/or a lavender-sleeve belt.

Q15: What are the associated symptoms?

- **A15:** Sometimes nausea and vomiting, but this is not always present. Also, from time to time, the patient feels sadness.

Q16: What is the interference with activities of daily living?

- **A16:** When the patient has BTCP, she is not able to do anything. Without these painful symptoms, she is able to go on excursions with her family and to have meals with them.

MANAGEMENT OF BTCP

Lifestyle changes: Encouraging the patient's self-management by using a PCA pump. Starting the day slowly is more comfortable for the patient.
Management of reversible causes: No reversible cause has been identified.
Modification of pathological processes: There was no possibility to modify the pathological process, so we treated the symptoms with antiemetic agents and finally with a nasogastric tube to release stomach secretions.
Non-pharmacological management: A warm abdomen pack, or a lavender-sleeve belt, is used for approximately 30 minutes once a day. When we applied the lavender-sleeve belt in the morning, the BTCP episodes were sometimes easier for the patient to handle. Time was set aside to listen to the patient and to address psychological concerns.
Pharmacological management: Adaptation of the background pain analgesic regimen and a PCA pump with rescue medication for the BTCP.

Evaluation: The measures helped the patient to adjust to her individual issues and deal with her disease. She was also able to manage her BTCP episodes. It was very important for her that she was also able to do something with her family and friends.

Case study 5: Non-BTCP

BASIC PATIENT DATA

Patient demographics: 65-year-old woman.
Patient history: Diagnosed with inoperable metastatic pancreatic cancer. Treatment consisted of chemotherapy with gemcitabine.
Pain presentation: The patient experiences a constant and poorly localised upper abdominal ache that limits her independence. The patient has visited the pain clinic of the oncology hospital where she has been treated. Based on her history and physical examination, the patient experiences visceral pain. She rates her pain intensity in the range of 7–10 on the Visual Analogue Scale (VAS).

ASSESSMENT OF PRESENCE OF BTCP

Q1: Does the patient have background pain?
- **A1:** Yes.

Q2: Is the background pain adequately controlled?
- **A2:** No.

IN-DEPTH ASSESSMENT OF UNCONTROLLED BACKGROUND CANCER PAIN

Q4: Describe the onset of pain?
- **A4:** A constant and poorly localised upper abdominal ache.

Q5: What is the frequency of pain?
- **A5:** The background pain is uncontrolled and constant in frequency.

Q6: Where is the site of pain?
- **A6:** The abdomen.

Q7: What is the radiation of pain?
- **A7:** The mid-back area.

Q8: What is the quality or character of pain?

- **A8:** The patient experiences a dull, fairly constant, pain.

Q9: What is the intensity or severity of pain?

- **A9:** The pain intensity is in the range of VAS 7–10.

Q10: What is the duration of pain?

- **A10:** The pain is constant.

Q11: What are the exacerbating factors?

- **A11:** There are no exacerbating factors.

Q12: What are the relieving factors?

- **A12:** A comfortable posture, or the use of heat packs, can alleviate the pain.

Q13: What is the response to analgesics?

- **A13:** Oral, short-acting, morphine can control the pain.

Q14: What is the response to other interventions?

- **A14:** Palliative chemotherapy seems to improve the pain intensity.

Q15: What are the associated symptoms?

- **A15:** The patient reports fatigue, discomfort, loss of appetite, and has trouble sleeping.

Q16: What is the interference with activities of daily living?

- **A16:** The patient feels limited in her independence and her physical functions have decreased. She has more or less been unable to take care of herself.

MANAGEMENT OF UNCONTROLLED BACKGROUND CANCER PAIN

Lifestyle changes: The patient spends most of her time in her house and takes long periods of rest through the day. She has a close relationship with her adult daughters who have been playing an active role in her care. The home-care nurse has been involved to monitor the symptoms and her condition.
Management of reversible causes: No reversible cause has been identified.
Modification of pathological processes: Systemic treatment with chemotherapy (gemcitabine).
Non-pharmacological management: The patient can alleviate her pain by using heat packs.
Pharmacological management: For moderate to severe visceral pain, oral morphine is the agent of choice. Regular dosing of oral short-acting morphine, beginning with 10 mg every 4 hours is prescribed.

Evaluation: After two days, the pain had decreased and the patient was satisfied. The total dose of short-acting morphine is switched to slow-release morphine twice a day, with short acting morphine as needed. Also, her functional status and confidence level has improved.

Appendix 2: Implementation of the EONS guidelines

Guidelines Implementation Toolkit

Implementing guidelines successfully is a challenge. Therefore, EONS has created a Guidelines Implementation Toolkit, entitled, 'Implementing guidelines – practical change', which can be useful to help overcome some of the challenges of implementing guidelines into practice.[78] This toolkit is available at the EONS website, under Education, Guidelines, Section 5, or via the following internet address: **www.cancernurse.eu/education/guidelines.html**

In summary, guideline implementation usually falls into three broad phases: Preparation, implementation and evaluation.[78] Each of these phases consists of a series of steps, which should be undertaken for successful implementation.[78] These steps are as follows:[78]

Preparation

- Step 1: Set up a team
- Step 2: Evaluate current practices
- Step 3: Set objectives
- Step 4: Prepare the way for implementation
- Step 5: Plan the implementation process
- Step 6: Get feedback on the tools

Implementation

- Step 7: Implement the plan

Evaluation

- Step 8: Evaluate the progress

For further, more detailed, information regarding these steps in the implementation process, we encourage the readers of this guideline to access the aforementioned toolkit from the EONS website.[78] The toolkit also includes practical examples to help understand some of the more complex parts of guideline implementation.[78]

Putting Evidence into Practice

In collaboration with the Oncology Nursing Society, EONS has developed a set of European 'Putting Evidence into Practice' guidelines (funded by the European Commission, as part of the European Action Against Cancer).[79] These guidelines provide a concise summary of the evidence-based interventions for the management of pain, including BTCP, in patients with cancer, along with expert opinions to guide nurses in the interpretation of European standards.

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