© Mattioli 1885

Breakthrough cancer pain

Renato Vellucci

SODc Palliative Care and Pain Therapy, Careggi University Hospital, Florence, Italy

The breakthrough cancer pain (BTcP) is defined as a "transitory flare of moderate to severe pain, interrupting mild background pain being controlled by chronic opioid therapy" (1) or as a "transient exacerbation of pain that appears in a situation of persistent pain otherwise stable" (2).

The clinical features of BTcP vary from individual to individual and the underlying mechanisms are not always clear.

BTP's clinical characteristics have been found to be mostly paroxysmal in onset, reaching maximum severity within 5 minutes (2-4), recurring in 4–7 pain episodes per day (1, 4, 5).

The BTcP is normally a therapeutic challenge, and when treatment is inadequate or absent, can have a terrible impact on patients quality of life, reducing his or her ability to work and participate in other daily activities.

Patients suffering from BTP feel poor and decreased satisfaction with overall pain control (6). Besides breakthrough pain may result in a number of other physical, psychological, and social problems (7). Really BTcP in patients further to be a significant clinical problem produces an increase in the economic burden for patients and the healthcare system (8). Also very often the poor management of this type of pain may reduce the estimate to the doctor.

Despite the clinical relevance of BTcP in the context of cancer related pain, there is increasing evidence that its assessment and diagnosis is often poor and treatment suboptimal (9), and this type of pain remains largely lacunous in many aspects, including terminology, definition and epidemiology.

BTP has been a topic of considerable semantic debate and subject of one of the major consensus meeting of an expert working group of the European Association for Palliative Care (2). In fact the term Breakthrough pain remained confusing for many European languages, because no translation existed (2). The expert working group of the European Association for Palliative Care suggested the use of a simpler term such as "transient" or "episodic" pain, as the English term "breakthrough" has no literal translation in many other languages. Although at present the term "breakthrough pain" remains widely and invariably used within the medical literature and other terms are confounding and unused in literature.

Breakthrough pain is a spectrum of very different entities and it is still today classified as incident pain (IP) and spontaneous pain (SP) (10-12). Incident pain's episodes are related to an identifiable precipitant. IP is usually sub-classified into three categories, volitional IP is brought on by a voluntary act (e.g., movement, activity), non-volitional IP is brought on by an involuntary act (e.g., bladder spasm), and procedural pain is related to a therapeutic intervention (e.g., wound dressing) (13). In SP no identifiable precipitant can be related to the episodes.

Based on the clinical features of BTcP it is recommended that it be managed with transmucosal rapid onset (ROO) formulations of fentanyl (oral or nasal). It is essential to consider that morphine sulphate immediate release, frequently used, does not show an efficacy profile superior to placebo first 45 minutes after, with pharmacokinetic characteristics inadequate to most of the episodes of BTcP and suitable only for the

12 R. Vellucci

treatment of pain foreseeable accident procedures, and persistent than 60 minutes (14-16).

BTCP' diagnosis can be a real challenge, nevertheless different author have suggested diagnostic criteria for breakthrough pain, and interestingly it was been recently emended by a task group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland (14). The term BTcP point out episodes of pain that occur in a context of managed baseline cancer pain. Obviously during the initiation and/or titration of opioids, patients does not have controlled background pain. The diagnosis of BTcP usually make one's way through patient's selfreport about pain experience, usable when patients have a normal mental status. To promote this process is crucial the empowerment of patients and caregiver. The term empowerments mean to implement the ability of the individuals to diagnose BTP in every-day life. This process can be realized trough a deep information about the types of pain and BTP, suggesting the correct contents and the modality of sharing information. Often can be useful to offer a pain day-book as multidimensional instrument, during the interval between the visits, were note all the characteristics of patients experience. Multiple sources can provoke BTcP and physicians need specific questions to investigate recent episode of pain to obtain details regarding the possible aetiology, severity, source, pattern, and subtype of the pain episodes must be carefully documented (16).

References

- 1. Portenoy PK, Hagen N. Breakthrough pain: definition, prevalence and characteristics. Pain 1990; 41: 273-81.
- Mercadante S, Radbruch L, Caraceni A, et al; Steering Committee of the European Association for Palliative Care (EAPC) Research Network. Episodic (breakthrough) pain: consensus conference of an expert working group of the European Association for Palliative Care. Cancer 2002; 94 (3): 832-9.

 Portenoy RK, Payne D, Jacobsen P. Breakthrough pain: characteristics and impact in patients with cancer pain. Pain 1999; 81: 129-34.

- Zeppetella G, O'Doherty CA, Collins S. Prevalence and characteristics of breakthrough pain in cancer patients admitted to a hospice. J Pain Sympt Manage 2000; 20: 87-92.
- 5. Hwang SS, Chang VT, Kasimis B. Cancer breakthrough pain characteristics and responses to treatment at a VA medical center. Pain 2003; 101: 55-64
- Bruera E, Schoeller T, Wenk R, et al. A prospective multicenter assessment of the Edmonton staging system for cancer pain. J Pain Symptom Manage 1995; 10 (5): 348-55.
- Skinner C, Thompson E, Davies A. Clinical features. In: Davies A, ed. Cancer-related breakthrough pain. Oxford: Oxford University Press, 2006: 13e22.
- 8. Fortner BV, Okon TA, Portenoy RK. A survey of painrelated hospitalizations, emergency department visits, and physician office visits by cancer patients with and without breakthrough pain. Pain 2002; 3: 38-44.
- 9. Gatti A, Mediati RD, Reale C, *et al.* Breakthrough pain in patients referred to pain clinics: the Italian pain network retrospective study. Adv Ther 2012; 29 (5): 464-72.
- 10. Gureje O, Von Korff M, Simon GE, *et al.* Persistent pain and well-being: A World Health Organization Study in Primary Care. JAMA 1998; 280 (2): 147-51.
- Abbott FV, Fraser MI. Use and abuse of over-the-counter analgesic agents. J Psychiatry Neurosci 1998; 23 (1): 13-34.
- 12. Ashby MA, Fleming BG, Brooksbank M, *et al.* Description of a mechanistic approach to pain management in advanced cancer: Preliminary report. Pain 1992; 51 (2): 153-61.
- Mercadante S, Vellucci R, Cuomo A, et al. Long-term efficacy and tolerability of intranasal fentanyl in the treatment of breakthrough cancer pain. Support Care Cancer 2014 Oct 29. [Epub ahead of print] PubMed PMID: 25351457.
- 14. Davies AN, Dickman A, Reid C, et al. Science Committee of the Association for Palliative Medicine of Great Britain and Ireland. The management of cancer-related breakthrough pain: recommendations of a task group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland. Eur J Pain 2009; 13 (4): 331-8.
- 15. Zeppetella G, Davies A, Eijgelshoven I, *et al.* A network meta-analysis of the efficacy of opioid analgesics for the management of breakthrough cancer pain episodes. J Pain Symptom Manage 2014; 47 (4): 772-785.e5.
- 16. Abrahm JL. Assessing the patient in pain. In: Abrahm JL, ed. A Physician's Guide to Pain and Symptom Management in Cancer Patients, 2nd edition. Baltimore, MD: Johns Hopkins University Press; 2005: 107-47.