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Research in Palliative Care: My Past, My Present, My Future

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As in all the fields of medicine, research is fundamental for a relatively young discipline, like palliative care. Research also means the need of expanding own knowledge, sharing discoveries, and providing new ideas for clinical application to improve patients' care. But above all, it is trasmitting a passion, which is possibly the sense of life for each of researchers. In this article I will describe some of data published by my froup in the last couple of years and future ongoing projects.

Cancer Pain Management

Opioid response has been my principal interest for years. The heterogeneity and complexity of patients with cancer pain have represented a relevant challenge for researchers in an attempt of grouping patients according to the characteristics of disease, pain, and patients. The intention of a cancer pain classification has been to improve pain management and to predict the likelihood of successful pain treatment, possibly identifying cancer patients who are less likely to respond to standard treatment. Among the possible factors, we have initially identified more relevant incident pain and psychological distress in studies with different designs [1,2]. In a subsequent study we also observed opioids are clinically effective in "definite NP" conditions although a more aggressive treatment requiring careful utilization of opioids and symptomatic drugs is strictly necessary [3]. Since the first publication on pain prognosis [4], a multitude of factors has been examined, including younger age, neuropathic pain, incident pain, psychological distress, and more recently, baseline pain intensity [5]. However, it is hard to state initial pain intensity may predict the outcome, whether an appropriate opioid titration is provided [6]. High level of pain intensity does not seem clinically an intrinsic factor, as may possibly depend on several factors, for example previous under treatment [7]. We are trying in a new trial to overcome, in a prospective way and with a homogeneous treatment, these criticisms on the existing factors of poor opioid response.

New opioids with interesting characteristics have been developed in the recent years. However, for most of them information is lacking in cancer patients. In preliminary studies we found that tapentadol was effective in opioid-naïve patients, with a low escalation index [8], and that an approximate conversion ratio with morphine may be 1: 3.3 [9]. Further studies are on ongoing to assess the safety and efficacy and conversion ratio in the range of higher doses. Finally, tapentadol is actually tested in animal models of bone cancer pain.

Breakthrough Pain

In the last two decades, hundreds of papers addressed breakthrough pain in terms of definition and treatment. In most epidemiological and clinical studies no clear distinction between background and BTcP pain intensity, and analgesic treatment was often poor or unreported. For example, from the clinical point of view, the meaningful pain intensity for asking for a BTcP medication was 7.1, with 77% of patients having a pain intensity of 7-8 on a numerical scale 0-10 [10]. We recently analyzed the relationship between background pain intensity, the background analgesic treatment, and the intensity of BTcP. Surprisingly, while optimization of background analgesia may help the treatment in terms of number of episodes to treat and efficacy of BTcP medications, it was unable to limit the global prevalence of BTcP in advanced cancer patients, which was quite high, about 75% [11]. On the contrary in a subgroup of patients with abdominal breakthrough pain, it has been estimated that breakthrough pain developed in 45% of patients with well controlled background pain after individualized treatment. This percentage was higher (about 80%) in patients who presented with uncontrolled background pain, underlying the need to better characterize patients with BTcP, only after a careful optimization of basal pain [12].

Many transmucosal (nasal and buccal/sublingual) fentanyl products have been licensed for BTP in opioid-tolerant patients [13]. These preparations, named rapid onset opioids (ROOs), have some advantages such as ease of administration, rapid onset of action, and avoidance of first-pass metabolism, which consequently offer an interesting alternative to intravenous, subcutaneous, oral or rectal administration in the management of BTP.

Most studies of BTP medication have suggested titrating the dose of ROOs given for BTP [14]. However, these randomized trials have never specifically examined this issue, and the information gathered is just consequential to the study design aimed to demonstrate superiority of ROOs over placebo, oral morphine or usual oral opioids, or to evaluate the safety and efficacy of ascending doses of ROOs in dose-finding studies. Many controversies surround this issue. We have been suggesting that doses of ROOs proportional to basic opioid regimen may be as effective as safe. A simulation of a calculation of doses of opioids used for background analgesia and those achieved after individual titration showed mean values of proportional doses very close to those found after titration [15]. In a"real world" study reproducing a clinical scenario of patients receiving opioids for BTP, while the dose of oral opioids used as rescue medication was 18% of the around the clock opioid dose, for oral transmucosal fentanyl titrated to determine the effective dose, the rescue dose was about 35% of the around the clock dose [16], suggesting that titration process may provide even higher doses than those expected by using proportional doses to the basal regimen. For instance, the only existing controlled study, performed with fentanl buccal tablet, has evidenced that proportional doses are more effective than the dose titration approach, without higher risks of adverse effects [17], confirming a series of open-label studies performed by my group in which proportional doses were highly effective and well tolerated [18,19], even at home

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[20]. Large epidemiological studies of characterization of BTP by using a predefinite algorithm and comparison studies of ROOs, used in proportional doses, are ongoing.

Home Care

Research in patients followed at home is a neglected area. However, this setting should be favored by patients and is the place where patients spend most of their life. As a consequence there is a need to implement the information on this kind of cancer population. The HOCAI (Home Care-Italy) group has been recently established with the intent to implement the information on cancer patients followed at home, given the paucity of existing data in this setting. A series of questions have been recently examined in multicenter studies.

Large multicenter prospective and retrospective studies provided new insights on home care patients. In a retrospective study the most frequent reason to switch at home was for convenience and to parenteral morphine. Patients who were switched to parenteral morphine a shorter survival in comparison with other opioid sequences. Opioid switching seems to be feasible in most patients, at least in less complex circumstances, in the home environment by experienced home care teams. Further prospective studies should provide information about the selection to admit to hospital and which predictive factors prejudice transportation in patients severely ill. Of interest, methadone was never used for switching [21]. In a large study it has shown how advanced cancer patients die at home. Most deaths were expected. Physicians and nurses visited the patient on the day of death, but were occasionally present at the moment of death. More than three people were generally present at time of death. More than two/third of patients died peacefully, without apparent suffering, and 35.7% of them received palliative sedation (PS) before dying. In the last two hours the most frequent clinical issues were in a rank order death rattle, dyspnea, and agitation. Home palliative care was an effective setting for death at home, particularly when relatives are actively involved [22]. Data regarding prognostication of life expectancy in patients with advanced cancer follone at home are of paramount importance to patients, families, and clinicians. However, data regarding patients followed at home are lacking. In 374 patients admitted to home care programs low systolic blood pressure and high heart rate, male gender, poor KPS score, anorexia, and dyspnea were correlated with a shorter serviva [23].

Subsequently, the profile of patients sedated at home has been characterized. PS was performed in 13.6% of patients and more frequently in younger patients. The principal reasons to start PS were agitated delirium and dyspnea. The duration of PS was about two days and the mean doses of midazolam were 23-58 mg/day. The level of satisfaction for the home care team and relatives was similarly good. PS did not influence survival and were a feasible and an effective technique minimizing a distressful death. Emergencies are another relevant issue at home [24]. Emergency calls are relatively frequent in patients followed at home by a palliative care team. Phone consultation or intervention at home has been found useful in limiting inappropriate hospital admission. Orphan symptoms are rarely assessed, particularly at home. In large multicenter prospective survey 48/362 patients admitted to home care presented one or more orphan symptoms, in a rank order sweating, pruritus, hiccup, tenesmus, and myoclonus. Although the symptoms examined have a low prevalence in advanced cancer patients admitted to home care, the distress for patients may be high and deserve further analyses. Given the low prevalence of these symptoms, large studies are needed to find possible associated factors [25,26]. The future home care research agenda includes the prevalence of breakthrough dyspnea, the prevalence of oral symptoms and sleep disturbances at home, of which data are in existent.

References

1. Mercadante S, Maddaloni S, Roccella S, Salvaggio L (1992) Predictive factors in advanced cancer pain treated only by analgesics. Pain 50: 151-155.
2. Mercadante S, Fulfaro F, Casuccio A, Barresi L (1999) Investigation of an opioid response categorization in advanced cancer patients. J Pain Symptom Manage 18: 347-352.
3. Mercadante S, Gebbia V, David F, Aielli F, Verna L, et al. (2009) Tools for identifying cancer pain of predominantly neuropathic origin and opioid responsiveness in cancer patients. J Pain 10: 594-600.
4. Bruera E, MacMillan K, Hanson J, MacDonald RN (1989) The Edmonton staging system for cancer pain: preliminary report. Pain 37: 203-209.
5. Fainsinger RL, Fairchild A, Nekolaichuk C, Lawlor P, Lowe S, et al. (2009) Is pain intensity a predictor of the complexity of cancer pain management? J Clin Oncol 27: 585-590.
6. Mercadante S, Gebbia V, David F, Aielli F, Verna L, et al. (2011) Does pain intensity predict a poor opioid response in cancer patients? Eur J Cancer 47: 713-717.
7. Mercadante S (2012) Cancer pain undertreatment and prognostic factors. Pain 153: 1770-1771.
8. Mercadante S, Porzio G, Ferrera P, Aielli F, Adile C, et al. (2012) Tapentadol in cancer pain management: a prospective open-label study. Curr Med Res Opin 28: 1775-1779.
9. Mercadante S, Porzio G, Aielli F, Adile C, Verna L, et al. (2013) Opioid switching from and to tapentadol extended release in cancer patients: conversion ratio with other opioids. Curr Med Res Opin 29: 661-666.
10. Mercadante S, Adile C, Torta R, Varetto A, Fulfaro F, et al. (2013) Meaningful cut-off pain intensity for breakthrough pain changes in advanced cancer patients. Curr Med Res Opin 29: 93-97.
11. Mercadante S, Valle A, Porzio G, Aielli F, Adile C, et al. (2013) Relationship between background cancer pain, breakthrough pain, and analgesic treatment: a preliminary study for a better interpretation of epidemiological and clinical studies. Curr Med Res Opin 29: 667-671.
12. Mercadante S, Adile C, Giarratano A, Casuccio A (2013) Breakthrough Pain in Patients with Abdominal Cancer Pain. Clin J Pain .
13. Mercadante S (2012) Pharmacotherapy for breakthrough cancer pain. Drugs 72: 181-190.
14. Davies AN, Dickman A, Reid C, Stevens AM, Zeppetella G, et al. (2009) 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 13: 331-338.
15. Mercadante S (2011) The use of rapid onset opioids for breakthrough cancer pain: the challenge of its dosing. Crit Rev Oncol Hematol 80: 460-465.
16. Mercadante S (2009) Breakthrough pain: on the road again. Eur J Pain 13: 329-330.
17. Mercadante S, Gatti A, Porzio G, Lo Presti C, Aielli F, et al. (2012) Dosing fentanyl buccal tablet for breakthrough cancer pain: dose titration versus proportional doses. Curr Med Res Opin 28: 963-968.
18. Mercadante S, Ferrera P, Adile C, Casuccio A (2011) Fentanyl buccal tablets for breakthrough pain in highly tolerant cancer patients: preliminary data on the proportionality between breakthrough pain dose and background dose. J Pain Symptom Manage 42: 464-469.
19. Mercadante S, Prestia G, Casuccio A (2013) The use of sublingual fentanyl for breakthrough pain by using doses proportional to opioid basal regimen. Curr Med Res Opin 29: 1527-1532.
20. Mercadante S, Porzio G, Aielli F, Averna L, Ficorella C, et al. (2013) The use of fentanyl buccal tablets for breakthrough pain by using doses proportional to opioid basal regimen in a home care setting. Support Care Cancer 21: 2335-2339.
21. Mercadante S, Valle A, Porzio G, Fusco F, Aielli F, et al. (2013) Opioid switching in patients with advanced cancer followed at home. A retrospective analysis. J Pain Symptom Manage 45: 298-304.

22. Mercadante S, Valle A, Porzio G, Costanzo BV, Fusco F, et al. (2011) How do cancer patients receiving palliative care at home die? A descriptive study. J Pain Symptom Manage 42: 702-709.

23. Mercadante S, Valle A, Porzio G, Aielli F, Adile C, et al. (2013) Prognostic factors of survival in patients with advanced cancer admitted to home care. J Pain Symptom Manage 45: 56-62.

24. Mercadante S, Porzio G, Valle A, Aielli F, Casuccio A (2013) Palliative sedation in patients with advanced cancer followed at home: a prospective study. J Pain Symptom Manage.

25. Mercadante S, Porzio G, Valle A, Aielli F, Costanzo V, et al. (2012) Emergencies in patients with advanced cancer followed at home. J Pain Symptom Manage 44: 295-300.

26. Mercadante S, Porzio G, Valle A, Fusco F, Aielli F, et al. (2013) Orphan symptoms in advanced cancer patients followed at home. Support Care Cancer.