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Cancer patients and their caregivers in the face of opioid analgesic treatment — opportunities and threats to the treatment process

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ABSTRACT

Failure to alleviate cancer pain may deteriorate mental functioning, increase depression symptoms, result in the clinical diagnosis of demoralization syndrome nonadherence of treatment, functioning discipline, which together, may precipitate desire for euthanasia. Increased incidence of pain in patients with advanced or terminal disease has been reported to range from 39% to 66.4% depending on the stage of the cancer being experienced. Further, the progressive aging of societies and increased life expectancy in cancer patients has changed the dynamics of modern treatment processes. Despite their efficacy, the use of opioids as an analgesic treatment during terminal disease has been affected by the quality, availability, and negative reputation of these scheduled drugs. This review aims to describe the specific factors and limitations of opioid pain management from the perspective of patients and their caregivers. Further, we aim to identify and discuss the key factors which determine the success or failure of opioid use for the treatment of pain with links to internationally recognized recommendations and current research.

Key words: analgesics, pain management, opioid, advanced cancer, palliative care

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Introduction

In 2007, a comprehensive review of pain prevalence research concluded that, despite clear recommendations from the World Health Organization (WHO), pain in cancer is still a problem for a large group of patients [1]. The International Association for the Study of Pain (IASP) declared the year between October 2008 and October 2009 as the year for the Global Fight Against Cancer Pain [2]. During this period, the IASP introduced many initiatives for both the medical community and the general public to raise awareness of cancer pain and to provide useful information in its management. Pain relief is considered a human right. In 2013, the

United Nations stated that the lack of effective treatment to assist those dealing with pain is a violation of the prohibition against torture and inhuman or degrading treatment [3]. Since the WHO announced the principles of the analgesic ladder in 1986, recommendations for the treatment of cancer pain have been increasingly published, both by recognized international and national organizations [4].

Global opioid use increased from 28 mg in 2005 to 42 mg morphine equivalents per capita in 2012 [5]. Additionally, opioid drug availability increased in 67 countries between 2006 and 2010 (ACM index increase) [5]. The understanding of the mechanisms of cancer pain, methods of pain assessment and treatment, and the

number of publications on this topic have all increased significantly. Despite these successes, pain is still the most common and one of the most severe symptoms accompanying disease and cancer treatment. According to a 2016 review [6] (4117 studies from 2005–2014), the prevalence of pain in patients with advanced or terminal disease was 66.4% (vs. 64% in 2007) [7], 55% (vs. 59% in 2007) during cancer treatment, and 39.3% (vs. 33% in 2007) in post-treatment patients.

From the perspective of patients and caregivers

Over the years, the ability to assess the effectiveness of pain relief strategies has been hampered by differences in the methods used to estimate pain prevalence [8] as well as differences in the index of adequacy of opioid consumption [9] (different lists of opioid drugs included in comparisons between countries [10]). These differences are often misleading or fail to explain the discrepancy between medical advances, increased availability of treatment, and the lack of expected improvement in the pain management caused by both the disease and its treatment.

The ability to globally assess the quality and availability of opioid analgesic cancer treatments is further undermined by the co-occurrence of extreme anti-opioid psychology in recent years — opioidophobia [11]. The problems of quality and availability have been highlighted in Poland [12] and the United States, respectively [13, 14]. While there is limited access to opioids in most countries, the misuse of controlled drugs is a major public health problem in some countries.

By 2030, it is estimated that 21.4 million new cases of cancer are expected worldwide [15]. Thus, for both clinical practice and research, the identification and understanding the conditions that determine effective pain therapy and investigating the other variables that model the treatment processes of specific patients are still urgently required.

The role of patients in pain management failure was recognized and identified as a significant factor in the 1994 Agency for Healthcare Research and Quality (AHCPR) recommendations [16]. In those recommendations, the AHCPR identified patient-specific barriers to the treatment of pain such as a resistance to communicate the severity of the pain being experienced due to fear of the side effects of the treatment, disbelief in its efficacy, fear of undermining the anti-cancer treatment, or a misunderstanding of the link between pain and disease progression due to incorrect information [17]. In recent decades, the contribution of both the patient and family attitudes to pain-treatment-failure has changed with social and cultural developments and needs to be

continuously monitored like other treatment success factors [18–20].

Quality of life as determined by health

The progressive aging of the human population in combination with the lengthening of survival periods in cancer patients are changing the dynamics of medical interventions. These have led to a shift from a “society at risk” in which disease was treated as a transitional state between lost and regained health to a “remission society” [21], in which prolonged and multistep treatment makes it possible to live with a chronically life-threatening disease at the expense of accepting the impact and regime of treatment. Chronic treatment requires the rebuilding of a lifestyle that may have been broken down by the diagnosis and is based on the values and relationships necessary to maintain it [22]. This new lifestyle requires perseverance to adapt to the limitations and recommendations of the primary healthcare persons and caregivers in the case of multimorbidity, coping skills in dealing with the health care system but also forces one to relate the proposed lines of treatment (including pain management) to all valued dimensions of life, not only somatic but also functional or psychosocial [23].

Additionally, it has been shown that patients may experience several deleterious health conditions due to a failure to manage pain and other debilitating somatic symptoms. These can include a deterioration in psychological functioning, exacerbating symptoms of depression [24], or clinical demoralization syndrome (in the ICD-10 International Classification of Diseases, category R45.3 Demoralization, and apathy) [25]. These by-products of ineffective pain management make it seem impossible for some patients to live with the rigors of treatment and can lead to the risk of desiring euthanasia [26]. Further, the feelings of hopelessness, helplessness, and a loss of purpose that are associated with demoralization symptoms can reduce compliance with longer-term treatment [27]. However, studies investigating this phenomenon have highlighted the importance of the patients’ maintenance of social relationships, a sense of being recognized in their subjective role as well as their relationship with the doctor as important factors which help with successfully combating demoralization.

Knowledge and attitudes can shape expectations

The results of Garzón’s 2018 study [28] support the hypothesis that demoralization is related to a poor-quality relationship with the treatment team. Additionally, Robinson et al. [29] highlighted the impact of patient-centered

communication on reducing feelings of hopelessness and increasing satisfaction with care. Their data points to the non-informational aspects of communication — such as feeling in control of one’s treatment, being involved in the decisions made about it, being seen as a person, and being able to personally contact the doctor when there are concerns or questions.

Patients’ attitudes and expectations about participating in long-term (months to years) cancer treatment process are shaped by stereotypes, publicly available information, and the knowledge they gain from physicians and other treatment team members during treatment.

A 2017 study by Jarosz et al. [30] indicated that the singular strategy of informing patients about the nature of opioid treatment without any other information or support is insufficient. Their data indicated that patients exhibited the least knowledge about opioids among the groups studied: doctors, nurses, students, and even lower than the general population.

In a study by Graczyk et al. (2017) [31], the negative effect of medical consultations on opioid aversion was assessed. In that study, the authors found that the triggering or reinforcing of a patient’s fear of opioid analgesic treatment occurred when patients interacted with physicians whose own fears about the use of opioids influenced their clinical practice. Undoubtedly, the process of informing patients about treatment options includes – in addition to information about the disease and its treatment — an insight into the attitude of the physician which may reinforce or weaken a patients’ defense mechanisms, attitudes, and expectations. Further, when an insufficient amount of time is taken by the physician to clearly explain both the disease and treatment regimens, the patient may go into a state of denial which makes their further cooperation in the treatment process difficult.

Early implementation of symptomatic treatment — an opportunity for compliance

Growing evidence suggests that the survival time for cancer patients is also dependent on the efficient control of disease symptoms [32]. Further, an increasing number of studies have shown that effective pain management contributes significantly to an improved quality of life [32]. Pain management therapy is already defined as an essential part of cancer treatment [32]. “Supportive care” [33] has become a part of the European Society for Medical Oncology’s (ESMO) 2018 proposed concept of “patient-centered care” [34] to include both supportive and palliative treatment. Moreover, studies have shown that the term “palliative” can have negative connotations for doctors, patients, and their caregivers and can cause significant delays in the referral of symptomatic

or interventional treatments, including those related to pain management [35]. The same document emphasizes the need for the provision of care from the moment of cancer diagnosis and its delivery in a way that tracks changes in patients’ needs and conducts a holistic assessment of the level of satisfaction of those needs — at the time of each consultation.

Also, in the 2016 recommendations, ASCO points to the need to integrate treatment and palliative care, which should involve, in addition to treating symptoms, including pain, the building of relationships with patients and their caregivers, educating both parties about the disease and its prognosis, setting treatment goals and supporting treatment decisions [36].

From the moment the diagnosis is communicated throughout the entire treatment process, there is room for building a therapeutic alliance between the physician/treatment team and the patient, leading to increased adherence to pain management recommendations, as well as concordance in making treatment choices and shared responsibility for making and carrying out decisions (self-management) [37, 38].

Patient and caregiver interactions shaping knowledge and attitudes

The National Institute for Health and Care Excellence (NICE) recommendations for the treatment of pain with opioid medications point first to the need for a conversation that includes elements of patient and caregiver education. Even before prescribing opioid medications, a physician-patient discussion about treatment concerns is recommended. These discussions should include a clarification of beliefs and concerns about potential addiction, tolerance, side effects, and disease progression that may be induced when using strong opioids. As a second step, an introduction of both verbal and written information regarding cancer treatment is recommended, including when and why they are used, their expected effectiveness, possible side effects, signs of toxicity, and other notable information [39]. An important element of education (both in countries with opioidophobia and those experiencing an opioid epidemic) is the consistency of information provided to patients at all stages of treatment: from family physicians [40, 41] to oncologists, to specialists in palliative medicine [42], pain management or pharmacists, whose role is not only to assess whether a prescription for opioid analgesics is correctly issued [43].

A poor response to pain management may be due to cognitive, psychological, social, cultural factors, or any combination of all four [this fact is addressed in Standard 4 of the European Federation for the Treatment of Pain in Cancer (EFIC) 2019 pain management standards] [44].

In each of these cases, low adherence or a complete lack of adherence disrupts the course of therapy and limits or nullifies, the treatment regimen's effectiveness [45].

The degree of compliance to therapeutic guidelines for opioid use is estimated in some analyses to be around 51–70%, however, in some studies, it is as high as 90% [46]. The high adherence is attributed to high levels of patient motivation and patient knowledge which is derived from the frequency and quality of the interactions with the interdisciplinary team during treatment during the onset of side-effects (such as constipation or nausea). Further, in that study, 8 of 198 patients exceeded the recommended doses by a small amount. This increase in dose was attributed to an enhanced tolerance to the medications the patients were taking. The lack of negative effects on patient cooperation in treatment, regardless of patient-specific belief barriers, is explained by adequate, early education and additional supportive treatment during cancer therapy.

Barriers to pain management due to knowledge and attitudes

A review of studies from 1986 to 2007 which tracked the relationship between barriers based on patients' cognitive rationale [knowledge, beliefs, attitudes as measured by Barriers Questionnaire (BQ)] [47] and the adequacy of the treatment regimen used for pain [Pain Management Index (PMI)] [48] showed that patients with a negative PMI, which defines a suboptimal use of analgesics, had a significantly higher BQ score than those who were treated adequately. Additionally, patients who were reluctant to tell their physician about their pain and were reluctant to take pain medication presented higher levels of cognitive barriers than those who did not exhibit hesitancy [49]. Deandrea et al. (2008) [50] retrospectively analyzed several studies from 1987 to 2007 which used PMI (26 papers) as a measure for the effectiveness of pain management treatments. Their data indicated that 43% of patients are treated with inadequate regimens (PMI defined as "an index that subtracts the patient's rating of pain from the rating of the strongest analgesic agent").

The inadequacy or ineffectiveness of adequate treatment can be influenced both intentionally or unintentionally by patients [51]. These patient-driven factors include whether patients report the pain they are experiencing, how adequately they describe the pain, whether they talk about their concerns, doubts about medication dosing, and finally, how they follow the recommendations in the long term (self-reported skipping of doses at lower pain sensations, increasing at higher ones).

A lack of current knowledge, false beliefs, and negative attitudes about opioid analgesic treatment are identified in many studies as common obstacles among patients, caregivers, and physicians. The most commonly shared beliefs in these groups are the fear of addiction, the development of tolerance, and the onset of unpleasant side effects during opioid use [52].

Specific concerns for patients are:

- concerns about distracting the physician's focus on the cancer treatment,
 - concerns about receiving the reputation as being a difficult or complaining patient,
 - the belief that pain is both an important informative indicator on the course of the disease as well as being necessary for its treatment,
 - fatalistic attitude to the possibility of pain relief.
- Beliefs shared by patients and caregivers affecting attitudes toward opioid analgesic treatment:
- opioids are used only in the last days of illness,
 - they cause cognitive impairment or limitation (or even euthanasia)
 - their use will be met with a negative reaction from the family when informed that they are taking narcotic drugs.

In addition, beliefs that are based on social stereotypes and religious beliefs, such as the value placed on experiencing suffering, are less well verbalized and difficult to disclose and research [53–58].

Opportunities for more appropriate use of opioid analgesic treatment due to knowledge and attitudes — communication and education

The positive evolution of the knowledge on the use of opioid analgesic treatment and its proper comprehension is possible if patients and caregivers are provided with useful, understandable, and current information. Educational programs and recommendations are dedicated to establishing and developing this educational change.

Interventions aimed at educating patients about pain management regimens in cancer have already been analyzed in systematic reviews [59], which highlighted the following key factors for patients: information about the nature and mechanisms of pain as well as advice on how to communicate and describe the pain. For clinicians, the key factors include: how to enhance pain assessment during consultations, how to deal with barriers to adherence, how to maintain regularity of pain assessment. These and other factors were described as elements of a multi-stage and staggered educational process. The pie chart in the middle indicates the process necessary for optimal

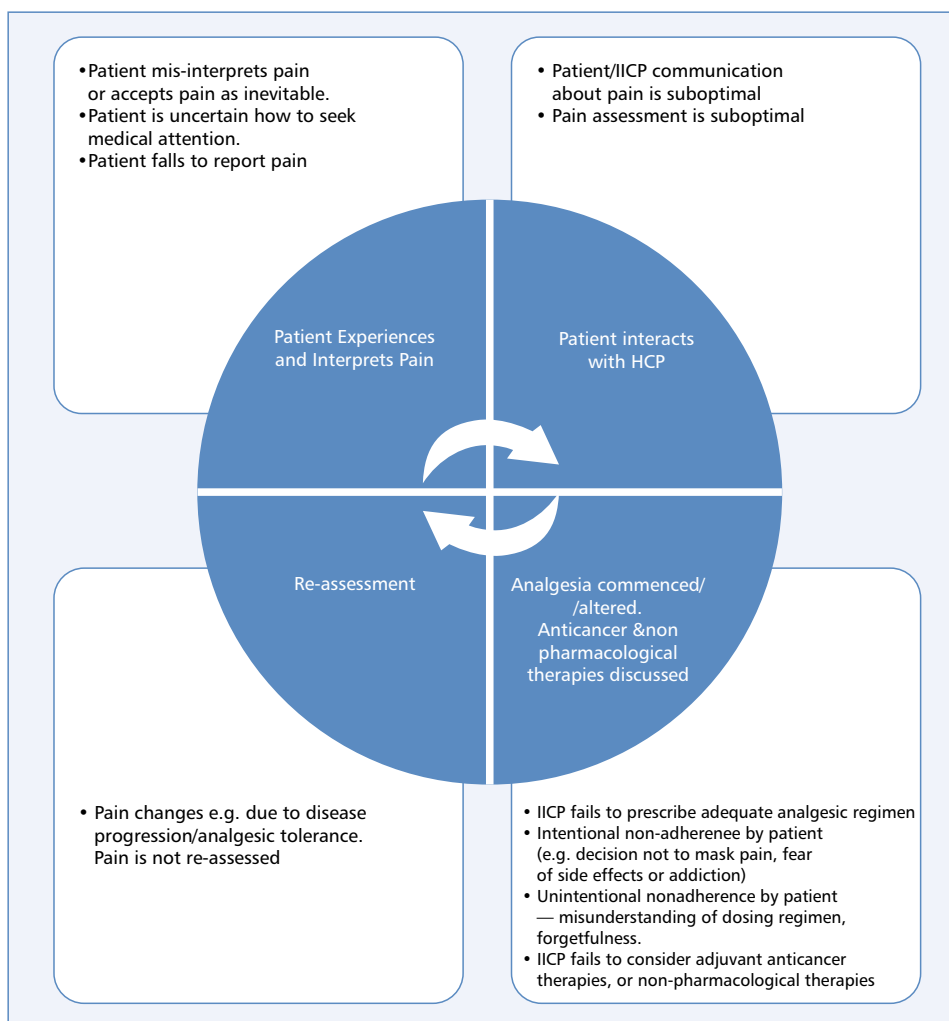


Figure 1. Essential steps for optimal cancer pain management [by: Adam R, Bond C, Murchie P. Educational interventions for cancer pain. A systematic review of systematic reviews with nested narrative review of randomized controlled trials. Patient Educ Couns. 2015]

treatment of cancer pain. External frames illustrate the barriers that can hinder the effective treatment of cancer pain. Educational interventions have usually dealt with one or more of these identified barriers (Fig. 1) [59].

Influencing the beliefs and attitudes of patients and their caregivers requires trust between the person providing the information and its source [60]. It is important to create and encourage an actively sustained patient-centered line of communication that relates to the patient’s values and goals. In their search for principles of optimal patient and caregiver education, Luckett et al. (2019) [61] based on a systematic review (353 publications) and meta-analysis of 15 studies, singled out interventions that focused on enhancing patients’ sense of self-efficacy as particularly effective. The authors emphasized that not only imparting knowledge but also learning new skills is crucial in pain management [61].

Summary

Ensuring that patients with pain have access [62] to analgesic treatment, including those which are based on opioid medication, is important. However, preparing patients to participate in the treatment process which will enable them to live with their disease to the highest possible quality whilst counteracting the adverse health effects of the substances themselves, are two sides of a single issue of the use of drugs based on controlled substances that still need to be urgently improved upon. Here, the studies reviewed have highlighted opioid dosage as an important factor for the inadequate pain management of patients with oncologic diseases. Both the inadequately low or high use of narcotic medications may be the result of an inconsistent and inadequately supported education process in the knowledge and skills of the medical community, patients, and their caregivers at various stages of treatment. Novel research

which elucidates knowledge and interrogates attitudes towards opioid analgesic regimens and regularly investigates the effects of disruptors (such as fashion, social trends, etc.) on this education can contribute to the early detection of adverse or harmful trends. However, this knowledge will not, by itself, change the attitudes and motivation of physicians and other members of treatment teams to use the available current knowledge, apply it in clinical practice, and communicate it to patients and caregivers. This task remains in physicians' hands, as does improving and applying knowledge of the processes that patients living with chronic life-shortening illnesses undergo.

The studies and recommendations described here indicate that with the development of ever more modern treatment lines, which determines the success or failure of physicians' work, the ability to keep a patient on several years or decades of treatment is enhanced. Further, the ability to build, correct, and maintain collaborative relationships with treated patients and their caregivers remains an essential aspect of palliative care.

The treatment of pain with controlled substances such as opioids requires a special approach and openness with patients. Since these drugs are often feared by patients and their relatives, and often even by medical personnel themselves; their use must be accompanied by a conviction that the prescription of opioids is appropriate. Additionally, patients should be informed from the beginning of treatment about the purpose, form, and limitations of pain therapy and, importantly, have a say in the therapeutic decisions made in this regard. As discussed in this review, the effectiveness of pain treatment is highly dependent on the level of patients' cooperation, which in turn, is derived from their knowledge, expectations, and beliefs about the therapy applied. Alternatively, inadequate knowledge among physicians and other medical personnel can lead to inadequate treatment regimens and doubts

about the right course of action among patients and their loved ones. Fortunately, the availability of numerous guidelines and recommendations in this area makes it possible to reach for reliable, transparent, and detailed sources of knowledge, which can not only further improve treatment outcomes but also reduce both opioidophobia and the opioid epidemic. Selected studies in Table 1.

Conflict of interest

The authors declared no potential conflict of interest with respect to the research, authorship and publication of this article.

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