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CONTENT

The drawing on the cover: *Pain* from William Lievens, Belgium (2010)

EDITORIAL

Pain undertreated

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All statistics show that all over the world, despite efforts in recent years, pain remains undertreated. Of all diseases, particularly cancer is associated with pain. The alarming pain signal that brings people to consult a doctor, is often not recognised in the early stages of the disease, but ironically, the pain is the symptom most feared after the diagnosis of cancer. Treating pain is by definition interdisciplinary and multidisciplinary team work, given the complexity of pain perception and expression.

One of the most discussed issues when it comes to people with cancer pain is opioid treatment: how does it work, when is it necessary, which opioid is chosen, what if the first choice proves to be suboptimal in practice, and many other issues. Underuse in practice of this class of analgesics occurs frequently due to the stigma related to treatment with opioids, which exists both in the population as among health professionals.

This issue of the journal PALIATIA presents different, sometimes controversial perspectives from various disciplines, i.e. pharmaceutical, medical oncologists, radiotherapists, specialists in palliative care, resident physicians. All these professionals and others individually contribute to the treatment of patients with cancer pain, demonstrating once again how important teamwork is in pain treatment and palliative care.

ORIGINAL PAPERS

Opioid switch: a therapeutic option for complex pain situation

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Abstract

A small group of patients with cancer pain will continue to suffer despite receiving appropriate treatment or will experience side effects from the opioids, which may limit the use of higher doses. Earlier experiences have shown that when a patient does not respond to a specific type of opioid, they may respond better to a different opioid. Opioid rotation or opioid switching is the name that has received this therapeutic approach.

Starting with a clinical case of rectal cancer and sacral pain treated with high doses of opioid, the article reviews the experiences of the authors with switching to methadone in a long stay palliative care unit and the published experiences of Mercadante with the opioid switching protocol of a acute palliative care Unit at a University Hospital. The patient presented was successfully changed to methadone with pain relief.

Several considerations of this procedure and practical consequences for the clinical practices are discussed. Specialists in frequent contact with advanced stage cancer patients should develop more experience in opioid switching.

Keywords: *opioid switching, palliative care, cancer pain, side effects*

Clinical case

A 54 year-old out-patient, who lives in a city far from our hospital, is referred to the Palliative Medicine Unit . The purpose of his visit to the clinic is to request a second opinion "because one cannot live with this pain", "I need you to do something because I cannot go on like this".

The patient was diagnosed nine years ago with a rectal adenocarcinoma and received treatment consisting of surgery, chemotherapy and radiotherapy. After a remission period of three years, presacral recurrence was found. This was treated with reirradiation, chemotherapy and biological therapy. Up to now the patient has responded well to the treatments applied remaining without distant metastasis.

He reports pain in the sacral region, irradiating to the posterior side of both limbs descending to the knee, with a maximum intensity of 8 (verbal numerical scale (VNS) 8-10/10, which worsens when sitting, walking or lying down the prone position ("he sleeps on his front"). In the interview, a significant component of reactive depression is evident. His general state is good but he has poor functionality. He came to the appointment with signs of anxiety from pain. Examination for opioid- induced side effects and neurotoxicity is negative. The patient

was not even constipated, despite taking laxatives from time to time. A recent PET-CT scan detected infiltration and metastatic bone destruction of the right sacral wing with soft-tissue mass enveloping the front and rear sides of the sacral promontory.

Current treatment: over the last year approximately, transdermic Phentanyl patches 225 microgram's/hour, replaced every 72 hours; Transmucous oral Phentanyl 800 microgram's, oral application when in pain; Ibuprofen 600mg, via oral every 8 hours; Pregabaline 75mg, tablets each 12 hours; Duloxetine: 60mg every 24 hours. He has undergone other treatments such as peripheral nervous blockers, botulinum toxin infiltration and multiple lumbar epidural blockers; spinal analgesia was offered but the patient declined.

The concept of opiod switching

Opioids are still the treatment of choice against cancer related pain and generally for advanced illnesses which include severe pain (1). Although most pain may be managed following the indications of the WHO pain ladder, a small percentage of patients will continue to suffer pain despite receiving appropriate treatment or will experience side effects from the opioids which may limit the use of higher doses. Earlier experiences have shown that when a patient does not respond to a specific type of opioid, they may respond better to a different opioid (2, 3). In these cases a change of opioid may lead to better pain management or to the disappearance of the undesirable effects of opioids.

The exact reason why an opioid switch is successful remains unclear (2). In some patients with poor response to pain, analgesic tolerance develops faster than the phenomenon of tolerance to side effects. In these cases, increasing the opioid dose might provoke greater toxicity. The best outcome would be to find an alternative opioid in which the situation would be reversed: where tolerance to the side effects develops faster than tolerance to the analgesic effect of the drug.

One important difficulty in opioid rotation is that there is no way of knowing whether the second opioid to be used will have a higher effectivity than the initial opioid. Another difficulty, which further complicates this therapeutic decision is that, it is impossible to know a priori the equivalent *equianalgesic* dose of the second opioid compared to the initial choice (4,5). Both these difficulties could be explained by the existence of individual factors that are still not well known: the diverse individual response to each opioid, different mechanism for each type of pain, pharmacogenetics and the varying degree of cross-tolerance between different opioids. Only the conclusions of prudent clinical experience in repeated situations will help. One good starting point to undertake initial opioid rotations may be a review of scientific experiences and communications, generally from palliative care teams.

The use of methadone at a palliative care unit for medium-stay patients in Salamanca

Our Group reviewed the experience of the use of Methadone at the Palliative Medicine Unit of the Hospital Los Montalvos, Salamanca, Spain for the treatment of cancer pain (6). In a descriptive retrospective study, a review was undertaken of the clinical histories of all terminal cancer patients treated with Methadone as an alternative opiod, over a period of 18 months. The cases detected were divided into 2 groups for independent analysis, depending on the main cause for the switch: insufficient neuropathic pain control and opioid induced neurotoxicity (OIN).

A total of 27 patients were studied, 9 belonging to the first group and the remaining 18 belonging to the second group. The equianalgesic dose is estimated according to findings reported by Ripamonti and colleagues (6) (See Table 1). After the switch, the adjustment and stabilisation of the Methadone dose required an average of 3-6 days. In the group of patients with neuropathic pain, the median daily Methadone dose at the moment of switching was

24mg (range 10-75). All patients reported significant pain relief from a median of 8/10 to 4/10 (VNS). In the group of OIN patients, the initial opioid was morphine in 12 patients and transdermic Phentanyl in 6 cases. The initial median dose expressed in the equivalent daily oral morphine dosage was 180 mg/day (range 60-974). The initial dose (Methadone median) was 20 mg (range 15-75). After the change, OIN symptoms were resolved in 14 out of the 18 patients. In all patients the median intensity of the pain decreased or remained the same as with the initial analgesic.

Table 1- Equianalgesic dose ratio between Morphine and Methadone according to Ripamonti and colleagues (7)

Morphine dose prior to switching opioid	*Rate of conversion: morphine: methadone*
30 – 90 mg/dl	4:1
90 – 300 mg/dl	6:1
> 300 mg/dl	8:1

Frequency, indications and results of opioid switch at a palliative care unit in Palermo

Recently, Professor Mercadante's team presented in a prospective study frequency, indications, results and predictive factors associated with opioid switching, using the same procedure applied for many years (8). The study monitored a group of consecutive patients, with cancer and who were receiving opioid treatment and who presented an unacceptable outcome of analgesia and side effects, despite attempts to establish standard symptomatic treatment for side effects. The initial rates for conversion between opioids were as follow (mg/day): oral morphine 100 = intravenous morphine 33 = Transdermic Phentanyl 1 = Intravenous Phentanyl 1 = oral methadone 20 = intravenous methadone 16 = Oral Oxycodone 70. A distress score was calculated using the total sum of the intensity of the symptoms. Opioid switching was considered successful when the intensity of pain and/or the distress score or the principal symptom necessitating the switch, decreased by at least 33% of the value registered prior to the changeover.

A total of 118 patients underwent opioid switching. The indications for opioid switching were poorly managed pain and side effects (51%), side effects (29%), unmanaged pain (15%) and convenience for the patient (4%). Of the total, 103 switches were successful, 96 switches were successful after the first change and a further switch was successful in 7 patients who had not responded to the initial switch. The median period to achieve dose stabilisation after the switch was 3 days. The simultaneous presence of poorly managed pain and side effects was related to failure of the switch. No statistical relationship was found between failure in opioid rotation and the initial dose, the type of opioid substituted, the pain mechanism and the use of adjuvant medication. Opioid switching was an effective method of improving the scope between analgesia and toxicity in over 80% of the cancer patients with poor response to the initial opioid. The simultaneous presence of pain and of side effects may be a contraindication in opioid switching.

Continuation of the clinical case

An opioid switch to Methadone was proposed. The dose of the initial opioid was calculated as the equivalent dose of oral morphine over 24 hours, of 600 mg (one 25 microgram/hour Phentanyl patch delivering 360mg morphine daily, applications of transmucous oral Phentanyl were 2400 micrograms of Phentanyl daily, equivalent to a tenth of the amount for morphine, meaning 240mg more oral morphine). Treatment was started with Methadone 10mg each 8 hours (the patient took more than 300mg morphine daily, ratio morphine:

methadone = 12: 1 following to Ripamonti et al (7) and was decreased by 30% as significant tolerance was deduced allowing for the many earlier months' treatment with Phentanyl). Intermittent pain allowed for the use of 2.5mg methadone for each episode.

Over the following days, the dose was adjusted to 15mg Methadone each 8 hours depending on the number of times extra medication was required for the pain. After 5 days the patient described his pain as moderate (VNS 4/10) and had improved his ability to sit and walk free from pain. He had also managed to rest most of the night lying in bed.

The patient returned to his city of residence after being advised of the possibility of once again considering spinal analgesia in case relief was not satisfactory. Monitoring by telephone over the last two months shows that the patient continues taking 20 mg of Methadone each 8 hours with pain of 3-4/10 and he continues to be acceptably active. He is currently undergoing further chemotherapy treatment.

Practical consequences

It is clear that success in opioid rotation in the two units described was high. Around 8 of every 10 patients showed drastic relief from the pain or side effects. The patient in the clinical case also improved significantly. Based on the experiences described here it seems evident that opioid switching in itself works as a therapeutic manoeuvre. That is to say, success does not depend on the type of opioid involved in the toxicity or poor pain management, or the type of opioid used as a replacement. It is the change in itself which is therapeutic. In many cases, the choice of the replacement opioid depends on the experience of the clinic where it is applied (methadone is often thought as a drug which is more suitable to treat neuropathic pain), on the availability of the opioid in each locality (in some countries Oxycodone or hydromorphone are still not available) or on the patient's clinical situation, which makes it preferable or advisable to use transdermic drugs or their administration by other routes.

Conclusions

We have seen that opioid switching is a very promising tool when administered properly. Specialists in frequent contact with advanced stage cancer patients should develop more experience in opioid switching. The use of methadone is an alternative which should not be discarded (9).

Opioid switching works but needs a certain amount of time to achieve good management with a stable dose of the new opioid, up to 3-4 days are required. In the early days, it may be better to use extra medication as a rescue tactic without increasing the originally prescribed opioid dose.

There is a small percentage of patients who will not experience complete relief after switching opioids. In these cases, the use of a second switchover in the opioid or an application of invasive techniques such as spinal analgesia, may be an alternative.

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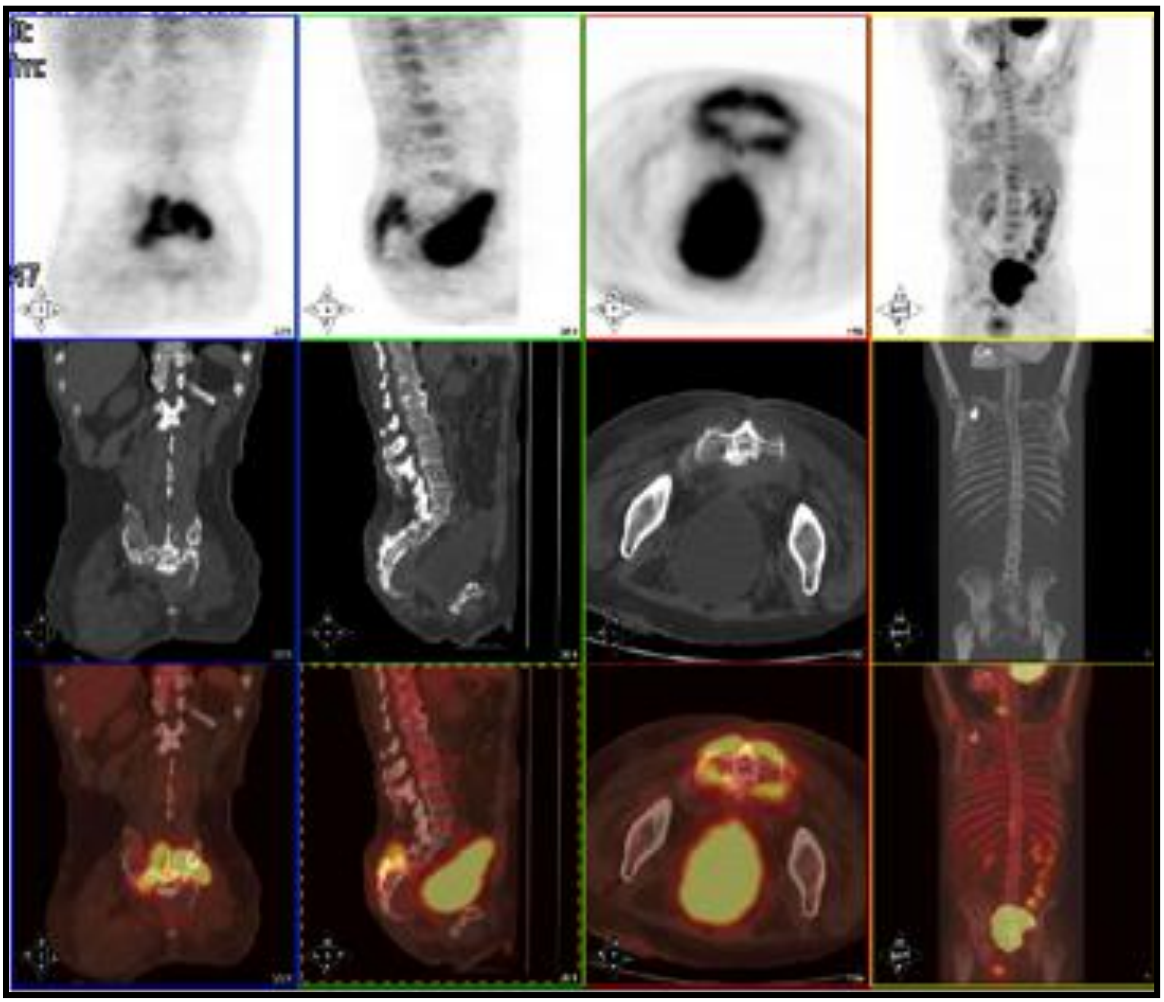
Figure 1- PET-CT image showing bone tumour affection and soft mass component enveloping the upper sacrum



CLINICAL LESSONS

Opioid pharmacology – short review

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Abstract

Opioids are a mainstream of treatment for acute pain and cancer-related pain. The literature offers also information about analgesic efficacy of opioids for some patients with chronic non-cancer pain.

For this reason it is very important for health care practitioners to be informed about pharmacokinetics and pharmacodynamics of natural, semi synthetic and synthetic opioids. Mechanisms of action, therapeutic indications and adverse effects are presented in this short review.

Key words: *opioids, pharmacokinetics, pharmacodynamics*

(Full text in Romanian)

Palliative radiotherapy of cancer pain

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Abstract

Radiation therapy is a local-regional treatment modality. Palliative radiation therapy (PRT) is an established tool in the management of symptoms caused by both locally advanced and metastatic cancer, including pain, bleeding or obstruction. The goal of PRT is to provide adequate symptomatic relief throughout a patient`s anticipated life span while limiting the risk of both acute and late treatment related complications.

Hypo fractionated radiotherapy delivers palliation that is time-efficient and minimally toxic. PRT is an important component in the multimodality approach to cancer pain management. While the mechanism of action remains unknown, RT has been shown to reduce cancer related pain, in addition to increasing the quality of life of patients who suffer from advanced cancer.

Although, most data on PRT are related to its use in the treatment of painful bone metastases, there are also data which support PRT for pain management in locally advanced gynecological malignancies, lung cancer, rectal cancer, or bladder cancer.

Key words: *pain, palliative radiation therapy, hypo fractionation, bone metastases, locally advanced cancer*

(Full text in Romanian)

Opiod treatment in chronic pain related to gastric cancer : a case report

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Abstract

Pain is a complex symptom with an important impact on quality of life of cancer patients. Recent advances in the medical field have led to improvements in palliative care to patients with cancer-induced pain.

We report the case of a 48 years old patient with a radical gastrectomy for gastric cancer and diagnosed with a local relapse involving the celiac plexus after 19 months from the surgery. The control of the pain was obtained, in terminal stage, with a daily dose of 2160 mg of morphine hydrochloride.

This case highlights the role of multidisciplinary approach of chronic cancer pain in a patient which required high doses of morphine.

Key words: *gastric cancer, cancer pain, morphine*

(Full text in Romanian)

MANAGEMENT

Management of pain in cancer patients

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Abstract

Evidence from clinical practice points out that pain related to cancer is still undertreated and consequently, pain management remains an actual subject. A didactic approach to pain management in cancer patients, in 3 steps, was offered by Portenoy. It shows how important is an acurate assessment of pain, as the first step towards a successful treatment. It also brings the existing conventions and resources in pain treatment and the need to tailor these to patient's individual situation to the attention of clinicians.

Pharmacologicat treatment represents the main resource for cancer pain, and it is based on the „WHO ladder". The ladder was designed as a model of how to use analgetics in an attempt to make opioid treatments more available worldwide. Hopefully the future will narrow the gap between what is possible in theory and what we see happening in clinical practice.

Key words: *cancer pain, pain management, analgetic approach*

(Full text in Romanian)

Neuropathic cancer pain: pathophysiology and management options

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Abstract

Neuropathic Pain (NP) in cancer disease is caused by a damage of the peripheral or central nervous system tissue, commonly due to tumour growth, compression, infiltration or destruction as well as to treatment-related toxicities or complications.

Increasing scientific evidence in the last decades did unfortunately not correlate with major improvements in available treatments and outcomes, being the management or at least the control of NP still a matter of disappointment for both patients and caregivers. Lack of standard procedures and poor response to available analgesic drugs are the major concerns in the management of this kind of pain.

Opioid analgesics, cornerstones in the management of nociceptive cancer pain, are, with some individual exceptions, often poorly effective in this setting. Steroids and anticonvulsants still represent the drugs of choice while antidepressants may just play a role as adjuvant drugs. Disease oriented treatments, such as radiation therapy, may be the treatment of choice in case of spinal compression.

Key words: *neuropathic cancer pain, management neuropathic pain*

Introduction

The management of Neuropathic Pain (NP) in medical practice has historically been an open challenge and a field of continuous frustration. In cancer medicine, the problem may become even more complex, due to the biological nature of the disease itself and the possible pathophysiological origins of pain. Neuropathic pain is caused by lesions (compression, infiltration or destruction) of either peripheral or central nervous system tissues. Although encouraging advances have been made in the last decades, the outcomes of treatment are usually unsatisfactory, being the pure symptom control the only realistic target. Furthermore in many cases, the duration of the therapeutic success is timely limited. The clinical importance of a proper initial assessment as well as the need of a continuous reassessment, have been underestimated, often resulting in inadequate and expensive therapeutic procedures.

In this short review, only NP associated to cancer disease (NCP) will be addressed and not all different possible origins of non-malignant NP. Along the available (but still limited) scientific evidence from clinical research, some suggestions regarding the management of NCP will be discussed in this paper.

Pathophysiology of neuropathic cancer-related pain

Neuropathic pain usually includes different clinical entities with typical characteristics varying according to their pathophysiology. A preliminary sub classification may easily be produced by discrimination between central and peripheral nervous origin of pain. A further distinction could be formulated considering cancer-related NP syndromes (1).

Neuropathic pain originating from the peripheral nervous system

Peripheral damage of neural tissue is very common in cancer, particularly in locally advanced or/and metastatic disease. Infiltrating tumour cells, nodules or masses may lead first to a local irritation and then evolve to partial or complete destruction of nerves commonly resulting in pain escalation. Neural or spinal compressions from the vertebral segments are feared complications of pathological neoplastic fractures, with pain usually anticipating the following neurological-neurosensitive impairments. Due to anatomic reasons, nervous plexi like the brachial, mesenterial and sacral ones are mostly exposed to the risk of external compression or infiltration by primary tumours or metastases arising from surrounding soft tissues and bones (2, 3).

The lesion of peripheral nerves can nevertheless produce persistent stimulation in the Central Nervous System finally resulting in escalating pain and possible related manifestations such as hyperalgesia and allodynia.

Neuropathic pain originating from the central nervous system

So-called deafferentation pains and complex regional pain syndromes are two main groups of NP sustained by “central” troubles. Well known deafferentation pains are typically the phantom (limb) pain and the post herpetic neuralgia (4). Complex regional pain syndromes are based on even more complicated pain transmission mechanisms and they will not be addressed by this paper.

Cancer-related NP syndromes

Common cancer-related NP syndromes, due to direct tumour involvement of nervous tissue, have been summarized in the work of Caraceni et al (5).

- Peripheral nerve damage (spinal/paraspinal mass, chest wall mass, retroperitoneal mass, soft tissue mass)
- Radiculopathy or “cauda equina” syndrome (vertebral, leptomeningeal, spinal metastases)
- Plexopathy (cervical, brachial, lumbosacral, sacral infiltration)
- Cranial neuropathy
- Perineal pain and tenesmus due to presacral mass

One should consider that NP may also be related to a iatrogenic-induced damage (6). Side effects of well-known cytotoxic drugs may produce clinically relevant pain and persistent neuropathies. Peripheral neuropathies and other nervous tissue-related dysfunctions may be generated by drugs of widespread use such as Cisplatin (and derivates), Vinca-alcaloids and Taxanes.

Management of neuropathic cancer pain (NCP)

General considerations

Despite a significant increase in general knowledge and slowly cumulating scientific evidence, only modest advances have been made in the management of NP. Some relevant papers issued in the last years, containing useful recommendations and guidelines (7, 8, 9, 10), contributed to a more structured approach to the problem. Even in an era of high-technology medicine, the importance of an exhaustive history-recording and of a proper clinical assessment cannot be emphasized enough. The identification of peculiar pain patterns and their anatomical origin should ideally result in patient-oriented, evidence-based and cost-effective approaches and treatment strategies. Neuropathic pain is consensually considered poorly responsive to common analgesic drugs, to anti-inflammatory drugs and even to opioids. The classical WHO scale basing on analgesic potency levels (11) is recognized as an inadequate procedure to approach NP Pain by recent reviews (7, 8, 9, 10).

The proper approach to NCP syndromes should be a multidisciplinary one, including a number of specialists like palliative care-, oncology-, and radiation therapy physicians, anaesthesiologists, neurologists, neurosurgeons and psycho-oncologists.
The importance of covering nursing and general supportive aspects can not be underlined enough.

Pharmacological treatment
Active antineoplastic treatments (chemotherapy and radiotherapy), should be included in the potential armamentarium against NCP. Cytotoxic drugs and ionizing rays may generate pain control by limiting neoplastic cell proliferation and dissemination thus reducing their devastating consequences on the neural tissue like compression, infiltration and/or destruction, finally resulting in pain stimuli.

Radiation therapy or local neurosurgery procedures may play a key role in the management of painful spinal compressions, common complications in metastatic cancer to the vertebral bone. Considering the pathophysiological complexity of NCP, pharmacological treatments should always be proposed within a treatment concept, where different measures may be helpful or act in a synergic way. Psychological and psychosocial issues may become relevant in some clinical settings (12) where the use of drugs alone may result in frustration for both patients and health care professionals.

1. Basic analgesic drugs
Paracetamol and anti-inflammatory drugs (level I drugs according to the WHO analgesic ladder) are only occasionally associated with significant clinical responses and satisfactory pain control outcomes. Consequently they should not be considered as standard drugs in the management of NCP. Furthermore they do not appear in the current management recommendations published by experienced groups (7, 8, 9, 10).

The use of basic analgesic drugs in combination with other more specific drugs for NCP may display some efficacy in selected clinical situations, particularly in mixed nocicepitive-neuropathic pain syndromes.

2. Opioid drugs
In NP of non-malignant origin, a review published by Eisenberg et al (13) demonstrated a significant efficacy of opioids over placebo. The role of opioids in the management of NP is currently matter of discussion. Their use is anyway recognized by different authors (7, 8, 9, 10) in relevant publications.

Morphine, the opioid of choice in the WHO ladder for pain management, is reported as poorly efficacious in NCP while its efficacy may probably increase if used in combination with other drugs (14, 15, 16, 17).
Methadone, a semi-synthetic opioid first introduced in 1930 and “re-discovered” in the last decades, is considered, even though a strong evidence is still lacking, the opioid which may have some efficacy in the management of NCP (18, 19). Although other strong opioids like *Hydromorphone, Oxycodone and Fentanyl* are not characterized by convincing evidence of efficacy (17); some selected patients may benefit from their introduction. The combination of opioids with anticonvulsants like Gabapentin or Pregabalin, seems to be a reasonable way to increase NCP control (7, 8, 9). Rotation to another opioid may be beneficial in some cases (20, 21). Oxycodone has been reported to be an effective analgesic option for the management of some cases of postherpetic neuralgia (22), but its efficacy should not be emphasized. Tramadol, a weak opioid (WHO level II), has been shown to have some activity in NP of non-malignant origin (23, 24). Possible benefits should be balanced towards the side effects potential of the drug, particularly in the elderly.

3. Corticosteroids

Despite many articles around this topic and the large clinical use, only limited evidence is available regarding the use of Corticosteroids in advanced cancer care and in NCP management particularly. Corticosteroids, Dexamethasone being the most documented drug, are generally active in the setting of NCP (25, 26, 27).

Over decades and still recognized as valid co-analgesic drugs in the management of NP, Corticosteroids are characterized by a great and usually rapid onset of activity due to their anti-inflammatory and anti-oedematous properties. The risk of treatment-related side effects needs accurate monitoring and follow up of the patients, particularly if the treatment is being continued over a long period of time.

4. Anticonvulsant drugs

Anticonvulsant drugs have been historically largely used in the management of NP. Since their introduction in the 1960s, many data have been reported and cumulated but the ultimate scientific evidence has been rather scarce until now, their use and analgesic efficacy still being a field of discussion and even of controversy (7, 8, 9, 10, 28, 29). They are generally accepted by the medical community as co-analgesic drugs in NP, rather used in combination schedules with other drugs. According to their characteristics and their potential side effects profiles, it is recommended that the administration of these drugs should be performed in collaboration with and under supervision of palliative care specialists.

Phenytoin, given as an intravenous infusion, has been demonstrated to be of some utility in the management of NP (30).
Carbamazepine, a well documented drug in NP of non-malignant origin like trigeminal or postherpetic neuralgia (28), is considered today by some authors (8, 29) less relevant than it used to be.
Gabapentin, first developed as an anticonvulsant drug and introduced in 1994, is a structural analogous of the Gamma Amino Butyric Acid (GABA). The efficacy of GABA in the management of NP of non-malignant origin has been reported in different studies regarding postherpetic neuralgias, diabetes mellitus-related neuropathias, phantom limb pain and other similar pathologies (31, 32, 33, 34, 35). Furthermore, evidence from clinical trials suggests that Gabapentin may be useful in the management of NCP as reported since the late 1990s (5, 36, 37). Various reviews published in the last decade seem to consolidate the use of Gabapentin in a broad number of NP settings (7, 8, 9, 38). The daily doses required to produce a clinical benefit may raise up to 3600 mg, the central nervous side effects representing the most important source of concern and commonly the leading reason for treatment interruptions.
The importance of a carefully, patient-specific dose titration cannot be emphasized enough.
Pregabalin, a newer and similar molecule, has rapidly become a valid alternative drug to Gapabentin. (7, 8, 9, 10, 39, 40).

5. Antidepressant drugs

Antidepressant drugs may play a significant role in the general management of chronic pain. Due to their modulating effect on pain threshold, they are able to produce clinical benefits in different clinical settings. Unfortunately there is only scarce literature comparing anticonvulsant and anti-depressant drugs in the management of NP. The few data available, referring to small patient populations and selected pathologies, did not show any advantage for a class of drug over another (41). Just like anticonvulsants, antidepressants should be considered as adjuvant analgesics, their efficacy being mostly displayed in treatment combination schedules, as suggested in recent review works (7, 8, 9, 10).

In the older reviews of Max et al (42) and Dworkin et al (12), the benefit was particularly underlined in NP of non-malignant origin. In the setting of chemotherapy-induced neurological toxicity, some benefits of the use of Nortryptiline has been reported for the

management of Cisplatin-related neuropathy (43). The role of newer anti-depressants like SSRIs (Selective Serotonine Reuptake Inhibitors), is still matter of debate since not all the questions raised by their use in NP management have been answered yet (44).

6. Calcitonine

Calcitonine is generally recognized as a drug with some effect in infusion schedules for the management of phantom limb pain, an usually treatment-refractory NP type (45). However the routine use of Calcitonine in the management of NP cannot be recommended.

7. Anaesthesiology

Anaesthesiological approaches may be indicated in selected patients with drugs-refractory NP. Neural blocks or spinal catheters may represent a valid way to obtain (rapid) pain control. In this setting, a patient-oriented multidisciplinary approach is strongly recommended since significant outcomes are usually obtained through a proper team work only.

Non pharmacologic treatment

Rehabilitation and physical therapies may help in the context of a differentiated multimodal strategy of pain management. The potential benefits of the physical exercise in NP have not been adequately studied; their role being probably underestimated. Even though all these different procedures can play a supportive role only, their systematic introduction, even in specialized institutions, is often poor. Surgery and surgical procedures may be indicated for the decompression of peripheral nerves, finally resulting in a (rapid) reduction of the pain intensity. Complex and aggressive procedures like rhizotomy or chordotomy, should be carefully considered for selected patients and carried out in centres with excellent expertise levels.

Psycho-oncological approaches, according to the frequent multidimensional nature of NP, could be introduced in the general management strategy for patients needing a particular support. Psychological issues and concerns should be included in the initial assessment.

Acupuncture and other procedures, generally classified under the definition of “Alternative and Complementary Medicine” may generate some clinical benefits in selected patients and situations but their role in a global treatment concept should not be overemphasized. For most of these procedures an adequate scientific evidence of efficacy is still lacking.

Conclusions

The management of NCP in our modern cancer medicine still represents a clinical challenge and major treatment successes are rather unusual. Some relevant scientific achievements along the last decades, led to a better assessment concept, to more structured and active treatment procedures and finally to a better comprehensive management of the clinical problem.

The combination of active drugs acting at different biological levels and on selected mechanisms, represents the strategy of choice at the moment and still is the best option available. Future improvements in this field will strongly depend on methodologically well conducted basic and clinical research and on carefully application of the available evidence.

Capillary education of patients, physicians and caring personnel working in this field, will further contribute to the progress in this complex field.

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COMMENTS, DISCUSSION

Adequat treatment of pain problems in current oncology network in Romania

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Abstract

There is still a large number of cancer patients whose pain is poorly treated. The present paper analyses the main reasons why this situation occurs in Romania, and discusses the consequences for clinical practice of oncology in Romania.

The main issues are insufficient resources (both human and material), a shortage in training of the medical staff and lack of health system management. The paper identifies ways to improve the current situation.

Key words: *cancer, pain, oncology network, management*

(Full text in Romanian)

NEWS

Training "Symptoms control in palliative care "

The Mobile Services Association for Palliative Care will organise again a course "Symptom control in palliative care ", to be held in Bucharest in October 2011 in partnership with the National School of Public Health Management and Health Improvement.

The course aims to increase knowledge about pain control and the most common symptoms in palliative care (pain, dyspnoea, anorexia and cachexia, anxiety and depression, nausea and vomiting, constipation and diarrhoea, sleep disturbances, hydration and symptom control features of the patient terminal), among physicians with clinical specialization through an interactive program during eight days.

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