DECISION MAKING ON REFRACTORY PAIN IN A YOUNG ONCOLOGICAL PATIENT

TOMA DE DECISIONES FRENTE A DOLOR REFRACTARIO EN PACIENTE ONCOLÓGICA JOVEN

DECISÃO FAZENDO CONTRA A DOR REFRATÁRIA NO PACIENTE ONCOLÓGICO

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SUMMARY:

The vast majority of cancer patients in advanced stages feel pain. Most are controlled with analgesics following the WHO analgesic ladder. However, a percentage of patients persist feeling pain. These are patients with difficult-to-control pain who often benefit from interventional measures. An even smaller percentage of patients keep on feeling pain as a refractory symptom despite adequate therapeutic measures. In these cases, palliative sedation is indicated. We present the case of a young patient with refractory pain who required palliative sedation in a palliative care unit of a private institution in Montevideo.

Keywords: Pain, clinical management, palliative care, sedation.

RESUMEN:

La gran mayoría de los pacientes oncológicos en etapas avanzadas presentan dolor. La mayoría de éstos son controlados con analgésicos siguiendo la escalera analgésica de la OMS. Sin embargo, un porcentaje de pacientes persisten con dolor. Estos son pacientes con dolor de difícil control que se benefician muchas veces de medidas intervencionistas. Un porcentaje aún menor de pacientes mantiene el dolor como síntoma refractario a pesar de las medidas terapéuticas adecuadas. En estos casos está indicada la sedación paliativa. Se presenta aquí el caso de una paciente joven con dolor refractario que requirió sedación paliativa, en una unidad de cuidados paliativos de una institución privada de Montevideo.

Palabras clave: Dolor, gestión clínica, cuidados paliativos, sedación.

RESUMO:

A grande maioria dos pacientes com câncer em estágios avançados têm dor. A maioria destas dores são controladas com analgésicos, de acordo com a escada analgésica da OMS. No entanto, uma porcentagem de pacientes continua sentindo dores. Estes são pacientes com dor de difícil controle que frequentemente se beneficiam de medidas de intervenção. Uma porcentagem ainda menor de pacientes mantêm a dor como um sintoma refratário, apesar das medidas terapêuticas adequadas. Nestes casos, a sedação paliativa é indicada. Apresentamos o caso de uma paciente jovem com dor refratária que precisou de sedação paliativa em uma unidade de cuidados paliativos de uma instituição privada em Montevidéu.

Palavras-chave: Dor, manejo clínico, cuidados paliativos, sedação.

INTRODUCTION

Pain, according to the International Association for Study of Pain (IASP) is defined as unpleasant sensory and emotional experience associated, or not, with actual or potential tissue damage described as a function of that damage. It has a great impact on the quality of life and a devastating effect on the terminally ill patient. When it is not relieved, it becomes the center of the person's life. Total pain affects the integrity of the person and can be seen as the tip of an iceberg, under which there are various physical, emotional, social and spiritual factors (1). The pain of difficult control may be due to its intensity, development of drug tolerance, inability to increase the dose due to side effects, to having special characteristics such as pain that is not sensitive to opioids, neuropathic pain or the sympathetic pain maintained, the incidental pain, or those instances where the emotional component predominates (2). Pain in patients under palliative care represents more than a nociceptive sensation and includes aspects related with the human condition, such as personality, affectivity, emotions, and psychosocial relationships (3). Sometimes this total pain becomes a symptom of difficult control, despite the adequate intervention of the entire palliative care team: psychologist, social worker, doctors, nurses, and it often becomes a refractory symptom, in which palliative sedation should be performed (4).

The case presented below is that of a young woman, mother of three girls, who comes from a low socioeconomic status. Total pain is diagnosed and must be sedated because it is refractory despite the interventions received, which we considered were adequate.

Description of the case

Female patient, 33 years old. No previous personal or family history. Lives with her partner and three daughters of 13, 3 years and 18 months. Receives a pension for sickness. Her partner, unemployed, is the primary caregiver. Her mother helps in caring for her daughters. Intervened in January 2016 (31 years old) due to a pigmentary lesion in her lower right limb, attending the puerperium of her third daughter (Pereira Rossell Hospital). The pathological anatomy shows a malignant melanoma of nodular histological type, Breslow 5 mm, Clark IV, margins compromised, with no deep involvement. A computerized axial tomography (CAT) scan is requested (3/16/2016) which shows encephalic, pulmonary, hepatic, bony, mammary, adrenal, peritoneal, inguinal and subcutaneous secondarism. Radiation therapy holocranial and spinal from T1 to T3 is started with good tolerance. In June 2016 begins the first series of chemotherapy with cisplatin, dacarbazine and vinblastine. Three series are performed with good tolerance. A new CAT scan was performed, which evidenced a decrease in brain, liver and lung lesions. Two more series are indicated with good tolerance.

In December 2016 a bilateral segmental mastectomy was performed (pathological anatomy: melanoma metastasis). In January 2017 the sixth series takes place. CAT of the skull and face is requested for a painful tumor in the lower jaw that reports a lytic lesion of the lower to the left maxilla compromising soft tissue. BAT of abdomen and pelvis reports no injuries in liver. Lithic lesion of sacrum. Consultation is requested with a radiotherapist who performs analgesic RT in the maxilla with good pain control. In March 2017 a severe spine pain is partially calmed with NSAIDs. Analgesia is adjusted, dexamethasone is added orally and a new CAT scan of the spine is requested, reporting: known lesion in T2, lytic lesion at the level of the posterior arch of T10 with compromise of the spinous process and both laminae. Extensive lytic lesion at sacral aileron level. Analgesic RT is again performed and then new QT with dacarbazine as monodrug. After that first cycle, severe thrombocytopenia. Consultation at 72 hs due to intense headache and tendency to sleep. Enter the Intensive Treatment Center for left temporal hematoma. Good evolution As a sequel, it maintains lower right limb paresis. Upon discharge (May 31, 2017) she is referred to the Palliative Care service. Until her admission we do not know what type of analgesia she has received and at what dose, since we do not have her previous medical history. We only have the oncological follow-up that refers to "good" or "bad" pain control. On admission to the service the symptoms were controlled with Dipirone with codeine (dipyrone 500 mg plus codeine 10 mg) every 8 hours, dexamethasone 24 mg/day and pregabalin 75 mg/day. Lactulose is added, 10 c every 12 hours, bisacodyl 5 mg every 8 hours and metoclopramide 10 mg every 8 hours.

The pain remains under control for two months. She is visited weekly by a palliative care doctor and biweekly by a psychologist. In those first interviews, although she knows her illness and sometimes mentions the prognosis, she prefers not to talk about it (avoidance). An interview was also carried out with the team´s Social Assistant, who contacted her eldest daughter high school to make them aware of the situation, and with the CAIF

(Center for Attention to Children and the Family) of the zone so that the eldest daughter can be seen by the school psychologist and her two younger daughters can attend the CAIF on mornings and afternoons, receiving three meals at the school. The patient has an ECOG 2-3 until then.

She gets out of bed to the couch, cleans herself with help, even performs some simple tasks inside her home. Two months after the first consultation, she reported increased pain in MID, neuritic type irradiated to the sole of the foot, without paresthesias. Analgesia is increased and immediate release morphine is indicated as oral solution, 10 mg every 4 hours (60 mg oral morphine per day) plus rescues (10 mg if pain is present) and 150 mg pregabalin at night. The rest of the medication stays the same (laxatives and antiemetics). It improves the pain control, but in 72 hs intense abdominal pain is added, colic type, with predominance of inferior hemiabdomen, which does not subside with rescues. Consultation with the emergency department, confirming fecaloma and acute urinary retention. A bladder catheter is put in place. Suspecting spinal cord compression, her hospitalization is indicated for studies. The patient refuses, not wanting to leave her daughters. A treating oncologist is consulted about the possibility of RT for pain control and treatment of probable compression, but it is contraindicated because she has already received maximum doses.

In 24 hours the pain increases. Analogic visual pain 10/10, of similar characteristics. Enters Sanatorium and starts with subcutaneous morphine, with rapid dose escalation up to 160 mg/day in 48 hours, in a continuous infusion pump. Continues with laxatives and antiemetics, and evacuation enemas are added as needed. Little pain control. After 72 hours, rapid rotation of morphine to methadone sc 30 mg/day[1], in continuous infusion pump plus adjuvants, dexamethasone 24 mg sc/day and pregabalin, 75 mg in morning and 150 mg at night. Rescues with methadone 5 mg sc/dose are made, scaled up to 60 mg/day in 72 hours, in a continuous infusion pump, plus adjuvants. Magnetic resonance imaging (MRI) performed, which reports total substitution of the sacrum. Pain therapist is consulted regarding possibility of interventional measures for pain control, but the team discards them.

Doses continue to escalate, without elements of intoxication, but pain control are not achieved, AVS 8-9/10. Very distressed by pain and separation of their daughters. The team's psychologist interview shows a great component of anguish for the future of their daughters. The social worker arranges that her husband can have legal custody of her eldest daughter (fruit of another relationship), alleviating some of her anguish. In this stage, she clearly states that he knows her short-term prognosis, sometimes expressing anger against the disease. She doesn't want her daughters to see her (even though visits had been authorized at any time).

Due to lack of methadone ampoules in the pharmacy, and since oral intakes are

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[1] EDOM (Equivalent Dose of Oral Morphine) 320. Metadone, would be10:1. Dose is reduced by 30% . In this case the reduction was smaller.

decreasing, a new rotation must be made to morphine, 400 mg/day in continuous infusion pump. Midazolam 15 mg/day, metoclopramide 30 mg/day, ranitidine 150 mg/day, and hyoscine butylbromide 60 mg/day are added to the pump. Rescues are made with morphine 10 mg when needed, and also dexamethasone, 24 mg/day. In 48 hours doses are increased for uncontrolled pain (up to 6 daily rescues), up to 500 mg sc/day by continuous infusion pump. At that time, the patient starts a tendency to sleep, although in moments of awakening she is lucid.

The pain cannot be controlled despite all these interventions and continues with severe pain (AVS 9/10). Seven days after the rotation pain control is not achieved. Patient and family are consulted and team members decide to initiate palliative sedation for total pain refractory to treatment. Start midazolam 30 mg sc/day in continuous infusion plus rescues of 7.5 mg if Ramsay less than 3[2]. Scale up to 90 mg sc/day. Patient dies after 72 hours.

DISCUSSION

Relatively old studies reported the incidence of cancer related pain at around 50-80% (5). In more recent communications, lower figures are reported, 24-60% in populations under active treatment, and higher incidence, 60-90%, in a population with advanced or terminal illness (6-8). These figures speak for themselves of the magnitude of the problem, especially taking into account the high prevalence and improvement in cancer survival figures in our times (9).

Symptomatic pain relief can be achieved in a good number of patients following the directives established in the different clinical guidelines, such as those of the World Health Organization (WHO) and those developed by different scientific societies of palliative care or oncology (10). The presence of pain and its inadequate management in patients with cancer has been documented extensively (11). In 2007 a meta-analysis was published that incorporated 52 studies, with a representative population of oncological patients in different clinical situations: after a curative treatment, during antitumor treatment, patients with metastatic disease and terminally ill patients. It was found that the prevalence is variable depending on the definition of pain used, but in any case it is higher than 50% in all types of cancer analyzed. In two recent systematic reviews, pain figures skyrocket to ranges of 62-86% in advanced stages of the disease (12, 13).

It was found that the following factors predicted a worse prognosis in terms of pain relief: intense psychological suffering, neuropathic pain, episodic pain, the need to increase the dose of opioids several times a week and a history of alcoholism or other drug addictions. In a series of almost 300 patients, in 93% of those who did not present any of these characteristics, adequate pain control was obtained, while in those presenting one or more of them, only 55% was obtained (14). From this data arises the Edmonton classification of pain prognosis (15).

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[2] Ramsay Sedation Scale: Grade1: patient is anxious and agitated. Grade 2: collaborative and oriented. Grade 3: Only responds to verbal orders. Grade 4: Asleep, responding to some auditive stimulus. Grade 5: Asleep, responding only to strong tactile stimulus. Grade 6: No response.

The emergence of pain therapy units and palliative care services in both the public and private sectors has meant an important advancement, but it is not enough to cover all the needs of this group of patients and their families (16). The approach to oncological pain remains a challenge, from a medical and ethical point of view.

The patients and very often the relatives refuse to accept the treatment with major opioids, given its social connotation to identify it with the near death. There are many myths about the use of these drugs, but the most deeply rooted in the population is that the analgesia itself triggers death.

Total pain is defined as that pain that becomes the center of a person's life, because it contains physical, emotional, social and spiritual elements (1). Flexibility is the key to pain control in patients. Patients are dynamic, depending on their stage, responses to therapy and personal preferences, so pain control must also vary. Despite having an impeccable strategy, with standardized and validated protocols, there are patients whose pain cannot be controlled. Up to 15% of oncological pain is resistant to morphine, requiring specific techniques for the treatment of pain units.

The majority of patients manage pain control with the measures recommended by the WHO. However, 10 to 20% of patients with advanced cancer do not manage to control pain, either due to the pathophysiology of the pain or due to the inability to absorb or administer drugs due to the disease itself or due to intolerance to opioids (17).

Therapeutic palliative sedation is defined as the deliberate administration of drugs, in the doses and combinations required, to reduce the consciousness of a patient with advanced or terminal disease, as necessary to adequately alleviate one or more refractory symptoms and with their explicit consent, implicit or delegated (18). According to the Palliative Sedation Guideline of the PRCPEX (Extremadura Regional Program of Palliative Care), for sedation to be considered ethical and legally lawful, it must meet certain conditions:

- There must be a refractory symptom
- The etiology of the symptom, established treatments and resistance to the same should be recorded in the clinical history.
- Must be intended to alleviate suffering using appropriate drugs at appropriate doses and proportionate to the symptom we want to relieve (minimum effective dose).
- The dose and combination of drugs should be adjusted to the reduction of consciousness sufficient for the relief of the symptom. The monitoring of the patient's response is essential to achieve relief.
- The patient's informed consent must always be obtained. If the patient cannot give consent, he can consider the one expressed by someone in the family in whom the patient has been able to delegate.
- There must be an interdisciplinary evaluation, provided by trained professionals and always under their direction.

There is no evidence that palliative sedation shortens life (19). The term “refractory” should be applied to those symptoms that can not be adequately controlled despite the best efforts to apply treatments that do not compromise the patient's conscience (20). The diagnostic criteria for refractory symptoms include that the physician must perceive that invasive and non-invasive procedures are incapable of providing adequate relief, or that they are associated with an intolerable morbidity for the patient, or that it is unlikely to improve the symptoms in a patient in a reasonable time. The implication of this term is that the pain may not be adequately relieved and that sometimes sedation may be necessary to adequately relieve the symptom.

In Uruguay there is a palliative sedation protocol in the Manual "Palliative Care. Symptom Control" of the National Palliative Care Plan. Palliative sedation is defined as "deliberately lowering the level of consciousness by administering appropriate drugs in order to avoid intense suffering caused by one or more refractory symptoms." Emphasis is placed on palliative sedation as a medical indication (21). It defines a refractory symptom as "one that can not be adequately controlled with the available treatments, applied by expert doctors, within a reasonable period of time and in the short, agonizing phase" (22).

Pain is generally " linked to massive tissue destruction by the tumor, which can not be controlled with protocolized analgesic treatment." To start palliative sedation, the following requirements must be met: the patient must have a documented terminal illness, death is imminent, there is a refractory symptom that determines suffering and that there is written, verbal or delegated consent to the family. Sedation should be indicated by the attending physician, analyzed with the head of the service, ensure the provision of medication and inform the patient of the procedure (and/or family) (18, 23).

The purpose of this work aims to highlight the importance of giving interdisciplinary care, avoiding unnecessary suffering to the patient and his family, and the early introduction of palliative care in cancer patients, at any age, at any stage of the disease and concomitantly with the onco-specific treatment. We know that young patients are later referred to palliative care and often receive more aggressive treatments, even if they are futile (24).

The intolerable and refractory character to the treatment of this situation forces in many occasions the assistance team to indicate the patient's sedation. In general terms, a good death is death without pain and without other poorly controlled symptoms, which is not prolonged artificially, with the company of family and friends, with the possibility of having been adequately informed about the disease, participating in making decisions, choosing where you want to die (home or hospital) and counting in each case with adequate health support (25). Palliative sedation is not euthanasia and the differences are in the objective, the process and the result (23).

late after a neurological complication. While we know that early introduction to the palliative care team does not change the patient's prognosis, it is proven that it improves the quality of life. While she was treated she made use of her autonomy, defining what was beneficial for her and her family. She was treated in a multidisciplinary team attending to all needs. We will focus the following paragraphs on the symptom, its treatment and the road leading to her sedation.

The causes of sedation described in the literature are delirium, dyspnea, pain, hemorrhage, nausea - vomiting, and psychological. Broeckaert in Germany in year 2000 obtained the following results as causes of sedation: 39% delirium, 38% dyspnea, 22% pain, 8.5% hemorrhage, 6% nausea and vomiting and 21% psychological (26). In 2008, the palliative care unit of the Central Hospital of the Armed Forces, in Montevideo, Uruguay, found that the causes of sedation were 60% delirium, 17% dyspnea, 45% pain, 0% hemorrhage, 2% nausea and vomiting and 0% psychological (23).

The analgesic escalation followed WHO protocols, reaching the third step with the use of strong opioids and adjuvants, needing to rapidly increase doses and rotation to higher potency opioids with less undesirable effects, since the symptom could not be controlled. Interdisciplinary work was done with Psychologist and Social Worker, since it was a total pain, which had to be addressed from all areas. At this point of refractory oncologic pain, invasive treatment was considered in consultation with anesthesiologists of pain therapy, but it was ruled out by the patient since she did not want new interventionist therapies and that, given the extent of the injuries and that the patient had received high doses of RT, these were not possible.

At this time, with a very short life expectancy and a refractory symptom, palliative sedation was proposed to the patient and her family. It was verbally consented by the patient (who remained lucid) and was accepted by her mother and her partner . It was indicated by two of the treating doctors, who had known the patient and her family for several months and tried to coordinate the palliative care team of the institution.

Sedation with midazolam was started without withdrawing the analgesic drugs that she had already been receiving parentally. In this case the basic requirements to initiate sedation were met: the patient had an advanced oncological disease, in terminal stage. She had a refractory symptom (total pain). Verbal consent was obtained from the patient and sedation was indicated by the attending physician in consensus with the rest of the team.

CONCLUSIONS

Although pain is a common symptom in patients with advanced oncological disease and in most cases we manage to control it, there is a percentage of patients who do not respond or respond badly to the usual therapy.

We must always keep in mind in our patients those personal and pathological factors that can indicate that we will be facing a patient with pain that is difficult to control. Keeping these risk factors in mind and knowing the resources that we have can be decisive in defining a difficult pain as refractory. This pain can have, besides the physical component, a psychological, social, spiritual component, which sometimes turn into a total pain, which must be addressed by all the members of the team. This total pain may also be refractory to treatment. If all the diagnostic and therapeutic steps are followed and we apply the national and international guidelines for palliative sedation, we must bear in mind that total pain must also receive palliative sedation and constitutes another therapeutic step to alleviate a symptom.

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