

Palliative Care in Children with Cancer in a Developing Country: Report of the Pediatric Oncology Cooperative Research Group

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Abstract

Background: In Mexico, the right to palliative care (PC) was established in 2012. Most of the pediatric oncology units (POU) do so in a non-systematized manner and by personnel not specifically trained.

Objective: To describe the characteristics of the PC that children with cancer received in 7 POU in Mexico.

Design: A retrospective, longitudinal, observational study was carried out in 7 POU between January 2010 and December 2016.

Measurements: We evaluated clinical-demographic characteristics, oncological diagnosis, and the cause of admission, duration and type of specific PC granted as chemotherapy, radiotherapy, surgery and nonspecific as analgesia, nutritional support, cause and place of death

Results: We included 414 patients: 40% adolescents, 53% male gender, 50% of parents had basic or no education. Residents of urban environment 57%. 80% profess the Catholic religion. 59% with soft tissue and metastatic bone sarcomas at diagnosis, most with therapeutic failure of 2 or more schemes. Metronomic chemotherapy was the most used as PC; pain control was achieved in 78%, nutritional support 40%, and 70% spiritual support. PC duration 0-40 months. 5% abandon the PC. 57% of deaths occurred at home.

Conclusions: The PC in our country is an emerging field that must be applied according to international standards to grant dignity to the death process in our patients. Our main limitation is the poor infrastructure in human and economic resources, the ignorance of its benefits to the patient, the family, its environment and therefore to the health system.

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Introduction

Despite all the advances in pediatric oncology, 20% of children with cancer will die from this disease^[1]. In our country, the official media reports an annual incidence of 9/100 thousand new cases of cancer in children under 18, with a general mortality rate of 5.1 / 100 thousand^[2]; 40% of the patients are in a very advanced stage of the disease making them candidates for palliative care (PC)^[3].

Pediatric cancer care in Mexico is composed by several health institutions. The Mexican Institute of Social Security (IMSS) provides health insurance to workers in the formal labor market and their families (65 million people). The Ministry of Health (MoH), National Health Institutes and State-level Ministries of Health provide care to people affiliated with the System of Social Protection in Health through its operational arm Seguro Popular (SP) (54 million). State workers, army, and navy workers (14 million) have their own social security institutions and healthcare provision mechanisms. Persons who have security care system do not pay. 7000 cases are diagnosed per year and are treated by 210 pediatric oncologists.

The European Palliative Care Association has established standards in the care of children with life-threatening or terminally illness and recommends to be offered to all children with cancer, to be introduced at the time of diagnosis, mainly those who are unlikely to be cured^[4-10]. The pain control and other symptoms in addition to psychological, social and spiritual problems is paramount. This requires the participation of an interdisciplinary team of health professionals^[10,14,15].

During the agonizing phase, PC must be more intense for the development of a normal grief^[10-15]. The pediatric oncologist plays an important role when a family faces the possibility of their child's death. However there is controversy among pediatric oncologists about when and who should be assigned to palliative care. It is generally accepted that these measures help to relieve the symptoms in children with incurable malignancies, at the time of diagnosis or after therapeutic failure to different lines of treatment^[6,11,14-18]. In 2009, the reform of article 184 of the General Health Law was enacted in Mexico and the 166 bis was added containing the Law on Palliative Care that recognizes the right to a dignified death^[19]. In 2012 the Official Mexican Standard (NOM 011-SSA3-2014) established the criteria for terminally ill patients care through palliative care, constituting a priority program of hospital quality^[20-23]. In Mexico, there is no formal PC groups. PC was initiated by the more engaged person in the team.

Objective

To describe the characteristics of PC that children with cancer received in 7 pediatric oncological units in Mexico.

Material and Methods

A retrospective, longitudinal, observational study was carried out. We evaluated clinical-demographic characteristics, oncological diagnosis, cause of admission, length and type of specific PC granted as chemotherapy, radiotherapy, surgery and nonspecific as analgesia, nutritional support, cause and place of death in 7 UOP from January 2010 to December 2016. Ethics Commit-

tees of hospitals approved research. The research committee of the Mexican Oncology Society invited all pediatric oncologists and only the members who answered are in this study.

We analyzed the patient's clinical files that were complete from 0 to 18 years with cancer histologically diagnosed that received PC according to the WHO definitions in the different POU of the participating hospitals. We analyzed the clinical-demographic characteristics such as age, gender, type of residence: rural, urban or suburban, the parent's maximum education, religion professed upon admission to PC. Also, we analyzed the basic oncological diagnosis as well as the initial stage of diagnosis in solid tumors and risk stratification in the case of leukemia, the number of treatments provided with curative intent prior to starting the PC, the reason of their admission to PC such as progression of the disease, the parents request and if it was related to an irreversible organic dysfunction secondary to oncological treatment such as cardiac, renal or hepatic insufficiency that conditioned the admission to PC. The duration was considered according to the follow-up time from the start of PC until the death or loss of follow-up.

Regarding the type of PC granted, those aimed at local or systemic control of the non-curative disease were defined as specific: palliative chemotherapy or metronomic chemotherapy considered as low doses of chronic antineoplastic drugs by oral route, radiotherapy and / or some kind of surgery and nonspecific care was defined as pain treatment according to the WHO analgesic scale; type of nutritional support: food supplement through enteral or parenteral route, treatment of nausea and vomiting, use of antidepressants, anxiolytics, administration of blood products for palliative purposes.

The spiritual support provided was given by specific personnel of each unit. The variables related to death, the motive and place reported in the clinical file were recorded. The spiritual support provided to the patient as well as bereavement therapy to the family was not analyzed in this series.

Results

The clinical files of 414 pediatric patients with cancer who received PC in their treating unit were evaluated. 220 of them were male gender representing the 53% and 194 of the feminine with 47%. The average age was 8 ± 5 years. 40% of the patients were older than 10 years and 10% were younger than 2 years. Regarding schooling, we observed no schooling in 16.5% of patients while only 20% had a higher level of education. 61% are living in fully urbanized areas and only 16% in rural areas, it should be mentioned that 50% of our patients reside in places far away from the treating center. When analyzing the religion professed by the families, it was observed that 76% profess the Catholic religion, while 7% reported not professing any. Regarding the type of cancer, it was observed that 247 had some solid tumor, the most frequent being osteosarcoma and soft tissue sarcomas. 41.4% (119) had been diagnosed with metastatic disease and had oncological treatment with curative purposes at the beginning. 167 patients (40%) had been diagnosed with some type of leukemia, the most frequent being high-risk lymphoblastic and 36 (7.7%) with myeloblastic leukemia before the onset of PC. The characteristics of all patients are shown in Table 1. The number of treatments prior to the onset of PC was 0 to 6. 67% (280) were

refractory to 2 or more oncological treatments with curative purpose. The main cause of admission was refractory disease to 2 or more treatments in 316 cases. 24 patients presented progression of the disease related to the abandonment of previous oncological treatment. 76 patients with serious complications related to treatment such as hepatic, renal failure and / or severe or irreversible brain or spinal cord injury, conditioned their curative treatment not to be possible and offered as a PC as an only option. We registered 24 cases in which at the request of the parents PC was initiated, 6 of them without any treatment of a curative type. The duration of PC was 0 to 40 months with a median of 4 months. It is striking that 40 patients had a survival rate of more than 10 months.

Table 2: Palliative care granted to children with cancer in different units of Pediatric Oncology in Mexico

Type	Patients (%)
Specific Palliative Care	
Palliative Chemotherapy	152(36.7)
Metronomic Chemotherapy	36 (8.6)
Palliative Surgery	37(8.9)
Radiotherapy	37 (8.9)
Immunotherapy	33 (7.9)
Non specific Palliative Care	
Thanatologic support	351(89)
Antidrepressant Manage	51(12.3)
Ansyolitic Manage	133(32)
Blood Product support	180(43)
Nausea and vomit control	186(37.6)
Nutricional support	
None	255 (61.5)
Food supplements	147 (34.5)
Parenteral nutrition	13 (3.1)
Pain manege	
Opiod access	323 (78)
Other analgesics	40(9.6)
None	51(12.3)

In relation to the specific PC, the most used modality was chemotherapy with palliative intention (36.7%), metronomic chemotherapy. Palliative surgery was used in 37 patients, the most frequent being disarticulation. 33 patients received palliative radiotherapy, mostly in solid tumors. Nonspecific care was provided to the total population studied. The most frequent was the administration of blood products for palliative purposes in 180 patients (43.4%). Crisis support was possible among 151 patients. However it was provided not specified what type of personnel provided it, given that in some units by volunteers. In relation to nutritional support, we observed 147 patients who had access to food supplements orally or through a nasogastric tube, and 14 received parenteral nutrition, some 4 in domiciliary form, while 255 did not register any type of nutritional support. Pain control is usually performed with the WHO analgesic scale;

Table 1: Clinical demographic characteristics in pediatric patients with cancer who received palliative care Pediatric Oncology units of Mexico

Characteristic	Patients (%) N 414
Gender	
Male	220 (53.1)
Female	194 (46.9)
Age group	
0-2 yo	42(10)
2 a 1 m -5 yo	81 (20)
5 a 1 m – 10 yo	127(30)
>10 yo	164 (40)
Residence	
Urban	235(61)
Suburban	94(23)
Rural	65(16)
Family's religion	
Catholic	316(76)
Other	68(17)
None	30 (7)
Cancer type Leukemia (n 167)	
ALL SR ¹	27(13)
LAL HR ²	75(45)
LAL VHR ³	35(10)
Myeloid	36(21.5)
Solid tumors (n247)	
Osteosarcoma	20 (8)
Soft tissue sarcoma	15(8)
Neuroblastoma	25 (10)
Other	187(74)
Cancer stage at diagnosis (Solid tumors)	
I	3(1)
II	4(1.3)
III	93(32)
IV	119(41.4)
Number of treatments with curative intent	
None	15 (3.6)
1-2	302(73)
3-5	97(23.4)
Cause of admission to Palliative Care department	
Refractory disease to 2 or more treatments	316(76.3)
Progression due to treatment abandonment	24(5.7)
Complications related to oncological treatment	76(18.3)
Parents request	24(5.7 %)

¹ Standard risk Acute Lymphoblastic Leukemia

² High risk Acute Lymphoblastic Leukemia

³ Very high risk Acute Lymphoblastic Leukemia

records indicated that 78% of patients had access to opioid analgesics without specifying the most commonly used medication. The other 22% had no access because of the lack of a specialist. No data related to pain control was recorded in the registers of 51 patients. In this series, we did not evaluate the quality of pain control since it was a retrospective study and most of the clinical records did not include it on a daily basis.

Table 3: Characteristics of death in patients receiving palliative care in different units of pediatric oncology in Mexico.

Characteristics	Patients (%)
Direct cause of death	
Bleeding	77 (18.5)
Respiratory failure	76(18.3)
Brain edema	75 (18.1)
Unknown due to abandonment of PC	24 (5.7)
Other causes (Septic shock, severe dehydration, etc.)	162 (39.1)
Place of death	
Hospital	162 (39.1)
Patient's home	228 (55)
Unknown due to abandonment of PC	24 (5.7)

Regarding the variables related to death, we observed that the most frequent cause referred in the clinical record was bleeding without specifying anatomical site in 77 patients, respiratory failure in 76, brain edema in 75. In the rest were recorded different causes such as sepsis, severe dehydration, etc.

In this series, the spiritual support in our patients and their family was not analyzed since in the majority of the units do not have this department.

Discussion

In Europe and the United States of America, 1 every 5 children with cancer do not survive the disease^[1-4]. Official data report that cancer is the second cause of death in children from 5 to 14 years-old as well as the second cause of request for attention by palliative care clinic in a third level center of our country (34%)^[23]. Even though there is a legal and regulatory framework to implement PC throughout Mexico^[17,19,23], given the modifications to the General Health Law, as well as the creation of the National Palliative Care Program^[27], included in the Integral System of Health Quality^[24] the efforts made, although they have been significant, have been dispersed and promoted from different angles and in different regions of the country^[25], otherwise, there is no public policy that meets the minimum requirements needed by international practices. In terms of PC: comprehensiveness, maximum coverage, equity and quality in the provision and access, effectiveness, science, accessibility, continued care, values, satisfaction of patients and families and commitment to evaluate and show results^[4,26-30]. The Atlas of Palliative Care in Latin America reports that there are 10 units of third level care that provide palliative care in Mexico; 4 of these are exclusively for palliative care and only one is specialized in pediatric patients; In 6 of these institutions, dual functions of pain and palliative care are carried out^[31]. Another fact is that in Mexico, this sub

specialty of pediatrics is incipient, so that personnel specialized in pediatric palliative care is practically nonexistent^[7,21]. Given these circumstances, the health personnel assigned to the different oncology units is responsible for providing the PC in pediatric patients as part of the comprehensive care for the child with cancer, although it has been demonstrated that the specialized units in palliative care usually have better plans of management and treatment of these patients in comparison with the oncology units^[32,33].

In our series, most of the patients are adolescents with metastatic solid tumors. The proportion of children under 2 years of age, with neuroblastoma and very high risk leukemia, is possibly caused by a late diagnosis of both cancer and complications that imply poor results compared with other groups^[1,2]. Our patients reside in urban-suburban areas and the level of education is low or null in 45% of the parents, which limits the socio cultural environment, which could contribute to the difficulty in achieving effective communication in relation to diagnosis, prognosis, treatment and complications. This limits the making of assertive and effective decisions related to the treatment of the patient regardless of the clinical stage and the type of cancer at diagnosis^[34,35].

Current standards state that PC in children should be provided from the moment of diagnosis, regardless of the prognosis, since the greatest benefit has been demonstrated when both the physician and the patient are made aware of their early onset^[4]. In this series, the high proportion of patients with metastatic disease and the number of treatments with curative intent are striking. The fact is that the parents of patients with very severe prognosis in the short and medium term, request multiple treatments with curative intent despite the low probability of success, as well as the lack of knowledge of the benefits of PC to the general population, to the parents as well as to the health personnel, making it difficult to include correct time as part of the integral care of the child with cancer^[34-36].

There are certain controversies about who should receive PC. Multiple circumstances may influence the decision of the pediatric oncologist to start PC. Studies have been published reporting some of the most important circumstances such as the fact that doctors infer that it would not benefit the patient. Likewise, the perception that upon interruption of curative treatment, the patient is doomed to certain death, leading to initiate controversial or heroic therapeutic measures involving a series of bioethical aspects^[33,37] reports that 79.4% of children with cancer included in a PC program received experimental chemotherapy and 40% of these were enrolled in a phase 1 study^[38]. However, in a country where resources are very limited and access to innovative or experimental treatments is a luxury, achieving the arrest of the progression of the disease with the resources available in a patient with a gloomy prognosis could be considered as a true success. Metronomic chemotherapy could positively influence the quality of life and the optimization of resources. Nevertheless, its benefits as a palliative treatment is still limited in our environment^[39,40]. The use of radiotherapy for palliative purposes is similar to that reported in the literature^[41,42].

In this series, nutritional support during this stage is recommended in a natural way according to the needs of each child. Enteral and parenteral nutrition is not recommended^[43,45]. In this series nutritional guidance could not be confirmed in the

majority of patients. This could correspond to the limitations of specialized human resources and especially to the lack of knowledge of the benefits that this type of support achieves in these patients. Pain control is a cornerstone in palliative care^[3,4,7,10,46,47]. We observed that most of our patients have access to opioid analgesia; a limitation of this study is that we do not know the quality of pain control or the actual number of patients that warrants it.

In pediatric patients who are in PC the place where death occurs has been studied^[48]. Kaye reports that more than half of the deaths of children with cancer enrolled in PC happen in a hospital, 40% of those undergoing through mechanical ventilation, invasive procedures and even cardiopulmonary resuscitation in an intensive therapy especially for those who were enrolled belatedly (1 month before death)^[38]. Gao reports that for these patients, the tendency to die at home or in a hospice goes up (more than 50%) and the factors that were related to the selection of the site of death of the minor was strongly related to the coverage capacity of their medical insurance as well as the distance of the oncological care center^[47]. Cárdenas-Turranza and colleagues reported that in our country 85% of children with cancer die intra-hospital, without specifying the stage of treatment in which the death occurred or the proportion of patients who were in palliative care in or in the end of life. They also imply that probability of the patient with a solid tumor dying at home is greater^[49]. In our country we do not even have hospices for patients in palliative care. The infrastructure we have is very poor compared with another countries^[50,51]. Despite this, the death of Mexican patients occurring in hospitals represents the 39% of cases and we are working on it to decrease it, although we did not investigate the exact place of the intra-hospital death or the circumstances in which it happened. Considering this fact it is important to mention that 6% of patients abandoned the treatment follow-up, which limits the knowledge of the circumstances of death and the factors related to the selection of the place of death, which may be linked to socio cultural as well as economic factors.

Being this the first report of the current status of PC in children with cancer in our country, we consider that one of the main barriers to achieve the inclusion of PC in the comprehensive care of children with cancer in our country is represented by the absence of the subject in the study programs of physicians, both undergraduate and postgraduate levels of pediatrics, pediatric oncology, as well as other related areas.

We establish that health professionals must acquire knowledge about patient care in the final phase of life, since it represents a measure that will benefit patients, their family and, without a doubt, the doctor himself. Only through consensus made by cooperative groups will it be possible to unify criteria and improve the quality of care for our patients and optimize resources in our country giving dignity to this process.

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