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Evaluation of Consultations of Pediatric Patients with Cancer Pain in a Tertiary Education and Research Hospital

Üçüncü Basamak Bir Eğitim ve Araştırma Hastanesinde Kanser Ağrısı Olan Pediatrik Hastaların Konsültasyonlarının Değerlendirilmesi

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ABSTRACT

Objective: The aim of this study was to evaluate the demographic and clinical data from pediatric consultations referred to the pain clinic and to identify the causes of pain and treatment methods used in children.

Method: All pediatric consultations referred to the Algology Clinic of Ankara City Hospital between January 1, 2019, and May 30, 2021, were retrospectively evaluated in terms of demographic and clinical characteristics, compliance with consultation recommendations, and changes in visual analog scale scores before and after consultation.

Results: The study included 74 patients. Of the patients, 44 (59.5%) were male and 30 (40.5%) were female. The mean age of the patients was 12.2 ± 5.2 years. All patients were followed for cancer diagnosis and treatment. Solid tumors and hematologic malignancies were present in 55.4% and 44.6% of the patients, respectively. More than half of the patients had localized pain, most often in the trunk (35%), and 24.3% had generalized pain. There was a significant difference in the mean visual analog scale (VAS) scores at the time of and after the consultation ($p<0.001$). There was no statistically significant difference in VAS scores between genders. In the post-consultation evaluation, 43 (58.1%) of the patients experienced a decrease in VAS values of 30% or more. There was a statistically significant decrease in VAS scores for patients who complied with treatment recommendations during the consultation compared to those who did not ($p<0.001$). There was no statistically significant correlation between gender, local or generalized pain, or cancer type with decrease in VAS scores.

Conclusion: In children suffering from chronic cancer pain, favorable outcomes can be achieved with appropriate medical treatment if adequate treatment compliance can be ensured.

Keywords: Children, neoplasm, pain

ÖZ

Amaç: Bu çalışmanın amacı algoloji kliniğine yönlendirilmiş pediatrik konsültasyonlardaki demografik ve klinik verileri değerlendirerek, çocuklardaki ağrı sebeplerini, ağrı tedavi yöntemlerini ortaya koymaktır.

Yöntem: 01.01.2019–30.05.2021 tarihleri arasında Ankara Şehir Hastanesi Algoloji Kliniği'ne yönlendirilmiş olan tüm pediatrik konsültasyonlar demografik ve klinik özellikleri, önerilen tedavi, konsültasyon önerilerine uyum, görsel analog skala puanlarındaki konsültasyon öncesi ve sonrası değişimler açısından retrospektif olarak değerlendirildi.

Bulgular: Çalışmaya 74 hasta alındı. Hastaların 44'ü (%59,5) erkek ve 30'u (%40,5) kadındı. Hastaların yaş ortalaması 12,2±5,2'tü. Hastaların tamamı kanser tanı ve tedavisi nedeniyle takip ediyordu. Hastaların %55,4'ünde solid tümörler, 44,6'sında ise hematolojik malignensi mevcuttu. Hastaların yarısından fazlasında lokalize ağrı vardı ve sıklıkla gövdeydi (%35), %24,3'ünün ise yaygın ağrısı vardı. Hastaların konsültasyon sırasındaki ve sonrasındaki vizüel analog skala (VAS) değerleri ortalamasında anlamlı farklılık saptandı ($p<0,001$). Hastaların VAS skorlarında cinsiyete göre istatistiksel olarak anlamlı bir fark bulunmadı. Konsültasyon sonrasındaki değerlendirmede hastaların 43'ünde (%58,1) VAS değerlerinde ≥%30 düşüş olduğu saptandı. Konsültasyon sırasındaki tedavi önerilere uyum gösterildiğinde hastaların VAS değerlerinde uyum göstermeyenlere göre istatistiksel olarak anlamlı azalma saptandı ($p=0,001$). Cinsiyet, ağrının lokal veya jeneralize olması ve kanser tipi ile VAS skorlarında saptanan düşüş arasında istatistiksel olarak anlamlı bir ilişki saptanmadı.

Sonuç: Kronik kanser ağrısı çeken çocuklarda, yeterli tedavi uyumu sağlanabilirse uygun medikal tedavi ile yüz güldürücü sonuçlar elde edilebilir.

Anahtar sözcükler: Çocuk, kanser, ağrı

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INTRODUCTION

Cancer pain in childhood is a significant cause of morbidity**.** Some studies have shown that the prevalence of pediatric cancer pain can be as high as 75% (1). Pain can develop as a consequence of the disease itself or the cancer treatments, such as surgery, chemotherapy, radiotherapy, and interventional procedures (2,3). The recurrent or persistent pain experienced by pediatric patients can lead to a reduced quality of life, functional limitations, emotional problems, school absenteeism, difficulties in developing social relationships, sleep disturbances, and decreased participation in daily physical activities (4-6). Psychological and social factors increase the risk of growing pain and psychiatric problems in adulthood (7). For this reason, effective management of chronic pain in childhood is critically important.

The treatment of children with cancer pain should be planned in collaboration with specialized physicians, especially pain specialists (5). A consultation with a pain specialist can provide more accurate information for determining clinical approaches and better treatment options for pain, thereby reducing the risk of chronicity and adverse outcomes. However, there is limited data on the reasons for referring patients to pain specialists and the treatment methods applied (8). Surveys, data from health service providers, and information from health service records are not sufficient to determine the prevalence of consultations.

In our study, we retrospectively reviewed the consultation records of patients referred from the pediatric clinic to the pain clinic. We aimed to identify the causes of pain and current pain treatment methods in children using demographic and clinical data.

MATERIAL and METHODS

In this study, data were obtained through a retrospective screening of demographic and clinical information from consultations of pediatric cancer patients aged 0-18 years at Ankara City Hospital between January 1, 2019, and May 30, 2021, after obtaining ethics committee approval (University of Health Science Clinical Research Ethics Committee, Date: 22/09/2021, No: E1-21-1791).

Demographic characteristics, pain etiology, pain localization, and severity, recommended treatments, International Classification of Diseases (ICD) codes, and the number of hospitalizations were recorded on the study form from the previous consultation forms recorded in the hospital information management system. The type of analgesics and route of administration used for treatment were recorded. The mean recommended oral morphine equivalent dose per patient was calculated in milligrams by dividing the total daily recommended opioid dose for all patients by the number of patients consulted. In morphine equivalent opioid dose calculations, oral morphine conversion ratios were accepted as oxycodone 0.75, hydromorphone 0.13, fentanyl 0.01, and oral/intravenous 3/1 (9). Additionally, the medical records of the patients were retrieved from the archives and reviewed retrospectively. Compliance with the consultation recommendations, the type of analgesics used, and the visual analog scale (VAS) scores at and after the consultations were recorded. A 30% decrease in VAS score was considered a significant reduction in pain. Patients with missing consultation data were excluded from the study.

Statistical Analysis

Recorded data were analyzed using the Statistical Package for Social Sciences, version 25.0 (SPSS Inc., Armonk, NY). The normality of numerical data distribution was examined using Kolmogorov–Smirnov and Shapiro-Wilk tests. Normally distributed continuous variables were presented as mean and standard deviation, while non-normally distributed ones were presented with median and interquartile range (IQR; 25^{th}-75^{th} percentile). Qualitative data were expressed as frequencies and percentages. The categorical variables were compared with the Pearson chi-square test. The numerical variables were compared using the Mann-Whitney U or the Independent samples t-test. The confidence interval was 95%, and the margin of error accepted was set to 5%. Therefore, the p-value was considered significant when $p<0.05$.

RESULTS

In our study, consultation records of 89 pediatric cancer patients referred to the pain clinic were retrospectively evaluated, and 15 patients with missing consultation data were excluded. Of the 74 patients in the study group, 44 (59.5%) were male and 30 (40.5%) were female. The ages of the patients ranged from 1 to 18 years, with a mean ± SD of 12.2 ± 5.1 years. The distribution of patients in the study group by gender, diagnosis, pain localization, and referring clinic is presented in Table I.

Solid tumors and hematologic malignancies accounted for 55.4% and 44.6% of the patient diagnoses, respectively. Of the patients consulted, 56% had pain secondary to cancer treatment, 36% had cancer-related pain, and 8% had pain associated with interventional procedures. Only 12% of the patients were recorded as having an ICD code for pain in their records.

Before referral to our clinic, 75% of the patients had received chemotherapy, 4% radiotherapy, and 0.3% hormone therapy. The pain was localized in more than half of the patients, with the most common localization being in the trunk (35%).

The 24.3% of patients experienced generalized pain (in more than three localizations). The number of hospitalizations ranged from 1 to 17, with a median of 5.2. The duration of hospitalization ranged from 1 to 77 days, with a median of 12.5 days. The VAS scores of the patients at the time of consultation ranged between 4.0 and 10.0, with a mean ± SD of 8.51 ± 1.53. The VAS scores of the patients after the consultation ranged from 2.0 to 9.0, with a mean of 5.59 ± 1.65. The mean VAS pain score was 8.47±1.4 in females and 8.27±1.60 in males. There was no statistically significant difference in VAS score according to gender. Following consultation, 43 (58.1%) patients experienced a decrease in VAS values of 30% or more. Patients who complied with the treatment recommendations during the consultation had a statistically significant reduction in VAS scores compared to those who did not ($p<0.001$). There was no statistically significant association between gender, pain localization, type of malignancy, and the decrease in VAS scores. The comparison of the significant relief in VAS scores of patients after consultation across variables is presented in Table II. There was no statistically significant difference in pain relief ratios in terms of gender, solid/hematologic malignancy, and local/generalized pain.

Significant pain relief was observed in 61.0% (25/41) of patients who were recommended nonsteroidal anti-inflammatory drugs (NSAIDs) and in 48.5% (16/33) of patients who were recommended opioids, with no statistically significant difference found between the groups in terms of the proportion of patients experiencing pain relief.

Before referral to the pain clinic, 80% of the patients were taking analgesics. The rate of strong opioid use before the consultation was 26%. The number of patients using opioids after consultation recommendations increased to 44%. The average recommended oral morphine equivalent dose per patient was calculated as 26.17 mg by dividing the total daily recommended opioid dose by all consulted patients. The types of analgesics and the frequency of recommendation after consultation were as follows: NSAIDs: 55.4%, morphine: 24.3%, oxycodone: 13.5%, fentanyl: 4.1%, and tramadol: 2.7%. Tramadol, fentanyl, and oxycodone were only found in the records of patients older than 12 years and with a body weight of more than 30 kg (Figure 1).

Table I. Distribution of the Patients According to Gender, Type of Malignancy, Diagnosis, Localization of Pain, and Referred Clinics

	n (%)
Gender	
Male	44 (59.5)
Female	30 (40.5)
Type of malignancy	
Solid	41 (55.4)
Hematologic	33 (44.6)
Localization of pain	
Local	56 (75.7)
Generalized	18 (24.3)
Consultant clinic	
Hematology	35 (47.3)
Oncology and other clinics	39 (52.3)

Table II. Comparison of the Significant Decreases in Visual Analog Scale Scores according to Some Variables

	Significant pain relief n (%) (n=41)	No significant pain relief n (%) (n=26)	p- value
Gender			0.857
Female	17 (57.7)	13 (42.3)	
Male	24 (54.5)	13 (41.5)	
Adherence to recommendations			**<0.001**
No, the recommended treatment was not applied	7 (17.1)	11(33.3)	
Yes, the recommended treatment was applied	31 (75.6)	7 (21.2)	
The recommended dose was decreased	3 (7.3)	15 (45.5)	
Localization of pain			0.269
Local	29 (70.7)	27(29.3)	
Generalized	12 (81.8)	6 (12.2)	
Type of malignancy			
Solid	20 (51.2)	21(48.8)	0.201
Hematologic	21 (63.6)	12 (34.4)	

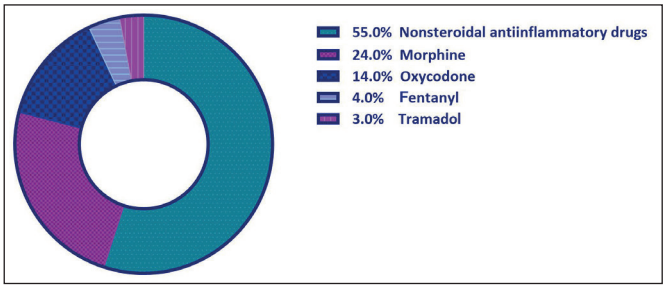

Figure 1. The distribution of recommended analgesics (%).

DISCUSSION

Although many pain departments report successful outcomes in the multidisciplinary management of chronic pediatric cancer pain, there is limited data about the records of referred patients and administered treatments (10). In our study, all of the pediatric pain referred to our clinic was due to pain related to malignancy. The number of patients with solid tumors was higher than the number of patients with hematologic cancers. The rates of pain related to cancer treatment, cancer itself, and interventional procedures were 56%, 36%, and 8%, respectively. These rates are similar to those found in the study by Shapiro et al (11).

A study found that the mean age of patients with cancer pain who admitted to the pain department was 8.9 (12). The mean age in the present study was 12.18 years, which is higher than that reported in the study mentioned above. The number of pediatric male patients admitted to our clinic is higher than that of females. This result may be attributed to the fact that pediatric cancers are more common in males (13). Medical treatment is the preferred treatment for most children with cancer pain. However, there is a lack of evidence regarding the selection and dosage of drugs in medical management. Opioids are the mainstay of treatment in cancer pain, with individual dosing and support by multimodal approaches (14). In our study, we followed the World Health Organization guidelines for the pharmacological treatment of cancer pain in children, specifically regarding analgesic selection and dosage (9). The mean daily oral morphine equivalent dose recommended in our clinic was found to be 26.17 mg. No comparison could be made because the data on the doses of opioid use in pediatric patients with pain were limited. Our study shows the results of the lack of opioid diversity and different forms of administration in our country. The absence of oral morphine solution in our country led to intravenous use only in children who could not use oral morphine solution.

Also, the absence of oral solution preparations of morphine may be the reason for the more frequent use of intravenous morphine in the treatment of unstable pain and breakthrough pain in this study. Unfortunately, the active ingredient hydromorphone is not available in our country. Non-compliance with recommended treatment is one of the most significant obstacles for clinical improvement. In our study, the rate of patients who did not follow the treatment recommendations partially or completely was 41%, which is slightly higher than the rate reported in other studies (36%) (15). Adequate clinical success, defined as a reduction of more than 30% in VAS levels, was not achieved in 42% of the pediatric patients in this study, in line with these ratios. Similar results have been reported in the literature (15). We suggest that the non-administration of the recommended treatments in our study might be due to the fear of health personnel and parents about the consequences of opioids, such as vital side effects and addiction.

In addition to pharmacological treatment in pediatric pain practice, psychological therapies should also be used to modify social-environmental factors to reduce the pain, disability, and negative mood associated with pain conditions and to improve the child's adaptive functioning (16). Age, female, gender, depressive symptoms, fatigue, and pain catastrophizing were associated with increased pain in a study by Klages et al (7). To improve pain management in pediatric cancer, a comprehensive approach using a biopsychosocial model of pain, with evidence-based pharmacology, complementary and alternative medicine techniques, technological modalities such as virtual reality, and, if necessary, interventional pain procedures, is recommended (17,18). Various interventional pain management modalities, such as nerve blocks and epidural and intrathecal treatments, are used less frequently in pediatric patient populations than in adults and often when other treatments have failed (19). This situation, may be attributable to the lack of randomized controlled studies on this topic. No interventional procedures were recommended for any of the pediatric patients consulted in this study.

We observed that favorable outcomes can be achieved with appropriate medical treatment in children with cancer pain if treatment adherence can be provided. Therefore, some barriers exist to providing compliance for proper treatment (20,21). Knowledge and training deficiencies, organizational and structural limitations, medication and prescription challenges, environmental and situational restrictions, communication gaps, technological barriers, parental factors, policy and systemic issues, logistical constraints, and context-specific limitations were identified as the leading barriers (21). For example, pain specialists may not be present in every hospital, and experience in this field is limited even among pain specialists. The number of pediatric pain clinics is also limited, even in developed countries (22). Therefore, training of physicians about pediatric cancer pain, improved communication with parents, and between healthcare professionals may exceed these barriers and provide better pain relief for

pediatric cancer pain (23). Further data on the prevalence, presentation, treatment, and long-term complications of chronic cancer pain in children are needed. In addition, opioids should be used in different routes and forms to titrate the dose, to increase analgesic efficacy, and for uncontrolled side effects following the guidelines establishing pediatric pain treatment standards (9). Therefore, there is an urgent need to resolve the issues of increasing the variety of opioids and eliminating difficulties in the bureaucratic process.

The limitations of this study include the lack of evaluation of functional improvement scales, the lack of knowledge of previous pain treatments, and the absence of long-term follow-up of the patients. The study's specificity in addressing cancer pain and evaluating treatment compliance can be considered a strength.

CONCLUSION

Favorable outcomes can be achieved with appropriate medical treatment in children with cancer pain, with proper treatment and compliance with the recommended medications.

AUTHOR CONTRIBUTIONS

Conception or design of the work: MB, EYA, SC
Data collection: MB, SSK, GY
Data analysis and interpretation: MB, HG, SSK, GY
Drafting the article: MB, HG, SSK
Critical revision of the article: MB, HG, SSK
Other (study supervision, fundings, materials, etc): EYA, SC, SS
The author (MB, SC, EYA, SS, HG, GY, SSK) reviewed the results and approved the final version of the manuscript.

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