CR Subscription Agency
Exploring and Distributing Knowledge Globally

International Journal of Neonatal & Pediatric Nursing
Volume 1 Issue 1

Use of Karnofsky Performance Scale for Assessing Pediatric Patients Undergoing Chemotherapy in Tertiary Care Hospital

Falguni Parande[1], Aanchal Anand[1], Mayuri Khaparde[1], Sunita Pawar[2*]
[1]Doctor of Pharmacy, [2]Assistant Professor,
[1,2]Department of Clinical Pharmacy, Poona College of Pharmacy Bharati Vidyapeeth Hospital and Research Center, Bharati Vidyapeeth University, Pune, India.

Corresponding Author
Email ID: sunita.reva@gmail.com

ABSTRACT

To Evaluate the performance status for pediatric patients experiencing Adverse Events during Chemotherapy. A Prospective and retrospective observational study was conducted over a period of six months in pediatric hematology oncology department. Patients aging 0-15 who were receiving chemotherapy for pediatric cancer were enrolled in the study. A self-designed Oncology patient profile form was used for collecting information like demographic details, cytotoxic drugs used during hospitalization and ADRs occurred. Follow ups were conducted for the first 4 consecutive chemotherapeutic cycles for duration of six months to interview the patient. A total of 50 patients (Male=33, Female=17) were included in the 6 months study. the pediatric cancers such (as Acute Lymphocytic Leukemia, Acute Myelocytic Leukemia, Burkitt's lymphoma, Hodgkin's Lymphoma, Wilm's tumor, Neuroblastoma, solid tumors, Nephroblastoma, Rhabdomyosarcoma, Ewing's Sarcoma, Clear cell sarcoma) were observed. The overall ADRs observed for all 50 patients in each cycle were segregated. Cycle 2 had most of the ADRs (n=184) and then Cycle 1(n= 178). Cycle 3(n= 151) and Cycle 4 (n=88) had lesser number of ADRs comparatively, on screening a total of601adverse drugs reactions, with an average of 3.02 adverse reactions per patient per chemotherapeutic cycle but the reactions reduce by fourth cycle with an average of 1.76 ADR per patient. The prognosis was quantified using Karnofsky Performance Score, which indicated better prognosis in the 3rd and 4th Cycle of Chemotherapy. The prognosis was observed to be poor in first two cycles, particularly in the 2nd Cycle.

Keywords*: Chemotherapy, Pediatric cancer, Chemotherapy induced ADRs, Karnosfsky scale.*

INTRODUCTION

Cancer in pediatric patients is rare with an incidence of 140–155 per million per year (age <15 years). This translates to ~1 in 7,000 children is diagnosed with cancer each year [1]. Children may receive more intense Chemotherapy (cancer treatment). Chemotherapy has different effects on growing bodies than adult bodies so cancer and its treatment are more likely to affect developing organs, and children may respond differently to drugs that control symptoms in adults [2]. Patients receiving chemotherapy often experience ADRs as the result of antitumor agents. Pediatric patients are susceptible to ADRs because they often cannot describe their symptoms and have small metabolic reserves [3]. The shortage of clinical trials in the pediatric population means that fewer pediatric patients are exposed to the drug before it is marketed. Thus, children are especially vulnerable to serious Adverse Drug Reactions (ADRs).

Cancer causes lag in a patient's activities. ADRs add on to it. The Pediatric group is at the highest risk of ADRs.Nearly three quarters of cancer survivors suffer an ADR related to their cancer therapy [4]. Adverse

drug reactions have a negative impact on the quality of life of affected children. Patient's daily living abilities (known to physicians and researchers as a patient's performance status), can and usually does change over time. Patients can experience a gradual worsening of their Performance Status as their cancer progresses, both from the cancer as well as from the cumulative adverse effects of treatments, thus leading to a decreased quality of life.

Various scales are used to assess or quantify such performance statuses of the patients undergoing chemotherapy. One of such popularly used scales is the Zubrod or ECOG (Eastern Cooperative Oncology Group) scale, it is endorsed by the World Health Organization (WHO). This scale ranges from 0 to 4, with 0 being "fully functional" and asymptomatic and 4 being "bedridden". Another scale used is the modified Lansky play-performance scale, developed in the late 1980s, to assess performance status in children aged 1 to 16 years [5]. Reuben *et al.* have created the Physical Performance Test (PPT) with the aim to objectively measure the physical functioning of elderly people [6]. But, this tool has been already validated in the geriatric population specifically. Functional Living Index-Cancer (FLIC), which is a Cancer-specific, functionally-oriented quality of life instrument, developed by H Schipper, J Clinch, A McMurray, M Levitt, [7] is one of the scales used to measure the Quality of life in Chemotherapy patients.

Karnofsky Performance Scale (KPS) has been used in this study. The Karnofsky scale is scored from 100 to 0, 100 score indicates perfect health and 0 indicates death. The scoring is majorly done in ranges of 10. This scoring system is named after Dr. David A. Karnofsky, who described the scale with Dr. Walter H. Abelmann, Dr. Lloyd F. Craver, and Dr. Joseph H. Burchenal in 1948 [8]. KPS has been be used to know the daily activities of the child, based on the information provided by the parent/caregiver after being interviewed by the practitioner. It describes a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, carrying out daily activities, *etc*) [9]. This can be used to quantify the quality of life for each individual patient [10]. The lower the Karnofsky score, the worse the prognosis for the illness.

Although ECOG performance scale, Lansky Scale and KPS, all rest on similar foundations to record performance status, their scales are not alike. The reason why we chose KPS for this study is because not only is this scale quick and simple, but it also gives an approximate assessment of the effects of treatment by physicians. It is more detailed and is described in 11 categories [11].

Changes in the treatment can be done by a routine assessment of KPS through a brief interview. These early referrals and changes may lead to better quality of life and care received by patients with advancing cancer. It not only covers the emotional, social and psychological aspects but also the physical aspects of the patient health. Moreover, KPS is considered the most appropriate scale for assessing the performance of pediatric patients, very much relevant to this study which is also based on pediatric population. The healthcare providers prefer KPS as it is highly reliable and its valid [11].

It is an instrument that translates feelings, perceptions, hope into numerical values on a scale, fit to be used in statistical calculations [12]. As comprehensive patient care that support the family as well is severely lacking in Indian practice [13]. We conducted this study with the objective to assess the quality of life for pediatric patients suffering from various

malignancies at diagnosis and four cycles after initiation of therapy, and to study the effect of type of cancer and type of chemotherapy they have been receiving, so that required interventions may be planned.

METHODOLOGY

Study setting

The present prospective observational study was conducted in Bharati Hospital and Research Centre (Paediatric Haematology/ Oncology Unit).

Inclusion and Exclusion Criteria

The sample size consisted of 50 patients, who have met the following inclusion criteria: Patients of 0–15 years of age, and patient diagnosed with cancer and were undergoing chemotherapy. Those excluded from the study were; patients other than paediatric age group, patients with more than one malignancy and non-co-operative patients.

Method

The Study was designed to evaluate the performance status for paediatric patients experiencing Adverse Events (AEs) during Chemotherapy for duration of six months. The informed consents were obtained from parents; since the patients were children. Every case that met the inclusion exclusion criteria were selected among the hospitalized patients. Follow ups were conducted for the first four consecutive chemotherapeutic cycles. A self-designed patient profile form was used for recording the data collected from patient files, patient or/and parent interviews if the patient was transferred the follow-up was conducted over the phone. The data included patient's information and the AEs reported by doctor or/and the patient. After the AEs were identified, they were classified according to the System Organ Class (SOC), as per MEDRA (Medical Dictionary for Regulatory Activities). In order to assess the daily activities of the child and to evaluate their performance status, Karnosfsky Performance Scale/Score was used. We enrolled patients who were hospitalized in between the year 2015–2017. The study was approved by the Ethics Committee of Bharati Medical College and Hospital following the completion of protocol design.

Assessment Tools Used

MedDRA system organ class is the highest level of the MedDRA terminology that has been applied to distinguish the symptom by its anatomical or physiological system, or its aetiology. Most of these describe disorders of a specific part of the body [14]. For example, Gastrointestinal System, Respiratory System, *etc*. The Karnofsky Performance score [9] runs from 100 to 0, where score 100 is perfect health and score 10 is death. Healthcare practitioners using the scale assign performance scores in intervals of 10.

This scoring system is named after Dr. David A. Karnofsky, who described the scale with Dr. Walter H. Abelmann, Dr. Lloyd F. Craver, and Dr. Joseph H. Burchenal in 1948. The primary purpose of its development was to allow physicians to evaluate a patient's ability to survive chemotherapy for cancer [15]. It is more detailed and is described in 11 categories. The lower the Karnofsky performance score, the worse the prognosis for an ongoing illness.

RESULT

A 6-month prospective observational study was conducted, in which a total of 50 pediatric oncology patients undergoing chemotherapy were included as per the inclusion and exclusion criteria.

There were 33 male patients (average age=5.9 years) and 17 female patients with an average age of 5.63 years. 58% of these cases were Acute lymphocytic leukemia (Pre-B, Pre-T and Ph +ve), 8% cases were Wilm's tumor, acute myeloid leukemia

(6%), Burkitt's lymphoma (6%), Hodgkin's lymphoma (4%), Rhabdomyosarcoma (4%), 14% other cases (Ewing's sarcoma, clear cell sarcoma of kidney, neuroblastoma, nasopharyngeal carcinoma, nephroblastoma and pre-yolk sac tumor).

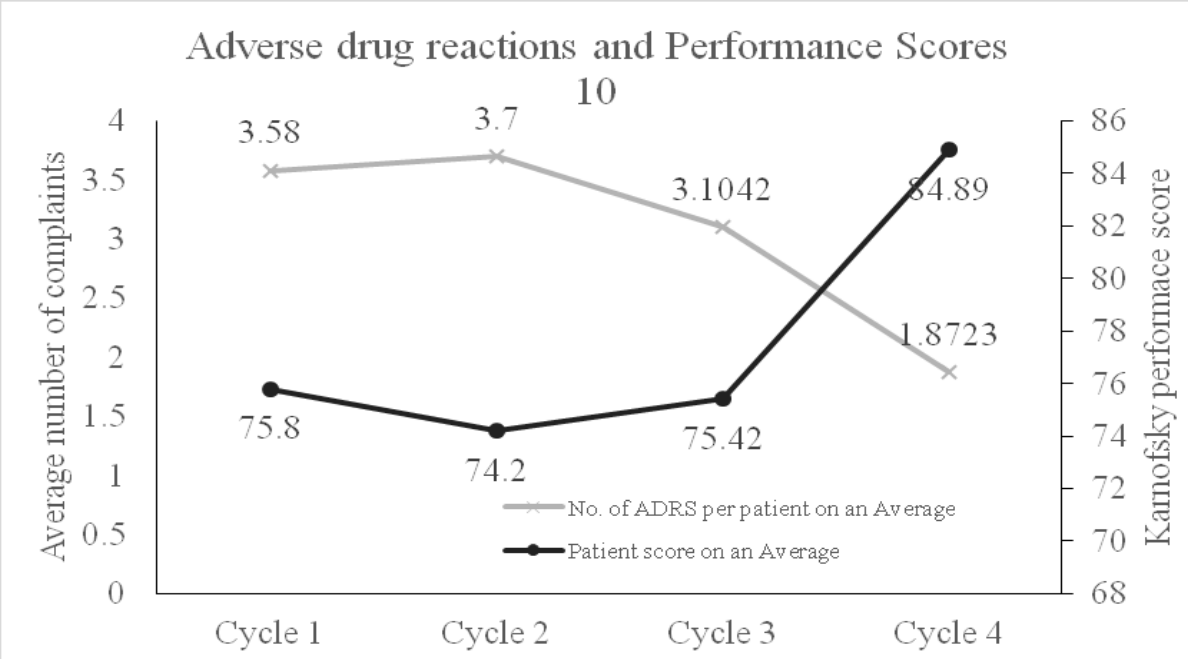

Fig 1. Chemotherapy Cycle

Table 1. Number of ADRs per Patients

	Number of patients (n)	Mean (c)	Standard Deviation	Standard Error
C1	50	3.58	1.90	0.26
C2	50	3.70	1.61	0.22
C3	48	3.10	1.85	0.26
C4	47	1.87	1.11	0.16

Table 2. Karnofsky Performance Scores

	Number of patients (n)	Mean (k)	Standard Deviation	Standard Error
C1	50	75.8000	21.00437	2.97047
C2	50	74.2000	18.41583	2.60439
C3	48	75.4167	17.97851	2.59497
C4	47	84.8936	11.00836	1.60573

The study included identification and classification of the observed Adverse Drug Reactions (ADRs) according to System Organ Class (SOC) and evaluation of the patient's performance score using Karnofsky Performance Scale. We considered two aims, of which the first one was based on the number of ADRs and the second one on the Performance Status of the patients. Since more than two

independent groups are involved, we have used one–way analysis of variance (ANOVA) and we used paired t-test to determine whether there are any statistically significant differences between the means of the groups. It should also be noted that although the sample size is 50 during the first two cycles, due to death incidences the number of patients has reduced in the third and fourth cycles. The number of ADRs per patient (as shown in table no.1) reduced in the fourth cycle (c = 1.76) significantly (p value <0.01) from cycle 1 (c=3.58), cycle 2 (c=3.7) and cycle 3 (c=3.02). The average complaints increase from cycle 1 to cycle 2(not significantly) and then gradually decrease. This depicts that the chemotherapy has shown its highest severity during the first cycle and since p value <0.05 with ANOVA, the level of significance; we can conclusively say the tolerance towards the chemotherapeutic agents becomes better by the fourth cycle.

To support this theory, we assessed the patient performance scores. The performance scores for the pediatric patients going through chemotherapy in cycle 4 (k=84.89) are significantly (p value <0.01) better than cycle 1 (k=77.4), cycle 2 (k=74.2), cycle 3 (k=74.2) as shown in table no. 2. Paradigm of inverse relation between adverse drug reactions and performance scores is shown in figure 1.

DISCUSSION

In patients with cancer undergoing chemotherapy, the most important predictive factor for prognosis is performance status. It measures how much patients can carry out their daily routine just as efficiently as before chemotherapy, as well as their energy and activity levels. In a study published in 2000 in The Journal of the American Medical Association, Wolfe and colleagues demonstrated that only 46% of parents who discussed the poor prognosis of their child understood that the children were terminal. When the physician and parent recognizes a patient's terminal condition beforehand, they were more likely to include a palliative treatment plan. [20] [16]

There are a few studies in which Karnofsky Performance Scale (KPS) has been used to evaluate the performance status in the oncology patients. One such study was on the effects of continuation of chemotherapy on the quality of life (QOL) of elderly patients with lung cancer which was conducted by Ryo Koyama and co-workers. A moderate correlation between KPS and the total score of the functional QOL domain was done. [17] Another KPS based study was done by Raymond W. Jang, MD, in University of Toronto, Canada, the purpose of which was to provide survival estimates for outpatients with advanced cancer, using KPS.[18]

In this study, the prognosis in each individual patient was assessed using KPS. Lesser the score as it nears scores like 20 and 10 the worse the chances of survival. [15] [21] Two aims were taken into consideration, of which the first one was based on the number of complaints (ADRs) while the second one on the Performance Status of the patients. Since more than 2 independent groups are involved, we have used one-way analysis of variance (ANOVA) to determine whether there are any statistically significant differences [22][21]between the means of the groups. Null hypothesis and alternative hypothesis have been used, in order to test them. During this 6-month study, 50 patients were taken but as the chemotherapy progressed there were death incidences which lead to a decrease in the sample size during the 3rd and 4th cycles.

A similar study was conducted by Vincent Mor, a PhD, in National Hospice Study (NHS) in which ANOVA with KPS as independent variable was used. It shows that as the KPS score decreases, the

proportion of patients unable to perform normal activities with or without help increases drastically. The findings suggested the utility of the KPS as a valuable research tool [22]

Another such study was done by DoritPud, a PhD. It was to determine if patients in oncology subgroups differed on functional status and quality of life (QOL). One-way ANOVA was used to demonstrate significant differences in KPS scores among the four subgroups ($P < 0.0001$). [23]

The first aim in this study was to test whether the numbers of complaints (ADRs) are same on an average for all the four cycles.When mean of complaints were plotted against the 4 Chemotherapy cycles, it was observed that the average complaints increase from cycle 1 to cycle 2& then gradually decrease, meaning that the average complaints are higher for cycle 2 (average - 3.7000) numerically but not significantly (p value > 0.05). However, the number of ADRs are significantly reduced in cycle 4 showing improving tolerance towards the treatment.

The second aim was to test whether Karnofsky Performance Score (KPS) is same for all the four cycles on an average. With the p value < 0.05 (P value =.012), there is a 99% significance that the patients perform better by the fourth cycle. The line plot graph between the Mean of Karnofsky Performance Score and Chemotherapy cycles showed that the average KPS decreases from C1 to C2 & then gradually increases.

We conducted this study to assess the Quality of life of children suffering from various malignancies at diagnosis and 4 cycles after initiation of therapy, and to study the effect of type of cancer and type of chemotherapy they have been receiving. The study basically confirms that cancer and chemotherapy along with its ADRs affects the performance status of the patients. Using a tool like KPS that can measure this performance status can at least help the health care team plan the required intervention and provide palliative care.

This study therefore supports that KPS is a reliable measure of functional status. Its ease of measurement and general acceptance of measure makes KPS a very reasonable candidate. In summary, the performance scale used was not only feasible but also useful.

LIMITATION

The study had a smaller sample size and duration of the study was six months, some data might have been missed because the parents/caregivers were not cooperative.

CONCLUSION

The adverse drug reaction monitoring and documenting is important it helps identify the absolute personalized treatment regimen most suitable for the patient's benefit. Use of tools like Karnofsky performance score helps clinicians, nurses in more efficient pediatric patient care.

REFERENCES

1) Federica Saletta, Michaela S. Seng, and Loretta M.S. Lau. Advances in paediatric cancer treatment. Translational Pediatrics. 2014 Apr; 3(2): 156–82.
2) Childhood Cancers; National Cancer Institute. https://www.cancer.gov/types/childhood-cancers
3) Akira Koizumi, Yoshinori Ohta, Mio Sakuma, Rika Okamoto, Chisa Matsumoto,, David W. Bates, Takeshi Morimoto. Differences in Adverse Drug Events among Pediatric Patients with and Without Cancer: Sub-Analysis of a Retrospective Cohort Study. Drugs - Real World Outcomes. 2017;4(3); 167–73

4) Geenen MM, Cardous-Ubbink MC, Kremer LC, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. JAMA 2007; 297(24); 2705-2715.
5) Forms Manual: Appendix L-Karnofsky/Lansky Performance Status; 2009 Marrow Donor Program and the Medical College of Wisconsin. 1-5.
6) Catherine Terret , Gilles Albrand, GéraldineMoncenix, and Jean Pierre Droz.Karnofsky Performance Scale (KPS) or Physical Performance Test (PPT)? That is the question. Critical Reviews in Oncology/Hematology. 77 (2011);142–147
7) American Thoracic Society, A quality of life resource, 1907.http://qol.thoracic.org/
8) Howard (Jack) West, MD; Jill O. Jin, MD, MPH. Performance Status in Patients with Cancer. JAMA Oncology Patient Page.October 2015.
9) KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA, http://www.npcrc.org/files/news/karnofsky_performance_scale.pdf[Accessed date: 3rd July 2020]
10) Chief Editor: Buck Christensen. Karnofsky Performance Status Scale.https://emedicine.medscape.com/article/2172510-overview [Accessed date: 3rd July 2020]
11) Cyndie Coscarelli Schag, Richard L. Heinrich, and Patricia A. Ganz.Karnofsky Performance Status Revisited: Reliability, Validity, and Guidelines.Journal of Clinical Oncology. (March) 1984; 2(3); 187-93.
12) Carsten Timmermann. 'Just give me the best quality of life questionnaire': the Karnofsky scale and the history of quality of life measurements in cancer trials: Chronic Illness. 2013 Sep; 9(3); 179–190.
13) PrernaBatra, Birendra Kumar, Sunil Gomber, MS Bhatia. Assessment of quality of life during treatment of pediatric oncology patients. Indian Journal of Public Health. 2014; 58(3);168-173
14) Medical Dictionary for Regulatory Activities – MedDRA. Therapeutic Goods administration. https://www.tga.gov.au/medical-dictionary-regulatory-activities-meddra[Accessed date: 3rd July 2020]