Original Article

The Evaluation of Quality of Life Associated with Peripheral Neuropathy in Patients with Hematologic Cancer

Oznur Usta-Yesilbalkan, RN, PhD
Associate Professor, Ege University, Faculty of Nursing. Department of Internal Diseases Nursing, Izmir, Turkey
Ayse Ozkaraman, RN, PhD
Associate Professor, Eskisehir Osmangazi University, Faculty of Health Sciences. Department of Nursing, Eskişehir, Turkey

Can Lafci, MSc Student
Ege University, Faculty of Nursing. Department of Internal Diseases Nursing, İzmir, Turkey

Correspondence: Ayse Ozkaraman RN, PhD, Eskisehir Osmangazi University Faculty of Health Sciences, Department of Nursing, Meselik Campus, Odunpazarı, Eskisehir, 26480 Turkey. E-mail: aozaydin26@hotmail.com.

Abstract

Objectives: The aim of this study was to evaluate peripheral neuropathy-related quality of life in chemotherapy-received patients with the diagnosis of hematological cancer.
Methods: This descriptive study was conducted on the patients who accepted to participate in the research and received chemotherapy for the first time and at least 3 cycles between January and October 2016 in a hospital in İzmir. The data of the study were collected by using the Individual Identification Form, the National Cancer Institute Common Toxicity Criteria Sensory and Motor Neuropathy Scale, and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy Scale (EORTC QLQ-CIPN 20). In the study, values belonging to categorical variables were presented as frequency and percentage. Mann Whitney U test was used in comparison of two groups with non-normal distribution.
Results: The mean age of 115 patients who participated in the study was 55.95±16.39 years, 56.5% of whom were male and 40% of whom have received RCHOP chemotherapy protocol. Peripheral neuropathy was detected in 36.5% of the patients. The EORTC QLQ-CIPN 20 sensory and autonomic subscale mean scores of patients with peripheral neuropathy were found to be statistically significantly higher than scores of those who were without neuropathy ($p = 0.001$, $p = 0.047$ respectively).
Conclusion: In our study, patients with peripheral neuropathy were found to have a lower quality of life related to CIPN than those without peripheral neuropathy.

Key words: Hematological cancer, peripheral neuropathy, quality of life

Introduction

Cancer is an important public health problem as it is related to a group of diseases characterized by uncontrolled growth and spread of cells and due to its high incidence and mortality rates (American Cancer Society, 2015; Public Health Agency of Turkey Ministry of Health, Department of Cancer, 2012). The incidence of the disease is high not only in other countries of the world but also in Turkey. (Public Health Agency of Turkey Ministry of Health, Department of Cancer, 2012). As time goes by, the number of hematological cancers among the patients with cancer has been increasing. Worldwide, more than 850.000 patients are diagnosed with hematologic cancer each year (Ferlay et al., 2016)

The treatment of hematological cancers is not only an urgent, lengthy and challenging process but also it may require special treatments such as a high-dose chemotherapy and/or hematopoietic stem cell transplantation (Li et al., 2015; Wang et al., 2016). These treatments, on the one hand, extend the life span of patients, but on the other hand cause the intense experience of physical and psychosocial problems related to conditions

arising from the disease course and side effects (Eyigor S, 2012; Fatal Injury Data, 2017). One of the frequently experienced neurological complications among these side effects is peripheral neuropathy (Ferlay et al., 2016; Seretny et al., 2014; Simon et al., 2017) The National Cancer Institute's dictionary of cancer terms describes peripheral neuropathy as "a nerve damage that causes pain, numbness, tingling, swelling or muscle weakness in different parts of the body" (Tofthagen, 2007). The frequency and severity of peripheral neuropathy varies depending on the cumulative dose and rate of administration of drugs such as platinum compounds, taxanes, vinca alkaloids, bortezomib, lenolidamide, thalidomide, interferon-a, brentuximab, and vetotin which are especially used in the treatment of the disease (Chu et al., 2015; Grisold et al., 2012; Jongen et al., 2015; Shimozuma et al., 2009; Wilkes, 2007; Wolf et al., 2008; Younes et al., 2012).

While making it difficult for patients to adhere to the treatment, chemotherapy-induced peripheral neuropathy (CIPN) also causes dose reduction in the treatment, discontinuation of the treatment, thereby leading to serious adverse effects on morbidity and mortality (Eckhoff et al., 2015; Ezendam et al., 2014; Kathleen Scott et al., 2016; Seretny et al., 2014). Patients suffer from CIPN-related tingling, numbness, cramps and pain in their hands, burning numbness in their hands or fingers and have difficulty in buttoning up their shirts, in holding a pencil or in opening a jar. In addition, due to the presence of these symptoms in the lower extremities, patients need to use the medical auxiliary equipment for standing, walking, climbing, stair climbing, driving a car or even for maintain balancing (Iżycki et al., 2016; Mols et al., 2014). In a systematic review of studies conducted on CIPN and quality of life, it was reported that CIPN has negatively affected the quality of life (Mols et al., 2014). In another study, it was found that patients with multiple myeloma and developed CIPN had a lower quality of life than those without peripheral neuropathy (Beijers et al., 2014). According to the information obtained from the literature, it has been identified that there is a limited number of studies on hematologic cancers in which solid tumors rather than CIPN and quality of life were evaluated (Fox et al., 2017; Seretny et al., 2014). Therefore, in our study, we planned to investigate the development status of peripheral neuropathy and peripheral neuropathy's impact on health-related quality of life in patients who underwent chemotherapy due to hematologic cancer.

Hypotheses of study

H1=There is relationship between quality of life and peripheral neuropathy

Methods

The aim and type of the research: This is a descriptive research conducted to evaluate the quality of life associated with peripheral neuropathy in chemotherapy-induced patients with the diagnosis of hematologic cancer.

The population and sample of the research: The universe of the research is comprised of hematologic cancer patients who were first treated with chemotherapy and at least 3 cycles between January and October 2016 in a hospital in Izmir, and the sampling is comprised of patients who accepted to participate in the research. The exclusion criteria in the study are: the nervous system, musculoskeletal system, skin-specific disease, and any disease affecting these regions (diabetes mellitus, elevated creatinine) and alcohol users.

Data Collection: This study was approved by the Ethical Committee, and we obtained written consent from the hospital management and patients before commencing the study. The data of the study were collected with the face-to-face interview technique by using the Individual Identification Form, the National Cancer Institute Common Toxicity Criteria Sensory and Motor Neuropathy Scale, and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy Scale.

The individual identification form: The individual identification form comprises of the sociodemographic characteristics of the patient, and the information related to the characteristics of the disease and its treatment.

The National Cancer Institute Common Toxicity Criteria Sensory and Motor Neuropathy Scale (NCI-CTCAE v 4.03): A scale assessing sensory and motor peripheral neuropathy, including objective and subjective measurements to assess chemotherapy-induced peripheral neuropathy (National Cancer Institute, 2010).

The European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy (EORTC QLQ-CIPN 20): The scale was developed by Postma et al. to evaluate the effect of the chemotherapy-induced peripheral neuropathy on quality of life; the Turkish validity and reliability study was conducted in 2015 by Onsuz. It is a 20-item assessment tool that is used to elicit chemotherapy-induced peripheral neuropathy symptoms and why this problem occurs, and the effect of functional limitations on the patients' lives. The scale has 3 sub-dimensions including sensory subscale (tingling, numbness, pain, unbalance when walking or standing, recognizing the temperature difference and hearing), motor subscale (cramps, writing, grasping small objects, weakness) and autonomic subscale (dizziness after changing position, vision, erectile dysfunction). There are 20 likert-type items in the scale and they are evaluated according to following options: "No-1 point", "A little-2 points"; "Fairly-3 points"; "Very Much-4 points". Receiving high scores from these sections indicates more symptoms and problems, while lower scores indicate less symptoms and problems. The Cronbach's alpha coefficients of the scale for the sensory and motor sub-dimension are 0.78 and 0.85, and -0.059 for the autonomic sub-dimension (Onsuz, 2015).

Data Analysis: The analysis of the data in the study was performed using the IBM SPSS 21.0 package program (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Values belonging to categorical variables were presented as frequency and percentage. The normal distribution of data was verified using the Shapiro-Wilk test. Mann Whitney U test was used in comparison of two groups with non-normal distribution. We considered $p < 0.05$ as statistically significant.

Results

The mean age of 115 patients who participated in the study was 55.95 ± 16.39 years, 56.5% of whom were male, 79.1% of whom were married, 45.2% of whom had non-hodgkin's lymphoma and 40% of whom have received RCHOP chemotherapy protocol (Table 1).

Table 1. Distribution of socio-demographic and disease characteristics

Characteristics	$\bar{x}$ **±sd (Min-Max)**	
Old(year)	55.95±16.39(18-83)	
Gender	**n**	**%**
Female	50	43.5
Male	65	56.5
Marital status		
Married	91	79.1
Single	24	20.9
Disease		
Hodgkin l*ymphoma*	19	16.5
Nonhodgkin *lymphoma*	52	45.2
Multıply myeloma	29	25.2
Acute leukemia	8	7
Chronic leukemia	3	2.6
Myelodysplastic syndrome	4	3.5
Chemotherapy		
R-CHOP	46	40
VAD	30	26.1
ABVD	15	13
Hiper CVAD	6	5.2
Vidaza	4	3.5
Mapthera	4	3.5
Nivolumab	3	2.6
CHOP	2	1.7
RFC	2	1.7

İmnovid	1	0.9
Darzalex	1	0.9
Dacogen	1	0.9
Number of cures		
Third	20	17.4
Fourth	34	29.6
Fifth	19	16.5
Sixth	10	8.7
Seventh and more	32	27.8
Total	115	100

Table 2. Distribution of NCI-CTCAE v4.03 grade

Grade	n	%
0 Asymtomatic	73	63.5
1 Moderate symptoms	32	27.8
2 Severe symptoms	10	8.7
3 Life-threatening consequences	0	0
4 Death	0	0

Table 3. Distribution of EORTC QLQ-CIPN 20 scores according to symptoms of peripheral neuropathy

Subscales	Peripheral neuropathy				p*
	Asymtomatic		Symtomatic		
	n	Median±sd	n	Median±sd	
Sensory subscale	103	25.72±8.33	12	36.16±7.12	0.001
Motor subscale	90	23.50±11.82	10	28.50±14.56	0.093
Autonomic subscale	83	36.33±18.92	10	37.33±10.29	0.047

*Mann Whitney U test

In the scope of the research, peripheral neuropathy was detected in 36.5% of the patients. Moderate symptoms were identified in 27.8% of the patients diagnosed with peripheral neuropathy, whereas severe symptoms were identified in 8.7% of the patients (Table 2).

According to the NCI-CTCAE v4.03, the mean score of sensory subscale in patients without peripheral neuropathy was 25.72±8.33, the mean score of motor subscale was 23.50±11.82, and the mean score of autonomic subscale was 36.33±18.92; the mean score of sensory subscale in patients diagnosed with peripheral neuropathy was 36.16±7.12, the mean score of motor subscale was 28.50±14.56, and the mean score of autonomic subscale was 37.33±10.29.

The sensory and autonomic subscale mean scores of patients diagnosed with peripheral neuropathy (from moderate to severe level) were found in the research to be statistically significantly higher than scores of those who were without neuropathy (p=0.001, p=0.047 respectively) (Table 3).

Discussion

In our study, it was identified that R-CHOP protocol consisting of cyclophosphamide, doxorubicin, vincristine, prednisolone and rituximab was administered to 40% of patients out of 115 patients, who underwent chemotherapy for the first time and at least 3 cycles due to hematological cancer, and VAD chemotherapy protocol consisting of vincristine, adriamycin and dexamethasone was administered

to 26.1% of patients out of the same 115 patients. The grade 1 peripheral neuropathy was detected in 27.8% of patients, while the grade 2 peripheral neuropathy was detected in 8.7% of patients. In our study, patients with peripheral neuropathy were found to have a lower quality of life related to CIPN than those without peripheral neuropathy. This result confirms our hypothesis.

Diouf et al (2015) reported grade 2 and 3 peripheral neuropathy in 28.8% of pediatric patients who received 36-39 doses of vincristine due to ALL (Diouf et al., 2015). Another study conducted on children with ALL reported that according to NCI-CTCAE v4.03 the sensory neuropathy frequency was between grade 1 (31%) and grade 2-3 (3.2-1.6%) and the motor neuropathy frequency was between grade 1 (18%) and grade 2-3 (4.4-1.9%) (Smith et al., 2015). When it comes to the meta-analysis of Scott et al. (2016), it was reported that peripheral neuropathy was found in 13.75% of patients using bortezomib due to multiple myeloma, and comparing to the control group, the risk of peripheral neuropathy was significantly high in patients treated with bortezomib (Kathleen Scott et al., 2016). In addition, in one case study, a patient who had been on imatinib (400 mg / day) for 10 years due to chronic myeloid leukemia was diagnosed with axonal neuropathy upon the complaints of burning sensation in extremities and the complaints of the patient were decreased by using nilotinib (300 mg 2 times / day) instead of imatinib (Kavanagh et al., 2018). Chi-Eun et al (2015) reported 19.7% tingling, 30.3% numbness, 15.2% burning sensation (in the fingers) in upper extremities and 36.4% tingling, 42.4% numbness, 30.3% burning sensation (in the fingers) in the lower extremities in patients (aged over 49 years) who underwent one or more administration of vincristine, thalidomide, bortezomib or lenalidomide due to hematological cancer (Eun, ChYoung and Sook, 2015). Agents such as vinca alkaloids, thalidomide, lenalidomide and bortezomib, which are used in hematological cancers, cause CIPN. While the mechanism of CIPN is not fully elucidated, chemotherapeutic agents damage neuronal bodies, myelin sheath and axonal components (Argyriou et al., 2012). The conducted studies have shown that the incidence and severity of CIPN in haematological cancers vary according to a drug and its duration of use (Diouf et al., 2015; K Scott et al., 2016; Smith et al., 2015). It can be said that this situation looks similar to the result of our research. Therefore, it will be beneficial in terms of the prevention of potential risks if nurses inform the patients who have undergone chemotherapy due to hematologic cancer and their relatives about CIPN and follow-ups of the patients are provided during and after the treatment.

In a study conducted, it was emphasized that the incidence of CIPN is increased in proportion to age of the children, and this is due to the fact that a child is able to better define and report the symptoms as age increases (Smith et al., 2015). Alberti et al (2014) emphasized that CIPN was seen at different rates according to patient and physician evaluations, thereby the evaluations should examined from both sides (Alberti et al., 2014). In our study, CIPN results are limited to the self-reports given by patients according to the NCI-CTCAE v4.03 scale. Therefore, we would recommend to researchers who will conduct studies regarding CIPN in hematological cancers to include the results of the physical examinations performed by health professionals and the information obtained from the patients.

According to the information obtained from the literature, it has been identified that there is a limited number of studies on evaluation of the quality of life associated with CIPN in patients with hematologic cancers (Beijers et al., 2016; Eun et al., 2015). Therefore, this part of the discussion continues with the results of limited number of studies conducted on patients with hematologic cancers and the quality-of-life outcomes associated with CIPN in patients with solid tumors. Beijers et al (2016) reported that the quality of life associated with CIPN was low in patients with multiple myeloma. Another study reported that the CIPN-related quality of life of hematological cancer patients was lower in the lower extremities than in the upper extremities (Eun et al., 2015). Varedi et al (2018) reported the long-term CIPN-related difficulty in walking and moving and sensory problems in the patients with ALL (Varedi et al., 2018). Two studies on solid tumors, in which the same with us an assessment tool was used, reported that as the severity and symptoms of CIPN increase, the quality of life decreases (Kutluturkan et al., 2017; Simon et al., 2017). Another study reported that CIPN was detected in the upper extremities (78.8%) and in the lower extremities (89.7%) during the evaluation performed 6

months after the last treatment of the patients who had been treated with taxane or oxaliplatin for 2 years, and as the result, 12.8% experienced difficulty in doing housework, 20.5% became dependent on someone else and 48.6% had a low quality of life (Beijers et al., 2014); while Egan (2015) reported that CIPN-related quality of life was minimally affected after an average of 5 weeks after completion of the platinum and taxane-based treatment (Egan et al., 2015). When the results of studies on solid tumors and hematological cancers are evaluated, it is seen that as the symptoms of peripheral neuropathy increase, patients experience difficulty in daily life activities and the quality of life decreases. As the authors of our research, we can state that these results are similar to the results of our research (Beijers et al., 2016; Varedi et al., 2018).

Conclusion

We believe that the results of our research contribute to the limited knowledge about the health-related quality of life associated with CIPN in patients with hematologic cancers. In this study, the responses to the CIPN-related quality of life scale are limited to the patients' self-reports. Meanwhile, since the sampling of the study was not large enough, and nonparametric tests were used, and the limited number of studies on this issue was conducted, comments on the results are brought into question. Therefore, we recommend that more studies with the large sampling are conducted on this regard and that results of physical examinations performed by nurses and patients' statements are included in the future conducted studies.

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