

Effects of reflexology on chemotherapy-induced peripheral neuropathy in patients with colorectal cancer referred to selected hospitals of Kerman University of Medical Sciences, Iran, in 2019

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Abstract

Background and aim: Colorectal cancer (CRC) is the third most common cancer and the fourth leading cause of death in the world. Systemic therapies for the early and advanced stages of the disease may develop chemotherapy-induced peripheral neuropathy (CIPN). The purpose of this study was to determine the effectiveness of reflexology on the CIPN in the patients with CRC. **Materials and methods:** The present interventional study was conducted on 70 patients with CRC randomly assigned in two equal groups (n=35) of experimental and control. Data were collected using S-LANSS scale and demographic information questionnaire. The executive protocol of reflexology was practically trained for the patient caregiver. After four weeks of intervention, the questionnaires were re-completed by patients of both groups. Data were analyzed by SPSS software using independent t-test and paired t-test. **Results:** A significant decrease in the mean score of pain intensity was observed in the experimental group after the intervention compared to the control group (p-value<0.001). **Conclusion:** Our findings demonstrated that the reflexology had a positive effect on improving the pain intensity of CIPN patients in the experimental group, so nurses can exploit the results of this study to improve patients' comfort and convenience.

Keywords: Chemotherapy-Induced Peripheral Neuropathy, Reflexology, Colorectal Cancer

INTRODUCTION

Cancer is one of the most common non-communicable diseases throughout the world, accounting for over 13% of deaths [1]. The American Cancer Society (ACS) declared more than 15.5 million Americans with a history of cancer as of January 1, 2016. The most common cancers in the United States are prostate, colon, rectal, and melanoma cancers in men, and uterine, colon, and rectal cancers in women [2]. In Iran, the prevalence rate of colorectal cancer (CRC) is 11.6 in men and 10.5 in women, with the 5-year survival rate of 41% [3]. Evidence suggests that high consumption of processed red meat and alcohol increases the risk of CRC, and milk and legumes may play a protective role against CRC [4].

The type of treatment is chosen based on the stage of the disease, and surgery is the definitive treatment in the early stage of the disease. Today, chemotherapy and sometimes radiotherapy are employed in certain stages of CRC [5]. Fluorouracil (5-FU) was the only drug available to treat CRC until the mid-1990s. The introduction of two new cytotoxic drugs, Irinotecan and Oxaliplatin in combination with 5-FU, led to significant advances in the CRC therapy, known as

first-line CRC therapy, and increased the mean survival rate to 14-19 months [6]. Chemotherapy in most cancers is a type of treatment that is associated with neurological complications [7]. Recipients of chemotherapy drugs develop the complication of Chemotherapy Induced Peripheral Neuropathy (CIPN) with different symptoms depending on age, drug dosage, cumulative dosage, duration of treatment, and other factors such as diabetes and alcohol abuse [8]. The CIPN is a common side effect caused by neurotoxic supplements, including platinum, taxanes and vinca

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How to cite this article: Beigmoradi, S., Nouhi, E., Movafegh, F., Ramazanpour, M., Soltani Nejad, E., Shakouri, A. Effects of reflexology on chemotherapy-induced peripheral neuropathy in patients with colorectal cancer referred to selected hospitals of Kerman University of Medical Sciences, Iran, in 2019. Arch Pharma Pract 2020;11(S4):103-8.

alkaloids, with a prevalence of 30 to 80%^[9]. It typically affects organs such as the hands and feet, with sensory symptoms (numbness, tingling, and pain), and neuropathic symptoms (cold and heat stimulation) as well as motor symptoms (muscle cramps, and balance and gait problems)^[10]. Park *et al.* (2013) found that 40% of cancer survivors experience persistent and debilitating symptoms of CIPN^[11].

The main symptoms of CIPN depend on the used drug and dose, and are usually associated with weakness and loss of sensations and reflexes^[7]. Reportedly, 68.1% of patients undergoing chemotherapy in the first month and 60% during 3 months after chemotherapy and 30% after 6 months develop the CIPN complications^[12]. About 60% of patients with CRC receive Oxaliplatin, and CIPN resolves over time in 48% of patients after receiving the drug^[13].

The most common complaint of patients with CIPN is loss of sensation^[14]. In approximately 90% of patients with acute neuropathy, the CIPN occurs within a week; and in 60% of patients, it persists for a year or more after stopping chemotherapy^[15]. Several studies have reported that static and dynamic balance maintenance in people with CIPN is significantly reduced^[16-18]. Turcot *et al.* found that people with peripheral neuropathy had poor balance^[19], and Alley *et al.* also showed an increase in sensory disturbance and balance in patients with peripheral neuropathy over time^[17].

Neuropathic pain is a chronic pain resulting from damage to the central or peripheral nerves. In this type of injury, sensory and motor fibers as well as fiber receptive field are disturbed and the most important symptom is increased pain intensity^[20]. The CIPN symptoms can be relieved with the use of vitamin E, carnitine, omega-3, glutamine, alpha-lipoic acid, glutamate, supplement therapy, massage therapy, acupuncture, yoga, Tai Chi exercise, physical activity and exercise^[21]. Factors such as lack of response to appropriate treatment of conventional medicine, coordination of complementary medicine treatments with the patient's own nature, low cost and simple treatment are among the reasons for patients' tendency to complementary medicine methods^[22].

Reflexology is a non-invasive, convenient and easy method of treating cancer patients, so that some patients consider this method as an alternative to drugs^[23], which improves the quality of life and reduces stress in such patients^[24].

Reflexology is a treatment in which the fingers are used to apply pressure to the feet or hands, and are prescribed to various patients such as migraine headaches, respiratory problems, pain, stress and anxiety^[25]. Pressure of the fingers on the centers stimulates hundreds of nerve terminals in the sole of the foot and releases endorphins, which prevent pain transmission and thus develop relaxation and numbness, thereby reducing tension and increasing peace of mind^[26].

Taso *et al.* found the positive effect of massage therapy on chronic non-cancer pain^[27].

Nursing is one of the first professions that can facilitate the use of complementary and alternative medicine (CAM) because nurses look at clients as a holistic view, and the CAM is the answer to this philosophy, which is used as an intervention for many nursing diagnoses^[28]. Massage is one of the most important complementary therapies in the science of nursing, which is considered valuable by many nurses; the massage in nursing increases the possibility of providing comprehensive care. One of the goals of nursing care is to provide comfort and convenience for patients, so experts recommend complementary medicine as a factor for patients' comfort^[25]. The nurses can perform complementary therapies such as reflexology in conjunction with routine care. However, because many of these treatments cannot be supported due to insufficient scientific evidence, the nurses are placed in a special position in terms of assessing and recognizing patients' need for such interventions and accepting evidence-based therapies^[29].

Since the massage is a nursing intervention that can be implemented for all individuals in any socioeconomic class, and on the other hand, due to limited studies on the effect of reflexology on peripheral neuropathic pain in the patients with CRC, the current study aimed to evaluate the effect of reflexology on the CIPN in the patients with CRC referred to Shahid Bahonar Hospital, Kerman Iran.

MATERIALS AND METHODS

The present interventional study was conducted in 2019 in the oncology wards of Shahid Bahonar Hospital affiliated to Kerman University of Medical Sciences, Iran. The study population was all cancer patients and the study sample was the CRC patients admitted to oncology wards 1 and 2 of Shahid Bahonar Hospital. The sample size was estimated to be 70 patients with CRC in the second or third stage according to the study of Kurt and Can (2018)^[30] in Turkey, with a confidence interval of $z = 1.96$, test power of 80% and using the formula of

$$n_{\text{ per / group}} = \frac{(\sigma_1^2 + \sigma_2^2) (z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2} \text{ considering}$$

10% dropout. Inclusion criteria were the age range of 18-85 years, awareness of time and place, informed consent to participate in the study, incidence of CRC in stages II and III, hospitalization in oncology ward, and having a permanent caregiver with the ability to perform reflexology at home. Exclusion criteria were a history of mental illness based on the information in the medical record, the patient's emergency condition, a history of taking any medication or supplement affecting neuropathic pain. Data were collected using the demographic information questionnaire and the Stands for Leeds Assessment Questionnaire of Neuropathic Symptoms and Signs (S-LANSS) scale. The S-LANSS scale consists of two parts. The first part includes interviewing the patient for

clinical evaluation based on the patient examination (two questions). In the first question, the areas of the body where the patient felt pain were hatched on the shape in the questionnaire. In this study, the patients with leg pain were considered. The second question is related to the severity of pain felt during the last week, indicating "score zero" as the lowest pain intensity and "score 10" as the highest pain intensity. The second part of the questionnaire was related to feeling pain (seven questions), with scoring based on "Yes" or "No". The total neuropathy score was obtained by adding the scores of the questions, which was a minimum score of zero and a maximum of 24. A score less than 12 indicated that neuropathic mechanisms had no effect on the patient's pain intensity and a score of 12 or higher indicated the effect of neuropathic mechanisms on the patient's pain intensity. First, the instrument was re-translated, the content and face validity of the mentioned instrument was performed using the opinions of 10 faculty members of the School of Nursing and Midwifery of Kerman University of Medical Sciences and three nurses working in the oncology wards of Shahid Bahonar Hospital. The reliability of the present questionnaire was measured using Cronbach's alpha coefficient and correlation coefficient ($r = 0.82$).

Data were collected through interviews and questionnaires completed by patients and reassuring about the confidentiality of information in both control and experimental groups before and after the intervention. The researchers collected samples after obtaining the approval of the Ethics Committee (IR.KMU.REC.1398.342), presenting a written letter of introduction, coordinating with the officials of the research environment, explaining the study objectives and obtaining informed consent from patients. Patients were randomly divided into control and experimental groups of 35 patients. There was no gender restriction (male or female) in the study; the two groups were homogenized in terms of treatment regimen, and age and sex distribution. In order to prevent information interference between the control and experimental groups, the days of the week were used as a criterion for random selection of samples. The control group received routine care measures of the center (follow-up tests and doctor's visits, etc.). In the experimental group, the intervention started from the second course of chemotherapy when the symptoms of taxane-induced peripheral neuropathy (TIPN) appeared in the patients. Prior to the intervention, the patient was given the necessary explanations about the importance of reflexology and its effect on improving the complications of CIPN. In this study, the intervener underwent theoretical and practical training in foot reflexology (performing relaxation and massage techniques on the soles of the feet) and proceeded to perform the intervention after obtaining a certificate. During the massage, the intervener took off their watch, ring and bracelet. They trimmed their fingernails. Sesame oil was used to reduce friction between the intervener's hand and the patient's legs^[31]. The reflexology intervention for the experimental group included preparation, warm-up, and stimulation and massage techniques in the reflection points of the spine and solar

plexus (back of the stomach, respiratory system, lungs, diaphragm, arm, knee and hip areas, eyes, ears, big toe, nails, face, head, brain, sinuses, parathyroid, thyroid, lymphatic system, stomach, pancreas, liver, gallbladder, adrenal glands, kidney, ureter, bladder, spine, small intestine, colon and pituitary gland) and treatment points on the left and right soles of the feet. The reflection point of the spine is located at the inner edge of the sole of the foot, which starts from the end of the first toe and leads to the heel of the foot, and the solar plexus is located at the end of the first metatarsal bone of the sole of the foot^[32], which was performed by warming the feet with the hands, doing specific movements of holding the over and under the feet with both hands, creating movements of bending backwards, bending the soles of the feet, and rotating outwards and inwards and movements in the heels. To stimulate the reflection points of the spine and the solar plexus, the massage was performed using the fingers as backward and forward movements and applying a pressure of about 0.5 cm^[33]. For the first time in the hospital, the intervener taught patients and their caregivers how to do massage in a practical way, and the caregivers practiced reflexology in the presence of the intervener, and their questions were answered. The patients and their caregivers were monitored by telephone during the intervention at home; they were also given a video on how to massage. The foot massage for patients in the experimental group was performed by the patient's main caregiver at home for four weeks, twice daily in the morning and evening for 10 minutes on each foot. The control group received no intervention. Two weeks after the intervention, the patients in both groups re-evaluated the signs and symptoms of neuropathic pain. Data were analyzed by SPSS version 22 software using analytical and descriptive statistics, numerical description of frequency distribution, mean and standard deviation. Due to the normal distribution of data, paired t-test was performed to analyze the data from before and after the intervention and independent t-test was used to compare the two groups.

RESULTS

Demographic information, including gender, age, marital status, educational level and occupational status, in the experimental and control groups are presented in Table 1. According to the results of the study, the participants in the study were 65% men and 34% women in the control group and 57% men and 42% women in the experimental group. The mean age of patients was 59.34 ± 14.54 years in the control group and 56.77 ± 15.67 years in the experimental group; 60% of the control group and 51% of the experimental group were married, but there was no significant difference in marital status between the two groups (p -value = 0.470). The highest number of patients in the control and experimental groups had the educational level of high school (40%) and higher (31%); there was no significant difference in the educational level between the two groups (p -value = 0.837).

The results of the disease stage showed that 57% of patients were in the second stage of the disease, and there was no

significant difference between the two groups in the disease stage (p-value = 0.473). Table 2 shows the overall pain score before and two weeks after the intervention. The mean pain intensity before the intervention was 6.37 ± 1.49 in the control group and 5.77 ± 1.83 in the experimental group (p-value = 0.138), indicating that the experimental and control groups were homogeneous for the contextual variables and pain intensity before the intervention.

In addition, the mean pain intensity after the intervention was 6.34 ± 1.53 in the control group and 4.94 ± 1.75 in the experimental group (p-value = 0.001). There was a significant difference in the mean pain intensity after the intervention between the control and experimental groups (p-value = 0.001).

Table 1- Demographic and contextual variables of the research units in the two experimental and control groups admitted to the Shahid Bahonar Hospital affiliated to Kerman University of Medical Sciences, Iran

Variables	Control group		Experimental group		Chi-square test results	P-value	
	Frequency	Percentage	Frequency	Percentage			
Gender	Male	23	65.7	20	57.1	0.543	0.461
	Female	12	34.3	15	42.9		
Age group	≤50	11	31.4	14	40.0	0.560	0.454
	>50	24	68.6	21	60.0		
Marital status	Married	21	60.0	18	51.4	0.521	0.470
	Single	14	40.0	17	48.6		
Educational level	<High school	10	28.6	8	22.9	0.536	0.837
	High school	14	40.0	16	45.7		
	>High school	11	31.4	11	31.4		
Occupational status	Unemployed	13	37.1	17	48.6	0.933	0.334
	Employed	22	62.9	18	51.4		

Table 2 - Comparison of the mean pain intensity score of the research units in the two experimental and control groups admitted to the Shahid Bahonar Hospital affiliated to Kerman University of Medical Sciences, Iran

Pain intensity score	Control group		Experimental group		Independent t-test results	P-value
	Mean	Standard deviation	Mean	Standard deviation		
Before intervention	6.37	1.49	5.77	1.83	1.50	0.138
After intervention	6.34	1.53	4.94	1.75	3.563	0.001

DISCUSSION

The aim of this study was to evaluate the effect of reflexology on CIPN in patients with CRC, the results of which showed that the mean pain score before the intervention in the experimental and control groups was not significantly different. However, the mean pain score after reflexology in the experimental group significantly decreased compared to the control group, indicating the positive effect of massage therapy intervention on patients' pain. The results of the present study are consistent with the findings of Stephenson *et al.* (2003) who investigated the effect of reflexology on pain in patients with breast cancer. In addition, the study reported that people in the experimental group had less pain in the experimental group 24 hours after the intervention than those who received opiates [34]. Wyatt *et al.* (2012) also

demonstrated that the foot massage can significantly affect the physical function and alleviate the dyspnea in the experimental group compared to the placebo and control groups, as well as reduce levels of fatigue, depression, anxiety, pain, nausea and vomiting in patients with breast cancer [35]. Ibrahim MM and Rizk SMA (2018) also indicated that patients' pain scores after reflexology were significantly lower than the control group [36].

Massage affects the sensation and perception of pain in different ways and is a method of physical removal of waste products from muscle tissue. Once the body is trained, stroked and warmed, the blood flow increases and nutrients and oxygen are delivered into the desired area [37]. The activity of the lymphatic system is increased, thus removing

waste products and reducing the effects of pain-inducing chemicals. This removal of chemical neurotransmitters is probably the best explanation for understanding the effects of massage. On the one hand, the massage reduces pain and discomfort by removing waste products in the tissues, and on the other hand, it leads to raising the pain threshold of nerve receptors, because if we start the massage gently and increase the intensity of its movements gradually, it will be possible to reduce the sensitivity of pain receptors and increase the pain threshold [38].

Deep tissue massage therapy relaxes and dilates blood vessels and stimulates nerve endings, although the massage does not directly improve muscle strength, but theoretically it can be said that the massage reduces fatigue and increases the possibility of muscle activity and indirectly increases endurance. Miladinia *et al.* [39] and Robinson *et al.* [40] reported that the foot massage in patients undergoing chemotherapy reduced pain, vomiting, fatigue and nausea. Bagheri-Nesami *et al.* (2014) also found that fatigue and pain intensity of patients in the experimental group were significantly different after the intervention compared to the control group [41]. Eom *et al.* (2019) also showed that the sleep quality and muscle strength of the experimental group increased after the onset of reflexology, and joint pain decreased four weeks after the intervention [42]. In contrast to the present study, Albert *et al.* (2009) did not find significant differences in pain intensity between the two study groups after massage therapy in patients undergoing heart surgery [43]. In a study by Pan *et al.* (2014), the patients with breast cancer who used massage continuously had significantly fewer symptoms of anger and fatigue; however, in their study, no significant differences were observed in the massage therapy group in terms of depression, anxiety, pain and upper extremity lymphedema, cortisol levels and quality of life [44]. Contradictory results of the present study can be due to individual differences and moods of the subjects in response to the intervention and its impact, as well as environmental and cultural factors affect the perception of the impact of massage technique. On the other hand, there may be differences in the practice of massage technique between caregivers, which can affect the results.

CONCLUSION

The results of the present study showed the important role of touch in stimulating the afferent receptors in individuals. Given that the mechanism of action of reflexology to some extent causes relaxation and that this does not happen with just a simple touch but also causes relief due to the application of this method on different parts of the sole of the foot and improves symptoms in people, as well as due to its simplicity and low cost, this method may be used as a complementary medical approach to pharmacotherapy and analgesics. Since non-pharmacological treatments along with specialized therapies are highly regarded to improve the symptoms of stress, pain and anxiety in patients with chronic diseases, but there is still need for further research to confirm the greater effectiveness of reflexology on the reduction of the pain and

symptoms caused by the chemotherapy-induced peripheral neuropathy in medical and educational centers to improve the quality of life of patients. One of the limitations of this study is the small number of oncology centers in Kerman and the implementation of the reflexology by the patient's caregiver.

ACKNOWLEDGMENTS

The current article has been adopted from a research project with the approval of the Ethics Committee (IR.KMU.REC.1398.342) of the School of Nursing and Midwifery at Kerman University of Medical Sciences, Iran. The researcher appreciates the Deputy of Research of the School of Nursing and Midwifery at Kerman University of Medical Sciences, the authorities of Shahid Bahonar Hospital and the participants in this project.

Conflict of interest

The authors declare no conflict of interest in all stages of the research.

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