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The effect of Peripheral Neuropathy Induced the Oxaliplatin in Patients with Colon Cancer

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ABSTRACT

Colon cancer is one the most common forms of cancer in both sexes. Due to important progress in the field of early detection and effective treatment, colon and rectal cancer survivors currently account for 10% of cancer survivors worldwide. However, the effects of anti-cancer treatments, especially oxaliplatin-based chemotherapy, on the quality of life (QoL) have been less evaluated. Oxaliplatin is a platinum compound that inhibits DNA synthesis, primarily by causing intrastrain cross-links in DNA. Oxaliplatin has a broad spectrum of antineoplastic activity and has demonstrated a lack of cross-resistance with other platinum compounds. Objective of the study: determining the effect of acute toxicity neuropathy caused by oxaliplatin and its effect on the lives of selected patients. Patients and methods A hospital-based observation study was conducted during a 4-month period on 50 patients with colon cancer who were interviewed and reviewed in the oncology department at Tripoli University Hospital. Results: A total of 50 patients participated in the study; the majority were male (70%) and were more than 50 years old (76.0%).Over three quarters (76.0%) of the patients work in an enclosed space. We found that the majority (86.0%) of patients were non-smokers, that two-thirds (66.0%) of patients were at stage 3 of the disease, nearly a quarter (26.0%) at stage 4, only four patients (8.0%) at stage 2, and no patient at stage 0 or stage 1. reported that (32.0%) of patients receiving oxaliplatin had kinetic symptoms, (48.0%) had sensory symptoms, and 20% had movement symptoms. As for neurotoxicity, 10 cases had chest pain only (20%), and 6 cases had difficulty breathing only (12%) and when we counted the cases that combined both symptoms together, they were 3 cases who showed symptoms of acute toxicity all at the same time. Conclusion: We concluded that males over the age of 50 are more likely to develop colon cancer and that neuropathy is not related to its effect by increasing the cumulative dose, but is related to the number of doses taken by the patient and the disease, and by neurotoxicity was 10 cases suffered from chest pain and 6 from difficulty breathing and 3 cases appeared on them symptomatic together, and in proportion to the symptoms of general neuropathy has appeared on all 50 cases that we conducted purely on them has suffered 16 cases out of 50 of the symptoms of subjective symptoms only 32%, and sensory symptoms appeared by 24 cases out of 50 cases by 48%, and motor symptoms on 10 cases out of 50 by 20%, the most targeted patients with oxaliplatin are patients of the third stage 66% were fourth 26% who suffer from chronic diseases such as sugar and blood pressure.

1. INTRODUCTION

Colon cancer is one the most common forms of cancer in both sexes. Due to important progress in the field of early detection and effective treatment, colon and rectal cancer survivors currently account for 10% of cancer survivors worldwide (Singh, V. P. et al. 2014). However, the effects of anti-cancer treatments, especially Oxaliplatin-based chemotherapy, on the quality of life (QOL) have been less evaluated. Although the incidence of severe chemotherapy-induced neuropathy (CIPN) in clinical studies is below 20%, data from real-world studies is scarce, and CIPN is probably under-reported due to patient selection and the patients' fear that reporting side-effects might lead to treatment cessation Oxaliplatin is a platinum compound that inhibits DNA synthesis, primarily by causing intrastrand cross-links in DNA (Timmins, H. C. et al. 2022). Oxaliplatin has a broad spectrum of antineoplastic activity and has demonstrated a lack of cross-resistance with other platinum compounds (Prutianu, I et al. 2022). Oxaliplatin accumulates in dorsal root ganglia, causing an axonal neuronopathy. Symptoms include numbness, pain and gait disturbance which may persist and impact on quality of life (QOL). Despite widespread use of this drug its late effects and patient satisfaction outcomes have not been widely reported (Tofthagen, C. et al. 2013). Furthermore, there has been limited qualitative research published in this Given that the clinical course of oxaliplatin-induced neuropathy is not well defined, the current study was performed to better understand clinical parameters associated with its presentation (Cavaletti, G et al. 2020). The neurological effect caused by oxaliplatin to colon cancer patients It affects the sensory and motor functions as well as the acute toxicity problems that were challenged to patients during the treatment leakage. Cancer refers to any disease within a large number of diseases characterized by the development of abnormal cells that divide in an uncontrollable way and have the ability to infiltrate and destroy normal body tissues (Labianca, R et al. 2010). Cancer often has the ability to spread throughout the body Cancer is the second leading cause of death in the world. But survival rates are improving for many types of cancer thanks to improvements in cancer detection, treatment and prevention (Griffith, K. A et al. 2017). Cancer is a leading cause of death worldwide, claiming nearly 10 million lives in 2020, or nearly 1 in 6 deaths The most common types of cancer are breast cancer, lung cancer, colorectal cancer, and prostate cancer About a third of cancer deaths are attributed to tobacco use, high body mass index, alcohol use, low intake of fruits and vegetables, and lack of physical activity Cancer-causing infections, such as human papillomavirus infection and hepatitis, account for approximately 30% of cancer cases in low- and lower-middle-income countries (Dault, R. et al. 2016). The most common cancer types are Breast cancer, Prostate cancer, Colorectal cancer, Melanoma, Bladder cancer, non-Hodgkin lymphoma, Kidney cancer…etc (Bodalal, Z. et al. 2014). This is a type of cancer that affects the colon, the colon is the last part of the large intestine of the digestive system Colon cancer is a cancer that occurs in the last 15 centimeters of the colon that meets a part of the rectal area and these two types of cancer are called colorectal cancer or colonic rectum cancer In most cases, colon cancer begins as a small mass of non-cancerous cells called adenomatous polyp, after a period of time the polyps that formed become cancerous masses in the colon. These strains may be small and accompanied by very few if any symptoms, and regular imaging scans can prevent the development of colon cancer by early detection of polyps before they turn into cancerous tumors (Comella, P. et al. 2009). Oxaliplatin plays a major role in the treatment of colorectal cancer (CRC), but is associated with the development of neuropathies (Zribi, A. et al. 2020, Hughes R. A. 2002). Oxaliplatin is a cytotoxic chemotherapy drug used to treat cancer (Jack, M. et al. 2012). It is a type of platinum drug and an alkylating agent Like other alkylating agents, oxaliplatin works by interfering with the development of DNA in a cell. It stops cells from growing and multiplying and kills them (Kaur, J.et al. 2020). This helps to treat cancer which is caused by cells rapidly growing and dividing out of control. It has connected connecters that lead to filament relapses and DNA is slowed down (Kim, S. H et al. 2018, Sugimoto, K. et al. 2008). The aim of the study to determining the effect of acute toxicity neuropathy caused by oxaliplatin and determining of symptoms in patients receiving oxaliplatin by sensory, motor or, kinetic type. Comparison of the severity and cumulative dose of neuropathy effect symptoms between doses from 2 to 3 weeks for three months with colon cancer patients. Comparison of neuropathy of patients receiving oxaliplatin between genders.

2. METHOD

Place of Study

Place of this Study at the oncology department in Tripoli University Hospital, starting from March to May 2023.

Study population

The study included 50 patients with colon cancer who were interviewed and reviewed in the oncology department at Tripoli University Hospital.

Study tool

The data was collected through a questionnaire, which included the following:

1. Demographic characteristics: age, gender, family history of chronic illness, marital status, nature of work, exposure to smoke and sources of environmental pollution, stage of the disease

2. Oxaliplatin dose and current dose, and when do you have the first signs and symptoms of neuropathy?

3. Questions regarding peripheral neuropathy symptoms, which include sensory symptoms, movement symptoms, and kinetic symptoms

Data management and statistical analysis

The collected data were sorted, coded, then entered and analyzed using SPSS, version 25.0. Quantitative data were expressed as numbers and percentages. We would compare the severity and cumulative dose of neuropathy effect symptoms between doses from 2 to 3 weeks for three months with colorectal cancer patients using Spearman's correlation. A p value of less than 0.05 was considered statistically significant.

3. RESULT

Demographic characteristic of participants

A total of 50 adults participated in the study with cancer of colon at Tripoli university hospital, Libya.

Gender

In total of patient with cancer of colon (n= 50), the study showed that female's percentage was about 30.0% (n=15) and males about 70.0% (n= 35) as showed in figure 1.

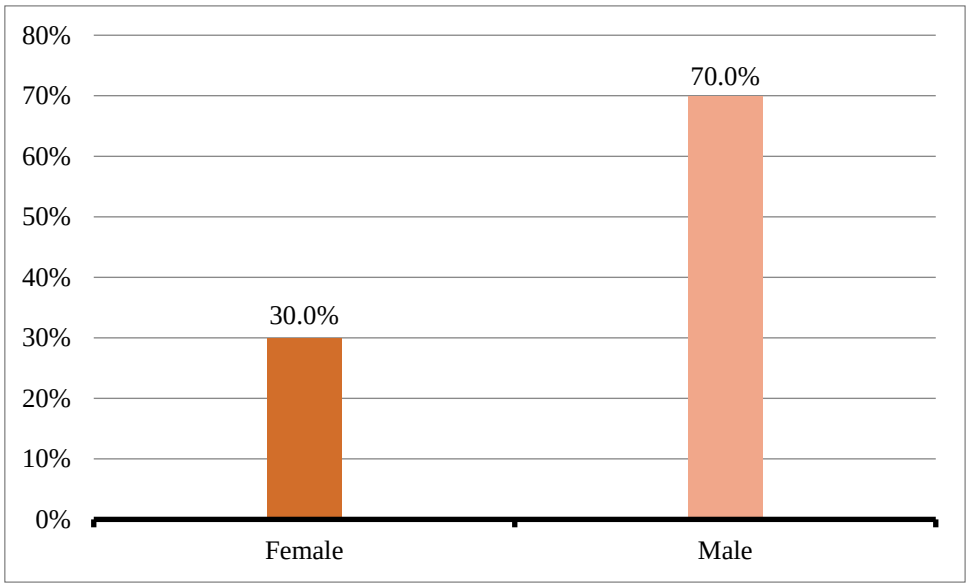

Figure 1: Distribution of patients according to sex.

Age: According to the distribution of age ranges, the highest group of patients with colon cancer were in age more than 50 years old by 76.0% in compare to age ranges 30-50 years was 24.0%, as showed in figure 2.

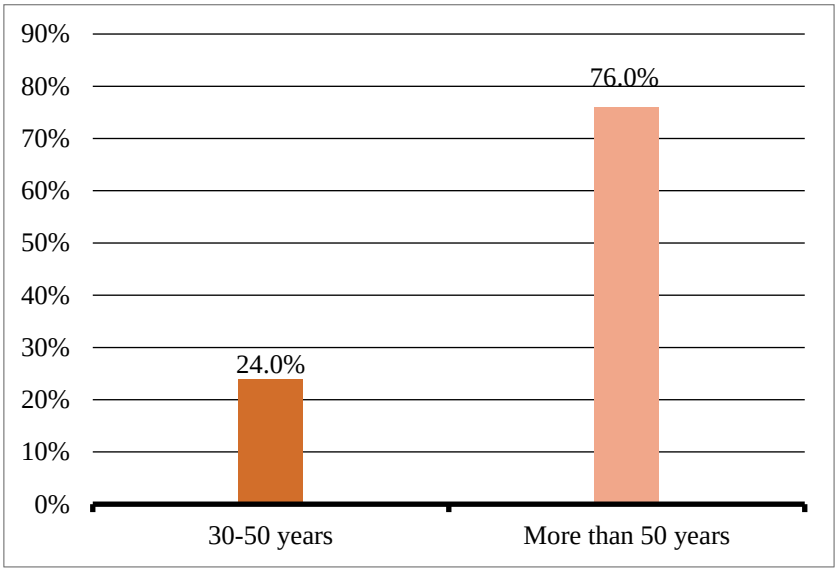

Figure 2: Distribution of patients according to age group.

Marital status : We found that majority (96.0%) of patients with colon cancer were married, while only two patients (4.0%) were unmarried as showed in figure 3.

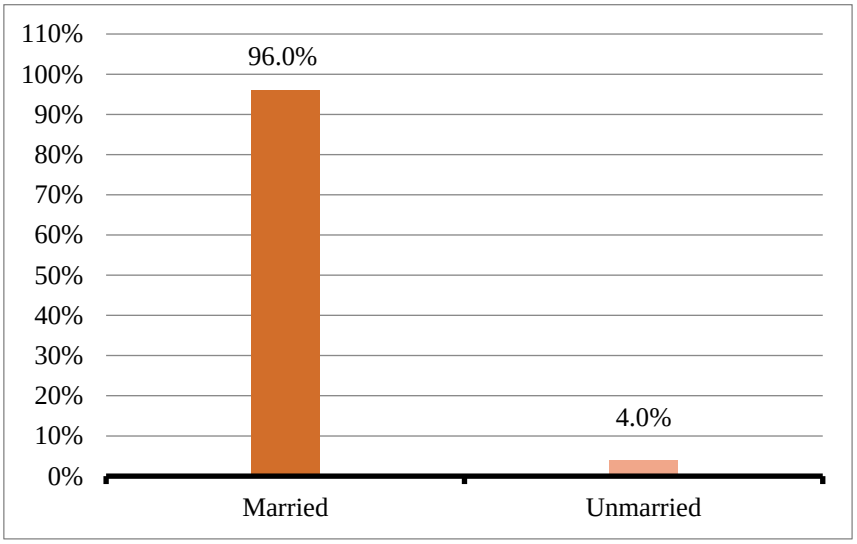

Figure 3: Distribution of patients according to marital status.

Nature of work: Over three quarter (76.0%) of the patients work in an enclosed space, two patients (4.0%) exposed to smoke and sources of environmental pollution, and ten patients (10%) had not previous exposure as showed in figure 4.

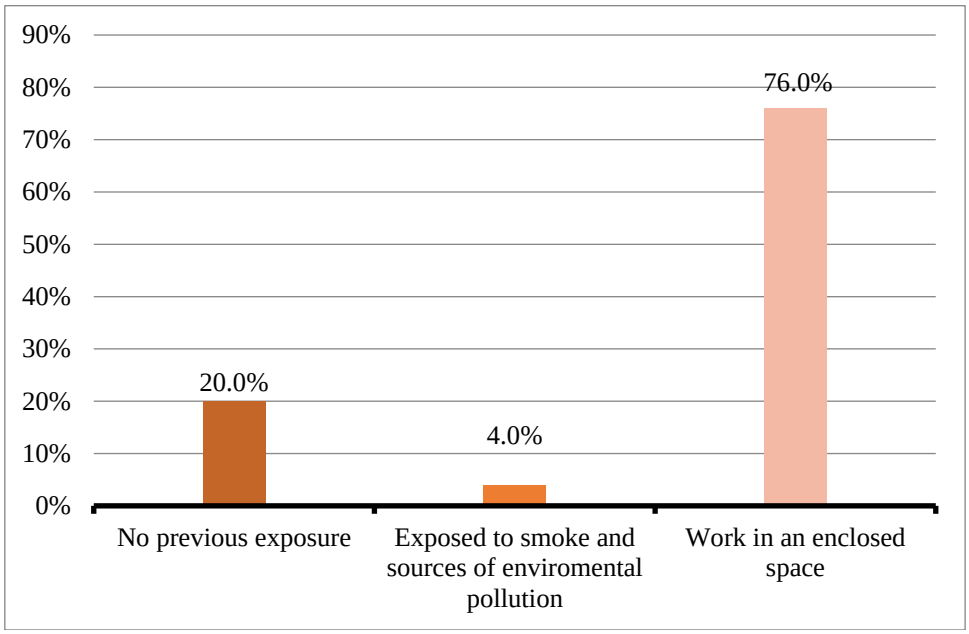

Figure 4: Distribution of patients according to nature of work.

History of smoking: We found that majority (86.0%) of patients with colon cancer were non- smoker, while only seven patients with colon and rectal cancer (14.0%) were smoker as in figure 5.

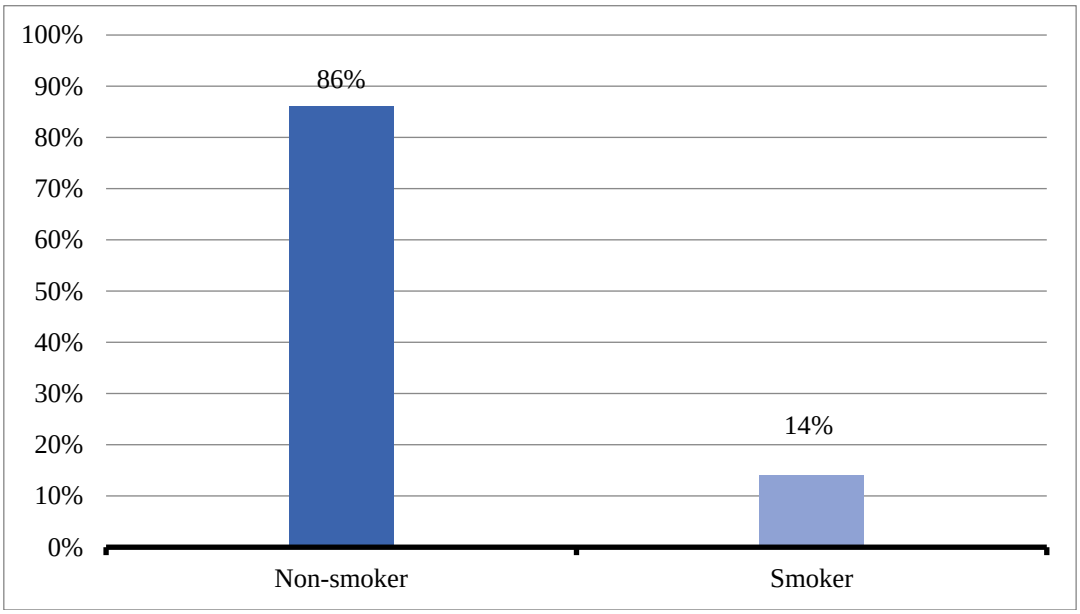

Figure 5: Distribution of patients according to history of smoking.

History of chronic disease: As in figure 6 revealed that twenty-nine (58%) of patients with colon cancer had chronic disease, and twenty-one (42%) of patients with colon cancer did not suffer from chronic disease.

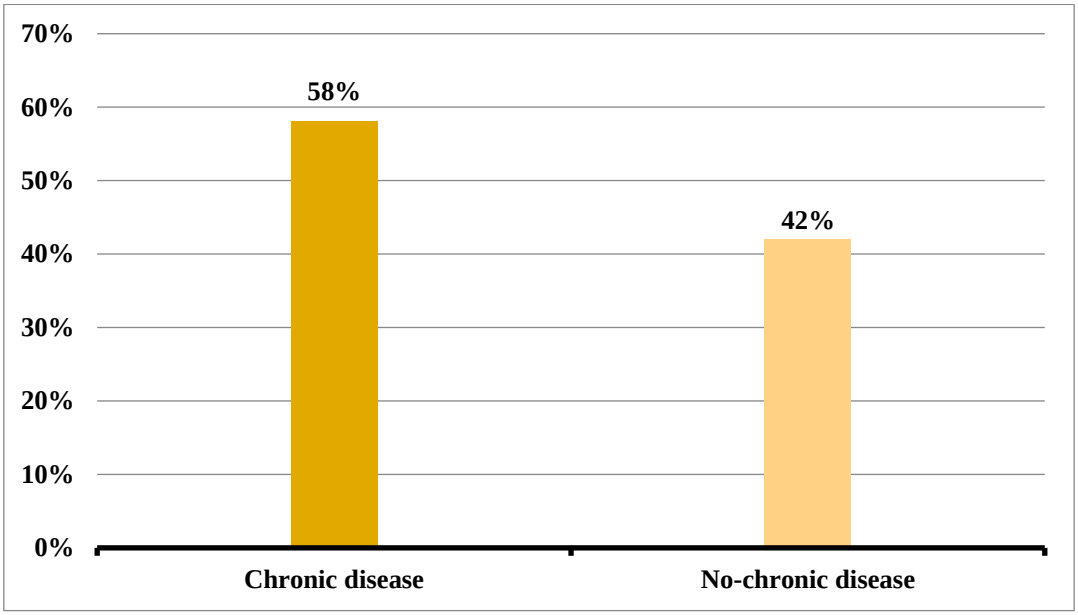

Figure 6: Distribution of patients according to history of chronic disease.

Stage of the disease: As in figure 7 revealed that two-thirds (66%) of patients were are at stage 3 of the disease, nearly a quarter (26%) at stage 4, only four patients (8%) at stage 2, and no patient at stage 0 or stage 1.

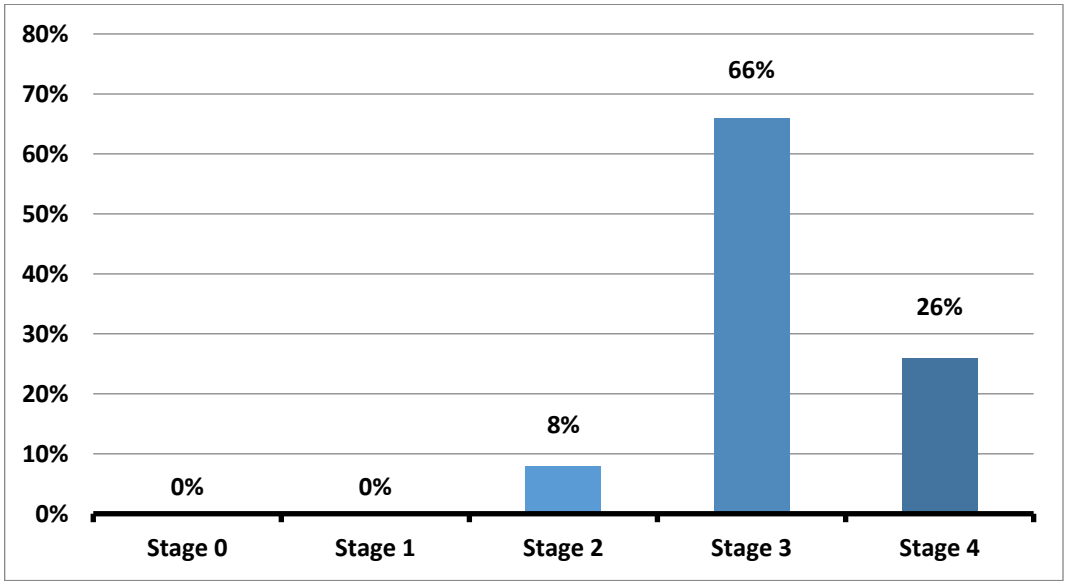

Figure 7: Distribution of patients according to stage of the disease.

Peripheral neuropathy symptoms in patients receiving Oxaliplatin: Figure 8 reported that (32%) of patients receiving Oxaliplatin had kinetic symptoms, (44%) had sensory symptoms, and (24%) had movement symptoms.

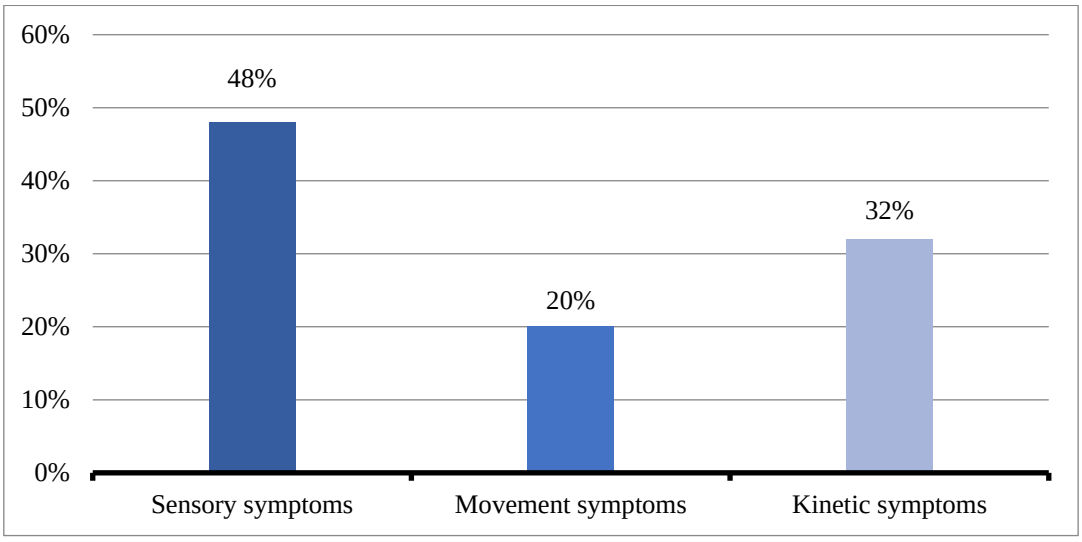

Figure 8: Peripheral neuropathy symptoms in patients receiving Oxaliplatin

Acute toxicity: In total cancer colon patients (n= 50), the study showed that ten patients (20%) had chest pain, while six patients (12%) had difficulty breathing during the infusion period. Only three patients had both chest pain and difficulty breathing during the infusion period, and thirty-seven patients did not had symptoms as in table 1.

Table 1: Distribution of patients according to acute toxicity

		Difficulty breathing during the infusion period.					
		Yes		**No**		**Total**	
		F	**%**	**F**	**%**	**F**	**%**
Chest pain	**Yes**	3	6%	7	14%	10	20%
	No	3	6%	37	74%	40	80%
	Total	6	12%	44	88%	50	100%

Cumulative dose of neuropathy effect symptoms between doses from 2 to 3 three months with colon cancer patients.

Table 2 shows the Pearson correlation coefficients of cumulative dose of neuropathy effect symptoms between doses from 2 to 3 months with colon cancer patients, where the relationships were with a correlation coefficient of (0.347) and aren't statistically significant at the level of significance.

Table 2: Correlation of cumulative dose of neuropathy effect symptoms between doses from 2 to 3 three months with colon cancer patients

Variable	**Correlation coefficient**	**P - value**
Oxaliplatin dose –symptoms of peripheral neuropathy	0.347	0.056

4. DISCUSSION

The results of the demographics of the participants and the comparison of the prevalence of the disease between both sexes in (50) samples, the result was varying in proportions, represented in the female (15) cases by 30%, and males by (35) by 70% and A comparison between the ages in (50) samples, so the cases whose age is from 30 to 50 years were (n=12) by 24%, and the cases that are older than 50 years, whose numbers are (38) cases, their percentage is 76%. As for the social status, the largest percentage belonging to married cases was 96% and (n=48) in the total number of cases and the lowest percentage to unmarried cases by 4%, which represents only two cases. According to the nature of the work, the largest percentage of people with colon cancer was so patients working in closed places by 76%, which is (38) cases, what cases are exposed to smoke in the workplace and their work environment is polluted, so their percentage was 4%, which is represented in only two cases, while the cases that do not work at all were 20%, which was represented in 10 cases, this indicates that the work environment has nothing to do with infection with Palmer. As for the smoking patients with a history of smoking, their infection rates were 14% with 7 cases, while the non-smoking cases were represented by 86% in the number of 43 cases. As for chronic diseases such as sugar and blood pressure, they accounted for about half of the number of cases, and this proves to us that chronic diseases have a relationship in the emergence of neuropathy in colon cancer patients, the percentages of cases with chronic diseases were 58% for the number of cases 29 cases out of 50, while other cases that do not suffer from chronic diseases represented 42% in the number of cases of 21 cases. Oxaliplatin was one of the chemical drugs for colon cancer patients and the patients were different in terms of the stage of the disease, the number of total referrals (50) was the largest percentage of patients receiving oxaliplatin are stage 3 patients, which was represented by 66% with 33 cases, while stage 4 patients, which were represented by 26% in the number of cases of 13 cases, and stage 2 patients were 8% in the number of 4 cases, As for the patients of stage 0 and 1, their case rate was 0%, i.e. the cases in both stages did not receive the dose of oxaliplatin , and this proves that the most frequent recipients of oxaliplatin are stage III patients. Patients showed different neuropathy symptoms, including sensory, motor and subjective different, we counted the most prevalent symptoms in 50 cases, the largest percentage was sensory-symptoms and represented 48%, which represents 24 cases out of 50, and the kinetic symptoms that followed 32%, which is 16 cases out of 50, and the motor symptoms were the least prevalent in patients, which represent 20%, which is returned to 10 cases out of 50 cases. We studied the symptoms of neurotoxicity, as they do not unite for most cases that receive oxaliplatin, as they appear during the infusion period only, and if they appear, the doctor must stop the infusion process for treatment, we counted each symptom separately, we counted the cases that showed them the two symptoms, the symptoms of neurotoxicity are chest pain and difficult of breath. The symptoms of chest pain appeared only in 10 cases out of 50 cases and represented 20%, As for the symptoms difficult of breath only, only 6 cases out of 50 cases appeared at a rate of 12%, while the cases that showed symptoms together at the same time during the leak were only 3 cases out of 50. As for the results of the cumulative dose of oxaliplatin and its association with the severity of the resulting neuropathy, we found in the data collected from 50 cases that there is no correlation between the amount of dose taken by the patient and the results of the symptoms of neuropathy, we conclude that the amount of dose taken by the patient of oxaliplatin does not change or affect the amount of neuropathy caused (no relationship) But the factor that affects is the number of doses he takes, so the more he increases the symptoms.

5. CONCLUSION

At the end of the project, we obtained the results and proved that neuropathy occurs in large proportions in males more than in women over the age of fifty, and that most of the symptoms were subjective and then sensory and then the motor symptoms and we also found that about half of the cases that suffered from neuropathy were patients with chronic diseases such as diabetes and blood pressure, and this increases the evidence that chronic diseases increase the severity of symptoms and that most of the symptoms are affected by chronic disease and by toxicity Nervousness.

We have presented our study on the two most of the symptoms, namely chest pain and difficulty breathing, were represented in 3 cases that showed the basic symptoms together, as for difficulty breathing, they appeared in 6 cases, and chest pain was represented in only 10 cases, as it turned out that most cases and the largest rates recipients of treatment compound consisting of Oxaliplatin were. In the third stage of the disease, by comparing the accumulated dose of Oxaliplatin with the severity of the symptoms shown on colon cancer patients, it became clear that there is no correlation between the dose of Oxaliplatin and the apparent symptoms, meaning that the symptoms and their severity are not affected by the strength of the dose taken but effected by amount and numbers of doses by cycles. We noticed all the cases that we dealt with inside Tripoli University Hospital before receiving doses were doing immunology analysis and some other tests to make sure that their bodies were ready and prepared for chemotherapy and after treatment they were given oral lotion, and oral moisturizing drugs, prevention of ulcers, medicines to prevent stomach irritation, and sometimes some envelopes, and dexamethasone has also been prescribed for some of them. Through research, we found that calcium gluconate reduces the symptoms of neuropathy if the patient receives it, but unfortunately, we did not get cases that received this treatment before receiving Oxaliplatin, so it was not possible to identify them.

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