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Eliminating Extravasation Events: Impact of Intervention Guidelines on Patients Receiving Chemotherapy

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Abstract: **Chemotherapy extravasation remains an accidental complication of chemotherapy administration and may result in serious damage to patients. Since patients are the first to feel any symptoms of possible extravasation and are relied upon to report them, their education is a crucial step in chemotherapy extravasation prevention and treatment.** ***Aim:*** **This study aimed to evaluate the impact of implementing interventional guidelines on eliminating extravasation events for patients receiving chemotherapy.** ***Design:*** **Quasi experimental research design was utilized.** ***Setting:*** **The study was conducted at the inpatient and out-patient departments at Oncology Hospital at Mansoura University Hospitals.** ***Subjects:*** **A purposive sample of (60) patients receiving chemotherapy was randomly divided into two groups with equal size (control and study).** ***Tools:*** **Three tools were used to collect the data and achieve the aim of the study as follows: Tool I: Structured Interview Questionnaire. Tool II: Factors contributing to venous extravasation questionnaire. Tool III: Extravasation assessment questionnaire.** ***Results:*** **There was an inverse relationship between patients' knowledge and the occurrence of extravasation, this was reflected in the fact that when patients' information increased, the extravasation occurrence in the study group was decreased at r = -0.468 and P 0.009, than that occur in the control group at r = 0.205 and P 0.276.** ***Conclusion:*** **The study concluded that; there were a numerous factors that can eliminates extravasation occurrence, which include improving patients' knowledge, appropriate; venous assessment, cannula size, cannula site, and efficient cannula secure, that can reduce the rate of extravasation.** ***Recommendation:*** **The current study recommended that Standardized teaching guidelines should be applied in Arabic, updated, colored booklet and be available at inpatients and outpatient for patients undergoing chemotherapy in order to help eliminating extravasation occurrence.**

Keywords: **Chemotherapy, extravasation, and intervention**.

1. INTRODUCTION

Intravenous infusion is the principal modality of administration of anti-cancer drugs for most types of malignant disorders with numbers more than 1 million infusions each day worldwide. These drugs can be classified into five categories according to their damage potential vesicant, exfoliants, irritants, inflammitants, and neutrals. **(Coyle et al., 2014).** It leads to many different Complications such as infection, phlebitis, infiltration, extravasation, soft-tissue necrosis, and compartment syndrome **(Dychter et al., 2012).**

Chemotherapy administration carries safety concerns to both patients and health care team. These concerns include extravasation of chemotherapy **(Schulmeister 2011),** which defined as a potentially severe complication or accidentally

leaks of chemotherapy into the surrounding tissue at the injection site ranging from local irritation to severe necrosis of the skin, subcutaneous tissue, peripheral vascular system, ligaments, or tendons. **(Maly et al., 2018 & Chang et al., 2014)**. The extent and severity of tissue damage depends on drug's properties, infusion site, how long it remains in the tissue, and the amount extravasated. Most lesions heal poorly and slowly. They may expand in size over weeks to months and if treatment is delayed, surgical debridement, skin grafting and even amputation may be the unfortunate consequences **(Bellin et al., 2010).** Many factors play a role in the potential development of extravasation including, injection technique, experience of personal giving injection, fragility of patient's veins, number of vein puncture attempt prior to establishing an operational intravenous line, site of injection, size and fixation of cannula and drug characteristics **(Upton et al., 2009).**

The patients are the first person to feel and report any symptoms of extravasation. Therefore patients must be educated to be aware of the class of drug, options of venous access, higher risk of extravasation, potential symptoms, and complications associated with it. Patients should be instructed to report any discomfort, pain, redness or swelling at infusion sites, and never underestimate any symptom. Moreover should be explained if they choose peripheral venous access over central, providing accurate history regarding previous manipulation in extremities, cooperation with the person performing the venipuncture, and reporting any symptoms that may arise during the infusion **(Kreidieh et al., 2016)**.

Significance of the study:

There are a scarce number of studies conducted in Egypt in relation to extravasations, so carrying out this research surely will add to the body of nursing knowledge in relation to this area as well as it will shed light on this problem in Egypt. Furthermore, understanding risk factors that might predispose to extravasations among patients receiving chemotherapy will certainly help in prevention of the adverse health effects caused by extravasations **(Schwab, et al., 2009**).

In addition, the exact incidence of chemotherapy extravasation varies greatly due to the general lack of reporting and absence of centralized registry of chemotherapy extravasation events. While center-based guidelines and policies attempt to minimize chemotherapy extravasation still has a prevalence that can range from 0.1% to 6% when administered through a peripheral intravenous access and from 0.26% to 4.7% when administered through a central venous access device (CVAD) (**Schulmeister 2011)**.

Extravasations increases morbidity, as it leads to some undesirable events such as prolonged times of hospitalization, unnecessary diagnostic procedures and treatments, extra workload for healthcare team, and the economic loss as well as threatening the lives of patients. In order to avoid additional chemotherapy adverse effects, every effort should be made to minimize the complications of chemotherapy administration **(Mader et al., 2009 & Wengström and Margulies 2008 & Schulmeister 2011)**. So this study was designed to evaluate the impact of implementing interventional guidelines on eliminating extravasation events for patients receiving chemotherapy.

Aim of the study

The aim of this study was to evaluate the impact of implementing interventional guidelines on eliminating extravasation events for patients receiving chemotherapy.

Research hypothesis

H (1). Patients' knowledge will be improved regarding chemotherapy extravasation in the study group than control group.

H (2). Extravasation events will be eliminated after implementing the interventional guidelines among the study group rather than control group.

2. MATERIALS AND METHOD

Research design: A quasi-experimental design was utilized to achieve the aim of the present study.

Setting: This study was conducted in inpatient and out-patient departments at Oncology Hospital at Mansoura University Hospitals.

Participants: A purposive sample of 60 patients, they were randomly divided into two equal groups as follows:

Group (I) study group: Comprised of 30 patients who received the interventional guidelines in order to enhance early reporting for any signs and symptoms of intravenous chemotherapy extravasation.

Group (II) control group: Comprised of 30 patients who exposed to hospital routine care only.

The sample of the study was selected according to the following criteria:

Inclusion criteria: Adult patients of both sexes ranged from 21 to 60 years old, newly diagnose and planned to receive chemotherapy, able to communicate and agree to participate in the study. The cases were randomly assigned into two equal groups (study and control group).

Exclusion criteria: Previous history of chemotherapy or hormonal treatment and previous venous complications.

The sample size: The sample size was calculated based on epidemiological information program, and the total of chemotherapeutic patients per year according to review of Mansoura university hospital statistical records. The final sample size was estimated to be 60 patients. The sample size of chemotherapy patients based on power analysis equation.

Equation to determine sample (n) at 95% confident power of the study.

Steven Thompson equation

N =N*p (1-p)/(N-1)*(d) n =sample size d= error percentage(0,05)

z =the correspond stander class of significance 95% (1.96)

p =percentage of availability of the objectivity (0.1)

Tools of data collection:

Three tools were used to collect the data and achieve the aim of the study as the following:

Tool 1: A Structured Interview Questionnaire: This tool was developed and used by the researchers after extensive literature review. It included four parts:

Part 1: Demographic characteristics and medical data such as sex, age, and marital status, level of education, occupation, residence, diagnosis and duration of the disease.

Part 2: Patient's knowledge regarding chemotherapy, it was include10 questions, 8 of them answered with true or false and the remaining 2 questions was multiple choice. The sum of the 10 question yields a patients general knowledge regarding chemotherapy medication. All question (true & false and multiple choice) questions were manipulated as, one point was given if the answer was correct and zero was given if the answer was wrong. The scores of the items were summed-up to give (10 marks). These scores were converted into a percent score, then the total patients' knowledge regarding chemotherapy was considered satisfactory if the percent score was 60% and more, and unsatisfactory if less than 60%.

Part 3: Patient's knowledge regarding venous extravasation, it was include 11 questions, 7 of them answered with true or false and the remaining 4 questions was multiple choice. The sum of the 11 question demonstrated patients' general knowledge regarding venous extravasation from chemotherapy. All question (true & false also multiple choice) questions were manipulated as, one point was given if the answer was correct and zero was given if the answer was wrong. The scores of the items were summed-up to give (11 marks). These scores were converted into a percent score, then the total patients' knowledge regarding venous extravasation was considered satisfactory if the percent score was 60% or more, and unsatisfactory if less than 60%.

Tool II: Factors contributing to venous extravasation Questionnaire:

This instrument was developed and used by the researchers after extensive literature review and it included three parts:

Part 1: Factors related to patients; which contained four items such as; history of atherosclerosis obesity, abnormalities of clotting factors, and peripheral neuropathy or other altered sensory perception.

Part 2: Factors related to medications; which contained four items such as medication name, period of treatment by chemotherapy, and numbers of cycle.

Part 3: Factors related to cannula that used such as cannula size, cannula site, type (peripheral or central), and inadequately secured.

Tool III: Extravasation assessment questionnaire:

This instrument was modified by the researchers and it was consisted of two parts:

Part 1: Vein quality assessment questionnaire (VAT): It was developed by Jacobson 1999 and adapted from (**Lenhardt et al 2002),** to assess the quality of vein before and after application of peripheral venous access, with reliability among oncology patients was 92% (SD 17.9; range 60% to 100%). Assessment of vein quality was restricted to upper limbs and classified according to the following criteria: Good (vein was easily visible and/or easy to palpate when tourniquet is applied), Fair (vein are small, scarred or difficult to palpate) and Poor (vein unable to be seen or palpated and require heat to aid vasodilation), plus location of catheter (forearm or hand). There were three categories of vein quality that ranged as following; (3)—Indicated good vein quality, (2)—Indicated fair vein quality and (1)—Indicated poor vein quality

Part 2: Extravasation of Chemotherapeutic agent Scale: First developed at 1997 and adapted from (**Mader, et al 2010 & Polovich et al 2014)**, to assess the severity of extravasation at the time of detection and determine the appropriate level of intervention. Assessment the severity of extravasation was classified according to the following criteria: skin color, integrity, temperature, edema, mobility, pain and fever. It was consisted of 5 items, each item grades from 0 – 4, can be classified as: (0)—No symptoms, (1)— Mild symptoms, (2)—Moderate symptoms, (3)—Severe symptoms, and (4)—Worst symptoms.

Validity and reliability:

For validity purposes, the researchers conducted an extensive literature review and developed the questionnaires from the previously used tools and reviewing the pertinent reviews. Tool I & II was designed by the researchers and revised by five experts in the field of medical-surgical nursing in the Faculty of Nursing of Mansoura and Aswan Universities (for content validity). While instrument III their validity and reliability was mentioned before. Reliability analysis was ascertained with Cronbach's alpha to determine the extent to which the items in all instruments are related to each other.

Pilot study:

A pilot study was conducted to assess the applicability of the tools, the feasibility of the study and to estimate the time needed for data collection. It was conducted on 10 % (6) of the total participants according to the selection criteria. All patients participated in the pilot study excluded from the study sample. Based on the results of the pilot study and expert's opinion, modifications and omissions of some details were done and then set the final fieldwork schedule.

Fieldwork:

This study was carried out through three consecutive phases: interviewing & assessment phase, implementation phase and evaluation phase. The data collection period was done for 8 months from the start of October 2018 to the end of May 2019.

1. **The interviewing and assessment phase:**

During this phase, the researchers explained the purpose of the study, tools components, and importance of early reporting of venous extravasation. The time needed for completing the questionnaire was ranged from 25 - 35 minutes for each patient.

2. **The implementation phase:**

- Based on the findings of assessment phase, goals and expected outcomes were formulated.
- In this phase, the selected patients who were recruited are randomly assigned to two equal groups. The study group (30) patients, who were exposed to the intervention guidelines that was designed and implemented by the researcher. While the control group (30) patients, who were exposed to routine hospital care by nursing staff.

- In this phase each patient was assessed three times regarding vein quality and the occurrence of extravasation.
- The first assessment was carried out by the researchers for each participant individually during the first time of receiving intravenous chemotherapy for collecting baseline data about their demographic data, assess their knowledge regarding chemotherapy and extravasation, also to assess vein quality. It took about 35 - 45 minute using tool (I, II, and III). The interventional guidelines was presented for the study group patient in a form of two session as followed;

- First session: The researchers gave guidelines to the study group while those participants were waiting to take the first cycle of chemotherapy on Sunday and Monday, regarding chemotherapy and the importance of early detecting of extravasation symptoms either during administration in the hospital or later in the home and what the proper action should be taken, using booklet, and PowerPoint.

- Second session: The researchers refreshed the previous given knowledge for the participant during receiving the first chemotherapy cycle.

- The second assessment done during receiving the fourth cycle of chemotherapy for each patient in both groups using tool II (part 2 and 3) & III.
- The third assessment was done during the six cycle of the administration for each patient in both groups using tool II (part 2 and 3) & III, the second and third time done in order to assess and determine factors that can affect extravasation occurrence, vein quality and chance of the occurrence of extravasation. Patients' interview done at 9 am to 12 md for 25 – 30 minute.
- The control group was assessed on a different day from the study group days (Wednesday and Thursday).

3. The evaluation phase:

This phase was emphasized on estimating the effect of an interventional guidelines for improving awareness regarding chemotherapy extravasation early reporting among patients under chemotherapy transfusion, through a comparison between control and study group after applying educational guidelines.

Ethical Considerations:

- An official approval was obtained from administrative authorities to carry out the study after explanation of the purpose of the study.
- Approaches to ensure the ethics were considered in the study regarding confidentiality and informed consent. Confidentiality was achieved by the use of closed sheets with the names of the participants replaced by numbers. All participants were informed that the information they provided during the study would be kept confidential and used only for statistical purpose.
- Written informed consent was taken from all participants before being enrolled in the study after explaining the purpose of the study.
- Participants were informed that their participation in the study was voluntary and they could withdraw from the study whenever they decide.
- The findings would be presented as group data with no personal participant's information remained.
- After completing the research, the researchers gave the interventional guidelines for each individual in the control group, in order to ensure the right of each patient to receive equal information and equal care.

Limitation of the Study:

There are different studies carried out on nurse's knowledge and practice regarding chemotherapy and extravasation while the patient aspect was neglected so there weren't enough researches found on patients' knowledge that covering all points and variables of our research.

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3. RESULTS

Table (1). Showed that 60.0% of the study group were in age group (41-50) with mean age 48.47 years, while the control group in the same table found that 43.3% in the same age group with mean 47.70 year. On the other hand 56.7% of the patient in study group were males and 33.3% of them had mid education, while 66.7% in the control group were females and with 53.3% of them had only basic education. The most frequent cancer diagnosed in the study group was 33.3% had cancer colon, and 26.7% had Lung cancer, while for the control group found that 43.3% had cancer colon and 40.0% had bone cancer.

Table (2). Illustrated that 46.7% and 56.7% of the study and control group respectively receiving medication group; Flurovracil, Oxaliplatin and leucovorin chemotherapy. In addition to 66.7% and 56.7% for study and control group respectively receive 6 cycle with duration between each cycle was 21 days. On the other hand the same table demonstrated the risk factors that can affect the occurrence of extravasation, were 26.7% of the study group had impaired in the peripheral feeling, and 23.3% of them had Hypotension also the same percent showed for atherosclerosis, while 36.7% of the control group had atherosclerosis as a risk factor and 30.0% of them had obesity.

Continued with the size of peripheral cannula as a risk factor this table showed that 76.7%, 100.0 and 96.7% in the study group were used blue cannula (22G) in the first cycle, fourth cycle and six cycle respectively, additionally 83.3%, 86.7%, and 93.3% of the control group was used blue cannula (22G) for receiving chemotherapy during first cycle, fourth cycle and sixth cycle respectively. According to peripheral cannula fixation, it was found that the entire sample of the study group in the three examined cycles had efficient fixation, while 13.3%, 20.0%, and 23.3% from the control group had inefficient cannula fixation in the first cycle, fourth cycle and sixth cycle respectively.

In addition, vein quality assessment in the same table showed that both groups had good vein quality in the first cycle of chemotherapy, while in the fourth and sixth cycle found that 73.3% of the study group had good vein. Also, percentage of 70.0% and 56.7% of the control group had fair vein quality in the fourth and sixth cycle respectively, while 10.0% of them in the sixth cycle had poor vein quality.

Table (3). Displayed that, the total patients' knowledge score regarding chemotherapy and extravasation, which found that, 100.0%, 90.0%, and 63.3% of the study group had good total knowledge score regarding chemotherapy during the first, fourth and sixth cycle respectively. While 56.7%, 53.3, and 60.0%, of the control group had fair total knowledge score. As regard to total patients' knowledge score regarding extravasation, the same table illustrated that 100.0%, 96.7%, and 80.0% of the study group had good total knowledge score during the first, fourth and sixth cycle respectively. On the other hand the control group represent 96.7% for fair total knowledge score regarding extravasation.

Table (1): Distribution of the studied subject according to their demographic data and medical data (n = 60)

	Study Group (n = 30)		Control Group (n = 30)		χ2	P
	No	%	No	%		
Age (years)						
31-40	1	3.3	5	16.7	4.033	0.133
41-50	18	60.0	12	43.3		
51-60	11	36.7	13	40.0		
Mean ± SD	48.47 ± 6.72		47.70 ± 8.18			
Sex						
Male	17	56.7	10	33.3	3.300	0.069
Female	13	43.3	20	66.7		
Education						
Basic	9	30.0	16	53.3	3.434	0.180
Mid education	10	33.3	6	20.0		
University	11	36.7	8	26.7		
Diagnosis						
Lung cancer	8	26.7	2	6.7	6.991	0.072
Cancer colon	10	33.3	13	43.3		
Cancer bone	6	20.0	12	40.0		
Breast cancer	6	20.0	3	10.0		

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Table (2): Distribution of the studied subject according to Extravasation's Risk Factors and Quality of Vein Assessment (n = 60)

Risk Factors	Study Group (n = 30)		Control Group (n = 30)		χ2	P
	No	%	No	%		
Factors Related to Treatment.						
▪ **Type of Chemotherapy**						
Adriamycin and cyclophosphamide	5	16.7	7	23.3	2.094	0.351
Flurovracil, Oxaliplatin and leucovorin	14	46.7	17	56.7		
Platinol used with Taxol, Taxotere, and GEMZAR	11	36.7	6	20		
Cycle of chemotherapy:						
14 days	10	33.3	13	43.3	0.635	0.426
21 days	20	66.7	17	56.7		
▪ **No of cycle:**						
6 Cycle	20	66.7	17	56.7%	0.635	0.426
16 Cycle	10	33.3	13	43.3%		
Factors Related to Patients:						
▪ Atherosclerosis	6	20.0	11	36.7	2.052	0.152
▪ Obesity	7	23.3	9	30.0	0.341	0.559
▪ Clotting	0	0.0	1	3.3	1.017	0.313
▪ Peripheral Impaired Feeling	8	26.7	5	16.7	0.888	0.347
▪ Hypotension	7	23.3	4	13.3	1.002	0.317

Con. Table (2): Distribution of the studied subject according to Extravasation's Risk Factors and Quality of Vein Assessment (n = 60)

Items	First Cycle				Fourth Cycle				Six Cycle			
	Study Group (n = 30)		Control Group (n = 30)		Study Group (n = 30)		Control Group (n = 30)		Study Group (n = 30)		Control Group (n = 30)	
	No	%	No	%	No	%	No	%	No	%	No	%
Factors related to Peripheral Cannula:												
▪ **Peripheral Cannula Size**												
Blue 22 G	23	76.7	25	83.3	30	100.0	26	86.7	29	96.7	28	93.3
Pink 20 G	7	23.3	5	16.7	0	0.0	4	13.3	1	3.3	2	6.7
	χ2 = 0.417		P = 0.519		χ2 = 4.286		P = 0.038*		χ2 = 0.351		P = 0.554	
▪ **Peripheral Cannula Site**												
Wrist	1	3.3	1	3.3	0	0.0	9	30.0	1	3.3	17	56.7
Fore arm	29	96.7	29	96.7	30	100.0	21	70.0	29	96.7	13	43.3
	χ2 = 0.0		P =1.0		χ2 = 10.588		P =0.001*		χ2 = 20.317		P =<0.001*	
▪ **Peripheral Cannula Fixation**												
Efficient	30	100.0	26	86.7	30	100.0	24	80.0	30	100.0	23	76.7
Not efficient	0	0.0	4	13.3	0	0.0	6	20.0	0	0.0	7	23.3
	χ2 = 4.286		P =0.038*		χ2 = 6.667		P = 0.010*		χ2 = 7.925		P =0.005*	
Vein Quality Assessment												
Good	30	100.0	30	100.0	22	73.3	9	30.0	22	73.3	10	33.3
Fair	0	0.0	0	0.0	8	26.7	21	70.0	8	26.7	17	56.7
Poor	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	10.0
	-				χ2 = 11.279		P =0.001*		χ2 = 3.863		P =0.145	

Fig. (1). According the occurrence of extravasation this figure represented that 6.70% and 10.0% of the study group had extravasation during the fourth cycle and sixth cycle respectively. While in the control group the extravasation occur as 20.0% and 26.70% during the fourth cycle and sixth cycle respectively, which reflect the effectiveness of the guidelines that given to the study group before the first cycle.

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Table (3): Distribution of the Studied Subject According their Total Knowledge Score Related Extravasation and Chemotherapy (n = 60)

Items	First Cycle				Fourth Cycle				Six Cycle			
	Study Group (n = 30)		Control Group (n = 30)		Study Group (n = 30)		Control Group (n = 30)		Study Group (n = 30)		Control Group (n = 30)	
	No	%	No	%	No	%	No	%	No	%	No	%
Total patients' knowledge score regarding chemotherapy												
Good	30	100.0	12	40	27	90.0	13	43.3	19	63.3	12	40.0
Fair	0	0.0	17	56.7	3	10.0	16	53.3	11	36.7	18	60.0
Poor	0	0.0	1	3.3	0	0.0	1	3.3	0	0.0	0	0.0
	χ^2 = 3.866		P =0.145		χ^2 = 14.795		P =0.001*		χ^2 = 25.714		P =<0.001*	
Total patients' knowledge score regarding extravasation												
Good	30	100.0	0	0.0	29	96.7	0	0.0	24	80.0	0	0.0
Fair	0	0.0	29	96.7	1	3.3	29	96.7	6	20.0	29	96.7
Poor	0	0.0	1	3.3	0	0.0	1	3.3	0	0.0	1	3.3
	χ^2 = 2.0		P =0.368		χ^2 = 60.0		P =<0.001*		χ^2 = 40.114		P =<0.001*	

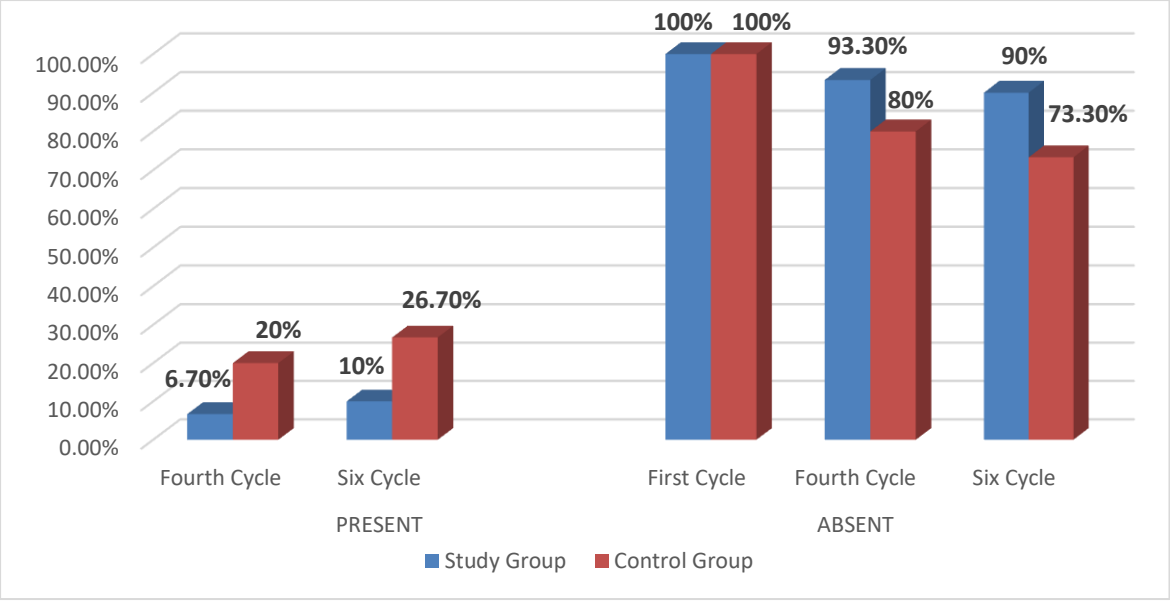

Fig. (1); Distribution of the Studied Subject According to the Occurrence of Extravasation (n = 60)

Table (4): Relation between Risk Factors and Occurrence of Extravasation (n = 60)

Risk Factors	Fourth Cycle								Six Cycle							
	Study Group				Control Group				Study Group				Control Group			
	Absent (n = 28)		Present (n = 2)		Absent (n = 24)		Present (n = 6)		Absent (n = 27)		Present (n = 3)		Absent (n = 22)		Present (n = 8)	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Factors related to type of chemotherapy:																
Adriamycin and cyclophosphamide	5	17.9	0	0.0	6	25.0	1	16.7	5	18.5	0	0.0	5	22.7	2	25.0
Flurovracil, Oxaliplatin and leucovorin	13	46.4	1	50.0	12	50.0	5	83.3	11	40.7	3	100.0	12	54.5	5	62.5
Platinol used with Taxol, and Taxotere	10	35.7	1	50.0	6	25.0	0	0.0	11	40.7	0	0.0	5	22.7	1	12.5
	χ^2 = 0.466		P =0.792		χ^2 = 2.584		P =0.275		χ^2 = 3.810		P =0.149		χ^2 = 0.385		P =0.825	
Factors related to patients																
Atherosclerosis	4	14.3	2	100.0	7	29.2	4	66.7	4	14.8	2	66.7	6	27.3	5	62.5
	χ^2 = 8.571		P =0.003*		χ^2 = 2.907		P =0.088		χ^2 = 4.537		P = 0.033*		χ^2 = 3.135		P =0.077	
Obesity	5	17.9	2	100.0	3	12.5	6	100	4	14.8	3	100.0	1	4.5	8	100
	χ^2 = 7.041		P =0.008*		χ^2 = 17.500		P =<0.001*		χ^2 = 10.952		P =0.001*		χ^2 = 25.455		P =<0.001*	
Clotting	0	0.0	0	0.0	1	4.2	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0
	-				χ^2 = 0.259		P =0.611		-				χ^2 = 0.376		P =0.540	
Impaired peripheral feeling	6	21.4	2	100.0	4	16.7	1	16.7	7	25.9	1	33.3	3	13.6	2	25.0
	χ^2 = 5.893		P = 0.015*		χ^2 = 0.0		P =1.0		χ^2 = 0.076		P =0.783		χ^2 = 0.545		P =0.460	
Hypotension	7	25.0	0	0.0	4	16.7	0	0.0	7	25.9	0	0.0	3	13.6	1	12.5
	χ^2 = 0.652		P =0.419		χ^2 = 1.154		P =0.283		χ^2 = 1.014		P = 0.314		χ^2 = 0.007		P =0.935	
Peripheral Cannula Size																
Blue 22 G	28	100.0	2	100.0	22	91.7	4	66.7	27	100.0	2	66.7	22	100.0	6	75.0
Pink 20 G	0	0.0	0	0.0	2	8.3	2	33.3	0	0.0	1	33.3	0	0.0	2	25.0
	-				χ^2 = 2.596		P =0.107		χ^2 = 9.310		P =0.002*		χ^2 = 5.893		P =0.015*	
Peripheral Cannula Site																
Wrist	0	0.0	0	0.0	4	16.7	5	83.3	0	0.0	1	3.7	11	50.0	6	75.0
Fore arm	28	100.0	2	100.0	20	833	1	16.7	27	100.0	2	66.7	11	50.0	2	25.0
	-				χ^2 = 10.159		P =0.001*		χ^2 = 9.310		P =0.002*		χ^2 = 1.493		P =0.222	
Peripheral Cannula Fixation																
Efficient	28	100.0	2	100.0	20	833	4	66.7	27	100.0	3	100.0	20	90.9	3	37.5
Not efficient	0	0.0	0	0.0	4	16.7	2	33.3	0	0.0	0	0.0	2	9.1	5	62.5
	-				χ^2 = 0.833		P = 0.361		-				χ^2 = 9.355		P =0.002*	

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Table (4). Illustrated that there was no statistically significant effect of the chemotherapy types, clotting abnormality, and hypotension on the occurrence of extravasation for both groups in the fourth and sixth cycle, while there was a significant effect of obesity on the occurrence of extravasation for both groups in the fourth and sixth cycle at $p < 0.05$. On the other hand this table found that patients on the study group whom had atherosclerosis had extravasation occurrence in the fourth and sixth cycle at $p < 0.05$, in spite of the control group there was no a significant effect at $p > 0.05$. Meanwhile patients with impaired peripheral feeling in the study group were developed extravasation occurrence in the fourth cycle at $p < 0.05$, otherwise the others from control group in fourth cycle and both groups in the sixth cycle extravasation not occur between them at $p > 0.05$. Additionally, the same table showed that there was a significant effect of the peripheral cannula size and site on the extravasation occurrence in both groups on the sixth cycle at $p < 0.05$. According to peripheral cannula fixation it was found a significant effect in the occurrence of the extravasation when there was improper securing of the cannula in control group especially in the sixth cycle.

Table (5). Portrayed that there was a strong significant effect of the vein quality and the occurrence of extravasation in both study and control groups at P 0.002 and < 0.001 respectively which means that extravasation can occur when the vein quality was decreased.

Table (6). Showed that there was an inverse relationship between patients' knowledge and the occurrence of extravasation, this was reflected in the fact that when patients' information increased, the extravasation occurrence in the study group was decreased at r = -0.468 and P 0.009, than that occur in the control group at r = 0.205 and P 0.276.

Table (5): Relation between Quality of Vein Assessment and Occurrence of Extravasation (n = 60)

Quality of Vein	Sixth Cycle							
	Study Group				Control Group			
	Absent (n = 27)		Present (n = 3)		Absent (n = 22)		Present (n = 8)	
	No	%	No	%	No	%	No	%
Good	22	81.5	0	0.0	17	77.3	0	0.0
Fair	5	18.5	3	100.0	5	22.7	5	62.5
Poor	0	0.0	0	0%	0	0.0	3	37.5
	$\chi 2$ =9.167		P =0.002*		$\chi 2$ =17.216		P =<0.001*	

Table (6): Relation between Total Knowledge Score and Occurrence of Extravasation (n = 60)

Knowledge	Extravasation scale							
	Study Group				Control Group			
	Fourth Cycle		Six Cycle		Fourth Cycle		Six Cycle	
	r	P	r	P	r	P	r	P
	0.105	0.582	-0.468	0.009*	0.237	0.208	0.205	0.276

4. DISCUSSION

Chemotherapy extravasation remains an accidental complication that may cause a serious damage to patients. Extravasation is manifested by a variety of symptoms including immediate effects as swelling at the infusion site, redness, and changes that may include a cold sensation, burning, stinging, or pain. In contrast, late effects include marked induration, dystrophy, and potential loss of function of the affected limb which might progress to blister formation and necrosis leading to amputation **(Doellman et al., 2009 & Al-Benna et al., 2013 & Schulmeister, 2011).** There are different studies carried out on nurse's knowledge and practice regarding chemotherapy and extravasation and patient aspect neglected, but the patient considered a main part in this process. The early reporting for signs and symptoms of extravasation is the responsibility of the patient **(Kee et al., 2014).** So, the present study was designed to evaluate the impact of implementing interventional guidelines on eliminating extravasation events for patients receiving chemotherapy.

Regarding demographic and medical data, the present study revealed that, there is no statistically significant difference between the two groups as regards demographic and medical data. This implies that both control and study group are homogenous and comparable. Moreover more than half of study group were in the age group from 41 - 50 years old. This

result contradicted with **(Ahmed et al., 2011)** in Egypt, who reported that more than one third of the total studied patients were in the age group from 51 - 65 years old. Regarding sex the result of the current study revealed most of control group belong to female sex, while study group belong to male sex. The finding concerned with control group was in agreement with (**Schulmeister and Camp-Sorrell 2000)** who mentioned that the majority of their participants with extravasation were females. In addition to the finding concerned with study group was in the same line with (**Sauerland et al., 2006)** who reported that fewer female patients than males.

Concerning to the commonest diagnoses (**Ibrahim et al ., 2014),** in Egypt found that the commonest diagnosis among their participants was more than one third for liver cancer and the minority of them founded for bladder cancer among men, while near to one third of their participants had breast cancer and the minority of them had liver cancer among women. On the contrary with the present study result, which illustrated that more than one third of the study group had colon cancer, and less than one third of them had lung cancer, breast, and bone cancer respectively. While near to half of the control group had colon cancer followed by cancer bone. This result might be explained by facts related to cancer prevalence worldwide, which reflected that the Colorectal cancer is the third most common cancer worldwide after lung and breast cancers with two-thirds of all colorectal cancers occurring in the more developed regions of the world.

According to the chemotherapy medication types as a risk factors for extravasation occurrence, the present study found that near to half of the study group received Flurovracil medication group followed by more than one third of them received Platinol medication group, while more than half of the control group participants received Flurovracil medication group followed by less than one third of them received Adriamycin medication group. In addition the majority of control group represented history of atherosclerosis and obesity respectively, while the majority of study group has peripheral Impaired Feeling. This result might be due to this group of medications was the most common among many others and suitable to previous mentioned diagnosis which concerned with our participants.

This finding was a consisted with (**Kreidieh et al., 2016)** in Lebanon, who found that the intravenous administered drugs can be classified into five categories according to their damage potential. Category one was Vesicants group that can result in tissue necrosis or formation of blisters when accidentally infused into tissue surrounding they include; Dactinomycin, Daunorubicin, and Doxorubicin. Category two was Exfoliants group that can cause inflammation and shedding of skin without causing underlying tissue death they include; Cisplatin, Docetaxel, and Paclitaxel. Category three was Irritants group that can cause inflammation, pain or irritation at the extravasation site, without any blister formation they include bleomycin, carboplatin and topotecan. Category four was Inflammitants group that cause mild to moderate inflammation, painless skin erythema and elevation at the extravasation site, they include bortezomib, and 5-fluorouracil. Category five was Neutrals group that neither cause inflammation nor damage upon extravasation include, Asparaginase, and bleomycin.

Another studies result adhered with the present finding which done by (**Ener and Malarvizhi 2004)** who found another certain factors that can increase risk of the extravasation rate which include, fragile, small, sclerosed veins, superior vena cava syndrome, lymphedema, peripheral neuropathy, decreased local blood flow, recent venipuncture at the same vein, and medications capable of altering mental status) plus insufficient training, poor infusion technique, and use of improper cannulas can increase the extravasation and should be taken into account before starting chemotherapy.

In relation to vein quality assessment the finding of the present study mentioned that both groups had good vein quality in the first cycle of chemotherapy, while in the fourth cycle less than three quarters of studied group compared to more than one quarter of control group had good veins. However, by the sixth session less than three quarters of studied group compared to more than half of the control group had fair veins quality. This result came in the agreement with (**Coyle et al., 2014)** who explained the fact regarding the effect of chemotherapy on vein quality, this fact was surely after four cycles the veins will be fragile. Which may explain why few number from study group developed extravasation even with proper intervention, this intervention provided for study group which may delay vein fragility or deterioration.

Regarding the assessment of patients' knowledge related to chemotherapy and extravasation, the current study showed that there was a statistically significant improvement in knowledge regarding chemotherapy and extravasation across intervention time especially fourth session, as the patient was exposed to more knowledge. This may be due to the effect of the intervention regarding chemotherapy. A similar improvement in level of knowledge was also observed in studies of (**Berger et al., 2018)** in Norway, who reported that, all patients acquired a higher level of knowledge after being informed

by physicians and other health care personnel throughout their treatment period. This might be due to many simple people in the Egyptian society had lack regarding the proper medical instructions about their condition, so when they are given these instructions that they are eager to learn, a large amount of it is stored, and this explains the noticeable improvement in the study group knowledge regarding chemotherapy extravasation.

As regard to the occurrence of extravasation, in the first cycle, there were no had extravasation in both groups. While in during the fourth cycle, the present study found that, six point seven of study group compared to twenty percent of control group suffered from extravasation symptoms, however in the sixth cycle found, ten percent of study group compared to twenty six point seven percent of control group had extravasation symptoms. This result occurred may be due to long time of treatment which in turn affects vein quality and in fact extravasation occur accidentally. Also, the higher rates of extravasation among control than cases may be explained by the effect of improved patients' knowledge toward early reporting about any sign and symptoms of extravasation occur, it is worth noting that the number of cases that had extravasation in the control group is not much. This also reflected that the nurses at the Oncology Hospital are trained, skillful and qualified to deal with these patients.

This result is synchronized with **Schulmeister (2011),** who stated that the incidence of chemotherapy extravasations among adults as published in the literature ranged from six to twenty percent. On the other hand, this result is inconsistent with (**Rose et al., 2008),** who stated that incidence rate of extravasation ranged between zero point one to six percent for chemotherapeutic agents. The variability of incidence rate could be explained as the published rate is likely to be underestimated, as many cases of extravasation go unreported and to the differences in the monitoring and notification systems for extravasation between hospitals.

Concerning to the relation between risk factors and occurrence of extravasation, the current study findings denoted that the incidence rate of extravasation occurrence was higher among studied patients with atherosclerosis, impaired peripheral feeling and who was obese. The result of this study is consistent with (**Kreidieh et al., 2016)** in in Lebanon who stated that factors related to patients that increase the risk of chemotherapy extravasation include small fragile veins, obesity, impaired level of consciousness, and who had previous multiple venipuncture. Similarly **(Ahmed et al., 2011)** in Egypt, stated that extravasation injuries are more severe in patients with arterial insufficiency such as atherosclerosis, diabetes mellitus and connective tissue diseases.

Regarding chemotherapy related factors, the result of the current study depicted a high incidence rate of extravasation among studied patients who had received the following chemotherapeutic drugs group named (Flurovracil, Oxaliplatin and leucovorin) as Inflammitants drug group, (Platinol used with Taxol, and Taxotere) as Exfoliants drug group and (Adriamycin and cyclophosphamide) as Vesicants drug group. The finding of the current study is an eye opener to (**Molas-Ferrer et al., 2015)** statement that every patient who receives irritant and vesicant chemotherapy is at risk for extravasation. In contrast, (**Ahmed et al., 2011)**, who clarified that no relation between extravasation occur and types of chemotherapy. Furthermore, (**El-Salaheen et al., 2018)** showed that extravasation highest among patient receiving nonirritant chemotherapy namely carboplatin.

In addition to (**Albain et al., 2008)** who found that Flurovracil and Gemzar is chemotherapy drug of choice to treat a number of forms of cancer including breast, colon, and lung, cancers. Owing to the fact that most participated patients were diagnosed either with colon or breast cancer and received these chemotherapeutic drugs as a treatment of choice according to their diagnoses and to international cancer management protocols. This result is supported by (**Coyle et al., 2014 & World Health Organization 2015**) which declared that women diagnosed with breast, uterine, and colon cancers are more liable to develop extravasation. This result could be explained, by the fact that the main protocol of care for patients diagnosed with breast cancer was adjuvant chemotherapy with four cycles followed by radiation therapy. Surely after four cycles their veins will be fragile**.** This might be explained that near to half of the both group of the present study receive Flurovracil and Gemzar is chemotherapy drug because this group of the medication that cause a mild to moderate inflammation, painless skin erythema and elevation at the extravasation site.

On the other hand the present study showed that, there was a significant effect of the choice peripheral cannula size and site as the fore arm on the extravasation occurrence in both groups on the six cycle. This might be due to pig cannula caliper become more suitable for the use of pressure bags also with bolus injections administered by hand, the pressure required pig cannula diameter and suitable length plus the veins that present in the fore arm were large, soft, and resilient

so it can tolerated the chemotherapy drug than that present in hand or in the antecubital fossa. This result consistent with (**Wienbeck et al., 2010)** who pointed out there was significantly higher rate of extravasations occurred with use of the 22G catheter as compared to the 20G and 18G and more extravasation occur when venous access was the dorsum of the hand. While the result done by (**Sinan et al., 2005**) opposite the present result, who revealed that there was no significant effect of cannula size and site on extravasation frequency. Furthermore, **(Schwab et al., 2009**) stated that no significant difference was observed between the two groups in their study that they found two to zero extravasations occurring respectively and no effect of the injection site on rate of extravasation.

As regard to relation between quality of vein assessment and occurrence of chemotherapy extravasation the present study portrayed that there was a strong significant effect of the vein quality status and the occurrence of extravasation in both study and control groups respectively which means that extravasation can occur when the vein quality was decreased. This in agreement with **(Duffy and McGowan 2008)** who implies the statement that the choice of which vein to puncture and size of the cannula should be based on the duration of the IV therapy, characteristics of the drugs, and state of the patient's peripheral venous network.

Regarding to the patients' knowledge regarding chemotherapy extravasation, **(Sakaida et al., 2014),** who proved in his study that the Communication with the patient plays a vital role in the recognition of extravasation and patients should be informed of the importance of reporting immediately any change in sensation, stinging or burning during the administration of chemotherapy. On the other hand, patients with communication difficulties who rely on careers or interpreters, it is important to establish that they understand the significance of reporting symptoms immediately. This agreed with the result of the present study that highlighted that there is an inverse relationship between patients' knowledge and the occurrence of extravasation; this was reflected in the fact that when patients' information increased, the extravasation occurrence in the study group was decreased.

5. CONCLUSION

Based on the results of the current study we concluded that although the chemotherapy extravasation was occur accidently but there were numerous factors that can eliminates extravasation occurrence, which include improving patients' knowledge regarding to chemotherapy extravasation, which motivate the patients to early reporting for any symptoms regarding extravasation occurrence. The other remaining factors as appropriate venous assessment, cannula size, cannula site, and efficient cannula secure can also reduce the rate of extravasation.

6. RECOMMENDATION

The present study recommended:

1. Replicate this study of large probability sampling and different hospitals in different geographical locations in order to determine factors that can affect chemotherapy extravasation.

2. Standardized teaching guidelines should be applied in Arabic, updated, colored booklet and be available at inpatients and outpatient for patients undergoing chemotherapy in order to help eliminating extravasation occurrence.

3. Further studies are needed in order to develop more accurate and realistic strategies for improving patients' knowledge for whom undergoing to chemotherapy.

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