Effect of Implementing A nursing Protocol on Patients' Outcomes Undergoing Trans-Hepatic Arterial Chemoembolization

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Abstract

Background: Careful monitoring for patient with hepatocellular carcinoma who receiving trans-arterial chemoembolization in adult intensive care units to reduce complications remains mandatory for nurses. The study aimed to evaluate the effect of implementing a nursing protocol on patients' outcomes undergoing trans-hepatic arterial chemoembolization. Quasi experimental research design was used in this study. Subjects: All adult patients who diagnosis with hepatocellular carcinoma and receiving trans-arterial chemoembolization at the liver intensive care unit and gastroenterology department at Al-Rajhi liver hospital were involved in this study. Two tools were used. Tool one: patient assessment questionnaire and includes 4 parts, tool two: patient outcomes assessment questionnaire. Methods: The nursing protocol on trans-arterial chemoembolization was implemented by the researcher from the day before procedure until discharge, the researcher assess site of insertion, post embolization syndrome after procedure and recorded it. **Results**: Findings of the present study revealed significant improvement in pain scores as it was 3.77±0.59 in the control group 4 hours after TACE while it was 3.19±0.63 in the **Study group**, and Mean ± SD was 3.95±0.58 in the control group 6 hours after TACE in comparison to 3.15±0.75 in the study group. Insertion site and ICU stay values of less than p=0.005, p=0.5 and p=0.05 respectively in response to implementing nursing protocol. Conclusion: implementing the nursing protocol on trans-hepatic arterial chemoembolization appear to be effective in terms of reducing incidence and consequences of post procedure complications. Recommendation: Patients and their caregivers need to be apprised of post embolization syndrome symptoms prior to TACE and provided with adequate nursing care for symptom control.

Keywords: Trans-hepatic Arterial Chemoembolization, Patients' Outcomes, Hepatocellular Carcinoma & Nursing protocol.

Introduction

Trans-arterial chemoembolization (TACE) is an invasive intervention that was first used to manage intrahepatic tumor growth in the 1980s and today is an established technique for treating hepatocellular carcinoma. Trans-arterial chemoembolization is now a prominent and standard palliative management for non-respectable liver metastases from primary colorectal cancer, others as neuroendocrine tumors and breast cancer. The high safe profile and clinical effectiveness of TACE have therefore meant that it is a viable option for patients with incurable disease. (Daniel, et al., 2012)

The administration of chemotherapeutic agents before embolization leads to exposure of the tumor to a higher concentration of chemotherapeutic agent and subsequent tumor necrosis due to vascular occlusion. (Fashiha, 2019). Embolization of the feeding arteries reduces arterial inflow and decrease washout of the chemotherapeutic agent, which importantly decreases systemic exposure. Drug-Eluting Bead TACE (known as DEB-TACE) is a newer intervention that uses

microspheres loaded with chemotherapeutic agents, which are administered into the tumor feeding artery with or without further embolization (Fashiha et al., 2019 & Heimbach et al., 2018)

Each medical intervention have benefits and complications and adverse effect. Complications associated with TACE includes post embolization syndrome (PES) which is commonest and is characterized by nausea, vomiting, pain in the right upper quadrant (RUQP), and fever; it requires hospital admission and at least a one night inpatient stay, PES remains the primary indication for acute inpatient management during standard admissions and is primarily responsible for increasing both the patient's TACE-related length of stay (LOS) and recurrent hospital admissions. Other complications as intra-peritoneal hemorrhage, liver failure, liver abscess, and cholecystitis are uncommon. Also others complications includes overt and covert bleeding at the femoral puncture site, neurovascular compromise of the affected leg, and sensitivity to the contrast medium. (Zhou, 2010)

The incidence of site insertion complications as hematoma at the puncture site is 5% to 23%. The main clinical findings are erythema and swelling at the puncture site, with a palpable hardening of the skin. Pain and decreased range of motion in the affected extremity can also occur. Simple hematomas exhibit a stable size and hemoglobin count and are conservatively. Initial managed management involves: marking the site and checking frequently for a change in size, as well as applying pressure. Strict bed rest is recommended, with the affected leg kept straight for 4 to 6 hours. The hemoglobin concentration and hematocrit should be monitored for acute blood loss. Simple hematomas usually resolve in 2 to 4 weeks. (**Kallini, 2016 & Miyayama, 2010**) Nursing management of the patient with TACE incorporates a variety of nursing interventions; protecting the patient from injury, providing comfort and emotional support, maintaining surveillance for complications, and educating the patient and family. Before the procedure, the patient should be asked about any sensitivity to contrast. Post procedural assessment involves monitoring vital signs, observing the injection site for bleeding, and assessing neurovascular integrity distal to the injection site every 15 minutes for the first 1 to 2 hours. Depending on how the puncture site is stabilized after the procedure, the patient may have to remain flat in bed for a specified length of time. Any evidence of bleeding and neurovascular impairment must be immediately reported to the physician. (Ay, et al., 2011, Lance, McLennan, & Obuchowski, 2011, Malagari, et al., 2010, Malagari, Pomoni, & Spyridopoulos, 2011)

Significance of the study

Various studies documented that the annual incidence of HCC showed a significant increase. If left untreated, liver cancer has a poor prognosis with more than 90% of patients dying of the disease within years of diagnosis. Trans-arterial chemoembolization (TACE) is the recommended treatment modality for asymptomatic, large or multifocal HCC. These patients are often followed by nurse because they are at high risk of developing post-procedure complications. Delayed recognition of major complications and subsequent ones can cause significant morbidity and mortality. The prevention of major complications following TACE therapy is critical.

Aim of the study

Was to evaluate the effect of implementing a nursing protocol on patients' undergoing trans-hepatic arterial chemoembolization.

Research hypothesis

A significant reduction in the incidence and consequences of post procedure complications in the study group compared to control group patients.

A significant reduction in ICU stay post procedure in the study group compared to control group patients.

Patients & Method

Research design: A quasi experimental research design was utilized in this to fulfill the aim of this study.

Setting: This study was carried out at adult intensive care unit and gastroenterology ward at Al Rajhi hospital

Sample: A convenience sample of all adult patients aged from (18—60) years old with hepatic cell carcinoma and had received trans-arterial chemoembolization were included in this study. They were assigned into study and control groups. The patients with advanced liver disease (Child –Pugh C), active GI bleeding, encephalopathy, refractory ascites, presence of vascular invasion or portal vein occlusion due to liver tumor, extra hepatic metastases, proto-systemic shunt, stage 3 or 4, and end stage tumor disease were excluded from the study.

Tools

The following two tools were utilized to collect data pertinent to this study. They were developed by the researchers after extensive review of the relevant literature. (Van, Borbath, Shim, et al., 2009, Frangakis, Geschwind, & Kim, 2011, Malagari, Pomoni, & Spyridopoulos, 2011)

Tool (1) Patient assessment questionnaire: to assess patients' demographic and medical data and consists of four parts:

Part 1- Demographic, history and clinical examination: This part was concerned to assess patients demographic data; patient's age and sex, history of previous liver diseases, presence of genetic and metabolic diseases affecting liver, history of onset and progression of symptoms, information from patient such as (jaundice, abdominal pain, nausea, vomiting, bowel disturbances, fever, appetite changes, neurological changes, changes in color of urine and stool, etc.). Complete physical assessment including vital signs, signs of liver damage, jaundice, bowel dysfunction, encephalopathy, and ascites, past and present history of any other disease, medications for other diseases.

Part 2- Laboratory and imaging assessment

It included fasting blood sugar and HbA1c in diabetic patient, kidney function tests (serum urea and creatinine), liver function tests (ALT, AST, prothrombin time and concentration, total and indirect bilirubin, serum albumin), complete blood picture and baseline level of viremia HCV using polymerase

chain reaction (PCR), AFP. Imaging assessment including; abdominal ultrasonography and fibro-scan. Part 3- Child-Turcotte-Pugh-score. This score was adopted from (Friedman, 2012). The Child-Pugh Score is a scoring system used to determine the prognosis with cirrhosis and need for liver transplantation. This part was concerned to assess the severity of the disease and predict mortality in patients with liver cirrhosis. This score includes three biochemical markers (serum albumin, total bilirubin, and prothrombin time, INR) and clinical features as the presence of ascites and hepatic encephalopathy. The Child score ranges from 5-15 with individual scoring; 5-6 being class A, 7-9 are being class B and 10-15 class C.

Part 4 - Visual Analogue Pain Scale: It was adopted from Flaherty (1996) and was used to assess pain intensity at the puncture site and around it after the procedure. The scale determines the level of pain intensity as follows: (0) no pain, (1-3) mild pain, (4-6) moderate pain and (7-10) severe pain.

Tool (II): Patients' outcomes assessment questionnaire

This tool was developed to evaluate patient's outcomes and complications of the diseases such as ICU stay, Post embolization syndrome (PES) and site of insertion complications as bleeding and hematoma.

Research implementation

This study was carried out in three phases:-

Phase (I): Preparatory phase

This study included sixty patients diagnosed with hepatic cell carcinoma who were recruited over a period of 6 months from January 2018 to June 2018 and received TACE.

Permission was obtained from authorities' personnel. Ethical consideration was approved from local ethical committee. Consent was taken from participating patients or relatives after explaining the nature and purpose of the study.

Content validity of tools: The tools were tested for content validity by jury of 5 experts in the field of critical care nursing and tropical medicine and gastroenterology at Asyut University and the necessary modifications were done.

Reliability was estimated by Cronbach's Alpha for tool 1 patient assessment sheet and its result was 0.89, for tool 2 patients' outcomes assessment sheet and its result was 0.87 which were accepted.

The pilot study was carried out on (6) patients who met the predetermined selection criteria to test applicability of the tools then necessary modifications were done according to the results of the pilot study and expertise opinions. The participants of pilot study were excluded from the main study.

Ethical considerations

the research proposal was approved from the ethical committee in the faculty of nursing, there was no risk of study subjects during the application of the research, the study followed common ethical principles in clinical research, an informed consent was obtained from each patient participate in the study, confidentiality and anonymity were assured and patient's privacy was considered during the collection of data.

Phase (II): Implementation phase

Data were collected from liver intensive care unit and gastroenterology department at Al-Rajhi liver hospital from the first day of admission till discharge then the data were recorded in the developed tools.

Study group

Before implementation of the nursing protocol, the researcher reviewed the patient's medical and surgical history which was followed by an assessment of patient's current level of consciousness. The researcher filled out the designed assessment sheet from one day before procedure until discharge.

The nursing protocol

Pre procedural considerations

The patient was admitted to the hospital the night before the procedure for correction of any coagulation or other abnormalities, patient monitoring before the procedure was performed with a blood pressure cuff, heart monitor, and pulse oximeter, vital signs (temperature, blood pressure, pulse), weight and height, physical examination (jaundice, palmer erythema, tremors, white nails, ascites, bruises, scratch marks, spider naevi, splenomegaly, lower limb edema, degree of edema). Abdominal ultrasound was done and laboratory investigation (fasting blood sugar and HbA1c if patient was diabetic, kidney function tests (S. Urea, creatinine), liver function tests (ALT, AST, prothrombin time and concentration and total and indirect bilirubin), complete blood picture, (PCR) quantitative, AFP at week (16-24) only and fibro scan (transient electrography) at the start and end of treatment.

Child turcotte Pugh (CTP) scoring system was performed, the researcher instructed the patient to fast at midnight the night before the treatment, medications routinely be checked with their physician, the researcher record and monitor for side effects, recorded any of the following conditions: asthma, diabetes, and allergies to iodine, shellfish, drugs, or latex, a venous access obtained before the procedure, drugs including pain medications, antiemetic agents and steroids were administered intravenously, bowel preparation the night before treatment was done and pretreatment with subcutaneous octreotide in patients with carcinoid

tumors to limit carcinoid crisis caused by hormonal dumping from tumor necrosis after embolization.

Post procedural considerations

The nurse assesses patient's vital signs every shift, ambulate with stand-by assist, intravenous fluids: 0.9% NS 150 mL/hr. were administered, pain control via intravenous , antibiotic treatment for 3–7 days following chemoembolization to cover Gramnegative enteric pathogens, Labs q8–12 hours: CBC, coagulation studies, basic panel, liver panel, 2 g Na diet.

Frequent assessment for the following: abdominal pain, nausea/vomiting, bowel changes, post-procedure bleeding, either at puncture site or internally, skin assessment q shift, prolonged table time in angio suite, radiation burns can occur anywhere on body (radiofrequency ablation only).

Monitor for signs and symptoms of acute liver failure as jaundice and encephalopathy, maintain a schedule of follow-up for laboratory tests and clinic visits 2 weeks after procedure and need for repeated CT scan or MRI 6 weeks after procedure, contact the patients regularly or when the patient needs and assure the patient medication adherence, ask about any side effects, any old or new drugs used by the patients and instruct regarding drug-drug interactions.

Control group

The control group received the routine care in the unit and were assessed by the researcher using first tool: assessed demographic data and medical data, past and present history of disease for patients, assess hemodynamic status manually laboratory investigation and imaging test, physical examination assessment on first visit and once per month for six months to fill the assessment sheet for patient according to routine of unit.

Evaluation phase

Patients were evaluated for the effect of nursing intervention on patient's outcomes (Study group) in comparison to the control group and to assure on the studied group patients compliance to the given instructions by using tool (1).

Statistical design

The collected data were reviewed, prepared for computer entry, coded, categorized, analyzed and tabulated. Descriptive statistics as mean, standard deviation, number, and percentage, were done using SPSS version 21 Statistically significant difference was considered at p-value less than 0.05(p< 0.05). The t-test was used to determine significant difference for the numeric variables. The chi-square test was used to determine significant difference in the non-parametric variables. Also correlation was done by Pearson Correlation.

Results

Table (1): Comparison between the study and control groups in relation to demographic variables.

Variables	Control	Control group (n=30)		Study group (n=30)		
	No	%	No	%	p-value	
Sex:						
Male	20	66.7	21	70.0	1.000ns	
Female	10	33.3	9	30.0		
Age (years):						
≤ 30	8	42.1	11	57.9	0.705ns	
31-50	9	52.8	8	47.1		
> 50	13	54.2	11	45.8		
Mean ±SD	45.1±16.65		40.7±19.6		0.357ns	

NS= no statistical significant difference; data described as (n & %), chi-square and (mean \pm SD) independent sample t-test

Table (2): Frequency and percentage distribution of patients (study and control) according to their medical data.

Modical data	Control group (n=30))) Stud	Study group (n=30)	
Medical data	N.	%	N.	%	
HBV:					
Positive	7	23.3	7	23.3	
HCV:					
Negative	7	23.3	7	23.3	
Positive	23	76.7	23	76.7	
Time of knowing infection with	hepatitis C/	year:			
Mean ± SD	1	11.47 ± 4.84		12.27 ± 4.14	
Liver:					
Abnormal Eco pattern	6	20.0	3	10.0	
Cirrhotic	24	80.0	27	90.0	
Portal vein:	•	·	•	•	
Thrombosis	6	20.0	4	13.3	
Ascites:		•			
No	18	60.0	17	56.7	
Yes	12	40.0	13	43.3	
Degree of ascites					
Mild	7	23.3	10	33.3	
Moderate	4	13.3	2	6.7	
Severe	1	3.3	1	3.3	
Site of hepatocellular carcinoma	a:				
Right side	22	73.3	24	80.0	
Left side	8	26.7	6	20.0	
Number of hepatocellular carci	noma lesions	S:			
One	13	43.3	16	53.3	
Two	10	33.3	10	33.3	
Three	4	13.3	2	6.7	
More than three	3	10.1	2	6.7	
Ablated for hepatocellular carc	inoma:				
No	21	70.0	23	76.6	
yes	9	30.0	7	23.3	
Ablation for hepatocellular card	cinoma:				
Successful	8	26.7	6	20.0	
Not successful	1	3.3	1	3.3	

data described as (n & %),

Table (3): Changes of pain scores in relation to time after TACE in the study and control groups post implementing the nursing protocol

	Control group (n=30) Study program (n=30)			
Time	$Mean \pm SD$	Mean ± SD	p-value	
T0	3.63±0.669	3.87±0.571	0.152ns	
T1	3.45±1.34	3.0±0.85	0.156 ns	
T2	3.77±0.59	3.19±0.63	0.023*	
T3	3.95±0.58	3.15±0.75	0.004*	

^{*}statistically significant difference (p<0.05) NS=no statistical significant difference

T0: immediately after TACE, **T1**: 2 hours after TACE, **T2**: 4 hours after TACE, **T3**: 6 hours after TACE, TACE: Trans-hepatic arterial chemoembolization

Control group Study group (n=30) **Outcomes** (n=30)p-value % N Post embolization syndrome 30 100.0 20 66.7 0.005* Insertion site complications 24 80.0 0.05* 20 66.7 1.3 ± 0.991 ICU stav 1.9 ± 0.232 0.05*

Table (4): Comparison between the study and control groups as regards arterial chemoembolization outcomes

Data described as (n & %), chi-square*statistically significant difference (p<0.05)

Table (1): Presents the demographic variables of the studied patients. It was found that there was predominance of male in both groups (70.0%, 66.7% respectively). The highest percentage of age was between 18 to 30 years (45.8%, 54.2% respectively), with a mean age of $(40.7\pm19.6, 45.1 \pm 16.65 \text{ respectively})$.

Table (2): Illustrates that; 23 patients (76.7%) were positive for HCV, regarding time of knowing infection with hepatitis C in both groups it was (12.27 \pm 4.14, 11.47 \pm 4.84 yrs. respectively). On the other hand, seven (23.3%) patients were positive for HBV infection. (80 % and 90 %) of patients were cirrhotic, (80 % and 86.7 %) were having a patent portal vein, (40 % and 43.3 %) had ascites out of whom 23.3 % and 33.3 % was mild, all patients were diagnosed as having a HCC mostly in the right side (73.3 %, 80 %) the highest percentage of them were having one lesion (43.3 % and 53.3 %) out of whom (30 %, 23.3 %) underwent previous ablation which was mostly successful (26.7 %, 20 %) respectively.

Table (3): Demonstrates the changes of pain scores in relation to time after TACE in the study and control groups, this table indicates that; there has been a statistically significant difference among study and control groups after 4hrs and 6 hours from TACE post implementing the nursing protocol.

Table (4): Shows that; there were significant differences between the two groups with regard to post embolization syndrome, insertion site complications and length of ICU stay.

Discussion

Despite the availability of curative treatment modalities, such as liver transplantation, surgical resection, and radio-frequency ablation, the outcomes of patients with hepatocellular carcinoma (HCC) remain poor. Accordingly, non-curative treatments, such as trans-arterial chemoembolization (TACE), radio-embolization, and sorafenib, are used in patients with advanced HCC. Hence, the aim of this study was to evaluate the effect of implementing nursing protocol on trans-hepatic arterial chemoembolization patients' outcomes.

In respect to demographic characteristics; the current study reported that there was a male predominance in both groups. This coincides with the results of (Ferlay et al., 2015) who reported that HCC predominantly affects males with incidence two to four times more common in males than females. The researcher point of view, this could reflect that the reasons for this gender disparity are complex and may stem from differences in behavioral risk factors, metabolic factors, tumor biology, and treatments received. The present study also, revealed that more than one fifth of both groups their age was >50 years, with a mean age of $(40.7 \pm 19.6, 45.1 \pm 16.65)$ respectively). This could be explained that HCC is the most common type of primary liver cancer in adults. This finding was in line with (European Association for the Study of the Liver, 2018) which reported that the highest prevalence of HCC was among age groups of 30 to 50 years. (Yuangan et al., 2019) conducted a study from May 2008 to July 2016, a total of 185 patients underwent cTAE/TACE therapy via extrahepatic collaterals for HCC were identified and included in this study. Of the 185 patients, there were 167 male and 18 female, with mean age of 50.7 ± 7.3 years (range, 32–81 years).

Concerning time of knowing infection with hepatitis C in both groups, the current study denoted that the mean time of all groups was $(12.27 \pm 4.14, 11.47 \pm 4.84)$ years respectively). This finding is consistent with (**Miki etal., 2008**) who said that the average time at onset of HBV related to HCC was reported to be at least 10 years earlier than that of HCV related to HCC.

According to medical data of the studied patients it was found that more than three quarters of studied patients were positive for HCV. On the other hand more than one fifth of them were positive for HBV, and all patients were diagnosed having a hepatocellular carcinoma on a background of liver cirrhosis mostly on the right side. These findings were in agreement with (Kumar et al., 2015) who mentioned that HCC is the most common type of primary liver cancer occurring most often in people with cirrhosis caused by hepatitis B or hepatitis C but HCV-related HCC is predominantly encountered. In my opinion viral hepatitis is the major infectious diseases in Egypt and needs to researchers to eradicate this problems.

The present study denoted that, there was a very highly statistically significant difference between both groups post implementing the nursing protocol with regards to their puncture site care. This study is in concordance with (Mendes 2015) who concluded that habitual performance of the nurses post procedure includes monitoring vital signs, close assessment, pain relief, management of complications and health education. Nurses should closely monitor patients who had undergone PCI post procedurally to avoid complications.

In this study, the statistical analysis showed that there has been a statistically significant difference among study and control after 4 hrs. and 6 hrs. from TACE post implementing the nursing protocol. This study was supported by (Skef et al., 2020) who stated that of all the post TACE syndrome events, pain is most frequently associated with an extended hospital stay. Thus, effective peri-procedural and immediate postprocedural pain control in patients treated by TACE are essential to reduce overall morbidity and the duration of the hospital stay. (Guido et al., 2010) stated that pain is one of the more troublesome symptoms reported by patients, and it may sometimes be a sign of a serious complication. It was reported in 250 out of 330 TACE procedures (75.8% of the total). (Lv et al., 2016) proved that the most frequently reported symptom was pain, followed by fever, however, which were also frequently encountered in patients without major complications.

As regards incidence of post-embolization syndrome, our findings indicate that all patients in the control group experienced post-embolization syndrome as compared to less than one fifth of the study group post implementing the nursing protocol. This is in agreement, with the study of (Mason et al., 2015) on Post-embolization syndrome as an early predictor of overall survival after trans-arterial chemoembolization for hepatocellular carcinoma who found that PES was the most common complication after TACE, occurring in over one-third of patients. Similarly, the study of (Quinto et al., 2018) concluded that PES is a type of minor and pathognomonic complication of TACE. It can appear immediately afterwards or in the 10 days following the procedure. It occurs in the form of fever, abdominal pain, nausea and/or vomiting and elevated transaminase levels. Also in this respect, (Gardini et al., 2018) stressed that post-embolization syndrome (PES) occurs in the majority of patients undergoing hepatic chemoembolization, and is the major reason for hospitalization after the procedure.

Considering hospital length of stay of the studied patient's results dedicated that the majority of patients in the study group had less than 2 days of hospital length of stay post implementing the nursing protocol,

while patients in the control group had more than 2 days of hospital length of stay. This results agree with the study of (Elsayed et al., 2016) entitled "Postembolization syndrome: Outcomes regarding the type of embolization" which revealed that PES developed in 16 patients (6.4%) with a median length of hospitalization of 4.4 days (range 1-7days). (Timothy & Clark, 2006) documented that because TACE can be performed through small-caliber diagnostic (4 to 5 French) catheters and micro-catheters, placement of large-diameter sheaths at the access site is seldom necessary. Therefore, complications related to puncture site access are uncommon. Access site hematoma is most frequently encountered and occurs in 2% of patients. Arterial pseudo-aneurysm and arteriovenous fistula develop rarely and can be minimized with meticulous puncture site planning to avoid puncture above the inguinal ligament or at the superficial femoral artery. PES remains the primary indication for acute inpatient management during standard admissions and is primarily responsible for increasing both the patient's TACE-related length of stay (LOS) and recurrent hospital admissions. The health care givers should be update their information introduce optimal nursing care. prevent complications and improve outcomes.

Conclusion

The present study concluded that implementing the nursing protocol on trans-hepatic arterial chemoembolization appear to be effective in terms of reducing incidence and consequences of post procedure complications, and length of hospital stay in the study group compared to the control group patients.

Recommendations

Based on the results of the current study it can be concluded that; a printed copy of the nursing protocol is to be distributed among patients undergoing trans hepatic arterial chemoembolization. A workshop for nurses working in liver ICU & gastroenterology department is to be organized for enriching nurses with recent guidelines related to trans-hepatic arterial chemoembolization. Patients and their caregivers need to be apprised of post embolization syndrome symptoms prior to TACE and provided with adequate nursing care for symptom control and replication of the study on a larger probability sample from different geographical areas for generalization of the results.

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