

## RESEARCH ARTICLE

# Side Effects of Chemotherapy among Cancer Patients in a Malaysian General Hospital: Experiences, Perceptions and Informational Needs from Clinical Pharmacists

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### Abstract

**Background:** This study aimed to assess the most common physical side effects experienced by local chemotherapy patients. Their perceptions of these side effects and informational needs from clinical pharmacists were also evaluated. **Materials and Methods:** This was a single-center, cross-sectional study. A face-to-face interview guided by a structured questionnaire with cancer patients admitted to receive repeated cycles of chemotherapy was conducted. Information collected included chemotherapy-related side effects after last chemotherapy experience, the most worrisome side effects, the side effects overlooked by healthcare professionals and the preferred method, amount and source of receiving related information. **Results:** Of 99 patients recruited, 90 participated in this survey (response rate: 90.9%). The majority were in the age range of 45-64 years (73.3%) and female (93.3%). Seventy-five (83.3%) and seventy-one (78.9%) experienced nausea and vomiting, respectively. Both symptoms were selected as two of the most worrisome side effects (16.7% vs. 33.3%). Other common and worrisome side effects were hair loss and loss of appetite. Symptoms caused by peripheral neuropathies were perceived as the major symptoms being overlooked (6.7%). Most patients demanded information about side effects (60.0%) and they would like to receive as much information as possible (86.7%). Oral conversation (83.3%) remained as the preferred method and the clinical pharmacist was preferred by 46.7% of patients as the educator in this aspect. **Conclusions:** The high prevalence of chemotherapy-related side effects among local patients is of concern. Findings of their perceptions and informational needs may serve as a valuable guide for clinical pharmacists to help in side effect management in Malaysia.

**Keywords:** Chemotherapy side effects - cancer informational needs - Malaysia

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### Introduction

Worldwide, more than 12 million individuals are newly diagnosed with cancer annually (Torpy et al., 2010). Of 8.2 million cancer deaths in 2012, 65% occurred in less developed regions. The most prevalent cancers were lung (13.0%), breast (11.9%) and colorectum (9.7%) (IARC, 2012). Cancer burden of Malaysia was reflected by the 18,219 new cases diagnosed in 2007 (The Ministry of Health, Malaysia, 2007). Increases in cancer prevalence have been leading to the ever-improving treatment modalities. On top of surgery and radiotherapy, the use of chemotherapy as well as targeted therapy has increased along with the availability of supportive treatment for its side effect management (Dohler et al., 2011).

Generally, physical side effects caused by chemotherapy have been well-characterized (Meirow and Nugent, 2001; Partridge et al., 2001; Shapiro and Recht, 2001; Sun et al., 2005; Arslan et al., 2013). Among the most common chemotherapy-induced side effects are bone marrow suppression, neuropathies, gastrointestinal disorders,

hair loss, fatigue and skin disorders. Some drug-specific side effects have also been identified. For examples, anthracyclines and bleomycin are associated with cardiotoxicity and pulmonary toxicity, respectively (Ismail et al., 2011). Effective management of chemotherapy-induced adverse effects is important to improve quality of life (QOL) of patients which may eventually influence their willingness to complete the treatment (Carelle et al., 2002; Kayl and Meyers, 2006).

On top of that, patients' perceptions of chemotherapy-related physical side effects were widely explored. Among the ovarian cancer patients, complete control of chemotherapy-induced nausea and vomiting (CINV) and absence of alopecia were identified as the most favourable health states (Sun et al., 2002; Sun et al., 2005). In contrast, multiple severe side effects and hepatotoxicity were the least preferred health states (Sun et al., 2002). Alopecia was also described as a distressing side effect by breast cancer patients as it had consistently affected their QOL and body image (Lemieux et al., 2008; Kim et al., 2012). As emphasized by studies since 1980's,

integrating patients' perceptions regarding side effects into decision making process during cancer treatment is always important (Coates., 1983; Carelle et al., 2002).

Cancer patients demand information to understand chemotherapy-related adverse effects and actions to be taken. Provision of sufficient pre-chemotherapy information including side effects and self-care strategies was proven to reduce certain treatment-related concerns and physical and psychosocial outcomes (Aranda et al., 2012). A study of Chinese breast cancer patients showed that side effects of chemotherapy and their management were given a higher priority among the information needed (Lee et al., 2004). According to a local survey, possible side effects, their management and prevention were ranked as the most important treatment-related informational needs besides rationale of treatment and how it would work against cancer. However, there is always a gap between patients' actual needs and information provided by healthcare professionals (Lei et al., 2011).

As indicted by numerous studies since the last decade, clinical pharmacists have been positively contributing to the reduction of chemotherapy-related medication errors (Goldspiel et al., 2000; Ghandhi et al., 2005), improvement of chemotherapy process safety (Bonnabry et al., 2006) and continuum of patient care (Coutsouvelis et al., 2010). Few studies had also described the impact of clinical pharmacy services on improving patient care and education (McKee et al., 2011; Valgus et al., 2011; Lihara et al., 2012; Tuffaha et al., 2012). However, patients' informational needs from pharmacists have not been fully studied.

To date, little is known about the local patients' experiences and perceptions of chemotherapy-related side effects and their expectations on related information provided by pharmacists. This study aimed to: 1) assess the most common physical side effects experienced by local chemotherapy patients; 2) evaluate their perceptions of these side effects; 3) investigate their informational needs from clinical pharmacist.

## Materials and Methods

### *Study Design and Setting*

This was a cross-sectional study undertaken in four selected wards within the Hospital Sultanah Bahiyah, Alor Setar. Two of these wards belong to the Department of Obstetrics and Gynecology and Surgery, respectively. Our hospital is the biggest general hospital in Kedah State, with approximately 1500 cancer patients receiving chemotherapy annually. This survey was registered with the National Medical Research Registry (NMRR) and approved by the Medical Research Ethics Committee (MREC) before any data collection procedures.

### *Patient Recruitment and Sampling*

This study involved patients with confirmed malignancies who were admitted to receive chemotherapy in any of the targeted wards. As we intended to assess their experiences of side effects, only those who had previously received at least one cycle of similar chemotherapy regimen were included. We excluded those who were

unable to communicate with pharmacist in the Malay Language or unwilling to be surveyed.

A two-month study period from April to May 2013 was planned. Number of patients receiving chemotherapy in these wards during February and March 2013 was used to estimate the sample size. In total, there were 248 patients scheduled for chemotherapy during this period. We applied Daniel's formula with finite population corrected and the projected sample size needed was 89 patients (Naing et al., 2006). Calculation was based on the estimation that about 90% of patients would have experienced chemotherapy-related side effects. We fixed the level of confidence and precision at 95% and 5%, respectively. Number of patients recruited was increased to account for a 10% non-response rate. They were selected using the convenient sampling technique.

### *Data Collection and Instrumentation*

Demographic information of recruited patients was collected from the e-Hospital Information System (e-HIS). After providing a written informed consent, each of them was interviewed by one of five appointed pharmacists prior to chemotherapy administration in the ward. A questionnaire consisting of three parts was used to guide the interview sessions. It was constructed in the Malay Language and the same language was used throughout the interviews.

First part of questionnaire is a checklist of common side effects experienced by patients after last cycle of chemotherapy. As recommended by the Multinational Association of Supportive Care in Cancer (MASCC), severity of CINV was assessed based on the nausea score and number of emesis episode if they experienced any of these two side effects (Molassiotis et al., 2007). Other possible side effects were assessed solely on a "yes" or "no" basis. Second part is two questions which evaluate patients' perceptions of side effects they were most worried about and being overlooked by healthcare professionals. Third part contains seven questions adapted from a similar study to explore patients' informational needs (Piredda et al., 2008). Forward translation of these questions from English to the Malay Language was conducted by a pharmacist who was proficient in both languages. Backward translation was done by another pharmacist. An option of "clinical pharmacist" was added to one of these questions which assessed the patients' preferred educator. Content of this questionnaire was validated by a panel of three (one oncologist and two oncology pharmacists). It was also piloted with 15 patients prior to data collection to make sure that they were able to interpret and answer all questions.

### *Statistical Analysis*

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0. Categorical data was described as frequencies and percentages, whereas continuous data was described as medians and interquartile ranges (IQR). Associations of two categorical variables were tested using the Pearson's chi-square or Fisher's exact tests, where appropriate. Considering convenient sampling was conducted, non-parametric tests including

Mann-Whitney (2 groups) and Kruskal-Wallis (more than 2 groups) tests were used throughout the comparisons of median differences. If a significant difference was detected in any Kruskal-Wallis test, pairwise comparisons were conducted using the Mann-Whitney tests with Bonferroni corrections. The levels of significance were fixed at 5%.

## Results

Of 99 patients recruited, 90 of them agreed to participate in this survey (response rate: 90.9%). The majority of patients were at age of 45-64 years (73.3%), female (93.3%) and Malay (86.7%). Approximately two third of them received only primary (36.7%) or secondary (40.0%) education. They mainly had ovarian (36.7%), uterine (23.3%), cervical (20.0%) and breast (6.7%) cancers. The most common chemotherapy regimens included paclitaxel and carboplatin (36.7%), gemcitabine (16.7%) and doxorubicin (13.3%).

In total, 75 (83.3%) and 71 (78.9%) of patients experienced nausea and vomiting after last cycle of chemotherapy, respectively. The median nausea score was 3.00 (IQR=5.00), whereas the median emesis episode was 4.00 (IQR=5.00). Differences of CINV severity among different patients' characteristics are summarized in Table 1. On top of CINV, most patients also experienced dry mouth or thirst (73.3%), hair loss (64.4%), tiredness or weakness (56.7%), loss of appetite (56.7%) and coldness (56.7%). Numbness in fingers or toes (46.7%), confusion or loss of concentration (43.3%), sadness or depression (43.3%) and reduced sense of touch (40.0%) were also reported.

Of all symptoms, patients were generally most worried about vomiting (33.3%), loss of appetite (23.3%), nausea (16.7%), hair loss (10.0%) and numbness (10.0%). Associations between patients' characteristics and side effects they were most worried about are described in Table 2. Majority of patients (86.7%) believed that none of these symptoms were overlooked by healthcare professionals. A small group indicated that neuropathy (6.7%), tiredness (3.3%) and bruises (3.3%) had been

**Table 1. Differences of CINV Severity among Different Characteristics (n=90)**

Variable	Median nausea score (IQR)	p-value	Median emesis episode (IQR)	p-value
Age Group (years)		<0.001*		0.028 <sup>b</sup>
20-44	5.50 (5.00)		5.50 (2.50)	
45-64	3.00 (4.00)		3.00 (6.00)	
≥65	4.50 (5.00)		4.50 (5.25)	
Gender		0.002		<0.001
Male	1.00 (2.00)		1.50 (2.25)	
Female	3.00 (5.00)		4.50 (5.00)	
Chemotherapy regimen		0.001 <sup>c</sup>		0.015 <sup>d</sup>
Paclitaxel and carboplatin	3.00 (5.00)		3.00 (6.00)	
Gemcitabine	2.00 (3.00)		0 (3.00)	
Doxorubicin	4.00 (4.25)		4.00 (5.25)	
Others	5.00 (5.00)		6.00 (3.25)	

\*Group 20-44 years versus 45-65 years (p = 0.003); <sup>b</sup>group 20-44 years versus 45-65 years (p = 0.024); <sup>c</sup>gemcitabine and doxorubicin (p = 0.036); gemcitabine and others (p = 0.009); <sup>d</sup>gemcitabine and doxorubicin (p = 0.036); gemcitabine and others (p = 0.003)

**Table 2. Associations between Patients' Characteristics and Side Effects, They Were Most Worried About (n=90)**

Variable	Number of patient (%)		p-value
	CINV	Non-CINV symptoms	
Age Group (years)			0.114
20-44	6 (33.3)	12 (66.7)	
45 and above	39 (54.2)	33 (45.8)	
Gender			0.026
Male	6 (100)	0	
Female	39 (46.4)	45 (53.6)	
Chemotherapy regimen			0.015
Paclitaxel and carboplatin	15 (45.5)	18 (54.5)	
Gemcitabine	3 (20.0)	12 (80.0)	
Doxorubicin	6 (50.0)	6 (50.0)	
Others	21 (70.0)	9 (30.0)	

**Table 3. Patients' Informational Needs for Chemotherapy-Related Side Effects from Clinical Pharmacists (n=90)**

Aspect	Number of patient (%)
When should they be informed	
As soon as one knows is going to be given chemotherapy	54 (60.0)
Between treatment decision and first cycle of chemotherapy	18 (20.0)
After the first cycle of chemotherapy	15 (16.7)
After side effects manifested	3 (3.3)
How much information would like to be received	
As much as possible	78 (86.7)
A lot	9 (10.0)
Enough	0
As less as possible	3 (3.3)
Not at all	0
The way being informed	
Personally, on their own	9 (10.0)
Personally, with a relative	81 (90.0)
Preferred sources of information <sup>a</sup>	
One-by-one conversation with healthcare professionals	75 (83.3)
Written (leaflets and pamphlets)	15 (16.7)
Preferred educator (if not necessarily pharmacist)	
Oncologist	39 (43.3)
General practitioner	6 (6.7)
Clinical pharmacist	42 (46.7)
Nurse	3 (3.3)

Other options given: Audio, video, radio or television broadcasts, specialized journals or magazines, interactive computer programmes and the Internet

overlooked.

A total of 54 (60.0%) patients perceived that information about chemotherapy-related side effects was important for them. It was almost equally important to information about the chances of recovery (70.0%) and more important than the information about the disease itself (53.3%), possible treatment (33.3%) and trajectory of illness (13.3%). Some other aspects which reflected patients' informational needs are summarized in Table 3.

## Discussion

To our knowledge, this is the first study that comprehensively described the chemotherapy-related side effect experiences of local cancer patients. This is also the first study in Malaysia that assessed the informational needs of cancer patients from clinical pharmacists.

Majority of recruited patients belonged to the middle-aged group and had only completed either primary or secondary education. Through ongoing observations, we found that they were generally from low socioeconomic backgrounds with relatively low income. Low education has been associated with the forgetting of medical information and more negative attitudes towards cancer (Kessels, 2003; McCaffery et al., 2003). Low socioeconomic status is also negatively correlated with health-related QOL among the cancer patients (Ashing-Giwa and Lim, 2009). Only by having a better grasp of patients' backgrounds, our healthcare professionals are able to implement an effective strategy in managing chemotherapy-related side effects and providing important information.

Nausea and vomiting were experienced by more than two-third of patients after last cycle of chemotherapy. CINV have been ranked as two of the most feared and distressing side effects since the last three decades (Coates et al., 1983; Schnell, 2003; Farrell et al., 2013). Consistent with these findings, Nausea and vomiting were selected by our patients as two side effects they were most worried about. Prevalence of vomiting was slightly lower than that of nausea but it remained as the most worrisome symptom. Male and elder patients have been associated with a lower risk of CINV (Jordan et al., 2007). However, just like those receiving moderately or highly emetogenic chemotherapy, they were more worried about CINV than other symptoms.

Similar to a previous study (Griffin et al., 1996), more than half and approximately half of chemotherapy patients experienced hair loss and loss of appetite, respectively. In our study, both of them were also selected as two of the most worrisome side effects. It is also important to note that numbness, confusion, loss of concentration and reduced sense of touch resulting from chemotherapy-induced peripheral neuropathies (CIPN) were experienced by nearly half of patients and believed to be the major symptoms being overlooked by healthcare professionals. In fact, CIPN has been described as an understudied and usually underreported side effect (Paice, 2007). Another side effect worthy of discussion is sadness and depression. Again, consistent with previous study (Griffin et al., 1996), it was experienced by more than 40% of patients. The relationship between psychological morbidities and cancer has actually been well-established (Lopez et al., 2011).

Different from an Italian study which highlighted the importance of information about the illness to patients (Piredda M), our patients were most interested with the information about chances of recovery, followed by information about treatment-related side effects. In contrast, both studies were consistent in terms of amount of information they wanted to receive. Majority of patients desired to receive as much information about chemotherapy-related side effects as possible. Both studies also demonstrated that the almost unanimously preferred method for receiving information was oral conversation. Oncologist remained as one of the preferred educators in both studies. It is pleasant to note that clinical pharmacists were almost equally well-accepted in patient education on chemotherapy-related side effects in our

study. Again, consistent throughout both studies, patients preferred receiving information along with their families and majority believed that it should be provided as soon as they knew they were going to be given chemotherapy.

A number of limitations in this study should be considered. It was a single-center study mainly involving female patients from the Department of Obstetrics and Gynaecology. As a study conducted within the referral center for gynecologic cancers in Northern Malaysia, our findings in chemotherapy-related side effects and patients' information needs may not be representative of other hospitals with different patients' characteristics. On top of that, this study had mainly focused on physical side effects resulting from chemotherapy. Future local studies should explore the changes of psychological state among patients. In addition, survey had required patients to recall their side effect experiences from the last cycle of chemotherapy. Recall bias was almost unavoidable during the data collection to a certain degree.

In conclusion, this study had revealed some of the chemotherapy-related side effects commonly experienced by local cancer patients. Though these symptoms have been well characterized, their high prevalence and impact on patients' QOL and psychosocial aspects were of concern. CINV remained as two of the most prevalent and worrisome side effects. CIPN was indicated as the major symptom being overlooked by healthcare professionals. Patients demanded as much information about these side effects as possible before chemotherapy was given. Pharmacists were well-accepted as patient educators in this aspect. In fact, findings of patients' perceptions and informational needs may serve as a valuable guide for clinical pharmacists to help in side effect management.

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