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Adverse drug reactions associated with chemotherapeutic agents used in breast cancer: Analysis of patients' online forums

Abstract

Background: Breast cancer is the most common type of cancer in women worldwide. The benefits of chemotherapy vary depending on the treatment regimen used and the characteristic of the tumour. However, adverse drugs reactions (ADRs) associated with chemotherapeutic agents can cause dose delays or reductions; thereby, affecting the treatment outcomes.

Objective To explore ADRs of chemotherapeutic agents used to treat breast cancer from the patients' perspective.

Methods: A total of 110 threads form nine online discussion forums were evaluated. They were exported into Nvivo for Mac where content analysis was applied. Threads were read carefully to observe emerging patterns which were then coded into subthemes and grouped into main themes.

Results: The participants characteristics on online discussion forums were often missing. 411 participants experienced 473 ADRs that were mainly associated with the nervous and immune systems. The forums' analysis yielded three main themes: patient-patient advice, self-medication and lifestyle changes.

Conclusion: Online discussion forums proposed valued source of data on ADRs associated with chemotherapeutic agents and overall patients' experience with cancer. The ADRs experienced by patients changed their priorities and the way the dealt with the disease. Therefore, healthcare professionals must consider the

patients' experience and attitudes towards cancer when designing a treatment plan. This can be established by increasing communication between healthcare professionals and patients.

Keywords

Adverse drug reaction, breast cancer, chemotherapy, content analysis, patient.

Introduction

Breast cancer is a heterogeneous disease that is characterised by carcinoma formation within tissues of the breast and can be categorised in multiple ways based on; clinical features, expression of tumour markers and histologic type and is the one of the most common types of cancer. In 2015, the UK statistic for new cases of invasive breast cancer was estimated at 55,122 [1].

Health-related quality of life (QOL) is an important outcome of chemotherapy among breast cancer patients. Many of the adverse drug reactions (ADRs) experienced by breast cancer patients as a result of chemotherapy can have a negative effect on the QOL during treatment and disease-free survival [2, 3].

Despite the increasing number of patients taking chemotherapy each year, there are no sufficient studies that look at the patients' perspective on ADRs associated with chemotherapeutic agents. Online discussion forums' use for reporting ADRs has increased markedly over the last few years with 90% of adults using the Internet [4]. Subsequently, online discussions forums provide a rich source of data regarding patients' experience as they deliver open and honest discussions [5]. Only two studies have assessed online discussion forums providing emotional support to breast cancer patients [6, 7], with no studies focusing on issues associated with anticancer treatment or patients' QOL.

The purpose of the study was to investigate ADRs associated with chemotherapy used among breast cancer patients.

Methods

Study design

A retrospective qualitative analysis of online discussion forums was conducted in order to explore breast cancer patients' perspectives of ADRs associated with chemotherapeutic agents. The research comprised an inductive approach, whereby observations were first made followed by the development of theories based on patterns that emerged from the observations [8]. Furthermore, the study involved observations of individuals in situ and was therefore classified as ethnographic [9]. During data collection, categories for interpretation were created for analysis, allowing the creation of themes and sub-themes within the study [10]. As the research carried out was from direct, first-hand observations of data from online sources available to other observers, which could be tested by other researchers for validity, the study was empirical [11].

Data Collection

An Internet search of widely available search engines (e.g. Google, Bing and Yahoo) was conducted to discover online forums. ADRs caused by various

chemotherapeutic drugs and chemotherapeutic drug combinations used to treat primary and secondary breast cancer were discussed publicly. Keywords used were ‘side effects’ OR ‘adverse drug reactions’ OR ‘adverse drug events’ OR ‘discontinuation’ AND ‘breast cancer’, to identify forums with threads referring to ADRs encountered during or after breast cancer treatment. The search returned approximately 987,000 results and the first 10 pages were inspected for relevant websites.

After inspecting multiple websites, the most relevant nine forums were selected and were: csn.cancer.org, breastcancercare.org, community.macmillan.org.uk, cancerresearchuk.org, stupidcancer.org, HealingWell.com, cancercompass.com, breastcancer.org and HER2support.org (Table 1). The forums did not require membership to view the content and were directly accessible. Internal searches were conducted on each of the nine forums for discussion threads regarding ADRs of chemotherapeutic agents used to treat breast cancer. Keywords used in the internal search were the specific drugs used to treat primary or secondary breast cancer: ‘breast cancer’ AND ‘adverse drug reactions’ or ‘adverse drug events’ or ‘side effects or discontinuation’ AND ‘cyclophosphamide’ or ‘fluorouracil’ or ‘epirubicin’ or ‘paclitaxel’ or ‘doxorubicin’ or ‘docetaxel’. The resulting threads were sorted by the date of the most recent

post. The first thirty threads were reviewed and based on the inclusion and exclusion criteria some were removed.

Inclusion criteria were created based on the National Institute for Health and Clnical Excellence (NICE) guidelines for the chemotherapeutic treatment of breast cancer in the UK [12] and on the National Comprehensive Cancer Network (NCCN) guidelines for the chemotherapeutic treatment of breast cancer in the US [13]. Metastatic and recurrent cancer threads were excluded, along with threads not written by the cancer patients themselves. After examination, 107 of the total of 164 threads over the nine forums were found relevant (Table 1).

Data collection took place in May 2018 and threads retrieved were created by users from 2004 until March 2018. In order to maintain the flow of the posts from individual users, including the time and date posted, the threads collected were saved as PDF files. This preserved the format of the discussion as viewed on the websites.

Table 1. Details of forums included in the study

FN	Forum name	Number of threads	Pages analysed	Number of members	Year(s) posted
F1	Breast Cancer Care	18	57	81	2017
F2	Breast Cancer Org	22	44	45	2010-2017

F3	Breast Cancer Topic	25	112	139	2008-2017
F4	Cancer Research UK	19	42	40	2009-2017
F5	Cancer Survival Network	6	47	66	2009-2017
F6	Macmillan Cancer Compass	3	10	8	2004-2008
F7	Healing Well	11	25	28	2004-2008
F8	Stupid Cancer Community	3	6	4	2017
	Total	107	343	411	

FN: Forum number

Data Analysis

Conventional thematic analysis was used for the interpretational meaning of the textual data found within the online threads (Figure 1). The technique specifically requires the generation of coding categories derived directly from the text data during analysis, as the themes are not predetermined [14, 15]. Computer-assisted qualitative data analysis software was used to analyse the material for emerging patterns. In this study, a collection of 110 threads from online breast cancer discussion fora were saved as PDF files and imported into Nvivo Pro 11 software. Nvivo contains the necessary tools for investigating patterns in textual data [16, 17].

All threads were analysed by another researcher (SA) following the inclusion and exclusion criteria to validate the outcomes. Data was analysed over a five-month period, between January and May 2018, each thread was read and then re-read line by line to familiarise the researcher with the content of the discussion. Concepts which could be coded into themes were searched for in the text. The unit coded for analysis may have been a word, sentence or paragraph. To ensure correct codification the context from the entire post of the user was considered. When the text was analysed and a new topic emerged, a new category was created for the data to be coded into. The categories were organised into themes and sub-themes to identify any recurring patterns. Threads that had already been coded were re-read to identify any comments containing the new topics in case they had been previously missed. Continually inspecting the raw data and coded themes maintained consistency within the analysis.

The end point of the study was indicated when saturation was reached and no new themes emerged from the text as all discussion topics had been exposed. Four main themes were identified through thematic content analysis relating to the demography, chemotherapeutic treatment plan, toxicity and patient perception and advice regarding chemotherapeutic treatment.

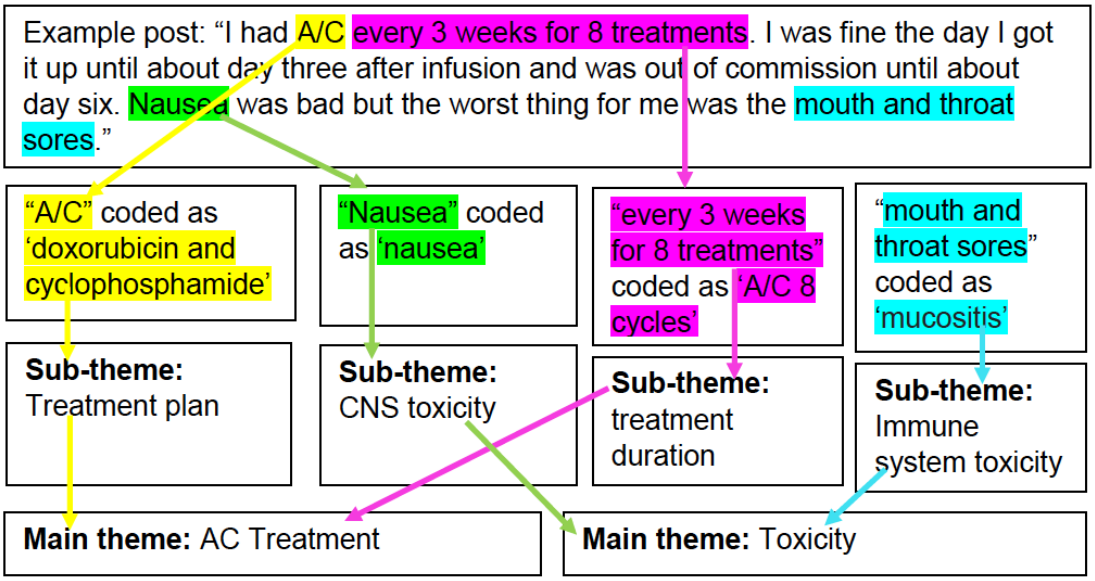

Figure 1. Example of codification and themes created in content analysis

Data Validation

Analysis of the data was completed with as little bias and preconception as possible in order to maintain an open attitude towards the hypothesis of the results. Many of the ADRs reported specific to the chemotherapy within the online forums had been previously discovered in clinical studies [18, 19]. Therefore, ADRs experienced and reported in online forums could be authenticated through the comparison of various scientific journal articles. Moreover, themes and sub-themes that emerged and were related to patients' perceptions and experiences of their treatment were validated internally by two researchers from the team and

externally by comparing them to outcomes of previous literature and medical reports.

Ethical Considerations

This was an observational study where all data collected had already been published on the online forums under usernames to create anonymity within the thread with no interference from the research team. Additionally, any identifying features for example real names were removed from the study in order to protect the identity of the users. During the coding process, all usernames were ignored and not referred to when citing quotes from individuals in the results. The URL addresses of the threads were anonymised to make user identification more difficult. This research was approved by Bournemouth University ethics committee and followed the Declaration of Helsinki (no data was shared outside of the study).

RESULTS

A total of 574 (139.7%) ADRs were reported by 411 patients (Table 2). The ADRs reported affected nine systems: nervous (n = 213), immune (n = 120), skeletal (n = 59), infectious (n = 29), cardiovascular (n = 17), skin (n = 14), endocrine (n = 11), ENT (n = 7) and respiratory (n = 3).

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166 Table 2. ADRs reported by the patients

Adverse effect	Drug/combination	N(%)
	Nervous system (n = 213)	
Neuropathy	AC (n = 25), FEC (n = 10), paclitaxel (n = 20), docetaxel (n = 6), TC (n = 3),	64 (15.6%)
Fatigue	"AC (n = 8), FEC (n = 16), paclitaxel (n = 4), docetaxel (n = 1), TC (n = 8)"	37 (9%)
Change in taste	AC (n = 16), EC (n = 2), FEC (n = 5), paclitaxel (n = 6), docetaxel (n = 3), TC (n = 5)	37 (9%)
Dizziness	EC (n = 5), FEC (n= 9), paclitaxel (n = 1), docetaxel (n = 1)	16 (3.89%)
Memory loss	AC (n = 3), EC (n = 1), FEC (n = 5), paclitaxel (n = 1), docetaxel (n = 2), TC (n = 3)	15 (3.65%)
Insomnia	AC (n = 2), FEC (n = 3), paclitaxel (n = 4), docetaxel (n = 1)	10 (2.43%)
Headache	A (n = 1), AC (n = 6), FEC (n = 1)	8 (1.95%)
Loss of appetite	AC (n = 4), paclitaxel (n = 1), docetaxel (n = 1)	6 (1.46%)
Anxiety	FEC	4 (0.97%)
Dry mouth	AC (n = 3), FEC (n = 1)	4 (0.97%)
"Abdominal and bowel pain"	"AC (n = 1), paclitaxel (n = 1), FEC (n = 2)"	4 (0.97%)
Hypothermia	AC	3 (0.73%)
Fever	AC (n =1), paclitaxel (n = 1)	2 (0.49%)
Paranoia	FEC	1 (0.24%)
Weakness	AC	1 (0.24%)
Mood swings	FEC	1 (0.24%)
	Immune system (n = 120)	
Alopecia	A (n = 2), AC (n = 30),EC (n = 5), FEC (n = 31), Paclitaxel (n = 18), docetaxel (n = 3), TC (n = 17)	106 (25.8%)
Allergic reactions	AC (n = 2), paclitaxel (n = 3), docetaxel (n = 4)	9 (2.19%)
Hair thining	FEC (n = 2), paclitaxel (n = 2), docetaxel (n = 1)	5 (1.21%)
	GIT (n = 101)	

Nausea	A (n = 1), AC (n = 29), EC (n = 1), FEC (n = 23), Paclitaxel (n = 5), docetaxel (n = 1), TC (n = 5)	65 (15.8%)
Vomiting	AC (n = 3), FEC (n = 3), paclitaxel (n =3)	9 (2.19%)
Constipation	AC (n = 6), FEC (n = 1), docetaxel (n = 1)	8 (1.95%)
Diarrhoea	FEC (n = 3), paclitaxel (n = 2)	5 (1.22%)
Heartburn	AC (n = 3), FEC (n = 1), paclitaxel (n = 1)	5 (1.22%)
Indigestion	FEC (n = 4), docetaxel (n = 1)	5 (1.22%)
Sickness	"FEC (n = 2), paclitaxel (n = 1), docetaxel (n = 1)"	4 (0.97%)
	Muscles, joints and bones (n = 59)	
Myalgia	"AC (n = 8), FEC (n = 5), Paclitaxel (n = 9), docetaxel (n = 3), TC (n = 1)"	26 (6.32%)
Joint pain	AC (n = 3), FEC (n = 8), paclitaxel (n = 6), docetaxel (n = 3)	20 (4.87%)
Bone pain	AC (n = 3), paclitaxel (n = 1), docetaxel (n = 4)	8 (1.95%)
"Pain in knees, legs and feet"	AC (n = 1), paclitaxel (n = 4)	5 (1.22%)
	Infection (n = 29)	
Mouth ulcer	A (n = 2), AC (n = 5), FEC (n = 1), paclitaxel (n = 2), docetaxel (n = 2), TC (n = 1)	13 (3.16%)
Flu-like symptoms	AC (n = 7), FEC (n = 1), paclitaxel (n = 2), TC (n = 2)	12 (2.92%)
Infection	FEC (n= 2), docetaxel (n = 1)	3 (0.73%)
Oral thrush	FEC	1 (0.24%)
	Cardiovascular (n = 17)	
Low RBC count	FEC (n = 1), T (n = 1)	2 (0.49%)
Low neutrophil count	AC (n = 1), FEC (n = 1), T (n = 1)	3 (0.73%)
Chest pain	AC	2 (0.49%)
Cardiomyopathy	A (n = 1), AC (n = 1)	1 (0.24%)
CHF	A	1 (0.24%)
Hypertension	docetaxel	1 (0.24%)
Fluid retention	FEC (n = 4), paclitaxel (n = 1), docetaxel (n = 1), TC (n = 1)	7 (1.7%)
	Skin (n = 14)	

Dry skin	A (n = 1), AC (n = 2), paclitaxel (n = 1), docetaxel (n = 1)	5 (1.22%)
Rash	FEC (n = 1), paclitaxel (n = 1)	2 (0.49%)
	Endocrine (n = 11)	
Watery eyes	AC (n = 3), FEC (n = 3), docetaxel (n = 1), TC (n =1)	8 (1.95%)
Weight gain	A (n = 1), paclitaxel (n = 1)	2 (0.49%)
Weight loss	FEC	1 (0.24%)
	ENT (n = 7)	
Hearing loss	FEC	4 (0.97%)
Change in smell	AC	2 (0.49%)
Nose bleeding	FEC	1 (0.24%)
	Respiratory (n = 3)	
Breathing problems	AC (n = 2), paclitaxel (n = 1)	3 (0.73%)

A: Adriamycin; AC: Adriamycin, cyclophosphamide; EC: epirubicin, cyclophosphamide; FEC: Fluorouracil, epirubicin, cyclophosphamide; TC: docetaxel, cyclophosphamide; T: docetaxel

Characteristics of the reported adverse effects

Nervous system

17 categories emerged under nervous system toxicity being: Neuropathy, fatigue, change in taste, dizziness, memory loss, loss of taste, insomnia, headache, loss of appetite, anxiety, dry mouth, abdominal and bowel pain, hypothermia, fever, paranoia, weakness and mood swings. The most prevalent categories were neuropathy, fatigue, change in taste, dizziness and memory loss, and were reported by 64 (15.6%), 37 (9%), 37 (9%), 16 (3.89%) and 15 (3.89%) respectively. This was followed by insomnia, headache and loss of appetite that

were reported by 10 (2.43%), 8 (1.95%) and 6 (1.46%) members respectively. Only 4 (0.97%) reported each of anxiety, dry mouth and abdominal pain. In addition, 1-3 members reported hypothermia, fever, paranoia, weakness and mood swings.

Neuropathy was mainly associated with the use of Adriamycin/cyclophosphamide (AC) (n = 25) or paclitaxel (n = 20) yet was encountered with other regimens including fluorouracil/epirubicin/cyclophosphamide (FEC), docetaxel and docetaxel/cyclophosphamide (TC). Neuropathy was described as worst with docetaxel than other drugs. Symptoms comprised numbness in fingertips, numbness or tingling in the feet, legs from the knee down, toes, face and fingertips. Facial numbness was described as ‘rare’ and ‘unusual’ whereas other types were more common. Additional symptoms associated with neuropathy included getting cold shivers out of a sudden, feeling of pins and needles in feet and constantly dropping things. Members described that symptoms improve ‘as the cycle goes on’. Neuropathy stopped either straight after completion of treatment or 4-5 weeks after completion.

Fatigue was associated with the use of AC, FEC, paclitaxel, docetaxel and TC. Fatigue was described as cumulative over the treatment and its intensity of fatigue varied depending on the regimen. With AC, FEC, TC and docetaxel, fatigue was described as mildly cumulative over the treatment duration, tiring,

affecting productivity, but ‘not so bad’. It started wearing off after the last infusion. Nonetheless with paclitaxel, fatigue was intense, felt the entire time and could last for years afterwards (up to five years).

Change in taste and loss of taste were associated with the use of AC, epirubicin/cyclophosphamide (EC), FEC, paclitaxel, Docetaxel and TC. Change in taste comprised several categories being ‘awful chemical taste’, ‘bad’, ‘’constantly horrible’, ‘salty’, ‘strange’, ‘metallic’, ‘nasty’, ‘unavoidable’, ‘loss of taste’. The change of taste was experienced at days 3-5 of each cycle and the taste buds were back normal 24 hours after the end of each infusion. In some cases, the change in taste lasted up to three days after the infusion.

Dizziness was associated EC, FEC, paclitaxel and docetaxel. Members experienced dizziness, spinning, light-headedness, fuzzy-headedness and loss of balance. Dizziness was encountered when in bed and when in walking. Moreover, 15 (3.65%) members reported memory loss that was associated with the use of AC, EC, FEC, paclitaxel, docetaxel and TC. Memory loss was labelled as ‘chemo brain’ where patients reported to forget everything and was associated with ‘lack of concentration’.

Insomnia, headache and loss of appetite were associated with Adriamycin (A), AC, FEC, paclitaxel and docetaxel. Patients felt sleepy yet were not able to fall asleep. Insomnia was worst with paclitaxel than the other derivatives. Headaches

were attributed to lack of sleep yet varied in duration and lasted up to four hours. Moreover, members reported loss of appetite where they could not eat anything all day.

Anxiety, dry mouth and abdominal pain were linked to FEC, AC and paclitaxel. Anxiety was described as ‘terrible’, ‘chipping constantly’ and often led to hospitalisation. Members also reported dry mouth that lasted up to 8 months after chemotherapy. In additional, abdominal pain was designated as severe and lasting for a long time.

Hypothermia, fever, paranoia, weakness and mood swings were less frequent effects experienced by members who had taken AC, FEC and paclitaxel. Members recommended checking temperature twice a day to monitor decrease or increase in temperature. Moreover, weakness and worrying about the condition were associated with paranoia and mood swings.

Immune system

Three categories emerged under immune system toxicity including alopecia, hair thinning and allergic reactions contributing to 106 (25.8%), 5 (1.21%) and 9 (2.19%) respectively.

Alopecia was the top reported ADR. It consisted of three subcategories including head hair loss (n = 83), eyebrow and eyelashes loss (n = 23). Hair loss was

described as an ‘unpleasant experience’, ‘not fun’, ‘unsettling’, ‘traumatic’ and ‘the worst ADR of treatment’. Members described losing either half or whole of their eyebrows and lashes. Hair loss was encountered at various intervals during the treatment being within 14, 16 or 21 days. The main two regimens associated with alopecia were FEC and AC that had been experienced by 31 and 30 users respectively. Other derivatives associated with alopecia were A, EC, paclitaxel, docetaxel and TC. Users reported the loss of mainly the head hair followed by eyebrow/ eyelashes and facial hair. Few members experienced hair thinning (n = 5) instead of alopecia and was mainly attributed to FEC, paclitaxel and docetaxel. After stopping the aforementioned regimen, users experienced the regrowth of hair but it was described as a slow growth, with super thin hair and ‘with severe chemo curls’. In other instances, the regrown hair was white or ash looking and thicker:

My hair also started off as pure white fuzz, but it’s slowly starting to fill in darker. I can’t tell what colour it is yet, very ash looking (yeah. Light & dark grey). But honestly it is getting thicker daily and I am happy to just have some hair up there. (Thread 97, page 8)

In other cases, the hair regrowth was described as ‘white’, ‘whitish non-colour’, ‘dark brown hair’ or ‘very grey’. On the other hand, eyelashes and eyebrows regrowth varied between users. In some cases, it was thinner and in others it was thicker and longer. The recovery of hair took between 8 -12 weeks after treatment.

Allergic reactions were associated with AC (n = 2),paclitaxel (n = 3) or docetaxel (n = 4). The allergic reaction varied between the three medicines. Allergic reactions resulting from AC use and affected the eyes, hands, feet and lower legs. Moreover, allergic reactions due to paclitaxel affected the face occurred during the infusion. With docetaxel, reactions were intense and encountered in every treatment with bright red face and tightness of chest. In the four cases encountered with docetaxel, members reported that the nurses had been quick in stopping the reaction.

Gastrointestinal

Seven categories emerged under GIT toxicity being nausea, vomiting, constipation, diarrhoea, heartburn, indigestion and ‘sickness’. The aforementioned categories contributed to 65 (15.8%), 9 (2.19%), 8 (1.95%), 5 (1.22%), 5 (1.22%), 5 (1.22%) and 4 (0.97%) respectively.

Nausea associated with A, AC, EC, FEC, paclitaxel, docetaxel and TC. It was 'very tiring', 'bad' and 'uncontrollable'. Though it was highly prevalent in AC (n = 29) and FEC (n = 23) regimens, it was worse with paclitaxel. Vomiting was associated with AC, FEC and paclitaxel. It lasted up to two days and in one instance led to hospitalisation. Constipation was associated with AC, FEC and docetaxel, was described as awful and lasted up to one week. Constipation was further described as the most difficult part and not cured all the time by medicines. Likewise, diarrhoea was not controlled by medicines and was associated with FEC and paclitaxel. Diarrhoea was described as one of the worst effects and lasted up to 4 weeks after the chemo finished. Heartburn, indigestion and 'sickness' were described as terrible yet tolerable and were associated with AC, FEC, paclitaxel and docetaxel. 'Sickness' occurred straight after the infusion but was controlled by combination of medicines.

Muscle, joints and bones

Four categories emerged under muscle, joints and bones toxicity and included myalgia, joint pain, bone pain and pain in knees, legs and feet. The aforementioned categories contributed to 26 (6.32%), 20 (4.87%), 8 (1.95%) and 5 (1.22%) respectively. Members reported aches in muscles and bones as well as stiffness. At one instance, the pain was described as 'debilitating at times',

‘horrible’, ‘tremendous’ and ‘being hit with sacks of flour’. Members also described joint pain as ‘awful’, ‘accumulative’ and mainly ‘in the legs and feet’. Pain was relieved by ibuprofen, paracetamol or loratadine and stopped within months of completion of the treatment.

Infection

A total of four categories were encountered and were mouth ulcers, flu-like symptoms, infection and oral thrush, and were reported by 13 (3.16%), 12 (2.92%), 3 (0.73%) and 1 (0.24%) respectively. Severe mouth sores and ulcers were experienced throughout the treatment and after the treatment. The mouth sores were described as severe and not always relieved by mouthwash, ice chips or popsicles. Infection was reported to be similar to flu. Flu-like symptoms comprised high temperature, body aches, body weakness, nasal drip, strange cough and in one instance led to hospitalisation. In other cases, members reported shingles that was secondary to low white blood cells (WBC) counts.

Cardiovascular

Cardiovascular toxicity comprised seven categories being fluid retention, low neutrophil count, low red blood cells (RBC) count, chest pain, cardiomyopathy, congestive heart failure (CHF) and hypertension that were stated by 7 (1.7%), 3

(0.73%), 2 (0.49%), 2 (0.49%), 1 (0.24%), 2 (0.49%) and 1 (0.24%) members respectively. Fluid retention was experienced where members reported severely swollen ankles. In one instance, the retention cleared 10 days after the treatment. Fluid retention associated with docetaxel resulted in severe hypertension with 'extreme pressure in the head'. Members also stated their experience with chest discomfort, low blood pressure, rapid heartbeats. Moreover, neutrophil count was very low that the patient ended up with a couple of blood transfusions and few hospital stays. Cardiomyopathy and CHF were associated with A's use that had been described as a 'wicked drug'. One member reported:

'I just found out I have congestive heart failure caused from receiving Adriamycin 10 years ago- never had muga or echo testing done before or after and now looking at having to get a pacemaker for the damage it caused.'

(Thread 2, page 8)

Skin

Skin toxicity had two categories being dry skin and rash that were informed by 5 (1.22%) and 2 (0.49%) members respectively. Members reported dry skin throughout their whole body during the treatment. Skin itching and skin flushing were experienced where members experienced itching without numbness. Skin

rash was experienced in the face (red), back of the hands (black) and fingers (red). The skin felt rough and sore and was cleared in one instance by doxycycline antibiotic. Members had also experienced loss of fingernails and toenails. Members reported brittle nails that have never disappeared. Fingernails have grown back six months post chemotherapy.

Endocrine

Endocrine toxicity encompassed three categories being watery eyes, weight gain and weight loss that were reported by 8 (1.95%), 2 (0.49%) and 1 (0.24%) respectively. Watery eyes were described as ‘terrible’ ‘ streaming’, ‘so bad’. The watery eyes associated with docetaxel use lasted for seven years after the completion of the chemotherapy. Patients gained up to 20 lbs on paclitaxel. On the other hand, one patient lost a third half of the weight when on FEC+T.

Ear, Nose and Throat

Members reporting ear, nose and throat (ENT) toxicity had experienced hearing loss (n = 4), change in smell (n = 2) and nose bleeding (n = 1). Members reported block in their ear with nothing to clear them. In two of the cases, it was important to use a hear aid in each ear. Members reported bad smell at the end of each infusion or the inability to smell anything at all (even flowers of skunk). Also,

exaggerated smells were reported. Nose bleeding was reported as mild and relieved using a cream (unspecified).

Respiratory

Respiratory toxicity had only one category that was breathing problems associated with AC and paclitaxel. Breathing problems were experienced when patients tried to inhale deeply that caused continuous coughing. The coughing was controlled using antihistamines and disappeared at the end of the chemotherapy. Taking a deep breath was difficult for patients and felt 'like coming out of bronchitis'.

Qualitative themes emerged

Theme 1: Patient-patient advice

Patients recommended medicines or lifestyle modifications to other patients for various conditions including: hair loss, nail loss, nausea, peripheral neuropathy and mouth sores.

For hair loss, the cold cap was recommended during chemotherapy after having a short haircut before the first session (in order to have less pressure on the roots). Other recommendations for prevention of hair loss comprised using a wide tooth comb, combing gently, washing less and using dry shampoo. Another

recommendation was to wash the hair once a week and Paxman shampoo and conditioner.

As preventive measure for nail loss different recommendations were given including: icing hands and feet, keeping the nails short, using vitamin E oil around the nails several times per day, having weekly bath salts (during paclitaxel).

For nausea, it was recommended to stay hydrated, drinking lots of water before the chemotherapy and taking nausea medicines on schedule. One patient reported:

Take your nausea pills like clockwork! Even if you don't feel nauseous, don't wait until you do feel sick, it's harder to get it under control at least for the first 4 days or so, keep a log book for your side effects and how you feel each day so when you get to round 2 etc…Drink a lot of water to help flush it out of your body. (Thread 105, page 2)

Moreover, frequent eating by having lots of light snacks was recommended as a prevention for nausea. Other patients recommended taking pills on time in order to overcome nausea.

For peripheral neuropathy, frozen water bottles were recommended as a preventive measure against burning hands and feet:

And I had peripheral neuropathy which caused burning pain in my hands and feet, but I found if I held frozen water bottles in my hands it helped drive the paclitaxel away from my hands and prevented the neuropathy (Thread 101, page 1)

Against mouth sores, chomping ice chips during the infusion was advised as a preventive measure. Other recommendations for mouth sores included rinsing with salty water, using Biotene, seeing a dentist about a dental hygienic regimen:

'Things that have helped me so far, include Biotene for my mouth (Thread 22, page 2)'.

Theme 2: Self-medication

Self-treatment has emerged among patients for few conditions where patients had taken medicines or alternative approaches in order to control certain effects. For instance, vitamin B12 was suggested as a preventive measure for neuropathy:

The only thing I would change is to start taking vitamin B12 to prevent the neuropathy that started near the end of Paclitaxel. It's gone now. I still take B12 (Thread 103, page 2).

In addition, drinking lots of water and sucking sweets was recommended for dry mouth. For loss of taste, patients recommended drinking lots of fluid, having lemon juice and/or eating stronger tasting food:

Lemon juice helps a bit (thread 99, page 2)

Furthermore, patients reported using oils, creams or wax for dry skin and chapped lips. Oil was recommended either by applying it directly to the skin or putting few drops in the bath at night. Nonetheless, creams and waxes were applied directly to the skin.

Theme 3: Lifestyle changes

Patients reported lifestyle changes relating to diet, exercise and stress management. Patients moved to having a healthy plant-based diet, having more vegetables, fresh juices, vitamins and exercising more. Patients also reported

going on stress management programmes but had not specified the types of programmes. One patient reported:

I'm trying to eat more greens, like kale, spinach, avocados, and trying (Thread 102, page 5)

Another patient reported:

I also turned to exercise and fresh carrot juice. I believe it had a lot to do with my recovery. I believe the carrot juice help remove the toxins from my joints and the exercise definitely rebuilt the muscles around the joints. (Thread 1, page 3)

DISCUSSION

This study utilised online discussion forums in order to explore the ADRs experienced by breast cancer patients. The findings of the study were important in uncovering the daily experiences of patients coping with the condition (breast cancer) and their attitudes towards the condition. Our research added to the existing significant research regarding ADRs experienced by cancer patients due to chemotherapeutic agents [20-22]. The aforementioned three studies focused on quantitative data regarding ADRs experienced by hospitalised patients during

[19] or qualitative data obtained from interviews/questionnaire with patients after hospitalisation [20-22]. None of the aforementioned studies used retrospective analysis of online discussion forums.

Online discussion forums data offer an advantage over interviews and questionnaires in obtaining further insight into the patients' own attitudes towards the condition and experience within the condition. Online patient communities propose a significant source of information particularly for excluded patients in traditional research studies [23]. The increased use of online discussion forums has increased substantially with the increased use of the Internet among individuals worldwide [23]. Patients utilise the Internet in order address their condition, access advise about the condition and manage their therapy [24, 25].

To date, there are limited qualitative studies that analyse the content of online discussion forums published by breast cancer patients who had experienced ADRs as a result of their chemotherapeutic treatment regimens. On the contrary the few studies that explored qualitative breast cancer patients' perspectives had focused on psychological distress following diagnosis [6, 26] or psychological support for patients [7].

Our study was the first qualitative study that explored the perspectives and attitudes of breast cancer patients towards ADRs experienced following treatment with chemotherapeutic agents. Online discussion forums allowed

patients to express their thoughts in unrestricted manner; hence, they provided a wealth of information about the physical and psychological ADRs experienced by patients [27]. In this respect, the findings of the study showed that patients experienced numerous ADRs associated with multiple systems of which the main ones were the nervous, immune and skeletal system. In dealing with the ADRs, three main themes emerged from the study related to patient-patient advice, self-medication and lifestyle changes.

Patient sought advice from other patients in order to deal with their condition, chemotherapeutic regimen(s) and their associated ADRs. Patients sought knowledge and emotional support from the online discussion forums mainly to deal with anxiety, depression and stress experienced as a result of their disease [6, 7]. The knowledge acquired from online discussion forums was perceived as more valuable to the patients as it had been obtained directly from available resources and not through an authoritative, filtering agent such as a doctor or nurse [28]. This showed that the patient-doctor relationship has changed and depended on the outcomes/lifestyle of patients and that coincided with the findings on other studies [29, 30]. Hence, the Internet era changed the behaviour of patients and made them rely on personalised information from the Internet rather than seeking it from experts [30, 31]. Patients' personalised behaviour was not only apparent in seeking advice about the condition and ways to cope with it

but also with patients' self-prescribing and self-medicating [32, 33]. Modern patients felt more convenient in managing their own illness and medication than visiting experienced healthcare professionals. This was attributed to several reasons being: urge of self-care in the Internet era, use of personalised information, financial constraints, lack of time, lack of adequate health services, health ignorance, extensive adverts of medicines and availability of medicines outsides pharmacies [32, 34-35]. Specifically, online discussion forums were convenient for patients because they provided a tool to exchange of knowledge, advice and provide relief from the stress associated with their conditions. Individuals had the ability to post anonymously and unrestricted manner. Hence, online discussion forums were a safe place for patients to express and discuss their thoughts and emotions in an uninhibited manner [27].

Strengths and Limitations

The findings of the study were extremely useful in providing in-depth information about the patients' experience of ADRs and their behaviour towards the condition. Patients felt more freely to express themselves in an honest and non-biased manner using online discussion forums than they would do face-to-face. The use of content analysis in exploring the results was advantageous as it required no cooperation from patients. As the content analysis was applied to retrospective

data, there was not bias as experienced in interviews or surveys where participants would be prompted to achieve a specific outcome. Currently, there are limited scientific literature on qualitative studies of ADRs experienced by breast cancer patients receiving chemotherapy treatment. This study determined detailed information on the toxicities associated with the administration of chemotherapy agents.

Nonetheless, several limitations were encountered in this study. As the project was retrospective in nature, there were gaps of information missing throughout the study. It was not always possible to obtain all of the information desired, for example, type of breast cancer, age, geographical location and drug dosage. However, in retrospective studies missing data is often reported as an issue. Another limitation of the study was that there had not been a way to authenticate the information claimed by patients regarding their condition and symptoms. Using online discussion forums, individuals feel invisible and thus have the courage to say things they may otherwise not [27]. Moreover, the study was limited to individuals that used the Internet discussion forums and that affected the generalisability of the results.

CONCLUSION

Online discussion forums provided valuable and detailed information regarding the toxicity of chemotherapeutic agents not currently present in scientific literature. By uncovering themes related to patient experience, the online discussion forums represented important source of qualitative data additional to traditional sources of information.

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