Patient perceptions of symptoms and concerns during cancer chemotherapy: ‘affects my family’ is the most important

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Abstract

Background Cancer chemotherapy is associated with a variety of side effects/adverse events. It is very important that patients adhere to the planned chemotherapy regimen, which necessitates a minimum of side effects and that these side effects be kept under control. We have investigated patients’ concerns and symptoms during chemotherapy with the aim to seek solutions that will improve patients’ quality of life during chemotherapy.

Methods Forty-nine patients with malignant diseases on parenteral antineoplastic agents were sequentially enrolled in this study. These patients completed a questionnaire consisting of 42 items related to non-physical concerns and 52 items of physical symptoms related to chemotherapy. Each patient was also asked to select the three items among these 94 items which affected him/her the most.

Results The median age of the cancer patients was 62 years and the male-to-female ratio was 18:31. Among the non-physical concerns, the most frequently chosen concern was ‘affects my family or partner,’ followed by anxiety related to treatment. Regarding the physical symptoms, the most frequent complaints were fatigue, alopecia and constipation, while the most troublesome symptoms were nausea, poor taste and paresthesia. Overall, the most frequently expressed concerns were ‘affects my family or partner’ and anxiety related to treatment. Male patients suffered most from fever, fatigue and nausea, and female patients complained more of poor taste and gastrointestinal problems.

Conclusion Patient perceptions of adverse events associated with cancer chemotherapy apparently have changed from physical symptoms to non-physical concerns. In our patient cohort ‘affects my family or partner’ was the most important concern. One important point to note is that female patients often complained of poor taste because this meant they were unable to cook well.

Keywords Chemotherapy · Side effects · Pain · Patient perceptions

Introduction

Cancer has been a leading cause of death in Japan since 1981, and one out of two Japanese people develops cancer during their life time [1]. Early detection and treatment are essential to cure this devastating disease. However, with a few exceptions, such as lymphoma, leukemia and germ cell tumors, advanced and relapsed cancers are rarely curable by any treatment modalities. Even patients who are thought to be cured have had to go through painful laboratory examinations and treatments consisting of surgery and/or radiation therapy and/or chemotherapy. Surgery and irradiation are local treatments that are completed within a couple of weeks, and usually only the local adverse sequelae are significant. In contrast, chemotherapy is scheduled over
months or even years in some diseases. It is a systemic
treatment often associated with a variety of side effects and
can occasionally be life-threatening. The emergence of
adverse side effects can negatively affect a patient in a vari-
ety of ways. Consequently, there is a need to control such
side effects since interruption of the chemotherapeutic regi-
men is detrimental to both a high cure rate or prolongation
of survival with a good quality of life (QoL).

In 1983, an Australian research group reported patients’
perceptions of the side effects of cancer chemotherapy. Emesis,
nausea and loss of hair were identified as major physical
symptoms, and anxiety when coming to treat-
ment, treatment time and fear of needles were major
non-physical concerns [2]. Ten years later, following the
introduction of a new group of antiemetics, the 5-hydroxy-
tryptamine 3 (5HT3) receptor antagonists into clinical use,
the same research group conducted a repeat study using the
same measures. This time, nausea overtook emesis, which
ranked fifth in the repeat study, and there was a clear shift
in patient concerns from those about physical symptoms to
psychosocial issues [3]. In 2002, a French group carried out
a similar survey and found that chemotherapy-induced nau-
sea and vomiting (CINV) was no longer within the top ten
of patient concerns and that ‘affects my family or partner’
ranked first [4].

In Japan, aprepitant, a neurokinin-1 (NK-1) receptor
antagonist, and palonosetron, a second-generation 5HT3
receptor antagonist, were approved for in 2009 and 2010,
respectively, and their use has gradually spread throughout
Japan. By 2011 these new antiemetics were routinely used
in medical practice. It is therefore timely to investigate
patients’ perceptions of the side effects and related issues of
cancer chemotherapy.

Methods

Patients and methods

We sequentially selected patients with pathologically docu-
mented malignant disorders who were being treated with
parenteral antineoplastic agents in our department. All solid
tumor patients had advanced cancer, and all hematologi-
cal malignancy patients were at advanced stages. Patients
who had received cytotoxic chemotherapy in the 4-week
period immediately prior to their interview were included
in the study. The study was approved by the Fukuoka Uni-
versity Hospital Review Board. A cancer research nurse
explained the aim and design of the study to the patients.
Those who consented to participate were asked to complete
a questionnaire consisting of 94 items on signs and symp-
toms potentially related to chemotherapy. Upon comple-
tion by the patient, the nurse checked whether all answers
were appropriately filled in and asked the patient to correct
any entry which was not completed or the answer unclear.
This questionnaire consisted of two categories of questions,
shop A and group B; for each item of group A the patient
was asked to choose between yes or no as answer, and
for the items in group B, the patient was asked to choose
one of five options, from the worst symptom (grade 4) to
no complaint (grade 0). The patient was also requested to
choose the three items that influenced/affected him/her
most, i.e., the most painful or most troubling events from
group A, group B, and the entire 94 items. Most patients
were able to choose three items which were most trouble-
some or painful. Patients who had difficulty in choosing
three items were offered help from the nurse in the form
of explanations. These nurses were members of the nurs-
ing staff who had no association with the patients in routine
clinical practice, and they intervened as little as possible
while the patient was filling in the questionnaire.

Creating a questionnaire

To be able to compare the perceptions of our Japanese
patients with those of patients in Western countries, we
used the questions covered by Carelle et al.’s study [4],
which used a questionnaire with items on 45 physical
symptoms and 27 non-physical concerns. Since there no
studies on patient perceptions of symptoms and concerns
who received chemotherapy in Japan have been conducted,
we had those items translated into Japanese. Some items
had to be changed and/or added to in order to facilitate
ease of answering for Japanese people. We changed “physi-
cal concerns” to descriptions easy for Japanese patients
to understand; for example, for “pain” we added items to each
specific site. We then rearranged the items in anatomical
order, again to make it easier for the patient to understand
the question. For “non-physical concerns”, we changed
items to correlate better with present-day life in Japan. Spe-
cifically, items of aging, social and economic problems,
and human relations were modified and/or added. Finally,
we added 11 and 26 items for “physical concerns” and
“non-physical concerns”. Thus, while several items have
been added to those in questionnaire used in Carelle et al.’s
study [4], all of their items were included, making it possi-
bile to compare our results with those of previous studies in
general and Carelle et al.’s study [4] in particular. The ques-
tionnaire which we created consisted of a group of ques-
tions pertaining to non-physical concerns (group A) and a
group of questions pertaining to physical concerns (group
B) (Tables 1, 2). Items in both group A and group B related
to potential adverse events of chemotherapy. The Japanese
version of the questionnaire is given in the Electronic Sup-
plementary Material.
Results

A total of 49 cancer patients receiving chemotherapy as an outpatient or an inpatient at Fukuoka University Hospital participated in this study during a period of 6 months from September 2011 to February 2012. The background characteristics of these patients are shown in Table 3. The median age was 62 (range 32–84) years, and the male-to–female ratio was 18:31. There were 21 patients with hematological malignancies and 28 with solid tumors. The anticancer agents used in 36 (74%) patients were categorized as highly or moderately emetogenic according to the CINV guidelines in Japan [5].

Patients with lymphoma, leukemia and breast cancer mainly received an anthracycline-based regimen while those with colorectal or lung cancer were treated with oxaliplatin or carboplatin combination chemotherapy.

A total of 91 symptoms were noted to be adverse events by the patients. Frequent painful non-physical concerns were ‘affects my family or partner’ followed in order by anxiety about difficulty in recovering from the previous chemotherapy, ‘affects my work or housework’, sick feeling, dissatisfaction about a change of primary care physician, and anxiety while on treatment and others (Table 4). The most troublesome non-physical concerns were almost the same as the high-frequency non-physical concerns; top of the list was ‘affects my family or partner’ followed by various anxieties and vague fears, but it is of note that the cost of medical fees ranked fifth (Table 6).

Among the physical symptoms, the most frequent complaints were fatigue, alopecia, constipation, loss of appetite, and paresthesia (Table 5). More than one-half of patients suffered a moderate to severe degree of fatigue, alopecia, constipation and loss of appetite. However, the most annoying problems were nausea, poor taste and paresthesia (9 patients each) followed by fatigue (8 patients), and fever and insomnia (7 patients each).

Nine patients complained of nausea as an unbearable experience. In five patients the nausea was associated with highly to moderately emetogenic anticancer drugs, while in the others the nausea was secondary to either opioid use, peritonitis carcinomatosa, tumor infiltration of the stomach or cerebral hemorrhage.

The clinical signs and symptoms that concerned the patients the most in the entire group were ‘affects my family or partner’ followed in descending order by anxiety about recovering from the previous treatment for the

### Table 1  Group A items in the questionnaire—non-physical concerns

| No. of item | Concerns                                           | No. of item | Concerns                                           |
|-------------|----------------------------------------------------|-------------|----------------------------------------------------|
| 1           | Forget things                                     | 22          | When do I have to go to a hospice care facility?  |
| 2           | Feeling low                                       | 23          | Cannot get clothes that fit                        |
| 3           | Feeling sick                                      | 24          | Affects my work/home duties                        |
| 4           | Easily excited                                    | 25          | Affects my family or partner                       |
| 5           | Cannot move forward                               | 26          | Can I return to my normal social life?            |
| 6           | Losing the will                                   | 27          | Affects social activity                            |
| 7           | Whimper/crying more often                         | 28          | Length of time treatment takes at clinic           |
| 8           | Irritable                                         | 29          | Presence of family members I have to take care of |
| 9           | Cannot concentrate                                | 30          | Cannot eat raw foods                               |
| 10          | Feeling fearful                                   | 31          | Can I get married?                                |
| 11          | Fear of death                                     | 32          | Effects delivery or infants or raising my children |
| 12          | Hard to understand what is going on               | 33          | Infertility                                        |
| 13          | Feeling anxious about treatment                   | 34          | Loss of sexual ability                            |
| 14          | Feeling anxious about being unable to recover from the previous therapy | 35          | Travel time to come to the hospital               |
| 15          | Feeling anxious about my life                     | 36          | Medical costs                                      |
| 16          | No adviser                                        | 37          | Relationships with medical staff                   |
| 17          | No supporter                                      | 38          | Relationships with other patients                  |
| 18          | I do not want others to know about my disease     | 39          | Problem with the hospital                         |
| 19          | Changing the primary physician                    | 40          | Contact methods for medical staff                  |
| 20          | Can I trust information on the internet?          | 41          | Can I call medical staff when I am sick?          |
| 21          | Hesitant to ask my primary physician to get a second opinion | 42          | Others ()                                          |

Please select the three most troubling items from items 1 to 42: (),(),()
next therapy, anxiety about treatment, nausea, poor taste, numbness, fatigue, vague fears and so on (Table 6).

There was no difference in symptoms between female and male patients for non-physical concerns, but for physical symptoms male patients suffered most from fever, fatigue and nausea, while females complained of poor taste, nausea, stomatitis, paresthesia, vomiting, and diarrhea (Table 7). Female patients felt that gastrointestinal problems were the most problematic side effects of chemotherapy.

**Discussion**

It is important to understand not only the significant physical symptoms but also non-physical concerns that patients feel or suffer from during systemic cancer therapy. Patients undergoing cancer chemotherapy can be made more comfortable by reducing the incidence and the severity of adverse events and by providing an appropriate dose and schedule of antineoplastic agents that will result in maximum antitumor effects with an improvement in QoL and survival.

In the early evolution of cancer chemotherapy in the 1970s and 1980s, severe CINV and emesis and nausea ranked first and second as the most troubling symptoms of cancer chemotherapy [2]. CINV in some patients was so serious that they refused to continue on their chemotherapeutic regimen despite the underlying disease being potentially curable. The situation improved with the approval of the 5HT-3 receptor antagonist as a prophylaxis for CINV in the 1990s, followed by the introduction of the NK-1 receptor antagonist at the beginning of the twenty-first century. The results of our study indicate that from the perspective of total management of cancer chemotherapy, CINV no longer ranks as a top concern among cancer patients undergoing chemotherapy.

Carelle et al. [4] reported a change in patient perceptions of the side effects of cancer chemotherapy. These authors found that ‘Affects my family or partner’ was ranked first, followed by anxieties and fears about a variety of events and non-physical concerns like ‘affects my work’ and

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**Table 2** Group B items in the questionnaire—physical symptoms

| No. of item | Concerns                      | No. of item | Concerns                      |
|-------------|-------------------------------|-------------|-------------------------------|
| 43          | Nausea                        | 69          | Pain during urination         |
| 44          | Emesis                        | 70          | Difficulty in urination       |
| 45          | Constipation                  | 71          | Nasal bleeding                |
| 46          | Diarrhea                      | 72          | Headache                      |
| 47          | Change in the way things taste| 73          | Dizziness                     |
| 48          | Taste nothing                 | 74          | Giddiness on standing up      |
| 49          | Poor appetite                 | 75          | Ringing in ears               |
| 50          | Sore throat                   | 76          | Difficulty in hearing         |
| 51          | Abdominal pain                | 77          | Bruise easily                 |
| 52          | Abdominal distension          | 78          | Urticaria/wheals              |
| 53          | Dry mouth                     | 79          | Change in skin color          |
| 54          | Change in how things smell    | 80          | Change in nails (color, pain, breaks) |
| 55          | Stomatitis/sore mouth         | 81          | Hot flush                     |
| 56          | Increase appetite             | 82          | Acne (pimples) or eczema      |
| 57          | Cheilosis                     | 83          | Dry skin                      |
| 58          | Difficulty in swallowing      | 84          | Itching                       |
| 59          | Numbness (Which part of body?)| 85          | Dermatitis sensitive to sun   |
| 60          | Pain in fingers and/or toes   | 86          | Fever                         |
| 61          | Dulling of senses             | 87          | Fatigue                       |
| 62          | Tingling sensation (Which part of body?) | 88 | Alopecia/loss of hair |
| 63          | Pain at injection site        | 89          | Weight loss                   |
| 64          | Poor veins                    | 90          | Weight gain                   |
| 65          | Anthralgia                    | 91          | Edema                         |
| 66          | Myalgia                       | 92          | Palpitation                   |
| 67          | Colored urine                 | 93          | Shortness of breath           |
| 68          | Amount of urine               | 94          | Insomnia                      |

Please select the three most troubling items from 43 to 94: (), (), ()
medical costs. The results of our study are in agreement with those of Carelle et al. [4]: ‘affects my family or partner’ was the most important concern of all 94 items in the questionnaire. This result suggests that patient perceptions of the side effects or experiences during systemic chemotherapy have shifted markedly from the physical symptoms, especially from CINV, to non-physical concerns.

For physical symptoms, the number of patients with symptoms in general and number of patients with the most painful symptoms were similar. However, the significant difference in complaints about physical symptoms between male and female patients was of interest. Female patients complained of difficulty in tasting foods properly, nausea, stomatitis, and dysesthesia, while male patients suffered most from fever and fatigue. Female patients felt that gastrointestinal problems were the most problematic side effects of chemotherapy. Women in Japan are still the predominant preparer of meals for their family, but gastrointestinal symptoms would seem to preclude the preparation of meals. In particular, difficulty in appreciating sweetness and saltiness properly makes it difficult for a housewife to prepare palatable food by checking the taste during cooking. Compared with men, women experience CINV more frequently and to a more severe degree [6].

Fatigue was the most frequent symptom reported among all physical symptoms, as shown in Table 5, not only by male patients but also by female patients. It is not easy for patients to differentiate chemotherapy-induced fatigue from fatigue due to their advanced underlying disease, and this study was not designed to address that distinction [7]. Anemia is a treatable pathophysiological state that induces fatigue and weakness. It has been treated with erythropoietin in Western countries, and improvement of anemia alleviates profound fatigue [8], but erythropoietin is not approved for cancer-related anemia in Japan. Considering the incidence and severity of fatigue in cancer patients on chemotherapy, it is to be hoped that erythropoietin will be approved for clinical use in the Japanese oncology field.

As shown in Table 6, concerns about their patient’s family or partner and anxiety related to treatment were the top three complaints among our cancer patients,
indicating an apparent shift from concerns regarding physical symptoms to psychosocial issues. These issues are quite subjective and difficult to measure even by appropriate instruments or tools. Therefore, unless patients express their concerns to medical staff, they may be easily overlooked or even ignored by healthcare providers. Our data and the results from a series of studies by an Australian group suggest the necessity of thorough physical symptoms and non-physical examinations before the start of chemotherapy. If a significant problem or concern is raised, it may have to be solved before treatment; otherwise, it may lead to an early interruption of the treatment and subsequent poor outcome.

Patient perceptions of the side effects of cancer chemotherapy based on the analysis of a thorough questionnaire have not previously been reported for Japanese patients. Yokoo et al. [9] carried out an Internet survey in which cancer patients’ concerns and their associations with QoL were assessed; 807 patients with all types of cancer who were older than 20 years participated in the survey, but no information on treatment was available. These authors reported that concerns about ‘self-management’ was the most common (61%) reported concern, followed by psychological symptoms (48%), medical information (46%), daily living (30%). Unfortunately concerns about family or partner were not included in this survey questionnaire. However, this Internet survey did illustrate that cancer patients in general seem to place a special emphasis on non-physical concerns rather than physical symptoms.

Patients experience a variety of side effects associated with chemotherapy. A major question to be asked by healthcare providers is whether chemotherapy is really good for patients in terms of QoL. In a prospective randomized phase three trial Dancey et al. [10] observed the superiority of second-line docetaxel over best supportive care in patients with lung cancer. The Australian–New Zealand Breast Cancer Trials Group conducted a study comparing continuous treatment with intermittent therapy in

### Table 5 Physical symptoms noted by patients

| Physical symptoms | Grade of symptom<sup>a</sup> |
|-------------------|-----------------------------|
|                   | 4  | 3  | 2  | 1  | 0  |
| Fatigue           | 7  | 14 | 26 | 10 | 20 | 6  | 12 | 13 |
| Alopecia          | 18 | 36 | 6  | 12 | 4  | 8  | 4  | 8  |
| Constipation      | 6  | 12 | 10 | 20 | 10 | 20 | 5  | 10 |
| Loss of appetite  | 10 | 20 | 10 | 20 | 7  | 14 | 3  | 6  |
| Paresthesia       | 10 | 20 | 5  | 10 | 5  | 10 | 8  | 16 |
| Loss of weight    | 9  | 18 | 5  | 10 | 4  | 8  | 9  | 18 |
| Shortness of breath | 3  | 6  | 5  | 10 | 9  | 18 | 10 | 20 |
| Stomatitis        | 5  | 10 | 2  | 4  | 5  | 10 | 15 | 30 |
| Change in the way things taste | 8  | 16 | 8  | 16 | 5  | 10 | 5  | 10 |
| Dry skin          | 4  | 8  | 4  | 8  | 11 | 22 | 7  | 14 |
| Insomnia          | 4  | 8  | 7  | 14 | 8  | 16 | 7  | 14 |
| Nausea            | 6  | 12 | 2  | 4  | 6  | 12 | 10 | 20 |
| Taste nothing     | 7  | 14 | 9  | 18 | 3  | 6  | 5  | 10 |
| Fever             | 5  | 10 | 6  | 12 | 7  | 14 | 6  | 12 |

Values in table are presented as the number of patients with the percentage in parenthesis.

<sup>a</sup> 0, No symptoms; 1, minimal symptoms; 2, mild symptoms; 3, moderate symptoms; 4, severe symptoms

### Table 6 Most serious concerns selected by patients from among all physical and non-physical concerns

| Rank | Most serious concerns                | No. of patients (%) |
|------|-------------------------------------|---------------------|
| 1    | Affects my family or partner         | 18 (36)             |
| 2    | Feeling anxious about being unable to recover from the previous therapy | 13 (26)             |
| 3    | Feeling anxious about treatment      | 10 (20)             |
| 4    | Nausea                              | 9 (18)              |
| 4    | Change in the way things taste      | 9 (18)              |
| 4    | Numbness                            | 9 (18)              |
| 7    | Fatigue                             | 8 (16)              |
| 8    | Feeling fearful                      | 7 (14)              |
| 8    | Medical costs                        | 7 (14)              |
| 8    | Fever                               | 7 (14)              |
| 8    | Insomnia                            | 7 (14)              |
| 12   | Fear of death                       | 6 (12)              |
| 12   | Anxiety to return to work           | 6 (12)              |
| 12   | Diarrhea                            | 6 (12)              |
| 12   | Loss of appetite                     | 6 (12)              |
| 12   | Pain at infection site               | 6 (12)              |
women with advanced breast cancer [11]. If disease did not progress in the patients receiving intermittent therapy, the treatment was withheld after three cycles. The same treatment was restarted only after the disease progressed, at which time three cycles were again given. This sequence was repeated until the disease no longer responded to the treatment. The survival did not differ significantly between the arms, but the QoL was worse in patients assigned to intermittent rather than continuous therapy, suggesting that QoL was improved by inducing and maintaining a tumor response despite the occurrence of side effects associated with chemotherapy.

A major limitation to our study is the small number of patients compared to previous studies, so it is difficult to draw comparisons for each gender, chemotherapy regimen, or disease, and in particular it is impossible to make statistical comparisons. However, in this study, 94 items pertinent to cancer patients undergoing chemotherapy were surveyed using a questionnaire, and important data on Japanese patients’ perception of concerns in this setting were obtained for the first time.

In conclusion, patient perceptions of adverse events associated with cancer chemotherapy have apparently shifted from physical symptoms to non-physical concerns. ‘Affects my family or partner’ is now the most important concern. A multi-disciplinary approach that includes the active involvement of medical social workers and medical staff is necessary to minimize their suffering. One interesting factor that appears not to have been noticed previously—or ignored—is the poor taste perception in female patients. This is particularly significant for Japanese women but has not been raised by women in Western studies, suggesting that the cultural background of the patient influences his/her perception of signs and symptoms associated with cancer treatment.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interests.

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Table 7 Difference in physical symptoms between male and female patients

| Symptoms                          | Male patients | No. of patients | Female patients | No. of patients |
|----------------------------------|---------------|----------------|----------------|----------------|
| Fever                            | 5             |                | Change in the way things taste | 5 |
| Fatigue                          | 5             |                | Nausea          | 5 |
| Nausea                           | 4             |                | Stomatitis      | 5 |
| Paresthesia                      | 4             |                | Paresthesia     | 5 |
| Change in the way things taste   | 3             |                | Vomiting        | 4 |
| Loss of appetite                 | 3             |                | Diarrhea        | 4 |
| Insomnia                         | 3             |                | Pain at injection site* | 4 |
|                                  |               |                | Insomnia        | 4 |

*a Includes fear of having multiple needle sticks for chemotherapy due to poor veins
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