Effect of Advanced Pharmaceutical Services for Chemotherapy on Length of Hospital Stay

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We prepared a chemotherapy information leaflet that helped to enhance patients’ understanding of chemotherapy and to reduce their anxiety about its adverse reactions. The aim of the present study was to evaluate pharmaceutical services with regard to the management of adverse reactions, length of hospital stay and the medical costs for women with gynecologic cancer who received chemotherapy. We carried out a retrospective chart survey of 28 ovarian cancer patients to clarify the effects of pharmaceutical care on their chemotherapy. Half of the patients were given chemotherapy information verbally and were assigned to Group A, and the other half were supplied with an information leaflet and a self-check list for adverse reactions and assigned to Group B. There were no significant differences between the two groups regarding the occurrence of adverse events, except for fatigue and insomnia. However, 50% (7/14) of the patients in Group A stayed longer in hospital to be free from adverse reactions, especially myelosuppression. The mean hospital days per cycle of chemotherapy in Group B (2.76±0.80 days) was significantly shorter than that in Group A (7.28±3.97 days, p<0.001). Thus, our pharmaceutical care using chemotherapy information leaflets had a favorable effect in terms of shortening the length of hospital stay.

Key words— chemotherapy information leaflet, retrospective chart survey, ovarian cancer, hospital stay, pharmaceutical care

Introduction

Recently, gynecologic cancer has become the leading cause of cancer deaths of women in Japan. In 2004, 20,468 Japanese women died of malignant neoplasms of the breast, uterus and ovary, with 22% having suffered from ovarian cancer and having received certain cancer therapies**. Currently, ovarian cancer chemotherapy is performed under various protocols including combination chemotherapy such as TJ (paclitaxel-carboplatin) or DJ (docetaxel-carboplatin) resulting in a remarkable improvement in cure rate***. However, adverse reactions frequently occur with antineoplastic drugs. Many patients are, therefore, extremely anxious about the severe adverse reactions since they are not aware of the symptoms, onset, and how to manage adverse reactions associated with their chemotherapy. Consequently, they feel anxious about leaving hospital earlier until they are free from adverse reactions.

In our previous study from June 1, 2002 to July 31, 2002 at the Kanto Medical Center NTT EC, Tokyo, Japan, we reported that before commencing the treatment, 98% (44/45) of the patients considered that chemotherapy could cause strong adverse reactions and only 49% (22/45) were satisfied with the relevant information about adverse reactions which consequently reduced their concerns about these reactions. A large majority, 93% (42/45) of the patients preferred to have explanatory leaflets on their chemotherapy. We found that most of the patients wanted to know more about the adverse reactions and in more detail than health care workers had imagined. Accordingly, since January 2003, the physicians have played a leading role in the medical care through daily rounds of patients in order to reduce their anxiety. Furthermore, the pharmacists have provided an information leaflet on the individual’s chemotherapy, and have given drug consultations to the patients. We found that all of the patients understood the information on chemotherapy described in the leaflet and 95% (42/44) were satisfied...
with it and their concerns about the adverse reactions were alleviated. Therefore, our pharmaceutical care in providing quality information for cancer patients was proved useful in reducing their anxiety\(^7\), but we recognized that a further assessment of our pharmaceutical service would be required.

In 1990, Hepler defined pharmaceutical care as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient’s quality of life (QOL)\(^5\). He reported that pharmaceutical services could reduce the number of adverse reactions, the length of hospital stay, and the cost of care. In the present study, we therefore evaluated our pharmaceutical services regarding the management of adverse reactions, the length of hospital stay and the medical cost to improve the care of 28 women with gynecologic cancer. We report here the result of a retrospective chart survey of 28 ovarian cancer patients from July 2001 to June 2004.

**Patients and Methods**

1. Chemotherapy information leaflet and self-check list

We produced a leaflet about chemotherapy for each patient according to a previously described method\(^3\), an example of which can be seen in Fig. 1. We also designed a self-check list of adverse reactions as is shown in Fig. 2. Before discharging the patient from the hospital, the pharmacist used the self-check list to explain about adverse reactions such as alopecia, leucopenia and nausea/vomiting. At the same time, we advised the patient to contact her physician if signs or symptoms of infection (fever or chill etc.) occurred, and determined whether she had sufficient knowledge about the adverse reactions of the antineoplastic drugs.

2. Patients

The subjects of this study included 28 postoperative ovarian cancer patients: (Group A: 14 were provided with the chemotherapy information verbally before 2003, Group B: 14 were provided with the chemotherapy information leaflet after 2003). All the initial chemotherapy (either TJ or DJ) was administered between July 2001 and June 2004 at the department of gynecology at the Kanto Medical Center NTT EC in Japan. Patients who had had prior chemotherapy were excluded from this study. The records of 28 patients were retrospectively reviewed. As is shown in Table 1, Group A consisted of 73 TJ cycles of chemotherapy and Group B consisted of 90 TJ and 12 DJ cycles of chemotherapy. The patients’ ages ranged from 45 to 68 years old (mean 56.8 years old) in Group A, and from 33 to 72 years old (mean 56.6 years old) in Group B.

3. Medical Survey

The age, chemotherapy regimen, number of cycles of chemotherapy, hospital days, occurrence of adverse events of nausea/vomiting, myalgia/arthralgia, neuropathy, alopecia, diarrhea, constipation, fatigue, anorexia, discomfort in stomach, insomnia, leucopenia, neutropenia, thrombocytopenia and anemia, and the drugs for prophylaxis or treatment of adverse reactions were recorded through inspecting medical charts between July 2001 and June 2004.

4. Statistical Analysis

Values are expressed as means±standard deviation (S.D.). P values less than 0.05 were considered as statistically significant. The difference in proportions was evaluated using Fisher’s exact test or the \(\chi^2\) test.

**Results**

1. The length of hospital stay per cycle of chemotherapy

Table 1 shows the patient demographics and the length of hospital stay per cycle of chemotherapy. The mean hospital days per cycle of chemotherapy in Group A with verbal information were 7.28±3.97 days, and ranged widely from 3 days to 15 days. Fifty percent (7/14) of the patients in Group A stayed in hospital for 8 to 15 days per cycle of chemotherapy until they were free from adverse reactions. On the other hand, the patients in Group B received the chemotherapy information leaflet and the self-check list of various adverse reactions with the pharmacist’s consultations. The mean hospital days per cycle in Group B were 2.76±0.80 days, and ranged from 1.57 to 4.67 days. All the patients in Group B left the hospital on their chemotherapy day or the next day. Therefore, the length of hospital stay per cycle of chemotherapy was significantly shorter in Group B than in Group A (\(p<0.001\)).

2. The occurrence of adverse events of chemotherapy

The occurrence of adverse events of chemotherapy is shown in Table 2. The incidence of nonhematologic toxicity was not significantly different between the two groups except for the higher incidence of insomnia (79% versus 29%; \(p<0.01\)) and the lower incidence of fatigue (0% versus 43%; \(p<0.01\)) in Group A in comparison with Group B. The patients in Group A who complained of insomnia needed more sleeping pills than those in Group B. In order to prevent vomiting and nausea, 93% (13/14) of the patients in Group A had intravenous injections of anti-emetics for 2 to 3 days (2 days for 4 patients and 3 days for 9 patients) whereas only 21% (3/14) in Group B had them for 2 days. Afterwards, 43% (6/14) of the patients in Group A used additional oral anti-emetics compared to 64% (9/14) in Group B.

The occurrence of most adverse events including severe myelosuppression such as leucopenia and neutropenia was not significantly different between the two groups. However, one case with neutropenic complications (grade 4 neutropenia for more than 7 days or with fever) occurred in Group B, but none in Group A. Following our guidance, she contacted her physician when she had a high fever at home, and was hospitalized for proper treatment.
Chemotherapy Leaflet

Your combination chemotherapy is Taxol® or Paraplatin®. We administer these drugs by intravenous injection. This combination of chemotherapy is the most effective therapy for your ovarian cancer now. However, if after trying this combination a couple of times and no effect on your cancer is found, we will change it to other combinations. Your doctor will decide the effect of chemotherapy on your cancer from overall aspects including your tumor marker (CA125, CA19-9), the results of CT or X-ray and your symptoms etc.

1 Reasons for Occurrence of Adverse Reactions of Anticancer Drugs

Taxol® or Paraplatin® is developed to interfere with the growth of cancer cells which multiply quickly. However, there are some normal body cells such as bone marrow, hair root, digestive mucous membrane which also multiply quickly. Since the growth of normal body cells can also be damaged by these anticancer drugs, adverse reactions frequently occur, such as leucopenia (low white blood cell count), thrombocytopenia (low platelet count in blood), anemia, alopecia (loss of hair), vomiting, nausea, diarrhea, anorexia (loss of appetite) and constipation etc. Some of these may be serious and others may not. These adverse reactions may not occur in every case. If you notice any signs or symptoms or have any questions, check with your doctor or pharmacist.

2 Prevention or Treatment of Adverse Reactions

Nausea - Vomiting

Nausea and vomiting occur more commonly. Anti-emetic drugs are used to prevent nausea and vomiting before anticancer drugs. These reactions may last for several days after treatment and can be treated by taking oral anti-emetic drugs for the first few days and then when necessary. (Anti-emetic drugs: Zofran®, Nazea OD®, Serotone® etc.)

Leucopenia (Neutropenia)

Leucopenia and neutropenia (low neutrophil cell count) occur more commonly. If these counts are low in your blood, there is an increased chance of getting an infection. Your doctor should watch out for these counts in the blood tests. If you get a fever, chill, cough, lower back pain or have difficulty in urination, check with your doctor immediately. To treat severe neutropenia, your doctor may use granulocyte-colony stimulating factors (G-CSF). (G-CSF: Neutrogen®, Gran®, Neup­up® etc.)

Myalgia - Arthralgia

Myalgia or arthralgia (pain in joints or muscles, especially in arms or legs) occur more commonly a few days after treatment with Taxol® and may last up to 5 days.

Pain is usually relieved by mild analgesics. (Analgesics: Voltaren®, Locon® etc.)

Thrombocytopenia

Thrombocytopenia increases the chance of bleeding. If you notice any unusual bleeding, bruising or red spots on your skin, check with your doctor immediately.

3. Intervention through pharmaceutical care reduced the length of hospital stay and medical costs for chemotherapy

Patients are usually hospitalized for 3 days including the dosage of antineoplastic drugs. Fig. 3 shows a case of chemotherapy associated with neutropenia-related complications which required 12 extra hospital days for the patient. Since the neutrophil counts of the patient failed to return to adequate levels before the 8th or 10th cycle of chemotherapy, the physician administered lenogastim, a granulocyte-colony stimulating factor (G-CSF) within 24 hours before the chemotherapy. Because of a neutropenic complication before the 9th cycle of chemotherapy, she was hospitalized for a further 5 days to be treated with lenogastim and antibiotics. After the 10th cycle of chemotherapy, the patient had to be further hospitalized for 7 days to control a recurrence of neutropenic fever. In four other cases, we found that physicians ordered G-CSF within 24 hours before the next cycle of chemotherapy.

On the other hand, in the case shown in Fig. 4, the intervention of the pharmacist resulted in discontinuing the order of administering lenogastim and reducing the dosage of antineoplastic drugs. In this case, the patient was administered lenogastim only four times at an outpatients’ department during the 10 cycle period of chemotherapy, and no neutro-
Alopecia

Taxol® usually causes a temporary and total loss of hair in more than 70-90% of patients. It starts 2 or 3 weeks after the first treatment. However, alopecia is a restorative adverse reaction so that after your treatment has ended, normal hair growth should return.

(Use of scarf, hat, wig)

Peripheral neuropathy

Peripheral neuropathy (numbness, burning, or tingling in hands or feet) is more common with the administration of Taxol®. This usually appears after multiple doses but decreases or disappears within several months after treatment has ended.

(Vitamins: Methycobal® etc.)

Constipation

Constipation is less common but it may occur during a long period of chemotherapy.

(Laxatives: Aloset®, Pursenid®, Magnesium Sulfate® etc.)

Diarrhea

Diarrhea occurs less commonly. Check with your doctor if you have black, tarry stools or blood in your stools.

(Antidiarrheal: Lacto®, Albumine tannate®, Lopermin®)

Fatigue

Unusual tiredness or weakness is more common after treatment and may last up to 5 days. When possible you should rest in bed.

Others

Hypersensitivity (skin rash or itching), shortness of breath, sores in your mouth, anemia, pain at injection site, etc.

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Fig. 1. Example of a TJ Chemotherapy Leaflet for Ovarian Cancer.

Penic complications occurred. In further three cases, the pharmacist intervened to reduce the dosage of antineoplastic drugs or to postpone the chemotherapy schedule instead of G-CSF administration. In total, the number of G-CSF dosages to prevent or treat severe neutropenia was 119 (85 in the inpatient ward and 34 in the outpatient department) in Group A and only 58 (22 inpatient and 36 outpatient) in Group B.

In terms of the health economy in the case of Fig. 3, the 12 extra hospital days cost the patient 388,885 Yen (room charges and the cost of therapeutic drugs), and 217,344 Yen for 16 lenograstim injections during the nine cycle period of chemotherapy.

Discussion

Our previous study demonstrated that the chemotherapy information leaflet improved the patients’ knowledge of the drugs and alleviated their concerns about drug adverse reactions. In this study, we reviewed 28 ovarian cancer patient’s charts to clarify further the effects of the quality of the information provided by pharmacists on the length of hospital
stay. Half of the patients were verbally given the chemotherapy information in Group A, and the other half, Group B, were supplied with an information leaflet and a self-check list of adverse reactions. We found that the mean hospital stay per cycle of chemotherapy in Group B was significantly shorter than that in Group A (2.76±0.80 days versus 7.28±3.97 days; p<0.001). In addition to the leaflet, we used the self-check list of drug adverse reactions in order to help the patient easily notice any primary signs or symptoms of a reaction, such as fever or chill. As a result, the patients in Group B left the hospital early because they knew how to manage any adverse reactions at home.

Regarding the adverse reactions, insomnia occurred in 79% (11/14) of the patients in Group A, which was much higher than the rate (≤5%) usually associated with antineoplastic drugs. Hospital life (less routine and not many social activities) might be the main cause of the high occurrence of insomnia in Group A. In contrast, a much higher incidence of fatigue was recorded in Group B (6/14) after discharge from hospital than in Group A (0/14), which seemed to be due to doing housework at home rather than adverse reactions.

Ishioka et al. have reported that the efficacy of oral 5-HT3 antagonists was almost equipotent to that of intravenous granisetron for TJ therapy. That report indicated that patients could control nausea by taking oral anti-emetics at home instead of intravenous anti-emetics at hospital. Generally, nonhematologic toxicity such as fatigue and vomiting/nausea does not require hospitalization after chemotherapy. Therefore, patients such as those in Group B can manage their adverse reactions at home if they are provided with quality information through appropriate pharmaceutical care.

Bone marrow suppression is one of the severest adverse reactions caused by antineoplastic drugs and is an usual
dose-limiting toxicity. The widespread use of prophylactic antibiotics and the availability of G-CSF has allowed the safe administration of myelosuppressive chemotherapy\(^7\). However, G-CSF should not be administered within 24 hours before or after a dose of chemotherapy drugs because potential sensitivity of rapidly dividing hematopoietic progenitor cells is reported to induce cytotoxicity\(^8\). Dosage reductions are often necessary when the neutrophil counts fail to return to adequate levels before the next course of chemotherapy\(^9\). The neutrophil complications observed in Fig. 3,
Table 1. Cycle of TIJ

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<th>Cycle of TIJ</th>
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<td>Carboplatin (mg)</td>
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<td>Drugs for ADRs</td>
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Fig. 4. The pharmacist intervened to discontinue the order of administering Lenogranim within 24 hours before the 4th cycle of chemotherapy and to reduce the dosage of Antineoplastic Drugs. ADRs: Adverse Reactions.

when G-CSF had been administered within 24 hours before the chemotherapy dosage, were possibly induced by the same mechanism as reported previously.

As health service workers, pharmacists have an important role to play in detecting the causes of unsatisfactory outcomes through careful monitoring. As is shown in Fig. 4, the pharmacist’s intervention achieved definite outcomes of without extra hospitalization and with less use of expensive G-CSF. The effectiveness of the pharmacist’s intervention not only improved the patient’s QOL but also reduced the medical costs. Hepler reported that pharmacists must abandon functionalism and adopt patient-oriented pharmaceutical care as their philosophy of practice and numerous reports describing the efficacy of pharmaceutical care have followed. Several studies have suggested a significant relationship between changes in pharmaceutical services and reductions in the length of hospital stay. The present study demonstrated that our advanced pharmaceutical services for each patient, such as providing quality information and evaluating the drug use for chemotherapy, reduced the length of hospitalization and thus reduced the medical costs. Therefore, we conclude that appropriate drug information and the promotion of pharmaceutical services are highly beneficial in chemotherapy, especially in improving cancer patients’ related-QOL. However, further studies are now underway to assess accurately the improvement of patient’s QOL involved in our pharmaceutical care during chemotherapy.

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References


