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Original article

Comparison of Therapeutic G-CSF Cycles and Prophylactic G-CSF Cycles in Patients Receiving Paclitaxel and Carboplatin Combination Chemotherapy for Ovarian Cancer: A Retrospective Study Report

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Abstract

Objective: The aim of the present study was to investigate the differences between therapeutic granulocyte-colony stimulating factor (G-CSF) cycles and prophylactic G-CSF cycles in patients receiving paclitaxel and carboplatin combination chemotherapy for ovarian cancer.

Material and Method: Medical records of 15 women who received paclitaxel and carboplatin combination chemotherapy for ovarian cancer between January 2003 and December 2012 were analyzed retrospectively. All 15 patients completed 6 cycles of paclitaxel and carboplatin as the first-line chemotherapy. The complications were compared between therapeutic G-CSF cycles and prophylactic G-CSF cycles.

Results: The number of chemotherapy cycles correlated with the ratio of prophylactic G-CSF cycles. It was considered that earlier prophylactic G-CSF injections were chosen due to a gradual decrease in WBC and neutrophil counts. The WBC and neutrophil counts were significantly higher in prophylactic G-CSF cycles than in therapeutic G-CSF cycles. However, there were no significant differences in the intervals of chemotherapy, delay of chemotherapy, and incidence of febrile neutropenia between the therapeutic G-CSF and prophylactic G-CSF cycles.

Conclusion: Prophylactic G-CSF injections were not effective in preventing the incidence of febrile neutropenia in patients receiving paclitaxel and carboplatin combination chemotherapy for ovarian cancer.

Key words: granulocyte-colony stimulating factor (G-CSF), ovarian cancer, paclitaxel and carboplatin combination chemotherapy

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Introduction

Chemotherapies often cause hypocytosis and lead to neutropenia and febrile neutropenia (FN). FN is one of the major dose-limiting toxicity and oncologic emergency diseases that requires the use of antimicrobial agents[1].

Primary prophylactic G-CSF for patients with a high risk of FN is reportedly effective[2]. Recommended guidelines for G-CSF injection were published by the American Society of Clinical Oncology in 2006[3].

The combination of paclitaxel and carboplatin therapy is one of the standard chemotherapies for ovarian cancer[4]. The FN risk induced by paclitaxel and carboplatin combination chemotherapy is considered to be lower, so primary prophylactic G-CSF injection is not commonly recommended[5, 6].

We investigated the differences between therapeutic G-CSF cycles and prophylactic G-CSF cycles in patients receiving paclitaxel and carboplatin combination chemotherapy for ovarian cancer in our hospital.

Material and Methods

Medical records of 15 women who received paclitaxel and carboplatin combination chemotherapy for ovarian cancer between January 2003 and December 2012 in our hospital were analyzed retrospectively.

All 15 patients completed 6 cycles of paclitaxel and carboplatin combination therapy as first-line chemotherapy. The chemotherapy consisted of intravenous paclitaxel at a dose of 175 mg per square meter of body surface area plus carboplatin at a dose of AUC 5 for every 22–29 days.

For therapeutic G-CSF cycles, we administered G-CSF when the neutrophil counts were < 500/μl. For prophylactic G-CSF cycles, we administered G-CSF when the neutrophil counts were 500/μl ≤ but < 1000/μl.

Table 1 Characteristics and conditions of the patients

Number of patients	n=15	
Age (years)	62.1 ± 9.5 (42–77)	
Stage of ovarian cancer	Stage I	6
	Stage III	7
	Stage IV	2
Histology of ovarian cancer	Serous adenocarcinoma	5
	Serous cystadenocarcinoma	2
	Serous papillary adenocarcinoma	4
	Serous papillary cystadenocarcinoma	1
	Endometrioid adenocarcinoma	1
	Clear cell adenocarcinoma	1
	Clear cell adenocarcinofibroma	1
Regime of chemotherapy	Paclitaxel, 175 mg/m^2; carboplatin, AUC5	
Cycles of chemotherapy	Total	90 cycles
	No G-CSF	22 cycles
	Therapeutic G-CSF	15 cycles
	Prophylactic G-CSF	53 cycles

Mean ± SD (range).

Table 2 Tendncies for therapy with G-CSF

Chemotherapy cycles	1	2	3	4	5	6	
No G-CSF (cycles)	9	4	3	2	2	2	24.40%
Therapeutic G-CSF (cycles)	4	2	3	2	2	2	16.70%
Prophylactic G-CSF (cycles)	2	9	9	11	11	11	58.90%

For both therapeutic G-CSF cycles and prophylactic G-CSF cycles, we discontinued G-CSF when the neutrophil counts were ≥ 1000/μl and there were no fever symptoms of FN.

Nartograstim (50 μg/body) or Filgrastim (75 μg/body) were used as G-CSF injections.

The minimum white blood cell (WBC) counts, minimum neutrophil counts, days with G-CSF, interval of chemotherapy, delay of chemotherapy, and incidence of FN were evaluated.

The complications were compared between therapeutic G-CSF cycles and prophylactic G-CSF cycles using the Wilcoxon signed-rank test and Fisher's exact probability test. All statistical analyses were done with the StatView 5.0 software for Windows (HULINKS Inc, Tokyo, Japan).

Results

The characteristics and conditions of the patients are shown in Table 1.

There were 15 patients. Their mean age was 62.1 years old. Six patients had stage I ovarian cancer, seven had stage III ovarian cancer, and two had stage IV ovarian cancer. There were five serous adenocarcinomas, two serous cystadenocarcinomas, four serous papillary adenocarcinomas, one serous papillary cystadenocarcinoma, one endometrioid adenocarcinoma, one clear-cell adenocarcinoma, and one clear-cell adenocarcinofibroma.

A total of ninety chemotherapy cycles were performed. There were 22 cycles with no G-CSF, 15 cycles with therapeutic G-CSF, and 53 cycles with prophylactic G-CSF.

The tendencies for therapy with G-CSF are shown in Table 2.

In the first round of chemotherapy, there were nine cycles with no G-CSF, four cycles with therapeutic G-CSF, and two cycles with prophylactic G-CSF. In the second round of chemotherapy, there were four cycles with no G-CSF, two cycles with therapeutic G-CSF, and nine cycles with prophylactic G-CSF. In the third round of chemotherapy, there were three cycles with no G-CSF, three cycles with therapeutic G-CSF, and nine cycles with prophylactic G-CSF. In the fourth round of chemotherapy, there were two cycles with no G-CSF, two cycles with therapeutic G-CSF, and 11 cycles with prophylactic G-CSF. In the fifth round of chemotherapy, there were two cycles with no G-CSF, two cycles with therapeutic G-CSF, and 11 cycles with pro-

Table 3 Comparison between therapeutic G-CSF cycles and prophylactic G-CSF cycles

	Therapeutic G-CSF cycles 15 cycles	Prophylactic G-CSF cycles 53 cycles	P value
Minimum white blood cell count (/μl)	1600 ± 325 (1100–2200)	2158 ± 493 (1400–3700)	<0.05
Minimum neutrophil count (/μl)	398 ± 104 (92–490)	841 ± 315 (409–1742)	<0.05
Frequency of G-CSF injection (times)	8.4 ± 4.3 (3–14)	6.3 ± 4.2 (2–19)	N.S.
Intervals of chemotherapy (days)	28.3 ± 6.7 (22–41)	27.7 ± 3.8 (22–36)	N.S.

Mean ± SD (range), Wilcoxon signed-rank test.

Table 4 Comparison between therapeutic G-CSF cycles and prophylactic G-CSF cycles

	Therapeutic G-CSF cycles 15 cycles	Prophylactic G-CSF cycles 53 cycles	P value
Delay of chemotherapy (cycles)	7	15	N.S.
Incidence of febrile neutropenia (cycles)	1	0	N.S.

Fisher's exact probability test.

phylactic G-CSF. In the sixth round of chemotherapy, there were two cycles with no G-CSF, two cycles with therapeutic G-CSF, and 11 cycles with prophylactic G-CSF.

Comparisons of the therapeutic G-CSF cycles and prophylactic G-CSF cycles are shown in Table 3 and Table 4.

The total number of therapeutic G-CSF cycles was 15 cycle, and the total number of prophylactic G-CSF cycles was 53 cycles. The minimum white blood cell counts were 1600 ± 325/μl in therapeutic G-CSF cycles and 2158 ± 493/μl in prophylactic G-CSF cycles ($P<0.05$). The minimum neutrophils counts were 398 ± 104/μl in therapeutic G-CSF cycles and 841 ± 315/μl in prophylactic G-CSF cycles ($P<0.05$). The frequencies of G-CSF injections were 8.4±4.3 in therapeutic G-CSF cycles and 6.3±4.2 in prophylactic G-CSF cycles. The intervals of chemotherapy were 28.3 ± 6.7 days in therapeutic G-CSF cycles and 27.7 ± 3.8 days in prophylactic G-CSF cycles. The delays of chemotherapy were 7 cycles in therapeutic G-CSF cycles and 15 cycles in prophylactic G-CSF cycles. Febrile neutropenia was confirmed in 1 case in the therapeutic G-CSF cycles and 0 cases in the prophylactic G-CSF cycles. Frequency of G-CSF injections, intervals of chemotherapy, delay of chemotherapy, and incidence of febrile neutropenia were not significantly different between therapeutic G-CSF and prophylactic G-CSF cycles.

Discussion

The number of chemotherapy cycles was correlated with the ratio of prophylactic G-CSF cycles. On the other hand, the ratio of therapeutic G-CSF cycles was almost the same. It was considered that earlier prophylactic G-CSF injections were chosen due to a gradual decrease in the WBC and neutrophil counts. G-CSF was administered in the case of higher level of WBC and neutrophil counts in prophylactic cycles thus, the WBC and neutrophil counts were significantly higher in prophylactic G-CSF cycles than in therapeutic G-CSF cycles. However, it was possible to improve the WBC and neutrophil counts more rapidly in prophylactic G-CSF cycles. There were no significant differences in the interval of chemotherapy, delay of chemotherapy, and incidence of FN between therapeutic G-CSF and prophylactic G-CSF cycles. We considered the prophylactic G-CSF injections to be not effective in preventing the incidence of FN.

Conclusion

There were no significant differences in the incidence of FN between prophylactic cycles and therapeutic cycles. Prophylactic G-CSF injections were not effective in preventing the incidence of FN in patients receiving paclitaxel and carboplatin combination chemotherapy for ovarian cancer.

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