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Comparison of quality of life in patients with advanced ovarian cancer treated with intravenous paclitaxel and carboplatin versus cyclophosphamide and cisplatin as first line chemotherapy – a preliminary report

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Introduction. Ovarian cancer is the fourth most common gynecological malignancy in Poland (after breasr cancer, lung cancer and cercical cancer) and the second leading cause of death from gynecological malignancy (after cervical cacer). An objective response to cytotoxic chemotherapy occurs in the majority of individuals with cancers of the ovary.
Material and methods. 54 patients (of 215), who were treated in our clinic between January 2000 and March 2001 were included in the study. Eligibility criteria were: 1) histologically confirmed diagnosis of advanved ovarian cancer, 2) primary cytoreductive surgery, 3) Karnofsky performance status 70% and cognitive abilities allowing for filling in the questionnaire. Quality of life was measured using EORTC-C30 (version 3.0) questionnaire.
Results. Higher score of nausea and vomiting was observed in the group of patients treated with PC regimen, as compared to paclitaxel and carboplatin. However, those patients had significantly better social functioning. Cyclophosphamide and cisplatin more often caused dyspnoea, sleeping and appetite problems. PC regimen affected cognitive functioning and role functioning less, as compared to paclitaxel and carboplatin. There was no significant difference in general functioning between the two groups.
Conclusions. Global quality of life in patients treated with paclitaxel/carboplatin was the same as in patients treated with PC regimen. Higher scores in symptom and single-item scale were observed in patients treated with the PC regimen. Paclitaxel/carboplatin regimen influenced the quality of life more in the functional scale. In order to obtain objective assessment of the quality of life larger population study is necessary.

Porównanie jakości życia chorych z zawansowanym rakiem jajnika w trakcie chemioterapii z zastosowaniem paklitakselu z karboplatyną oraz tradycyjnego schematu PC w pierwszej linii leczenia – doniesienie wstępne

Wstęp. W Polsce rak jajnika jest czwartym pod względem częstości występowania nowotworem u kobiet (po raku piersi, płuca i szyjki macicy) i drugą co do częstości przyczyną zgonów z powodu nowotworów narządów rodnych (po raku szyjki macicy). Celem naszego badania było porównanie wpływu tradycyjnego schematu PC, zawierającego cyklofosfamid i cisplatynę oraz nowoczesnego leczenia paklitakselem z karboplatyną na jakość życia pacjentek z zaawansowanym rakiem jajnika.
Materiał i metody. Jakość życia mierzona była za pomocą kwestionariusza QLQ-C30 (wersja 3.0), opracowanego przez EORTC. W badaniu wzięły udział 54 pacjentki spośród 215, z histologicznie potwierdzonym rakiem jajnika, leczone wg schematu PC lub paklitakselem z karboplatyną jako chemioterapia pierwszego rzutu. W grupie chorych leczonych schematem PC, w porównaniu do paklitakselu z karboplatyną, obserwowano częstsze występowanie nudności i wymiotów, duszności, zaburzeń snu oraz łaknienia. Jednakże schemat PC w mniejszym stopniu wpływał na społeczny aspekt życia. Zaobserwowaliśmy także mniejszy wpływ schematu PC na funkcje poznawcze i pracę. Nie stwierdziliśmy natomiast różnic w ogólnej jakości życia chorych leczonych obiema metodami leczenia.
Wnioski. Ogólna jakość życia chorych leczonych z zastosowaniem paklitakselu i karboplatyny jest taka sama, jak chorych leczonych według schematu PC. Zaobserwowano większy wpływ schematu PC na jakość życia w skali objawowej. Natomiast paklitaksel z karboplatyną wywierał większy wpływ na jakość życia w skali funkcjonalnej. W celu obiektywnej oceny wpływu obu metod leczenia na jakość życia konieczne jest objęcie badaniem większej liczby chorych.

Key words: quality of life, chemotherapy, ovarian cancer
Słowa kluczowe: jakość życia, chemioterapia, rak jajnika

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Introduction

Ovarian cancer is the fourth most common gynecologic malignancy in Poland (after breast cancer, lung cancer and cervical cancer) and the second leading cause of death from gynecological malignancy (after cervical cancer) [1]. An objective response to cytotoxic chemotherapy occurs in a majority of individuals with cancers of the ovary. Cisplatin-based combiantion chemotherapy allows a high clinical response rate in ovarian carcinoma. Before the introduction of paclitaxel, cyclophosphamide and cisplatin (PC regimen) was the only first line treatment of advanced ovarian cancer. Adminisrtation of paclitaxel in combiantion with cisplatin as first line treatment resulted in longer overall and disease-free survival [2, 3]. It is suggested that cisplatin could be repalced with carboplatin in order to decrease nephro- and neurotoxity. Several prospective randomized trials comparing cisplatin to carboplatin have demonstrated similar efficacy and little nephro- and neurotoxity of carboplatin in combiantion with paclitaxel [4, 5]. However, carboplatin has been shown to cause myelosupression [4]. Prolongation of life expectancy and tumor shrinkage have traditionally been taken as outcome measures when evaluating the efficacy of medical treatment on cancer. Despite the substantial side effects and functional impairment often associated with cancer treatment, only recently attention has been given to the assessment of quality of life [6, 7].

Aim of study objectives

The purpose of our study was to compare the effect of intravenous cyclophosphamide/cisplatin and paclitaxel/carboplatin as first line chemotherapy in patients with advanced ovarian cancer after primary cytoreductive surgery.

Material and methods

54 patients (of 215), treated in our clinic between January 2000 and March 2001, were included in the study. Eligibility criteria were: 1) histologically confirmed diagnosis of advanced ovarian cancer, 2) primary cytoreductive surgery, 3) Karnofsky performance status 70% and cognitive abilities allowing for filling in the questionnaire. 24 patients received the PC regimen (cyclophosphamide 750 mg/m^2 and cisplatin 75 mg/m^2). The remaining 30 patients were treated with paclitaxel and carboplatin (paclitaxel 135mg/m^2 in 24 hour intravenous infusion and carboplatin administration according to the Calvert formula – carboplatin (mg)=AUCx (GFR+25)). Quality of life was measured using EORTC QLQ-C30 (version 3.0) questionnaire. QLQ-C30 has been carefully developed in a multi-cultural setting by the European Organiztion for Research and Treatment of Cancer in 1986. The instrument has been shown to be valid, reliable and responsive to change. Disease-specific modules are available to supplement the core questionnaire. Study results can be compared across trials. The questionnaire can be easily understood by most patients and is quick to complete (mean time 11 minutes). QLQ-C30 consists of 30 items and a number of scales (5 functioning scale-physical, role, cognitive, emotional, social; 3 symptom scales – fatigue, pain, nausea/vomiting; 1 global health status and supplementary modules containing additional items and scales – constipation, diarrhoea, sleep, dyspnoea, appetite, financial.

A high score for functioning scales and the global scale indicate a high level of functioning or quality of life. A high score for a symptom scale or a single-item scale reveal a high level of symptom or problem (8, 9).

Quality of life questionnaire was handed to patients at subsequent 3rd or 4th chemotherapy course, after their consent to participate in the study. Whenever instructions were not understood or questions were confusing additional explanation was given. Questions were read out and questionnaire filled in when a patient was unable to fill in the questionnaire herself.

The analysis comprised age, FIGO stage, economic status, education and residual disease after primary cytoreductive surgery and Ca 125 antigen level. There were no statistically significant differences between the two groups apart from age (p=0.038). In the group of patients treated with paclitaxel and carboplatin the age was significantly lower comparing to the group of patients treated with PC regimen.

All scores were obtained from scales and single-item measuring range from 0-100 according to the guidelines provided by EORTC [10]. Patients characteristics and quality of life scores were analysed with statistical Mann-Whitney U Test.

Results

Patients characteristics are summarized in Table I. Figures 1 and 2 show quality of life scores in functional, global and symptom scales. Patients treated with PC regimen presented higher scores in the functional scale – social functioning. There were no differences between the two groups in the remaining aspects of the functional scale. Patients treated with paclitaxel and carboplatin reported fewer symptom scores in the following items: nausea/vomiting, sleeping and appetite problems. Global quality of life was the same in the two groups.

Discussion

Introduction of paclitaxel to the treatment of advanced ovarian cancer resulted in a better response rate and improvement of a progression-free interval. Combination

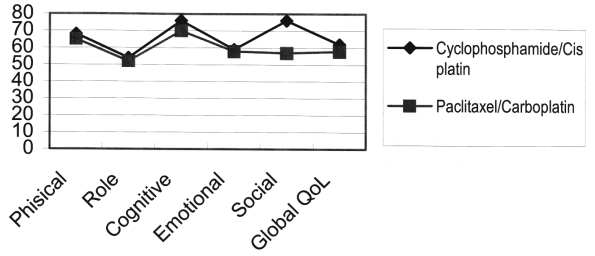

Figure 1. QoL RESULTS functional scales and global quality of life

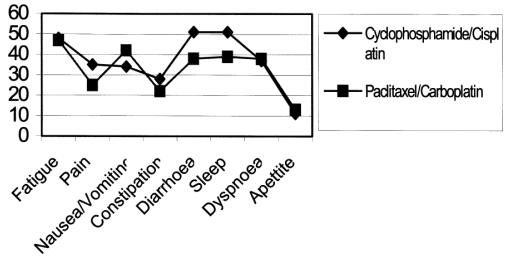

Figure 2. QoL RESULTS symptom scales and single items

Table I. Patients, characteristics

Characteristics of patients		Number of patients		
		All	First line pc	First line paclitaxel/carboplatin
Number of patients	N	54	24	30
Age	mean	55	60	51
	(range)	(27 – 78)	(40 – 78)	(27 – 71)
FIGO stage	Ic	4	1	3
	IIb	6	2	4
	IIc	4	3	1
	IIIc	35	17	18
	IV	4	4	-
CA 125 (u/ml)	mean	134.74	98.45	163.76
Time from diagnosis	<30 mths	54	24	30
	>30 mths	-	-	-
Education	<high school	14	12	2
	high school	19	6	13
	graduate school	12	2	10
	missing	9	4	5
Economic status	low	9	2	7
	average	33	15	18
	high	12	7	5

of paclitaxel and platinum compound has recently become the new standard of care for advanced ovarian cancer. The use of paclitaxel and cisplatin, even in therapeutic doses, has been shown to develop dose-limiting general toxicity. Both paclitaxel and cisplatin are neuro- and nephrotoxic agents. For this reason the use carboplaitn (a less toxic platinum compound) instead of cisplatin is thought to be feasible. Current data has shown that paclitaxel in combination with carboplatin produces an identical response rate, progression-free interval and median overall survival [11]. However, those two agents appear to cause myelotoxity [11].

It is only recently that attention has been given to the assessment of quality of life despite the substantial side effects and functional impairment often associated with cancer treatment.

In our study we have compared the effect of intravenous cyclophosphamide/cisplatin and paclitaxel/carboplatin as first line chemotherapy on physical and psychological aspects of quality of life in patients with advanced ovarian cancer. Nausea and vomiting were observed more frequently in the group of patients treated with the PC regimen. However, those patients had significantly better social functioning (p=0.012).

The global quality of life was the same in both groups.

The interpretation of the results remains essentially qualitative. Clinical significance is subjective and is a matter of opinion. The values and opinions of individual patients will differ, as will the opinions of the treating clinician and those of society in general. Thus, for a quality of life measurement scale, it is unlikely that a single threshold value will be universally accepted as a cut-off point that separates clinically important changes from trivial and unimportant ones. However, many investigators are finding that, for a variety of scales assessing overall quality of life and some of its dimensions, changes of between 5% and 10% (5 and 10 points on the 1-100 scales of QLQ-C30) are noticeable by patients and regarded as "significant" [12-14]. Osoba et al. asked patients to complete the QLQ-C30 on repeated occasions, and the patients also related their perception of change since the previous time they completed the QLQ-C30. Physical, emotional, social functioning and global quality of life scales were evaluated [13]. It was found that when the scale scores changed by 5 to 10 points, patients describe their condition as "a little" better (or worse). A change of 10 to 20 was described as "a moderate" change. A change greater than 20 was "very much" better (or worse) [9, 13].

Our results were interpreted according to the outcome measurement proposed by Osoba et al. and recommended by EORTC.

Patients treated with the PC regimen, apart from significantly more frequent nausea/vomiting and less social functioning impairment, presented changes in other aspects of functioning and symptom scale. We observed that the PC regimen less influenced cognitive and role functioning (average difference of successively 6 and 7 points in comparison to paclitaxel/carboplatin regimen). PC caused dyspnoea, sleeping and appetite problems more often (average differences successively 6, 6 and 13 points). Our results suggest that the PC regimen affects the quality of life more. The fact that there was statistically significant difference in age between the two groups (median 63.5 versus 54.0, p=0.038) could have affected our results. Currant et al. observed that age, apart from general health status and psychosocial functioning, appeared

to be the most important risk factor of bad general functioning among patients with early diagnosis of breast cancer [15].

Despite the fact that there were no significant differences in the global quality of life, we cannot definitely say that our results were not influenced by a limited number of patients. Thus, in order to obtain objective assessment of quality of life larger population study is necessary.

Conclusions

Global quality of life of patients treated with paclitaxel/carboplatin was the same as of patients treated with the PC regimen. Higher scores in symptom and single--item scale were observed in patients treated with PC regimen. Paclitaxel/carboplatin regimen more significantly influenced the quality of life in functional scale. In order to obtain objective assessment of the quality of life a larger population study is necessary.

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