THE INFLUENCE OF PACLITAXEL TREATMENT ON SELECTED BIOCHEMICAL AND MORPHOLOGICAL BLOOD PARAMETERS IN PATIENTS DIAGNOSED WITH BREAST CANCER

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Abstract

Introduction: Breast cancer is the most commonly diagnosed cancer in women and second only to lung cancer as the leading cause of death in women. These statistics necessitate seeking new solutions for the prevention and treatment of cancer. In recent years, taxanes have emerged as one of the strongest groups of anticancer drugs. Paclitaxel is a drug with proven clinical efficacy in the treatment of breast cancer. However, as with all other cytostatics, Paclitaxel is not free from side effects. Despite its proven effectiveness during the therapy and after its termination, it is necessary to monitor the patient for side effects. The aim of the present study was to assess the impact of treatment with Paclitaxel on blood test results. This paper analyzes the results of these tests before therapy and after its completion.

Material and methods: The study included 40 patients diagnosed with breast cancer, treated with Paclitaxel at the Chemotherapy Outpatient Clinic of prof. F. Łukaszczyk Oncology Center in Bydgoszcz. The study was conducted from November 2009 to May 2010. All the patients underwent a mastectomy. The research method was a survey and an analysis of blood tests before and after Paclitaxel treatment. Based on the data, the influence of Paclitaxel treatment on changes of selected blood parameters was evaluated.

Results: As a result of Paclitaxel therapy, for the entire group, an average increase of GPT (AIAT), GOT, hemoglobin /HGB/ and erythrocytes was observed, along with an average decrease in blood urea, creatinine and blood platelets. The level of leukocytes remained on the same level. The results of the evaluation of red blood cells, platelets, GPT (AIAT) and creatinine before and after Paclitaxel treatment differed significantly. The results for urea, GOT (AST), hemoglobin and white blood cells before and after Paclitaxel treatment did not differ in a statistically significant way.

Conclusions: There is a need for continuous monitoring of blood parameters, so that the body's response to treatment may be predictable and that treatment does not pose a significant risk to the patient's life. The patients should be informed about the side effects of chemotherapy, and methods of their prevention.

Keywords: treatment of breast cancer, Paclitaxel, blood tests.

Introduction

Breast cancer is a major cause of death in women between 25 and 60 years of age. The incidence of this cancer increases with age, peaking between 50 and 70. Treatment of breast cancer is a comprehensive, individually selected therapy, depending on tumor staging (TNM) and risk of relapse based on predictive and prognostic factors. Chemotherapy has been a universally applied form of treatment for breast cancer since the 1970s. Adjuvant chemotherapy (originally used after radical topical treatment) is used in order to destroy micro metastases. Qualification of a patient for chemotherapy should take place no later than eight weeks after the surgery. Postoperative chemotherapy is used according to specific schemes [1, 2].

Paclitaxel is a new drug for breast cancer used in chemotherapy; it was originally isolated from the bark of the yew tree *taxus brevifolia*, which is currently produced in a semi-synthetic process from the needles of the European yew *taxus baccata* [3]. The antitumor activity of paclitaxel consists in increased polymerization of tubulin proteins in the microtubules of the karyokinetic spindle and in depolymerization of microtubules. The drug also acts on cell-cycle proteins (MAPS) and apoptosis pathways. Paclitaxel's pharmacokinetics is non-linear – its concentration in the serum is variable, depending on the dose [4]. Paclitaxel enables achieving a remission in about 60 percent of the patients with breast cancer who have not previously been treated with chemotherapy. The drug has proven to be very active in patients previously treated with anthracyclines. In this group of patients, a remission can be achieved in 20-40 percent of the cases. [1] During the application of Paclitaxel, bone marrow suppression may occur, usually expressed as short-term leukopenia, thrombocytopenia, and in particular as neutropenia, which is dose-dependent. Paclitaxel also shows hepatotoxic activity.

In oncology, Paclitaxel is administered intravenously, in doses calculated per square meter of

body surface, following time schedules strictly determined by the physician. The drug may be administered over one hour, three to four hours, or even over a 24-hour period. The aim of this study was to assess the impact of Paclitaxel treatment on the results of blood tests. The study included the following parameters: leukocytes, erythrocytes, platelets, GOT (AspAT), GPT (AIAT), creatinine and urea.

Material and methods

The study included 40 Patients treated with paclitaxel at the Outpatient Clinic of Chemotherapy at the F. Łukaszczyk Regional Oncology Center in Bydgoszcz, and diagnosed with breast cancer. Neoplastic disease in the breast and the monotherapy with paclitaxel administered intravenously constituted the basic selection criteria for selecting the patients for the present study. The study was carried out between November 2009 and May 2010. For all patients, the second medication was applied after a previous therapy with anthracyclines. All of the patients had undergone a mastectomy. Paclitaxel was administered intravenously in standard doses of 175 mg/m2 of body area, over three to four hours. The research method used was a survey poll and an analysis of blood tests before and after Paclitaxel therapy.

For the evaluation of hematological toxicity, blood counts were used. The blood tests were performed before each course of chemotherapy. All laboratory tests were performed at the Oncology Centre in Bydgoszcz and interpreted according to its existing range of norms. The study included the following parameters: leukocytes, erythrocytes, platelets, GOT (AspAT), GPT (AIAT), creatinine and urea. Filling out of the questionnaire and participation in the study were voluntary on the part of the patients. Before deciding to participate in the survey, the patients were informed about the purpose and nature of the study and they signed a written informed consent form. The study was conducted on the basis of approvals form:

- The Bioethics Committee at Collegium Medicum, Nicolaus Copernicus University in Torun,
- The Director of the Oncology Center in Bydgoszcz.

The presentation of the results includes numbers and percentages, arithmetic means, standard deviations, Wilcoxon signed-rank tests (the level of significance of $p \geq 0.05$), and tables presenting the numbers and percentages of individual responses to questions. The calculations were performed using the Microsoft Excel spreadsheet.

Results

The analysis of the responses given in the survey and the results of the blood tests yielded the following results.

The study group was characterized in terms of age. The results are shown in Table 1.

Table 1 The average age of the patients.

N- number of patients	Mean	Standard deviation	Minimum	Maximum	Median
40	54,7	10,23368	31,0	74,0	55,5

The patients were aged from 31 to 74. The average age was 54.7 years.

The frequency of treatment with Paclitaxel of the patients was also determined. The results are shown in table 2.

Table 2. The frequency of Paclitaxel administration in the study group.

The incidence of Paclitaxel	N-number of respondents	% of respondents
Every 21 days	36	90.0
Every7 days	4	10.0

For 36 patients, i.e. 90 percent, 21-day protocols were used, while 7-day protocols were used

in 3 cases.

The average dose of Paclitaxel administered to the patients was also calculated. The results are shown in Table 3.

Table 3. The average doses of Paclitaxel used.

N-number of respondents	Average	Deviation Standard	Minimum	Maximum	Median
40	40284.5	62.70033	100.0	370.0	300

The doses administered to the patients were between 100 and 370 mg. The doses from 100 to 145 mg were used in patients with 7-days chemotherapy protocols. The other doses were administered to the patients treated every 21 days.

An analysis of selected blood test results was also conducted. The study included the following parameters: leukocytes, erythrocytes, hemoglobin, platelets, GOT (AspAT), GPT (AIAT), creatinine and urea. The results obtained are presented below.

Table 4 Evaluation of the changes in blood parameters before and after treatment with Paclitaxel in relation to the number of patients.

The evaluated parameters of blood	N-Number of persons assessed	Situation before therapy				Situation after treatment		
		Normal	Above normal	Below normal	Standard	Normal	Above normal	Below normal
Leukocytes / WBC /	40	30	5	5	31	31	7	2
Erythrocytes / RBC /	40	25	2	13	32	32	2	6
Hemoglobin / HGB /	40	26	0	14	29	29	0	11
Platelets / PLT /	40	25	15	0	36	36	4	0
GOT (AST)	34	24	10	0	21	21	13	0
GPT (ALT)	34	23	11	0	18	18	16	0
Creatinine	34	25	3	6	22	22	3	9
Urea	33	30	33	0	32	32	1	0

After Paclitaxel treatment the following changes were observed:

- an increase in the number of patients whose results concerning leukocytes were within the norm from 30 to 31 patients; in 24 cases the results remained normal, and in 5 patients, the results increased above the norm.

- an increase in the number of patients whose test results for erythrocytes were within the norm from 25 to 32 individuals; 17 patients maintained normal results, in 4 patients, the results fell below normal, and in two they were raised above normal. In 11 patients, results rose from below-normal to normal,

- an increase in the number of patients whose hemoglobin levels were normal from 26 to 29 patients; 24 patients remained within the normal range, in 2 patients the results fell from the normal range to below-normal; in the case of 9 patients the previous results below the norm remained on the same level, and 5 cases they increased and reached the normal range,

- an increase in the number of patients whose platelet counts ranged within the norm from 25 to 36 persons. The results of 24 patients remained normal, and in 12 patients the results fell from above-normal to normal,

- a decrease in the number of patients whose GOT (AspAT) levels were normal from 24 to 21 presons; 18 patients maintained normal levels both before and after the therapy, in 6 patients, the normal results increased to above-normal levels, above-normal levels were maintained in 7 cases, while in 3 cases the above-normal results fell and reached the normal range,

- a decrease in the number of patients whose GPT (AIAT) levels ranged within the norm from 23 to 18 persons; in 17 patients the results remained normal, and in 6 patients, the previously normal levels increased above the norm,

- a decrease in the number of patients whose creatinine levels remained normal from 25 to 22 patients; 20 patients maintained normal results, in 4 patients the levels fell below normal.

- an increase in the number of patients whose urea levels were within the norm from 30 to 32 persons; 30 patients remained within the normal range, the results remained above normal in 1 patient, and in 2 patients the levels fell from above-normal to normal.

The levels of blood parameters during and after Paclitaxel therapy, and differences between them are detailed in Table 5.

Table 5 Blood parameters during and after Paclitaxel therapy, and differences between them.

The evaluated parameters of blood	N-number of respondents	Results before therapy Paclitaxel		Results after treatment Paclitaxel		Difference	
		Average	SD	Average	SD	Average	SD
Leukocytes / WBC /	40	7,11	2,8128	7,11	2,6821	0,006	2,8245
Erythrocytes / RBC /	40	4,13	0,4073	4,24	0,5404	0,111	0,5350
Hemoglobin / HGB /	40	12,4	1,1387	12,56	1,1721	0,163	0,9470
Platelets / PLT /	40	315,05	88,2642	278,15	59,6896	-36,900	92,0902
GOT (AST)	34	27,49	12,1236	30,29	9,9260	2,08	11,3957
GPT (ALT)	34	33,7	32,8873	39,16	23,8640	7,577	35,2900
Creatinine	34	60,3	28,8341	56,03	30,3781	-4,901	12,0489
Urea	33	5,36	2,4329	4,95	1,9334	-0,373	1,7118

- as a result of Paclitaxel therapy, in the entire group, an average increase in the levels of GPT (AIAT), GOT (AspAT), hemoglobin / HGB /, and erythrocytes was observed.
- as a result of Paclitaxel therapy, in the entire group, an average decrease in the level of urea, creatinine, platelet count was observed.

- the leukocyte level remained the same.
- In the study of selected blood parameters before and after Paclitaxel treatment, a Wilcoxon test was used (the adopted level of statistical significance was $p < 0.05$)

Table 6 Differences in blood parameters before and after therapy – Wilcoxon test.

Evaluated blood parameters before therapy & after therapy	N-number of people who have been evaluated different parameter	T	Z	Level p
Leukocytes / WBC /	40	409	0,01	0,989276
Erythrocytes / RBC /	40	242	2,26	0,023938
Hemoglobin / HGB /	40	201	1,87	0,061871
Platelets / PLT /	40	238	2,31	0,020784
GOT (AST) *	34	200,5	1,66	0,097245
GPT (ALT) *	34	145	2,61	0,009129
Creatinine*	34	161	2,33	0,019613
Urea*	33	250	0,54	0,585775

*The results of GOT (AspAT), GPT (AIAT), creatinine and urea were taken into account only for some of the patients, as for the rest of them they were unavailable.

As shown in the table, the level of significance p was <0.05 for erythrocytes, platelets, GPT (ALT) and creatinine. The measurement results for these parameters before and after Paclitaxel therapy differed significantly. However, the results for urea, GOT (AST), hemoglobin and white blood cells before and after therapy Paclitaxel did not differ in a statistically significant way (p> 0.05).

Summary and Conclusions

In the chemotherapy of patients with generalized breast cancer, Paclitaxel can achieve a remission in about 60 percent of patients with breast cancer who have not previously been treated with cytostatics, and in patients who had previously been treated with anthracyclines a remission can be achieved in 20 – 40 percent of the cases. [5] In Paclitaxel monotherapy, the drug administered once a week was more effective and less toxic than when a the three-week treatment protocol was followed [6]. Studies indicate that Paclitaxel is effective in monotherapy, and its

activity is comparable to FAC. [7] Despite the proven effectiveness of Paclitaxel in the treatment of breast cancer during treatment with this drug and after its completion, it is necessary to monitor the patients for side effects.

The Analysis of the blood tests performed before and after Paclitaxel treatment showed that the drug did not cause a statistically significant reduction in the level of leukocytes, erythrocytes or hemoglobin. However, there did occur a statistically significant lowering in the level of platelets. Yet it should also be noted that none of the patients ever showed platelet levels below normal – neither before nor after the treatment. Similar results were obtained by other authors [7]. A comparison in the levels of erythrocytes before and after treatment revealed that the values were below the norm in 15 patients before treatment and in 8 patients after it. Levels of leukocytes within the normal range were maintained in 24 patients, the level of erythrocytes in 17, and that of hemoglobin in 42. The blood morphology analysis presented here shows that Paclitaxel administered in standard doses over 3-4 h does not cause significant bone marrow suppression. The analysis of blood chemistry confirmed Paclitaxel's hepatotoxicity.

AspAT levels in the group increased after treatment, in comparison with the levels before treatment. Nonetheless, this increase was not statistically significant. Yet it should be noted that before the treatment 10 patients had AspAT levels above the norm, and after treatment this number rose to 13 patients. In contrast, the analysis of AIAT levels in the blood showed an increase of statistical significance. Before starting the treatment, 11 patients had results above the norm, and after the treatment 16 patients had AIAT values exceeding the normal range. Determining the effect of Paclitaxel on the liver is very difficult because the patients were receiving a multidrug therapy, which included painkillers. Liver damage by cytostatic drugs consists in a transient increase in liver enzymes (which typically return to normal within several weeks after administration) as well as intrahepatic cholestasis.

In the study group, a comparison of the levels of creatinine and urea in the blood before the administration of Paclitaxel and after treatment revealed a reduction in the values of these parameters. Only the decrease in creatinine was statistically significant. The likely cause of a statistically significant decrease in serum creatinine level was premedication consisting of steroids and antihistamines, administered to all of the patients receiving Paclitaxel.

In summary the study yielded the following conclusions:

- Paclitaxel therapy had a statistically significant impact ($p < 0.05$) on the values of red blood cells, platelets, GPT (ALT) and creatinine,

- the therapy had no statistically significant effect ($p > 0.05$) on the values of the leukocyte count, hemoglobin, GOT (AspAT) and urea.

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