PSA LEVEL AND ADVERSE EVENTS IN SIXTH AND TENTH SERIES DOCETAXEL CHEMOTHERAPY IN CASTRATE-RESISTANT PROSTATE CANCER (CRPC) PATIENTS

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ABSTRACT

Objective: *This study aims to compare the efficacy of docetaxel on PSA levels and to analyze the adverse events caused by docetaxel.* ***Material & Methods:****The study design was retrospective cohort. Participants were prostate cancer patients at Saiful Anwar Hospital who received androgen deprivation therapy with increased PSA level 3 times the nadir or 2 bone lesions or soft tissue lesions > 2cm. PSA levels were assessed monthly. Participants were grouped into 6 and 10 series regimens. Adverse events of nausea, diarrhea, alopecia, SGOT SGPT abnormailties, creatinine abnormalities, anemia, and neutropenia were observed.Statistical analysis was performed usinga differential T-test.* ***Results:****A total of 32 participants were involved. The PSA levels between 6 and 10 series groups were as follows: 1st month (142.2 vs 28.24 ng/mL,p=0.000), 2nd month (101.78 vs 16.98 ng/mL,p=0.001), 3rd month (472.35 vs 13.95 ng/mL,p=0.439), 4th month (120.64 vs 4.0 ng/mL,p=0.180), 5th month (64.325 vs 24.6 ng/mL, p=0.015), 6th month (41.915 vs 20.7 ng/mL,p=0.497). Adverse events in the 6 and 10 series regimens were nausea (25% vs 81.25%), diarrhea (37.5% vs 50%), alopecia (6.25% vs 43.75%), SGOT SGPT abnormalities (25% vs 56.25%), creatinine abnormalities (6.25% vs 37.5%), anemia (18.75% vs 31.25%), leukocytosis (6.25% vs 0%), and neutropenia (25% vs 12.5%). Adverse events in 6 series regimen began to occur in 3rd series with 1 participant experiencing nausea, and the most were 3 participants experiencing diarrhea in 6th series.Adverse events in 10 series regimen began to occur in 4th series with 1 participant experiencing nausea, 1 participant experiencing SGOT SGPT abnormalities, 1 participant experiencing diarrhea, and the most were 4 participants experiencing nausea in the 9th series.* ***Conclusion:*** *The 10 series of docetaxel chemotherapy is not superior to 6 series. Adverse events are more prominent in the 10 series.*

Keywords: *Docetaxel, PSA, adverse events.*

ABSTRAK

Tujuan: *Penelitian ini bertujuan untuk membandingkan efikasi docetaxel terhadap kadar PSA dan menganalisis efek samping yang ditimbulkan docetaxel.* ***Bahan & Cara****:Desain penelitian ini adalah kohort retrospektif. Partisipan merupakan pasien kanker prostat RSUD Dr. Saiful Anwar yang menerima androgen deprivation therapy dengan peningkatan kadar PSA 3 kali dari nadir atau didapatkan 2 lesi tulang atau lesi jaringan lunak > 2cm. Kadar PSA dinilai setiap bulan. Partisipan dikelompokkan menjadi regimen 6 seri dan 10 seri. Adverse events mual, diare, alopesia, abnormalitas SGOT SGPT, abnormalitas kreatinin, anemia, leukositosis, dan neutropenia diamati. Analisis statistik dilakukan menggunakan uji-T diferensial.* ***Hasil:*** *Sebanyak 32 partisipan dilibatkan. Perbedaan kadar PSA kelompok 10 dan 6 seri meliputi: bulan 1 (142.2 vs 28.24 ng/mL, p=0.000), bulan 2 (101.78 vs 16.98 ng/mL, p=0.001), bulan 3 (472.35 vs 13.95 ng/mL, p=0.439), bulan 4 (120.64 vs 4.0 ng/mL, p=0.180), bulan 5 (64.325 vs 24.6 ng/mL, p=0.015), dan bulan 6 (41.915 vs 20.7 ng/mL, p=0.497). Adverse events regimen 6 dan 10 seri adalah mual (25% vs 81.25%), diare (37.5% vs 50%) (p=0.03), alopesia (6.25% vs 43.75%), abnormalitas SGOT SGPT (25% vs 56.25%), abnormalitas kreatinin (6.25% vs 37.5%), anemia (18.75% vs 31.25%),leukositosis (6.25% vs 0%), dan neutropenia (25% vs 12.5%). Adverse events pada regimen 6 seri mulai terjadi pada seri 3 dengan 1 partisipan mengalami mual, dan terbanyak adalah 3 partisipan mengalami diare pada seri 6. Adverse events pada regimen 10 seri mulai tejadi padaseri 4 dengan 1 partisipan mengalami mual, 1 partisipan mengalami abnormalitas SGOT SGPT, 1 partisipan mengalami diare, dan terbanyak adalah 4 partisipan mengalami mual pada seri 9.* ***Simpulan:*** *Kemoterapi docetaxel 10 seri tidak superior dibandingkan 6 seri. Adverse events lebih prominen pada 10 seri*

Kata kunci: *Docetaxel, PSA, adverse events.*

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INTRODUCTION

Prostate cancer is the most common malignancy found in male patients with the fifth highest mortality rate due to malignancy.[1] Prostate cancer is the most commonly diagnosed malignancy in more than half of the world's countries. Epidemiological data shows that in 2020, more than 1.4 million people are diagnosed with prostate cancer and of these, 375.000 patients die from prostate cancer.[2] Men over 65 years of age have a higher risk of developing prostate cancer, where the incidence can increase to 60% in the population. In Indonesia, research in Jakarta showed that prostate cancer occupies the top ten most common malignancies.[3] The trend of these incidents has increased since the 1990[s] and is believed to continue to increase over time. Prostate cancer mortality rates range from 1.2 to 26.8 cases per 100.000 population. Prostate cancer becomes dangerous because generally this cancer does not show clinical manifestations in its early stages. When it reaches an advanced stage, prostate cancer can manifest as obstruction to the flow of urine, bone pain, paralysis due to bone metastases, to kidney failure. In addition, there are no definite recommendations regarding how to prevent the growth of prostate cancer.

The diagnosis of prostate cancer includes several tests, including digital rectal examination (DRE), prostate specific antigen (PSA) examination, magnetic resonance imaging (MRI) to identify local spread, and trans perineal or transrectal ultrasonography (TRUS) guided biopsy (Descotes, 2019). PSA levels, a serine kinase enzyme belonging to the human kallikrein (hK) family, between 4 mg/dl to 10 mg/dl have a positive predictive value (PPV) of 20% to 30%. PSA levels that exceed 10 mg/dl have a higher PPV, which ranges from 42% to 71.4%. However, based on the Prostate Cancer Prevention Trial (PCPT) study, there is no PSA level associated with a 0% risk of prostate cancer, so the higher the PSA level, the higher the risk of prostate cancer.

Docetaxel is an anticancer agent which is a taxane or antimicrotubule agent. This agent is commonly used in cases of prostate cancer which has resistance to hormonal therapy or also called metastatic castrate-resistant prostate cancer (mCRPC) since its use was recognized by the Food and Drug Administration (FDA) in 2004.[4] Docetaxel works by binding to beta-tubulin which further increases proliferation and stabilizes the conformation. This event will inhibit the incorporation of microtubules into the mitotic spindle, which as a consequence, will inhibit the cell cycle in the G2/M phase.[4] Another mechanism for docetaxel is to inhibit the expression of Bcl2, which is an antiapoptotic gene whose expression increases in cancer cells.[5] Apart from being related to cancer progression and local therapy, several previous studies stated that the addition of docetaxel managed to reduce PSA levels and was associated with a higher overall survival rate.[5-6] However, the use of docetaxel cannot be separated from various kinds of adverse events, where anemia and neutropenia are the most common adverse events. In addition, docetaxel adverse events include alopecia, dysgeusia, peripheral neuropathy, skin and nail toxicity, and gastrointestinal complications.[7-8] However, these adverse events are transient and can be managed with supportive therapy.

OBJECTIVE

This study aims to compare the efficacy of docetaxel on PSA levels and to analyze the adverse events caused by docetaxel

MATERIAL& METHODS

The design of this study used a retrospective cohort design. Subjects were male patients with prostate cancer who received chemotherapy at the Saiful Anwar Regional General Hospital, Malang, obtained from the period 2017 to 2022. The inclusion criteria were male patients with prostate cancer who received castration therapy with androgen deprivation therapy (ADT) which has an increased PSA level of 3 times the upper limit of the normal range or two metastatic bone lesions or soft tissue lesions measuring >2 cm.

The data collected is the result of an analysis of information originating from the medical records of patients with mCRPC at the relevant hospital. Data recording in the form of patient identity consisting of name, medical record number, telephone number, year of birth, PSA level at diagnosis, testosterone level at diagnosis, specimen type, histology interpretation, pathology anatomy number, Gleason score, staging, type of castration, chemotherapy used undertaken, chemotherapy schedule, post-chemotherapy PSA levels, and adverse events experienced.

The numerical data of this study will be displayed in the form of the mean along with the

standard deviation (SD) presented in the form of a histogram. Meanwhile, categorical data will be displayed as a percentage in a pie chart. The normality test was carried out using the Shapiro-Wilk or Kolmogorov-Smirnov test, while the homogeneity test was carried out using the Levene test. Data comparison tests were performed using a paired T-test if the data were normally distributed or the non-parametric Wilcoxon signed rank test if the data were not normally distributed. Statistical analysis was performed using the IBM SPSS version 23.0 application.

RESULTS

A total of 32 participants with mCRPC were included in this study. Of the 32 participants, 16 participants (50%) received a 10 series docetaxel chemotherapy regimen, while the other 16 participants (50%) received a 6 series docetaxel chemotherapy regimen.

Table 1 shows the list of participants and their PSA levels in certain months after receiving chemotherapy regimens.

Table 2 shows a comparison of PSA levels each month between groups of participants who received 6 series of chemotherapy with 10 series of chemotherapy. The PSA on chemotherapy 2, 7, 8, 9, and 10 was incomplete, so a comparison between the 6 series and 10 series groups could not be tested.

Based on the comparison results in the table 2 for PSA at 1st chemotherapy between 6 series and 10 series, a p value of 0.000 ($p < 0.05$) was obtained, so it can be concluded that there was a significant difference in PSA at 1st chemotherapy between 6 series and 10 series, where the 1st chemotherapy PSA in the 10 series group had a higher median (median=142.2 units) than the 1st chemotherapy PSA in the 6 series group (median=28.24 units).

The comparison results in the table 2 for PSA on the 2nd chemotherapy between 6 series and 10 series, a p value of 0.017 ($p < 0.05$) was obtained, so that it can be concluded that there was a significant difference in PSA on the 3rd chemotherapy between 6 series and 10 series, where the 3rd chemotherapy PSA in the 10 series group had a higher median (median=148.01 units) than the 3rd chemotherapy PSA in the 6 series group (median =38.28 units).

The comparison results in the table 2 for PSA on the 3rd chemotherapy between 6 series and 10 series, a p value of 0.065 ($p > 0.05$) was obtained, so it can be concluded that there was no significant

Table 1. Characteristic of Study Participants.

Variables	Chemotherapy Regimen		P value
	6 series	10 series	
Body Mass Index (BMI)	21.30 ± 1.41	20.61 ± 0.95	0.917
Quality of Life (QoL)	59.16 ± 2.31	65.82 ± 4.11	0.836

Table 2. PSA Levels between groups 6 series and 10 series.

Series	6 series			10 series			P value
	Median	Min	Max	Median	Min	Max	
1st	32.45	1.44	106.7	174.3	36.66	1367	0.001
2nd	38.28	1.02	92.78	148.01	20.26	1557.98	0.017
3rd	13.38	0.83	103.8	81.64	19.74	1863.59	0.065
4th	22.15	1.17	78.99	57.58	0.49	2383	0.181
5th	22.33	1.01	149.28	83.99	0.56	819.21	0.033
6th	23.71	0.92	223	55.92	0.34	714.6	0.031
7th	-	-	-	49.19	0.81	621.69	-
8th	-	-	-	61.06	0.35	582.39	-
9th	-	-	-	40.49	0.44	566.19	-
10th	-	-	-	34.40	0.2	531.3	-
Post	20.7	0.74	1836	41.91	0.12	527.3	0.497
Post-pre	-27.99	-1357.79	1516	-48.11	1357.79	150.68	0.651

difference in PSA on the 3rd chemotherapy between 6 series and 10 series, where the 3rd chemotherapy PSA in the 10 series group had a higher median (median=81.64 units) than the 3rd chemotherapy PSA in the 6 series group (median=18.36 units).

The comparison results in the table 2 for PSA on the 4th chemotherapy between 6 series and 10 series, a p value of 0.181 (p> 0.05) was obtained, so that it can be concluded that there was no significant difference in PSA on the 4th chemotherapy between 6 series and 10 series, where the 4th chemotherapy PSA in the 10 series group had a higher median (median=57.78 units) than the 4th chemotherapy PSA in the 6 series group (median=22.15 units).

The comparison results in the table 2 for PSA on the 5th chemotherapy between 6 series and 10 series, a p-value of 0.033 (p <0.05) was obtained, so that it can be concluded that there was a significant difference in PSA on the 5th chemotherapy between 6 series and 10 series, where the 5th chemotherapy PSA in the 10 series group had a higher median (median=63.99 units) than the 5th chemotherapy PSA in the 6 series group (median=22.33 units).

The comparison results in the table 2 for PSA on the 6th chemotherapy between 6 series and 10 series, a p-value of 0.031 (p <0.05) was obtained, so it can be concluded that there was a significant difference in PSA on the 6th chemotherapy between 6 series and 10 series, where the 6th chemotherapy PSA in the 10 series group had a higher median (median=55.92 units) than the 6th chemotherapy PSA in the 6 series group (median=23.71 units).

The comparison results in the table 2 for PSA on the 7th, 8th, 9th, and 10th chemotherapy there is only data in the 10 series group, while in the 6th series there is no data, so a comparison test for PSA on the second chemotherapy cannot be carried out. -7, 8, 9, and 10 between 6 draws and 10 draws.

The comparison results in the table 2 for PSA post chemotherapy between 6 series and 10 series, a p-value of 0.497 (p> 0.05) was obtained, so that it can be concluded that there was no significant difference in PSA post chemotherapy between 6 series and 10 series, where PSA Post chemotherapy in the 10 series group had a slightly higher median (median=41,915 units) than post chemotherapy PSA in the 6 series group (median=20.7 units).

Based on the table 2, it is known that the post chemotherapy PSA in the 10 series group had a slightly higher median than the post chemotherapy PSA in the 6 series group. Because the differences in post-chemotherapy PSA between 6 series and 10 series were not too large, the results of the tests were not significant.

The comparison results in the table above for the PSA delta (PSA post deducted by the 1st chemotherapy PSA) between 6 series and 10 series, a p-value of 0.651 (p> 0.05) was obtained, so it can be concluded that there was no significant difference in PSA delta (PSA post minus PSA chemotherapy 1st) between 6 series and 10 series, where the PSA delta (PSA post minus PSA chemotherapy 1st) in the 10 series group had a slightly lower median (median = -48.12 units) than the PSA delta (Post PSA reduced by 1st chemotherapy PSA) in group 6 series (median = -28.0 units).

Table 3. Comparison of Adverse Events of Chemotherapy in the 6 Series and 10 Series Groups.

Adverse events	Chemotherapy Regimen		P value
	6 series (n total=16)	10 series (n total=16)	
Nausea	4 (25%)	13 (81.25%)	0.03
Alopecia	1 (6.25%)	7 (43.75%)	
SGOT SGPT Abnormality	4 (25%)	9 (56.25%)	
Creatinine Abnormality	1 (6.25%)	6 (37.5%)	
Anemia	3 (18.75%)	5 (31.25%)	
Neutropenia	4 (25%)	2 (12.5%)	
Leukocytosis	1 (6.25%)	0 (0%)	
Diarrhea	6 (37.5%)	8 (50%)	

Table 3 shows a comparison of the various types and numbers of adverse events observed in participants who received the docetaxel chemotherapy regimen in the 6 series and 10 series groups. Adverse events of nausea were found in 4 (25%) participants in the 6 series regimen group and 13 (81.25%) participants in the 10 series regimen group. Alopecia adverse events were found in 1 (6.25%) participant in the 6 series regimen group and 7 (43.75%) participants in the 10 series regimen group. Adverse events of abnormal SGOT SGPT levels were found in 4 (25%) participants in the 6 series regimen group and 9 (56.25%) participants in the 10 series regimen group.

Adverse events of abnormal creatinine levels were found in 1 (6.25%) participant in the 6 series regimen group and 6 (37.5%) participants in

the 10 series regimen group. Adverse events anemia were found in 3 (18.75%) participants in the 6 series regimen group and 5 (31.25%) participants in the 10 series regimen group. Adverse events neutropenia were found in 4 (25%) participants in the 6 series regimen group and 2 (12.5%) participants in the 10 series regimen group. Adverse events leukocytosis was found in 1 (6.25%) participant in the 6 series regimen group and 0 (0%) participants in the 10 series regimen group. Adverse events leukocytosis was found in 6 participants (37.5%) in the 6 series regimen group and 8 participants (50%) in the 10 series regimen group. There was a significant difference in the adverse events of chemotherapy 6 series and 10 series (p=0.03).

Table 4 describes the time of occurrence of adverse events in the 6 series chemotherapy regimen. A total of 1 participant experienced nausea after series 3 chemotherapy, 1 participant after series 4 chemotherapy, 1 participant after series 5, and 1 participant after series 6. A total of 1 participant experienced alopecia after series 6 chemotherapy. A total of 1 participant experienced SGOT and SGPT abnormalities after chemotherapy series 5, 3 participants after series 6. A total of 1 participant experienced creatinine abnormality after series 5 chemotherapy. A total of 1 participant experienced anemia after series 4 chemotherapy, 1 participant after series 5, and 1 patient after series 6. A total of 1 participant experienced neutropenia after chemotherapy series 4, 2 participants after series 5, and 1 participant after series 6. A total of 1 participant had leukocytosis after series 5 chemotherapy. A total of 2 participants experienced diarrhea after series 4 chemotherapy, 1 participant after series 5, and 3 participants after series 6.

Table 5 describes the time of occurrence of adverse events in 10 series chemotherapy regimens. A total of 1 participant experienced nausea after chemotherapy series 4, 1 participant after series 5, 1

Table 4. Time of Adverse Events Appearance on Docetaxel 6 Series Chemotherapy.

Adverse event	Total of patients (n)					
	Series					
	1	2	3	4	5	6
Nausea	0	0	1	1	1	1
Alopecia	0	0	0	0	0	1
SGOT SGPT Abnormality	0	0	0	1	1	2
Creatinine Abnormality	0	0	0	0	1	0
Anemia	0	0	0	1	1	1
Neutropenia	0	0	0	1	2	1
Leukocytosis	0	0	0	0	1	0
Diarrhea	0	0	0	2	1	3

Table 5. Time of Adverse Events Appearance on Docetaxel 10 Series Chemotherapy.

Adverse event	Total of patients (n)									
	Series									
	1	2	3	4	5	6	7	8	9	10
Nausea	0	0	0	1	1	1	2	1	4	3
Alopecia	0	0	0	0	0	2	1	1	2	1
SGOT SGPT Abnormality	0	0	0	1	0	1	2	2	1	2
Creatinine Abnormality	0	0	0	0	1	0	2	0	0	3
Anemia	0	0	0	0	0	0	2	0	1	2
Neutropenia	0	0	0	0	0	0	1	0	1	0
Leukocytosis	0	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	1	1	0	2	0	3	1

participant after series 6, 2 participants after series 7, 1 participant after series 8, 3 participants after series 9, and 4 participants after series 10. A total of 2 participants experienced alopecia after series 6 chemotherapy, 1 participant after series 7, 1 participant after series 8, 2 participants after series 9, and 1 participant after series 10. A total of 1 participant experienced SGOT and SGPT abnormalities after series 4 chemotherapy, 1 participant after series 6 , 2 participants after series 7, 2 participants after series 8, 1 participant after series 9, and 2 participants after series 10. A total of 1 participant experienced creatinine abnormalities after chemotherapy series 5, 2 participants after series 7, and 3 participants after series 10. A total of 2 participants experienced anemia after series 7 chemotherapy, 1 participant after series 9, and 2 patients after series 10. A total of 1 participant experienced neutropenia after series 7 chemotherapy and 1 participant after series 9. None of the participants in the 10 regimen group experienced leukocytosis. A total of 1 participant experienced diarrhea after chemotherapy series 4, 1 participant after series 5, 2 participants after series 7, 3 participants after series 9, and 1 participant after series 10.

DISCUSSION

Docetaxel was the first drug that was recognized for its efficacy in treating mCRPC.[9] Apart from prostate cancer, the efficacy of docetaxel has been proven to treat non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, and pancreatic cancer.[10-11] The CHAARTED clinical trial described significant clinical improvement in patients with hormone sensitive prostate cancer with docetaxel administration, marked by an increase in overall survival (OS) from subset analysis.[12] This study assessed the effect of chemotherapy with docetaxel on PSA levels as the main biomarker for prostate cancer cases. PSA levels were measured every month until the 6th month, then the levels at the end of the intervention were compared. In this study, there was a significant difference (p=0.001) in PSA levels at the 1st month between regimens 6 series and 10 series. Similar results were also observed for PSA levels at the 2nd month, with a value of p=0.017.

However, at the 3rd and 4th months there was no difference in PSA levels between the 6 series regimen and the 10 series regimen with p = 0.065 and p = 0.181. Comparison of PSA levels at the 5th month showed significant results with a value of p = 0.033. At the 6th month, there was a significant difference (p=0.031) in PSA levels between the 6 series regimen and the 10 series regimen. However, after analyzing post-chemotherapy PSA levels, there was no difference between the 6 series regimen and the 10 series regimen with p=0.497. In a study with HER-2 positive metastatic breast cancer, similar results were observed that the docetaxel regimen for 6 months did not result in significant differences in progression free survival (PFS) (p=0.0640) or OS (p=0.3073).[13]

This is supported by research using paclitaxel which states that the addition of 6 to 8 cycles of chemotherapy does not improve PFS and OS in breast cancer patients. In addition, some participants had elevated PSA levels in their first or second chemotherapy series. This is a natural phenomenon experienced by patients receiving chemotherapy with docetaxel, which is then followed by a response of PSA levels to chemotherapy so that the event should not be used as an indicator of stopping the chemotherapy regimen.[14]

To date, there is no consensus recommending the exact number of cycles of docetaxel chemotherapy that is optimal.[15] The minimum number of cycles of docetaxel chemotherapy is 4 times and generally docetaxel chemotherapy is given in 6 to 10 cycles, with 1 dose given every 3 weeks.16 Giving chemotherapy 4 times is recommended to provide benefits before the patient can finally stop treatment. Nakai et al. (2020) reported that more than 8 cycles of docetaxel chemotherapy were associated with improved OS, but taking into account the adverse events of chemotherapy, 8 cycles of chemotherapy was considered the optimal number of cycles.[16]

Kato et al. (2021) reported similar findings that the docetaxel regimen more than 7 times increased the survival of patients with mCRPC.[17] However, adding docetaxel chemotherapy cycles to more than 10 cycles did not improve OS.[18] Docetaxel chemotherapy regimens exceeding 10 cycles were more commonly used prior to 2012, where there was no alternative chemotherapeutic agent available in case docetaxel failed to provide the expected efficacy. In contrast, administration of many cycles of docetaxel chemotherapy actually worsens a person's quality of life because it is closely related to docetaxel toxicity.

Docetaxel is a drug that is metabolized in the liver, so its excessive use can cause liver damage to

fulminant hepatocellular necrosis, characterized by increased levels of non-functional liver enzymes, namely AST and ALT. In addition, the addition of docetaxel chemotherapy cycles is also associated with increased incidence of peripheral neuropathy and bone marrow damage. Docetaxel levels of 675 mg/m^2 are associated with peripheral neuropathy adverse events. Therefore, it is necessary to consider determining the maximum number of chemotherapy cycles with docetaxel, so that second-line mCRPC treatment can be considered which is expected to increase patient survival.[19]

Even so, the results of research related to this matter are still inconsistent, in which other literature states that the addition of chemotherapy cycles with docetaxel or paclitaxel provides an increase in PFS and OS. de Morrée et al. (2016) reported that administration of docetaxel for more than 10 cycles was associated with a higher OS with a median of 33.0 months. Meanwhile, study participants who only got 8 to 10 cycles and 5 to 7 cycles had a median OS of 26.9 months and 22.8 months.[20] Even so, the occurrence of adverse effects of docetaxel administration is an indication for discontinuation of chemotherapy.

In this study, an analysis of adverse events from docetaxel chemotherapy was performed between participants belonging to the 6 series and 10 series regimen groups. The adverse events observed in this study included nausea, alopecia, abnormalities in SGOT SGPT levels, abnormalities in creatinine levels, anemia, neutropenia, leukocytosis, and diarrhea. Although docetaxel is well tolerated by most patients, adverse effects of docetaxel administration include acute and long-term effects, such as infusion reactions, febrile neutropenia, fatigue, fluid retention, pneumonitis, skin and nail toxicity, epiphora and lacrimal duct stenosis, gastrointestinal complications, and neuropathy.[7] However, the adverse events of docetaxel are reversible, so they are not observed between treatments and when the patient has stopped chemotherapy.

In the present study, more therapeutic adverse events were observed in the participants in the 10 series, in which the most frequent adverse events were gastrointestinal adverse events. This is in accordance with previous literature that a longer duration of chemotherapy is associated with more prominent adverse events.[21] Moreover, increasing patient efficacy of longer chemotherapy regimens is also still being questioned.

CONCLUSION

Prostate cancer is still a challenge in the world of health because prostate cancer is the most common malignancy found in male patients. The difficulty of detecting prostate cancer due to clinical manifestations that often do not appear at an early stage contributes to delays in diagnosis and treatment, resulting in increased patient mortality. Docetaxel is the first taxane class chemotherapeutic agent approved for use in mCRPC cases. In conclusion, in this study, there was no significant difference in the levels of a prostate cancer biomarker, namely PSA, in docetaxel chemotherapy with 6 cycles or 10 cycles.

So there is no improvement in chemotherapy performance by adding chemotherapy cycles of more than 6 series. Moreover, docetaxel adverse events are also more common in regimen 10 therapy, where the most adverse events involve the gastrointestinal system in the form of nausea and diarrhea, so that the addition of a series of therapy is associated with an increase in adverse events. However, further research is needed regarding the duration of chemotherapy in mCRPC cases.

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