Journal of Engineering Science and Technology
Vol. 16, No. 1 (2021) 209 - 223

CHEMOTHERAPY FOR CERVICAL CANCER PATIENTS: IS IT A "NIGHTMARE"?

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Abstract

Chemotherapy in cervical cancer is the most widespread type of therapy because it is used as a support for other types of therapy as well. Given the widespread use of chemotherapy in cervical cancer patients, evaluation of the success of chemotherapy in cervical cancer management is very important. In this study, a comprehensive evaluation of the results of chemotherapy on cervical cancer was carried out from the aspect of the clinical picture and humanistic outcome based on cancer stage. The test subjects were cervical cancer patients at a government hospital in the city of Bandung, Indonesia who went through three cycles of chemotherapy and met the inclusion criteria. Evaluation of the clinical features includes observation of relief of symptoms of vaginal discharge, bleeding, vaginal discharge, vaginal irritation, vulvar mucosal irritation and pain and general condition. Humanistic outcome was evaluated using the EORTC QLQ-C30 questionnaire. The data obtained on the conditions before and after chemotherapy were statistically evaluated using the t-test (p<0.05). Administration of chemotherapy has been shown to have an impact on improving the clinical picture and humanistic outcome for all stages. This proves that patients with a lower stage tend to acquire better improvements. The side effects of chemotherapy that tend to exacerbate some aspects of humanistic outcomes are overcome by pharmacological and non-pharmacological therapies and by providing health care services that pay attention to the psychological aspects of the patient.

Keywords: Cervical cancer, Chemotherapy, Clinical picture, Humanistic outcome.

1. Introduction

Cervical cancer is a disease with a high rate of incidence and mortality in the world [1]. Treatment of cervical cancer can be in such forms as surgery, radiotherapy, or chemotherapy. Chemotherapy in cervical cancer is the most widely used compared to other treatment options as it can be applied for all levels of cervical cancer severity and is very much needed as a supporting management, both in surgery and radiotherapy [2, 3]. Given the wide use of chemotherapy in cervical cancer patients, evaluating the success of chemotherapy in cervical cancer management is very important. Evaluation of the success of chemotherapy in cancer is carried out not only by monitoring the clinical features but also must be accompanied by monitoring of humanistic outcomes [4]. This is because cancer survivors not only suffer from clinical symptoms but also experience a decrease in quality of life. In patients with advanced cancer, chemotherapy often does not show improvement in the clinical features but shows improvement in humanistic outcomes [2]. The decline in the patients' quality of life is not only due to the illness, but also the side effects of chemotherapy. The success of coping with the adverse side effects of chemotherapy was also evaluated based on monitoring humanistic outcomes. In cancer therapy, success is also determined by the severity of the disease suffered by the patient or the stage [5-7] so that evaluation must pay attention to these factors.

Research related to the evaluation of the success of cancer therapy is still largely carried out separately, whether it focuses only on clinical features [7-13] or humanistic outcomes alone [5, 6, 14-18]. Research evaluating clinical and humanistic outcomes simultaneously is quite limited. Likewise, research on the adverse side effects of chemotherapy [19-21] and the success of chemotherapy has also been largely carried out separately. Integrated studies of the adverse side effects of chemotherapy associated with the evaluation of the efficacy of cervical cancer therapy are still limited.

Based on the above conditions, the aim of this study was to assess the success of chemotherapy in cervical cancer patients by evaluating the clinical features and humanistic outcomes simultaneously based on stage. In addition, this study also evaluated the impact of adverse side effects from chemotherapy on the patients' quality of life and was integrated with the evaluation of the success of chemotherapy. Thus, by conducting this study, the results of the overall evaluation of the success of chemotherapy in cervical cancer both from the aspect of the clinical features and humanistic outcomes based on stages can be achieved. The novelty of this study is the overall result of chemotherapy evaluation in cervical cancer, both from the aspect of clinical features and humanistic outcome based on stage.

2. Methods

This cross-sectional study was conducted in a public hospital located in Bandung, West Java Province, Indonesia. The sample of the study comprised patients diagnosed with cervical cancers and hospitalized in the first, second, and third-class hospital wards from June 2015 to October 2016. Inclusion and exclusion criteria were applied in the sample selection. Patients diagnosed with cervical cancer without comorbid conditions, patients with stage 1 to 4 cancer undergoing chemotherapy or other combined therapies for curative, control, palliative purposes, patients having medical records and undergoing first-time chemotherapy

and absolute three cycles of chemotherapy were included in the study. Patients transferred from other hospitals, patients who died before the administration of three-cycle chemotherapy, and patients leaving the hospital against medical advice were not included in the study.

110 cervical cancer patients had been hospitalized in the hospital from June 2015 to October 2016, where 97 of them underwent chemotherapy and the rest of 13 had no chemotherapy. Of 97 patients, 23 patients were excluded in the study (four patients transferred from other hospitals, eight patients having incomplete three cycles of chemotherapy administration, and eleven patients declining their participation in the study). Among the 8 patients who had not completed the three-cycle chemotherapy administration, two patients were self-quitting from the therapy, three patients were dropping out from the chemotherapy, and three patients died before the chemotherapy completed. Finally, 74 patients involved as the participants in this study, ranging from 21 to 62 years old (mean = 47.6, SD = 8.6). Most of the participants (71.6%) were at the age group of 45-64 years old and obtained degree of education below senior high school level (60.8%). Most of them were unable to fill out the questionnaire by themselves, and thus requiring a guidance or an interview during the completion of the questionnaire. The average parity of the participants was 2.6 ± 1.4, and most of the patients (44.6%) had stage 2 cancer.

This study had an ethic clearance number Ref: KE/FK/426/EC dated on 29 April 2015 from the Ethics Committee of Faculty of Medicine, Universitas Gadjah Mada. The patients completed and signed a consent form witnessed by their family members. Clinical data of the patients were collected based on medical professionals' observations written on the medical records. The observed clinical displays included vaginal discharge, bleeding, vaginal secretion, vaginal irritation, vaginal vulva mucosa irritation, and pain.

Data were also collected from a questionnaire administered specifically for cancer patients, EORTC QLQ C-30 version 3. The instrument was developed by EORTC Quality of Life Group and used to measure the quality of life of cancer patients. It consists of 30 items categorized into three main domains: functional, symptoms, and status of global health/quality of life. In this study the Indonesian version of the instrument was administered to the participants. Data collected from pre- and post-chemotherapy during the three cycles of chemotherapy were evaluated statistically using t-test with $p < 0.05$.

3. Results

3.1. Clinical feature

Based on the results of the evaluation of clinical features based on stage, data on the percentage of patients who no longer experience clinical symptoms after chemotherapy for three cycles are listed in Table 1. For all observed symptoms, there is a tendency for the percentage of patients to experience symptom relief to decrease along with the higher the stage. Symptoms of vaginal discharge and bleeding appeared in all patients. In the symptoms of vaginal discharge and bleeding, it was observed that the higher the stage, the lower the percentage of patients who experienced symptom relief. Symptoms of vaginal secretions appeared only in stage III patients and all patients experienced symptom relief after

chemotherapy. Symptoms of vaginal irritation did not appear in stage I patients. In stages II, III and IV patients, all patients experienced relief of vaginal irritation symptoms. Symptoms of vulvar mucosal irritation only appeared in stage IV patients and disappeared in all patients after chemotherapy.

Table 1. Percentage of clinical descriptions as symptom relief and post- chemotherapy general condition based on stage after receiving chemotherapy for three cycles.

Clinical description (%)	Stage			
	I (*n*=12)	II (*n* =33)	III (*n* =25)	IV (*n* =4)
Symptom relief				
leukorrhea	100	96	93.3	25
bleeding	100	68	53.3	0
vaginal secretion	(-)	(-)	100	(-)
vaginal irritation	(-)	100	100	100
vulvar mucosa irriations	(-)	(-)	(-)	100
Post chemotherapy general condition				
improvement	100	96.0	93.9	75
no improvement	0	4.0	6.1	25

(-) = the patient had no symptoms at pre- chemotherapy

In Table 1, it can be seen that after chemotherapy, there is a tendency that with increasing stages, the percentage of patients who experience improvement in their general condition decreases. The highest percentage who experienced improvement in the general condition occurred in stage I patients. All stage I patients experienced an improvement in their general condition after chemotherapy. The lowest percentage of patients showing improvement in the general condition occurred at stage IV.

The results of the pain symptom observation are stated by the pain score. Pain score is set on a scale of 0-10. Score 0 indicates that the patient does not feel pain. The higher the pain intensity is indicated by the increasing pain score. Pain scores of patients before and after chemotherapy are listed in Table 2. Based on Table 2, after chemotherapy for three cycles at all stages, there was a tendency to decrease pain scores compared to before chemotherapy. In stage I to III patients, there was a significant decrease in pain score after chemotherapy, while in stage IV patients, the decrease in pain score was not significant.

Table 2. Pain score of cervical cancer patients pre- and post- chemotherapy based on stage.

Stage	*N*	Pain score		*p*
		Pre chemotherapy	Post chemotherapy	
I	12	2.9±1.9	0.9±0.9	0.000*
II	33	3.3±1.4	1.0±1.5	0.000*
III	25	4.2±1.7	1.4±1.4	0.000*
IV	4	4.8±1.5	3.5±1.9	0.391

* = different significantly (p<0.05)
± = standard deviation

3.2. Humanistic outcome

The results of the humanistic outcome evaluation are listed in Table 3. After chemotherapy, stage I to IV patients have an increasing trend in all aspects of the functional domain. In stage I patients, the improvement in all aspects of the functional domain was not statistically significant. The significant increase in stage II patients occurred in two aspects, namely physical and emotional functions. In stage III patients, there was a significant increase in three aspects, namely role, emotion and cognitive. In stage IV patients, there was a significant increase in one aspect, namely the role function.

Table 3. The average value of the quality of life domain of cervical cancer patients pre- and post –chemotherapy.

	Cervical Cancer Patients Receiving Chemotherapy							
Domain	**Stage 1 (n=12)**		**Stage 2 (n=33)**		**Stage 3 (n=25)**		**Stage 4**	
	Pra	**Post**	**Pra**	**Post**	**Pra**	**Post**	**Pra**	**Post**
Functional								
Physical	83.6 ± 14.8	88.9 ± 9.6	68.3 ± 22.6	80.0 ± 17.8*	54.4 ± 31.8	66.4 ± 27.9	38.3 ± 24.0	38.3 ± 19.2
Role	84.9 ± 21.7	93.9 ± 7.8	75.8 ± 31.0	85.6 ± 19.6	52.7 ± 30.0	71.4 ± 27.5*	33.3 ± 27.2	45.0 ± 23.3*
Emotional	77.2 ± 14.7	98.6 ± 4.8	72.7 ± 24.0	98.9 ± 3.6*	65.3 ± 25.5	97.2 ± 7.6*	83.3 ± 19.3	95.8 ± 8.3
Cognitive	94.7 ± 10.6	100.0 ± 0.00	89.9 ± 19.1	96.2 ± 10.3	78.0 ± 18.4	94.4 ± 9.4*	83.3 ± 19.3	87.5 ± 16.0
Social	79.5 ± 15.8	81.9 ± 16.6	71.2 ± 26.2	75.3 ± 22.3	65.3 ± 23.8	71.5 ± 2.8	79.2 ± 25.0	83.3 ± 23.6
Symptom								
Fatigue	17.9 ± 18.3	7.41 ± 18.3*	34.7 ± 26.7	14.3 ± 19.9*	52.8 ± 26.1	26.9 ± 20.2*	66.7 ± 24.0	33.3 ± 24.0
Nausea and vomiting	11.2 ± 16.4	20.83 ± 16.4	23.7 ± 25.3	17.2 ± 18.0	39.3 ± 27.8	25.0 ± 20.9	50.0 ± 30.4	29.2 ± 8.3
Pain	22.9 ± 19.5	11.11 ± 19.5	33.0 ± 27.6	15.6 ± 19.7*	41.3 ± 27.4	25.0 ± 24.1	34.7 ± 11.5	50.0 ± 13.6
Dyspnoea	6.4 ± 10.8	1.39 ± 10.8	12.6 ± 21.5	5.4 ± 15.2	26.0 ± 26.5	8.3 ± 20.3*	29.2 ± 21.0	16.7 ± 19.3
Insomnia	22.9 ± 21.5	2.78 ± 21.5*	26.3 ± 29.2	3.2 ± 10.0*	32.0 ± 25.6	9.7 ± 18.3*	50.0 ± 30.4	25.0 ± 31.9
Appetite loss	22.1 ± 17.8	33.33 ± 17.8	29.8 ± 31.2	34.4 ± 26.5	33.3 ± 23.5	54.2 ± 19.2*	29.2 ± 21.0	58.3 ± 16.7
Constipation	12.1 ± 17.4	0.00 ± 17.4	24.6 ± 32.4	6.7 ± 18.4*	23.1 ± 26.9	2.8 ± 9.4*	62.5 ± 28.5	0.0 ± 0.0
Diarrhoea	11.3 ± 16.3	0.00 ± 16.3	11.6 ± 19.6	0.0 ± 0.0*	22.0 ± 29.4	6.9 ± 19.6*	36.1 ± 42.0	0.0 ± 0.0
Financial difficulties	15.2 ± 21.2	8.33 ± 21.2	33.7 ± 32.1	31.1 ± 33.8	32.9 ± 26.5	31.9 ± 36.1	16.7 ± 21.3	8.3 ± 16.7
Global health status/ Quality of Life	33.3 ± 35.5	79.17 ± 35.5*	75.0 ± 14.2	79.2 ± 7.5*	29.3 ± 14.1	59.7 ± 19.3*	29.2 ± 16.0	39.6 ± 26.7

*=significantly different (p.0.05)

In the symptom domain, in stage I patients, there was a tendency to decrease except for nausea and vomiting and decreased appetite. Symptoms of nausea and vomiting as well as decreased appetite tend to increase although it is not significant. There are two symptoms that significantly decrease in stage I patients, namely fatigue and difficulty sleeping. In stage II patients, there is a tendency to decrease in the symptom domain, except for loss of appetite. There was an increase in

symptoms of loss of appetite, although it is not statistically significant. In the symptoms of nausea and vomiting, there were differences between stage II patients and stage I patients. In stage II patients, the symptoms of nausea and vomiting tended to decrease, although not statistically significant. In the symptom domain, there was a significant decrease in stage II patients compared to stage I, namely five types of symptoms. Symptoms that significantly decreased in stage II patients were fatigue, pain, difficulty sleeping, constipation and diarrhea. In stage III patients, the symptom domain tends to decrease except for decreased appetite. The decrease in appetite symptoms in stage III patients showed a significant improvement. Symptoms that have decreased in stage III patients consist of five aspects, namely fatigue, shortness of breath, difficulty sleeping, constipation and diarrhea. In stage IV patients, as with the other three stages, there was also a tendency for symptom reduction, although it was not significant, except for pain. Although the pain symptom showed an increasing trend, it was not statistically significant. For the domain of global health status (quality of life), all patients in stages I to III showed a significant improvement after chemotherapy. Stage IV patients also showed an increasing trend in global health status although it was not statistically significant.

4. Discussion

This study aims to evaluate the clinical picture and humanistic outcome of cervical cancer patients after receiving chemotherapy. Evaluation of the success of cancer therapy does not only involve clinical features or humanistic outcomes but also must be done simultaneously [4]. This is because cancer survivors not only suffer from clinical symptoms but also experience a decrease in quality of life.

For patients with advanced cancer. the success of therapy is often difficult if only evaluated based on clinical outcomes. Patients with advanced cancer often do not show improvement if only evaluated based on clinical outcomes. but show improvement in humanistic aspects [2]. Comorbid factors (comorbidities) can affect the humanistic outcome of therapy in cancer patients [22-24]. However, this study did not account for comorbid problems in patients. This is because in this study most of the patients did not have comorbid (73%).

The comorbid in the patient is also thought to have no direct impact on the clinical features but may have an impact on humanistic outcomes. Patients at the same stage often use chemotherapy with different drugs. Different drugs in patients with the same stage can affect clinical outcomes [8. 10. 25] and humanistic patients [14-17. 26. 27]. Of the 74 patients evaluated. 67 patients (90.5%) received cisplatin-based chemotherapy. Thus. in this study. most patients used chemotherapy on the same basis. The remaining 9.5% of the patients received carboplatin-based chemotherapy.

According to the Clinical Practice Guidelines in Oncology Cervical Cancer. basically, cisplatin and carboplatin are the main choices in cervical cancer therapy [28]. Cisplatin is cheaper than carboplatin [29]. The difference between the two chemotherapy drugs is the side effects to the kidneys. Cisplatin causes side effects in the form of kidney problems. However, these side effects can be overcome by administering mannitol [30. 31]. Based on the above analysis. it is estimated that the difference in the baseline chemotherapy regimen between cisplatin and carboplatin will not affect the evaluation of humanistic outcomes.

4.1. Clinical feature

Based on the results of the evaluation of clinical features. data on the percentage of patients who no longer experience clinical symptoms after chemotherapy for three cycles are shown in Table 1. For all observed symptoms. there is a tendency for the percentage of patients to experience symptom relief to decrease along with the higher the stage. Two of the symptoms include vaginal discharge and bleeding. Symptoms of vaginal discharge appeared in all patients. In the symptoms of vaginal discharge based on Table 1 it is observed that the higher the stage. the lower the percentage of patients who experience symptom relief. Leucorrhoea is a symptom that must also be observed to see the success of cervical cancer therapy. Based on research at a hospital in Lampung. Indonesia. it was concluded that there was a statistically significant relationship between continuous and untreated vaginal discharge and the incidence of cervical cancer. Decreasing symptoms of vaginal discharge after chemotherapy shows that there has been good progress in cervical cancer patients [11]. As is the case with vaginal discharge. bleeding symptoms occur in patients of all stages. After getting chemotherapy. there was an improvement in the form of the percentage of symptom relief which was getting higher with the lower the stage. This was also observed in the results of research in the United States in the form of improvement in bleeding symptoms in patients after receiving chemotherapy [13].

Based on the results of the observation. it was found that symptoms of vaginal secretions only appeared in stage III patients and all patients experienced symptom relief after chemotherapy. These results are in line with research in Serbia. In cervical cancer patients who were observed in this study. it was observed that there was a decrease in symptoms of vaginal secretions after chemotherapy [32]. Two other symptoms observed were vaginal irritation and vulvar mucosal irritation. Symptoms of vaginal irritation did not appear in stage I patients. In stage II. III and IV patients. all patients experienced relief of vaginal irritation symptoms. Symptoms of vulvar mucosal irritation only appeared in stage IV patients and disappeared in all patients after chemotherapy. Based on the results of research in China it was observed that after chemotherapy the patients experienced improvement. including the disappearance of symptoms of vaginal and vulvar mucosal irritation [10].

One of the symptoms felt by cervical cancer sufferers is pain [12]. Based on Table 2. after chemotherapy for three cycles at all stages. there was a tendency for a decrease in pain symptoms to be represented in a decrease in "pain score" compared to before chemotherapy. In stage I to III patients. there was a significant reduction in "pain score" after chemotherapy. while in stage IV patients. a decrease in "pain score" was not significant. The tendency to decrease pain symptoms in all patients was thought to be due to analgesic administration. This has been proven based on the results of research in Nigeria. Based on the results of this study in Nigeria. giving palliative therapy with analgesics in cervical cancer patients has been shown to reduce pain symptoms [9].

In this study. the evaluation of tumor size parameters was not possible. which is one of the important clinical outcomes. This is because there are too few data. namely from 74 patients. only three patients had tumor measurement data. The reduction in tumor size is one of the parameters in assessing the effectiveness of a therapy in the treatment of cervical cancer. The results of a study in Austria showed

that after chemotherapy with cisplatin until the end of therapy. tumor size decreased in 66% of patients [8]. The results of research at the Dr. Soetomo Hospital. Surabaya. Indonesia. shows that there is a decrease in the average size of the tumor after giving chemotherapy in the form of a combination of carboplatin-paclitaxel [33]. Although the tumor size was not evaluated. the overall clinical picture showed improvement after chemotherapy.

After chemotherapy. the percentage of patients who experienced improvement in their general condition increased with the lower the stage (Table 1). The highest percentage who experienced improvement in general condition occurred in stage I patients. All stage I patients experienced improvement in their general condition after chemotherapy. The lowest percentage of patients showing improvement in the general condition occurred at stage IV. This is in line with research in several countries. including Slovenia [25]. Malaysia [7] and China [10]. Observations in Austria even showed that a total of 97% of patients experienced improvement in their general condition after chemotherapy [8]. The above results indicate that the sooner cervical cancer is detected and the sooner it is treated with chemotherapy. the more likely it is to experience improvement in the clinical feature.

4.2. Humanistic outcome

4.2.1. Functional domain

Quality of life observations with the EORTC QLQ-C30 questionnaire were evaluated in the study based on different stages. As can be seen in Table 3. after chemotherapy. stage I to IV patients have an increasing trend in all aspects of the functional domain. This can be seen from the trend of increasing scores after chemotherapy compared to before chemotherapy. In stage I patients. the improvement in all aspects of the functional domain was not statistically significant. In comparison. the results of a study in Malaysia showed that the one that most affected the quality of life of cervical cancer patients due to chemotherapy was stage III and IV [7]. This is presumably because in the early stages. patients generally have not felt any significant complaints.

The functional aspect that has significantly improved is physical function in stage II patients. Another study conducted in China. showed that giving chemotherapy significantly increased the value of physical function [10]. Role function has increased in stage III and IV patients. The increase in role function is related to the tendency to improve physical function and the tendency to decrease most of the symptoms after chemotherapy. Both things make patients feel more comfortable. So, they can return to play a good role in family life and in the environment where they live [2]. Based on the results of a study in Poland. cervical cancer patients did not experience a significant reduction in function. There is a possibility that the decline in this role tends to be on a psychological aspect. Another possibility is because the patient is undergoing treatment in the hospital and must rest completely after undergoing chemotherapy. So, it is not possible to play a role in the family or the environment in which he lives [6]. Emotional function experienced a significant increase in stage II and III patients. After chemotherapy. the patient is psychologically accepted that he has cancer and realizes that chemotherapy is needed. This is what causes the emotional condition to be better which is indicated by a significant increase in the value of the emotional domain. In a study of cervical cancer patients in India [16] and Austria [17] it was

observed that after chemotherapy there was a tendency to increase emotional function. Apart from psychological factors from the patient. external influences such as counselling. education and information were also very important in fixing the patient's emotions. What also has a major influence in improving patient emotions is family support as has been studied in cervical cancer patients at a government hospital in Surakarta. Indonesia [34].

Suffering from cancer. including cervical cancer. can have several effects that can worsen a person's functional status. one of which is anxiety. Anxiety affects cognitive function in patients [35]. Giving chemotherapy actually has the potential to cause cognitive decline [26]. This happens because chemotherapy causes myelosuppression. Myelosuppression causes a decrease in the production of red blood cells which results in decreased cognitive abilities. After receiving chemotherapy. the patients showed a tendency to improve cognitive function and this occurred significantly in stage III patients. The tendency to improve cognitive function occurs in addition to the decline in cancer pathological conditions due to chemotherapy. On the other hand, the side effects of cancer in the form of myelosuppression are thought to be overcome by giving vitamin B6. Vitamin B6 plays a role in increasing the process of red blood cell formation [36. 37]. The results of research in India also show that there tends to be an improvement in cognitive function although it is not significant [16]. The effect of chemotherapy on social function is that the value of social function tends to decrease because patients are undergoing treatment and must undergo complete rest after chemotherapy. so that their social activities tend to be disrupted. However, since the patients undergo chemotherapy not continuously but only at certain times according to the therapy cycle. the patient can still carry out his social activities between the therapy cycles [2]. Based on the results of this study. social function shows an increasing trend after chemotherapy although it is not significant. These results are in line with those of studies in India [16] and in China [10].

4.2.2. Symptom domain

In general, there was a tendency for symptoms to decrease in patients at all stages after receiving chemotherapy. as listed in Table 3. However, there were symptoms that tended to increase. namely nausea and vomiting. decreased appetite and pain. Based on the results of this study. at all stages showed a tendency that fatigue symptoms decreased after chemotherapy. A significant reduction was shown by stage I to III patients. In stage IV patients the reduction in fatigue was not significant because the patient was in the most severe condition. In addition to being a symptom experienced by cervical cancer sufferers. fatigue is also a common symptom experienced by chemotherapy because of the side effects of myelosuppression that cause anaemia. Anaemia condition causes symptoms of fatigue [36]. Reduced fatigue symptoms are thought to be due to treatment of anaemia with iron and vitamin B complex supplements or blood transfusions. In addition, most of the sufferers also experienced a decrease in symptoms. So, the symptoms of difficulty sleeping decreased. The reduced symptoms of insomnia lead to improved sleep quality. Improved sleep quality leads to decreased fatigue symptoms. The decrease in these symptoms is thought to be due to the administration of drugs to reduce these symptoms. as observed in a study in India [16].

Symptoms of nausea and vomiting tend to increase yet not significant in stage I patients. Chemotherapy can cause side effects of nausea and vomiting in patients. Nausea and vomiting during chemotherapy are caused by stimulation of receptors in the gastrointestinal tract and receptors in the chemoreceptors trigger zone (CTZ) that send messages to the nucleus tract fracture solitaries of the brain. It can stimulate salivation. contraction of the diaphragm. respiratory muscles and abdominal muscles. Chemotherapy drugs can induce nausea and vomiting both directly on the mucosa and through the blood and stimulate enteroendocrine cells. The stimulation of enteroendocrine cells leads to the release of a number of endogenous mediators. These endogenous mediators then bind to the appropriate receptors on adjacent vagal fibers and cause stimulation of the afferent nerves terminating in the brainstem. particularly at the nucleus of the tractus solitaries. Furthermore. there is a process of activating the nausea center. Serotonin (5-HT) is a mediator responsible for the emergence of nausea and vomiting responses [36. 38]. In stage II. III and IV patients the symptoms of nausea and vomiting tended to decrease although it was not statistically significant. There was no significant increase in symptoms of nausea and vomiting in stage I patients and the tendency to decrease symptoms of nausea and vomiting in stage II. III and IV patients were thought to be due to the use of the antiemetic ondansetron. Ondansetron acts as a selective antagonist and is competitive at the 5HT3 receptor. by inhibiting the activation of vagal afferent nerves so as to suppress the vomiting reflex [20].

Based on this study. it was found that there was a tendency to reduce pain after the patient received chemotherapy in stage I to III patients. Significant reduction in pain occurred in stage II patients. The tendency of decreasing pain symptoms in stage I to III patients and not significantly increasing pain in stage IV. is thought to be caused by giving analgesics. Likewise, the results of research on cervical cancer patients in Nigeria. Based on the results of this study in Nigeria. providing palliative therapy with analgesics in cervical cancer patients is proven to reduce pain symptoms so that the patient's quality of life improves [9]. Chemotherapy causes side effects of shortness of breath. Cisplatin has a broncho constrictive effect which can occur several minutes after administration. This bronchoconstriction effect is an anaphylactic reaction which also causes facial edema. tachycardia and hypotension. Symptoms of shortness of breath tend to decrease at all stages. although it is not significant. This is thought to be due to the treatment of these effects by administering intravenous injection of epinephrine and administration of corticosteroids or antihistamines [39]. Likewise, in research in India. it was found that in patients who received chemotherapy. there was no significant increase in symptoms of shortness of breath [16]. The pain due to cancer and the side effects of chemotherapy can cause symptoms of insomnia.

Based on the results of this study. after chemotherapy there was a significant reduction in insomnia symptoms in stage I to III patients. In stage IV patients. there was a tendency to decrease symptoms of insomnia. although it was not significant. Research in India Singh [16] and Austria [14] also showed that after chemotherapy there was a decrease in insomnia symptoms. Different results were shown in studies in the United States. Based on this study. it was found that there was an increase in insomnia complaints after patients received chemotherapy [27]. This difference is thought to be due to differences in fatigue symptoms. In this study in the United States. patients experienced a significant increase in symptoms of fatigue and depression after the first and second cycles of

chemotherapy [27]. In this study. patients experienced a reduction in fatigue symptoms after chemotherapy because anemia was treated with iron and vitamin B complex supplements or blood transfusions.

Chemotherapy can affect appetite. Chemotherapy can inhibit the patient's appetite through the role of chemoreceptors in the brain. causing anorexia. Symptoms that arise in the digestive tract due to chemotherapy such as mouth sores. sprue. and inflammation of the salivary glands can also reduce appetite [24]. Patients at all stages tended to show an increase in symptoms of loss of appetite. although this was significant only at stage III. Although the observation of the symptoms of nausea and vomiting did not increase significantly due to the use of ondansetron. because the cisplatin used by 90.5% of patients was a chemotherapy drug with high emetogenic levels [40]. its effect on decreased appetite still tend to appear even though they do not show a significant increase. These results are in line with research in China. namely that after receiving chemotherapy. symptoms of loss of appetite tend not to show any changes [10].

Chemotherapy can have neurological effects that lead to constipation [41]. The results showed that after chemotherapy. patients showed a significant decrease in constipation symptoms. even in stages II and III. a significant reduction in constipation symptoms occurred. It is suspected that patients are given laxatives such as bisacodyl [21]. With these two efforts. after chemotherapy there was no increase in constipation symptoms in patients. In fact, it tended to decrease. The results of the above studies are in line with studies in Ethiopia. Based on this study. there was no constipation in patients who received chemotherapy [42]. Apart from neurological effects on the gastrointestinal tract. chemotherapy also influences the intestinal mucosa. namely mucosal ulcers. This can cause diarrhea. The symptoms of diarrhea can be overcome by administering antidiarrheal such as loperamide [19]. Based on the results of the evaluation. after receiving chemotherapy. the patient tended to decrease diarrhea symptoms. Those who showed a significant reduction were stage II and III patients. An outcome consistent with this study was an evaluation of patients receiving chemotherapy in France. Based on the results of the study. it was found that there were no patients who experienced diarrhea due to side effects of chemotherapy.

Chemotherapy. including handling its side effects in cervical cancer patients. requires a high cost [29]. so that it can increase financial difficulties for patients. The results of this study indicate that there is a tendency to decrease financial difficulties after chemotherapy although it is not significant. The tendency to decrease in financial difficulties is due to the existence of health insurance that covers the cost of chemotherapy treatment. so that psychologically it can ease the financial burden and reduce anxiety of the patients. Patients feel calm because they no longer need to pay for expensive chemotherapy costs. The fewer financial disturbances experienced by patients. it will have an impact on improving the patient's quality of life [43].

4.2.3. Global health status

The results showed that there was a trend towards a significant increase in the domain of global health status. although the significance was in patients with stage I. II. and III. The patients felt that their overall quality of lives had improved when compared to before receiving chemotherapy for three cycles. This is caused by

clinical symptoms such as bleeding. vaginal discharge and pain that have decreased or disappeared. These results are in line with the those of research in Austria [17]. The trend of increasing global health status at all these stages is not only due to the decreasing severity of cancer. but also because of the use of drugs to treat the side effects of chemotherapy. Another aspect that is thought to have an effect is the service of health workers at the hospital. Good service from doctors and nurses while the patient is receiving therapy is thought to also affect the quality of life. This is proven based on the results of research in Greece [18]. Based on the evaluation on humanistic outcomes. after chemotherapy. there tends to be an improvement in the quality of life in patients with cervical cancer. This increase in the quality of life occurs because of the patient's health condition. Although there is a tendency for a decrease in some aspects of the patients' quality of life due to the side effects of chemotherapy. patients do not need to worry about undergoing the therapy. With proper treatment. the adverse side effects of chemotherapy can be treated properly. This will minimize the adverse effects of side effects felt by patients during therapy.

5. Conclusion

After chemotherapy for three cycles. it was observed that there was a trend toward improvement in clinical features and humanistic outcomes in cervical cancer patients at all stages. This indicates the lower the stage each patient has. the better the improvements they get. The side effects of chemotherapy that reduce several aspects of the humanistic outcome have been successfully overcome with pharmacological and non-pharmacological therapies as well as by providing health care services that pay attention to the psychological aspects of the patient.

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