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The cortisol level, depression anxiety stress score, and quality of life in patient with advance stage cervical cancer after two years of psychorative intervention

Soetrisno,[1*] Erindra Budi Cahyanto,[2] Sri Mulyani,[2] Angesti Nugraheni,[2] Hafi Nurinasari,[1] Rubin Enhui Tjiang[1]

ABSTRACT

Background: Cervical cancer is the second most cancer in women after breast cancer. Emotional stress is the most common comorbid attacking women with advanced-stage cervical cancer, where 13- 40% are depressed which can increase mortality by 39%. Management of cervical cancer has so far focused on standard chemoradiation treatment, but has paid less attention to other aspects such as cognitive, psychological, spiritual and physical. The study aims to determine cortisol levels, Depression Anxiety Stress (DAS) score and quality of life for patients with advanced-stage cervical cancer after two years of psychocurative intervention

Methods: The pretest-posttest group design experimental study, continued previous studies, 30 subjects with advanced-stage cervical cancer patients, divided into 15 subjects received standard and psychocurative treatments, the other 15 as controls only received standard therapy. Psychocurative is done independently three times a week for two years based on psychocurative smart books. Home visits are conducted once per week to monitor, motivate the subject to do the psychocurative independently properly and discipline. Cortisol levels, DAS scores and quality of life were measured before and after treatment, the data were analysed by paired t-tests in the SPSS 25 program.

Results: One control group subject died before the study was completed. Before and after psychocurative, cortisol levels in the treatment group were 12.29 ± 4.36 and 6.71 ± 3.88 with $p<0.05$. The Depressive scores were 14.13 ± 3.02 and 8.46 ± 3.07 with $p<0.05$. The Anxiety scores 12.13 ± 1.64 and 6.73 ± 2.40 with $p<0.05$. The Stress scores were 14.40 ± 2.64 and 7.27 ± 2.81 with $p<0.05$. The quality of life score of the physical domain were 55.00 ± 6.54 and 62.67 ± 8.63 with $p <0.05$. The Psychical domain was 57.00 ± 9.41 and 65.66 ± 8.42 with $p <0.05$. The Social domain was 33.67 ± 9.15 and 41.67 ± 10.29 with $p <0.05$. The Environmental domain was 63.00 ± 1.93 and 69.33 ± 7.76 with $p <0.05$

Conclusions: Psychocurative decreases serum cortisol levels, decreases depression, anxiety, and stress scores and improves the quality of life of the physical, psychological, social and environmental domains.

Keywords: psychocurative, cortisol, DASS, quality of life, cervical cancer

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[1]Departement of Obstetrics and Gynecology, Medical Faculty, Universitas Sebelas Maret-Dr. Moewardi General Hospital Surakarta, Indonesia
[2]Bachelor of Midwifery Programme, Medical Faculty of Sebelas Maret University Surakarta

[*]Correspondence to:
Soetrisno, Departement of Obstetrics and Gynecology, Medical Faculty, Universitas Sebelas Maret-Dr. Moewardi General Hospital Surakarta, Indonesia
soetrisno_spogk@yahoo.com

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BACKGROUND

Cervical cancer is currently the fourth most common malignancy in women after breast, colorectal, and lung cancer, with 527,600 new cases and 265,700 deaths annually.[1] Cervical cancer and breast cancer are the most common cancers in Indonesia; in 2013, the incidence of cervical cancer was 0.8 ‰ and breast cancer 0.5‰.[2] In patients with advanced cervical cancer, stress occurred both physiological stress (disease progression and therapy), psychological stress (anxiety related to diagnosis, prognosis, treatment costs medical, fear of death), and social stress (family support, economic pressure, and environment).[3] As a result of long-term stressors exposure, depression can occur which reduces the quality of life.[4] Many researchers have made efforts to reduce stress as a way to improve the quality of life and endurance.[5] The relationship of psychological factors and immune system function, inflammation, blood vessel growth, and tumor development has led many researchers to the question whether psychocurative interventions can help reduce stress symptoms, inhibit recurrence, and improve endurance, and quality of life of patients cervical cancer.[6-9]

Psychocurative is a psychological intervention, created with the aim of ensuring that a person has a better chance to adjust to their mental conditions and situations, so that they can change the components of previous knowledge and gain new understanding to change behaviour for the better. Treatment efforts in the form of psychocurative interventions are intended to ensure that a person has a better chance to adjust to their mental conditions and situations and to build interpersonal, harmonious

and integral relationships to improve psychological stability and ability to live. Psychocurative consists of cognitive, spiritual, social and physical support that can change the condition of distress into eustress.[8]

This study aims to analyze differences in cortisol levels, anxiety scores, and quality of life of patients with advanced-stage cervical cancer, after 2 years of psychocurative.[7]

Specific response to stress is the release of the hormones adrenocorticotropin and cortisol into the bloodstream as a result of activation of the hypothalamic-pituitary-adrenal axis. Cortisol is a glucocorticoid hormone that is synthesised from cholesterol in the adrenal cortex. Cortisol is commonly known as a "stress hormone", which is only released during stressful conditions. [10,11]

DAS score is an emotional score in the form of a self-report format, consisting of three scales, designed to measure negative emotional states, depression, anxiety and stress.[12]

Quality of life is defined as "the perception of individuals about their position in the life of the cultural context and value system in which they live, in relation to their goals, expectations, standards, and concerns". Quality of life on a global scale, broader than health status, subjective inheritance and related to all aspects of life that are important to that person. There is evidence that dissatisfaction with environmental, psychological and / or social problems can have an impact on the physical health and well-being of individuals.[13]

Previous studies have shown that psychocurative interventions can significantly reduce cortisol levels, DAS scores, and improve quality of life.[14] This study aims to further analyze differences in cortisol levels, DAS scores, and quality of life for patients with advanced-stage cervical cancer after two years of psychocurative intervention.

METHOD

Study Design

An experimental study of pretest-posttest group design was conducted in the ward and outpatient clinic of the Department of Obstetrics and Gynecology Dr. Moewardi / Faculty of Medicine, Universitas Sebelas Maret, Surakarta

Research population

The subjects of study were advanced stage cervical cancer patients, treated at the Dr. Moewardi General Hospital/ Medical Faculty of Sebelas Maret University Surakarta from August 2017 - August 2019, as many as thirty patients, divided into 15 patients in treatment and control groups. Inclusion criteria; stage IIB-IV cervical cancer, can speak Bahasa, communicate well, have at least graduated from elementary school education, are willing to participate in research and sign informed consent. Exclusion Criteria; suffering from cancer other than cervical cancer, pregnancy, endocrine abnormalities, severe mental disorders (psychotic), and a history of depression treatment.

Instrument

Serum cortisol measurement by Prodia Surakarta Central Java Indonesia Clinical Laboratory. The time of blood sampling before 8 am, because blood cortisol levels increase in the morning (highest at around 8 am) and decreases at night and during the early phase of sleep.[10]

Three survey instruments were used, the first was a demographic and clinical characteristics data questionnaire that included age, body mass index, occupational status, education level, number of children (parity), marital status and hemoglobin levels.

Second instrument; DASS 42 questionnaire, is a screening instrument used to identify stress levels. The DASS is a format that contains three self-report scales, which are designed to measure negative emotional states namely depression, anxiety and stress. Each of the three DAS scales contains 14 questions, divided into subscales of 2-5 questions with similar meanings. The Depression Scale assesses dysphoria, life devaluation, self-humiliation, lack of interest/involvement, anhedonia, and inertia. Anxiety Scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experiences of anxious influences. The Stress Scale is sensitive to the level of chronic non-specific stimuli, for example emotional stress.[12]

The third instrument is a question about quality of life according to WHO-QOL-BREF which must be answered by the subject who is able to read; if not, use the help form filled in by the interviewer. In clinical practice, the WHOQOL-BREF assessment helps clinicians make an assessment of the areas in which subjects are most affected by the disease, and make treatment decisions. The WHOQOL-BREF domain score contributes significantly, explaining differences in general aspects related to overall quality of life and general health, with the physical health domain making the highest contribution, compared to the psychological, social and environmental domains. This shows that all four domains must be considered when evaluating overall quality of life.[21]

Procedure

The treatment group was conducted to psychocurative intervention for 60 minutes per week for

four weeks in a lecture and practice session at the Dr.Moewardi General Hospital/Medical Faculty of Sebelas Maret University Surakarta, which was continued three times per week of independent psychocurative at home of each subject. The lecture and practice session of psychocurative was provided by the researcher and the team that had been previously trained, according to the modified psychocurative smart book module. Before getting the next lecture and practice of psychocurative intervention, the subject of the treatment group conducted a discussion and explored the experiences after undergoing a psychocurative procedure. Research variable data before and after psychocurative showed significant benefit for patients with advanced cervical cancer.[14]

This study is a continuation of previous research, subjects were instructed to do psychocurative independently three times a week at home for two years based on the psychocurative smart book guidelines that have been given by researchers. Researchers make home visits to each subject once a week, to monitor and motivate the subject as well as discussion and exploration of matters relating to research.

The control group only received standard therapy (chemoradiation). The research variables in control group were the same as the treatment group, examined before and after two years psychocurative intervention.

Examination of cortisol levels, DAS scores and quality of life was carried out on different days from the treatment group as in the first phase of the study, so that it did not violate ethics and still respect patients' rights to receive comprehensive services according to hospital standards.

Statistic analysis

All data were entered and analyzed using SPSS version 25.0 for windows. Patient characteristics were summarised using descriptive statistics. All continuous data are presented as mean ± SD while categorical data are presented as frequency and percentage (%). All numerical variables are tested using independent t-test.

The dependent variable is cortisol hormone level, DAS score, and quality of life. Characteristics of the subjects were: age <45 years and ≥ 45 years, Body Mass Index <24 and ≥ 24 kg/m^2, primiparity and multiparity, elementary and intermediate schools, employed and not employed, married and single, Hb levels <10 g% and ≥ 10 g%, p-value≤0.05 was considered statistically significant.

Table 1 **Subjects Characteristics**

Characteristic	Group		p *value*
	Intervention	Control	
Age (year)			
< 45	4 (26.7%)	4 (28.6%)	0.670
≥ 45	11 (73.3%)	10 (71.4%)	
BMI (kg/m2)			
< 24	13 (86.7%)	12 (85.7%)	0.725
≥ 24	2 (13.3%)	2 (14.3%)	
Occupation			
Employed	6 (40.0%)	5 (35.7%)	0.622
Not employed	9 (60.0%)	9 (64.3%)	
Parity			
Multi	13 (86.7%)	11 (78.6%)	0.604
Primi	2 (13.3%)	3 (21.4%)	
Education			
Elementary	8 (53.3%)	4 (78.6%)	0.594
Intermediate	7 (46.7%)	10 (71.4%)	
Marital status			
Married	13 (86,7%)	11 (78.6%)	0.604
Single	2 (13.3%)	3 (21.4%)	
Hb Level (gr%)			
< 10	6 (40%)	3 (21.4%)	0.231
≥ 10	9 (60%)	11 (78.6%)	

RESULT

Table 1, shows that the characteristics of the subjects in terms of age, BMI, occupation, parity, education level, marital status and Hb level showed p>0.05, meaning there were no significant/ homogeneous differences between the treatment and control groups.

Table 2, shows that the mean difference of serum cortisol levels in the treatment group before and after psychocurative showed a significant difference (p<0.001) while the control did not have a significant difference (p=0.083). The mean difference test of cortisol levels in the treatment and control groups before psychocurative there was no significant difference (p =0.989). The t-test of cortisol levels in the treatment and control groups after psychocurative showed a significant difference (p<0.001).

Table 3 shows that the mean different DAS Depression scores in the treatment group before and after the psychocurative showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.151). The mean difference in DAS Depressive scores in the intervention and control groups before psychocurative was not significantly different (p=0.258), after psychocurative it was significantly different (p<0.001). Meanwhile, DAS Anxiety score in the treatment group before and after the psychocurative

Table 2 The differences in cortisol levels between the intervention and control groups

		Cortisol						
		Pre-test			Post-test			
Group	n	Mean ± SD	Mean difference	CI 95%	Mean ± SD	Mean difference	CI 95%	*p-value*
Intervention	15	12.29 ± 4.36	0.022	-3.15 – 3.19	6.71 ± 3.88	-5.21	3.26 – 7.89	<0.001*
Control	14	12.07 ± 3.87	0.022	-3.14 – 3.18	11.60 ± 3.85	-5.21	-0.97 – 1.64	0.083
p-value			0.989			<0.001*		

* significant p<0.05

Table 3 The differences in DAS scores between the intervention and control groups

		Pretest			Posttest			
DAS Score	n	Mean ± SD	Mean diff	95% CI	Mean ± SD	Mean diff	95% CI	p value
Depression								
Intervention	15	14.13 ± 3.02	1.20	-.935 – 3.34	8.46 ± 3.07	-3.96	-6.11 – (-1.80)	<0.001*
Control	14	12.92 ± 2.55	1.20	-.923 – 3.33	12.42 ± 2.53	-3.96	-6.10 – (-1.82)	0.151
p-value		0.258			<0.001*			
Anxiety								
Intervention	15	12.13 ± 1.64	-.438	-1.98 – 1.10	6.73 ± 2.40	-5.26	4.16 – 6.63	<0.001*
Control	14	12.57 ± 2.38	-.438	-2.02 – 1.14	12.00 ± 1.75	-5.26	-.20 – 1.34	0.135
p-value		0.566			<0.001*			
Stress								
Intervention	15	14.40 ± 2.64	-2.1	-3.92 – (-0.272)	7.27 ± 2.81	-8.23	6.02 – 8.23	<0.001*
Control	14	16.50 ± 2.10	-2.1	-3.91 – (-0.285)	15.50 ± 2.68	-8.23	0.359 – 1.64	0.640
p-value		0.111			<0.001*			

* significant p<0.05

Table 4 The differences WHOQOL BREF between the intervention and control groups

		Pretest			Posttest			
WHOQOL	n	Mean ±SD	Mean diff	95% CI	Mean ± SD	Mean diff	95% CI	p-value
Domain 1/ physical								
Intervention	15	55.00 ± 6.54	8.87	-2.69 – 20.54	62.67 ± 8.63	7.30	.802 – 13.81	<0.001*
Kontrol	14	46.12 ± 20.97	8.87	-3.47 – 21.23	55.35 ± 8.42	7.30	.807 – 13.81	0.127
p-value			0.127			0.029*		
Domain 2/ psychological								
Intervention	15	57.00 ± 9.41	4.14	-2.62 – 10.90	65.66 ± 8.42	11.73	5.17 – 18.30	<0.001*
Kontrol	14	52.85 ± 8.25	4.14	-2.59 – 10.87	53.92 ± 8.80	11.73	5.15 – 18.31	0.336
p-value			0.220			0.001*		
Domain 3/ social								
Intervention	15	33.67 ± 9.15	-1.54	-9.46 – 6.37	41.67 ± 10.29	8.11	-15.60 – (-.631)	<0.001*
Kontrol	14	41.78 ± 10.48	-1.54	-9.47 – 6.38	43.21 ± 10.48	8.11	-15.65 – (-.580)	0.218
p-value			0.692			0.035*		
Domain 4/ environment								
Intervention	15	63.00 ± 1.93	7.28	1.82 – 12.74	69.33 ± 7.76	12.19	6.00 – 18.37	<0.001*
Kontrol	14	55.71 ± 6.75	7.28	1.84 – 12.72	57.14 ± 8.48	12.19	5.97 – 18.40	0.234
p-value			0.084			0.001*		

* significant p<0.05

showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.135). The mean difference in the DAS Anxiety score in the intervention and control groups before psychocurative was not significantly different (p=0.566), after psychocurative it was significantly different (p<0.001). Another parameter of DAS Stress score in the treatment group before and after the psychocurative showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.640). The mean difference in the DAS Stress score in the intervention and control groups before psychocurative was not significantly different (p=0.111), after psychocurative it was significantly different (p<0.001).

Table 4, shows that the mean difference in physical domain score of the treatment group before and after psychocurative showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.127). The mean difference in physical domain score of the intervention and control groups before psychocurative was not significantly different (p=0.127), after psychocurative significantly different (p=0.029).

Table 4, shows that the mean difference test of the psychological domain score of the treatment group before and after the psychocurative showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.336). The mean difference test score of the psychological domain of the intervention and control groups before psychocurative was not significantly different (p=0.220), after psychocurative significantly different (p<0.001).

Table 4, shows that the mean difference test of the social domain score of the treatment group before and after psychocurative showed a significant difference (p <0.001), in the control group there was no significant difference (p=0.218). The mean difference in social domain score of the intervention and control groups before psychocurative was not significantly different (p=0.092), after psychocurative significantly different (p=0.035).

Table 4, shows that the mean difference test score of the environmental domain of the treatment group before and after the psychocurative showed a significant difference (p<0.001), in the control group there was no significant difference (p=0.234). The mean difference in environmental domain score of the intervention and control groups before psychocurative was not significantly different (p=0.084), after psychocurative significantly different (p<0.001).

DISCUSSION

This study is a continuation of previous study that shows that psychocurative significantly reduces cortisol levels, reduces stress and improves the quality of life of patients with advanced cervical cancer.[14,15]

This follow-up study initially included thirty subjects of advanced stage cervical cancer patients who met the inclusion and exclusion criteria. But in its development, one of the subjects in the control group died, therefore at the end of the study, there were only twenty-nine subjects.

Psychocurative is a psychological intervention that is created, with the aim of ensuring that a person has a better chance to adjust to their mental conditions and situations, so that they can change the components of previous knowledge and gain new understanding to change behaviour for the better. created to ensure that a person has a better chance to adjust to their mental conditions and situations and build harmonious and integral relationships to improve psychological stability and ability to live. Psychocurative consists of cognitive, spiritual, social and physical support that can change conditions distress becomes eustress.[8,16,17]

The results in table 2, show that the mean cortisol levels in the treatment group after second-year treatment were lower than in the control group, statistically significant. This indicates that psychocurative for two years is very useful, which also means more refined standard chemoradiation therapy which is now applied to patients with advanced stage cervical cancer.

Cortisol is a glucocorticoid hormone that is synthesised from cholesterol in the adrenal cortex. Cortisol is commonly known as the "stress hormone", which is only released during stress conditions.[10] Cortisol is one of the main biomarkers of depression and is often used for depression monitoring therapy.[11,19]

By providing psychocurative therapy, emotional stress decreases, cortisol production from the adrenal cortex decreases in subjects with advanced stage cervical cancer.[8,20] The results of this study are also consistent with the research of Soetrisno et al. who get a significant decrease in cortisol levels in patients with psychiatric advanced cervical cancer.[14,21]

Table 3 shows that the mean DAS scores in the treatment group decreased more than controls. The paired t-test results showed that there were significant differences in the mean DAS scores in the treatment group before and after psychocurative, the control was not significant. The paired t-test DAS scores in the treatment and control groups before psychocurative were not significantly different. This all shows that psychocurative after two years is very useful, which means that it is also perfecting the standard chemoradiation therapy which is now applied to patients with advanced cervical cancer.

Psychocurative is a branch of modern psychology or psychiatry which makes the meaning of life the central theme. In general definition, psychocurative can be described as a psychology/ psychiatric style that recognizes the spiritual dimension in humans in addition to the physical and psychological dimensions, and assumes that the meaning of life and the desire for meaningful life (the will to meaning) are the main motivations of humans to achieve the coveted meaningful life.[8] In patients with advanced stage cervical cancer, the main psychological problem is the patient's fear of the disease. This fear arises because of the patient's lack of understanding of the disease.[22]

Psychocurative administration can cause DAS scores decrease, because the provision of appropriate psychocurative interventions including cognitive, spiritual, social, and physical support will change the distress to eustress, causing positive emotional changes, can trigger beneficial gene expression.[8,14]

Table 4, shows that the average quality of life scores in the physical, psychological, social, and environmental domains in the treatment group before and after the psychocurative increase, greater than in the control group. The mean difference in quality of life scores of the four domains in the treatment group before and after the psychocurative showed a significant difference. In controls not significant. The mean difference test of the four domains of quality of life of the treatment and control groups before psychocurative did not show any significant difference, whereas after psychocurative there was a significant difference.

The study found substantial levels of depression, anxiety, stress and quality of life among cancer patients undergoing standard therapy (chemoradiation). The level of depression found in this study is inversely related to previous studies conducted in Taiwan, where cancer patients did not show significant differences in the development of depression.[7] Depression, anxiety and stress were found to be one of the most common symptoms among patients undergoing chemotherapy and radiotherapy at the Dr. Moewardi General Hospital/Medical Faculty of Universitas Sebelas Maret Surakarta. Previous studies have reported that depression and anxiety generally form one group of symptoms among cancer patients.[14] The levels of depression, anxiety and stress in the control group were higher than in the intervention group.

Limitations of this study are confounding variables that are not fully controlled such as blood chemistry (liver function, kidney function), comorbid conditions such as diabetes mellitus and cerebrovascular disease, as well as drugs used for comorbidities not assessed.

CONCLUSION

Two-year psychocurative interventions have been shown decreases in cortisol levels, DAS scores, and improve the quality of life of patients with advanced stage cervical cancer. The results of this study further refine the previous study which also means more refined therapy of advanced stage cervical cancer

CONFLICT OF INTEREST

There are no conflicts of interest regarding this research and publication.

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ETHICAL CONSIDERATIONS

Ethical considerations in this study are in accordance with the Ethical Feasibility Letter issued by Dr. Moewardi General Hospital No. 642/VIII/HREC/2018. All patient had received signed informed consent prior to any data collection. All procedures performed in research involving human participants are in accordance with the ethical standards of the Institutional Research Committee based on the 1964 Helsinki Declaration.

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