ORIGINAL ARTICLE

The correlation of nutritional status with hematology toxicity of adjuvant chemotherapy in ovarian cancer

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ABSTRACT

Objectives: To observe correlation of nutritional status using Nutritional Risk Index with the side effects of adjunctive haematological chemotherapy.
Materials and Methods: This study was a retrospective cohort study observing whether or not hematologic side effects occurred during chemotherapy based on medical records of postoperative ovarian cancer patients receiving adjuvant chemotherapy.
Results: Sixty-eight subjects with age range of 31-50 years (44.1%) multipara (68.8%), and advanced stage (52.1%) were observed. An increase was found in the diagnosis of malnutrition between the IMT method and NRI, which was 18.7% compared to 43.7%. A significant correlation was found between preoperative malnutrition and the incidence of anaemia after adjuvant chemotherapy for ovarian cancer patients (p=0.002). Whereas, in the event of leukopenia and thrombocytopenia, there were no significant correlations with p=0.675 and p=0.415, respectively.
Conclusion: There was an increase in malnutrition rate with the use of NRI compared with BMI and there was a significant correlation between malnutrition and side effects of anaemia in patients with ovarian cancer who underwent surgery and continued with adjuvant chemotherapy.

Keywords: ovarian cancer; nutritional status; adjuvant chemotherapy; maternal health

ABSTRAK

Tujuan: Mengetahui hubungan status nutrisi menggunakan Nutritional Risk Index dengan efek samping hematologi kemoterapi ajuvan.
Bahan dan Metode: Penelitian ini merupakan suatu studi kohort retrospektif yang mendata terjadi atau tidaknya efek samping hematologi selama kemoterapi berdasarkan data rekam medis penderita kanker ovarium pasca operasi yang mendapat kemoterapi ajuvan.
Hasil: Didapatkan 68 subyek dengan rentang usia terbanyak 31-50 tahun (44,1%) multipara (68,8%), dan stadium lanjut (52,1%). Didapatkan peningkatan diagnosis malnutrisi antara metode IMT dengan NRI, yaitu 18,7% dibandingkan 43,7%. Didapatkan hubungan yang bermakna antara malnutrisi pra operasi dengan kejadian anemia pasca kemoterapi ajuvan pasien kanker ovarium (p=0,002). Sedangkan pada kejadian leukopenia dan trombositopenia tidak didapatkan hubungan yang bermakna p= 0,675 dan p=0,415.
Simpulan: Didapatkan peningkatan angka malnutrisi dengan penggunaan NRI dibandingkan dengan IMT dan hubungan yang bermakna antara malnutrisi dengan efek samping anemia pada penderita kanker ovarium yang menjalani operasi dan dilanjutkan dengan ajuvan kemoterapi.

Kata kunci: kanker ovarium; status nutrisi; kemoterapi ajuvan; kesehatan ibu

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INTRODUCTION

Cancer is still a health problem in the world. Each year 240,000 women in the world are diagnosed with ovarian cancer with a five-year survival rate of only about 45%. There are 3 types of ovarian cancer which are named according to the cells they originate from. Ninety percent of ovarian cancers originate from the epithelial lining that covers the surface of the ovary. This group is known as epithelial cancer.[1]

The principles of management of ovarian cancer are the same as the principles of handling other malignant diseases, namely the treatment of primary lesions operatively and the handling of potential sites of tumor metastases with chemotherapy. Handling or main treatment of ovarian cancer to date includes surgery and chemotherapy.[2]

Ovarian cancer sufferers experience changes in body composition as a result of their own disease which causes an increase in energy requirements to meet the increase in body metabolism, but conditions due to cancer also result in decreased appetite so that the body is unable to meet energy needs. This condition causes the catabolic process to increase so that there can be a change in the nutritional status of ovarian cancer patients. Other conditions that can cause changes in nutritional status are therapeutic modalities including chemotherapy.[2]

Chemotherapy is a cancer therapy that involves the use of chemicals or drugs whose purpose is to kill cancer cells. Side effects caused by chemotherapy can cause nausea, vomiting, diarrhea, stomatitis, alopecia, susceptibility to infection, thrombocytopenia, neuropathy and myalgia.[3] Chemotherapy can be done with several chemotherapy drug regimens. Combined chemotherapy regimen Platinum and Taxane is known to increase the life expectancy of ovarian cancer patients. The use of the Taxane class chemotherapy regimen has the effect of leukopenia, neutropenia, and thrombocytopenia.[4]

Cancer therapy including surgery and chemotherapy has the effect of anorexia, nausea, vomiting and diarrhea which will aggravate weight loss. Malnutrition changes physiologically at the organ to cellular level, affecting post-therapy morbidity and quality of life, therefore, a strategy to determine comprehensive nutritional status needs to be found. The results found that patients with good nutritional status since the start of therapy had significantly better survival than those who had poor nutritional status.[5]

Not many studies have looked at the effect of nutritional status on ovarian cancer patients, especially in Dr. Soetomo Hospital, so in this study we tried to find a correlation between nutritional status using the Nutritional Risk Index with the hematological side effects of ovarian cancer patients who received adjuvant chemotherapy.

MATERIALS AND METHODS

This research is a retrospective cohort study that records whether or not hematologic side effects occur during chemotherapy based on medical records of postoperative ovarian cancer patients receiving adjuvant chemotherapy. The research was conducted at the Gynecology Oncology Clinic and Gynecology Ward, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, by collecting medical records of ovarian cancer patients who underwent surgery and continued with the provision of adjuvant chemotherapy for 3 cycles in January 2018 - December 2018.

Nutritional status calculated by NRI scoring was calculated based on the formula (1.519 x serum albumin gr/L) + (41.7 (current weight/ideal weight)). Then divide the results into 2 groups only not malnutrition (NRI $\geq$97.5) and malnutrition (NRI <97.5). Hematological side effects that occur in ovarian cancer who receive adjuvant chemotherapy based on the National Cancer Institute (NCI) Toxicity Criteria, namely anemia grade 1 (mild): Hb <LLN - 10g/dL, anemia grade 2 (moderate): Hb <10.0- 8.0 g/dL, anemia grade 3 (severe): Hb <8.0 g/dL, grade 1 leukopenia (mild): WBC <LLN-3,000 mm3, leukopenia grade 2 (moderate): WBC <3,000-2,000 mm3, leukopenia grade 3 (weight): WBC <2,000-1,000 mm3, grade 1 thrombocytopenia (mild): PLT <LLN-75,000 µL, grade 2 thrombocytopenia (moderate): PLT <75,000-50,000 µL, grade 3 thrombocytopenia (severe): PLT <50,000-25,000 µL.[6]

RESULTS AND DISCUSSION

There were 68 ovarian cancer patients who matched the inclusion criteria of the study, namely surgery at Dr. Soetomo Hospital Surabaya and with the results of PA epithelial ovarian cancer during 2018 and continued with adjuvant chemotherapy. Then 20 patients (29.4%) did not undergo further therapy or adjuvant chemotherapy because they did not control or refused chemotherapy.

The age range of study subjects was between 22 and 71 years with a composition of 1 (2.1%) non-malnutrition

group and 2 (4.2%) malnutrition group under 30 years of age, 16 (33.3%) non-malnutrition group and 10 (20.8%) aged between 31 and 50 years, and 10 (20.8%) were not malnourished and 9 (18.8%) were malnourished by more than 51 years. There was no significant difference between the non-malnourished and malnourished groups (p=0.595).

Ovarian cancer is generally found in women of older age or post-menopausal age. Ovarian cancer is rarely found under 40 years of age. The incidence rate increases with increasing age.[7] Increasing age in women may give time for genetic changes to the ovarian surface epithelial cells.[8]

There were 14 (29.2%) of the research subjects with parity 0, 17 (35.4%) with parity 1, 8 (16.7%) with parity 2, 5 (10.4%) with parity 3, and the rest 2 (4.2%) each. The number of live births (parity) is thought to have an effect on reducing the risk of ovarian cancer. Some studies have shown that a first birth can reduce the risk of ovarian cancer compared to subsequent births, but other studies have shown that the protective effect against ovarian cancer increases when there is a second birth.[9]

Early stage cancer staging results based on nutritional status were 13 (27.1%) in the non-malnutrition group, 10 (20.8%) in the malnutrition group. And advance stage 14 (29.2%) were not malnourished and 11 (22.9%) were malnourished and there were no significant differences (p=0.601). The calculation of the Body Mass Index in this study resulted in 9 (18.75%) in the underweight category (undernourished), 27 (56.25%) with normal weight or normal nutritional status, and 12 people (25%). with overweight and obesity. Meanwhile, the calculation of nutritional status using the Nutrition Risk Index/NRI found 27 (56.25%) in the normal category or no malnutrition and 21 (43.75%) obtained malnutrition ovarian cancer. Calculation of nutritional status correctly can reduce delays in identifying malnutrition diagnosis in ovarian cancer patients, thereby reducing morbidity and mortality.[10]

The results of this study indicated that of the 3 parameters of chemotherapy adjuvant side effects, only Hb levels had a significant correlation with the assessment of nutritional status using NRI. Anemia is a common finding in cancer patients, with an incidence between 30% and 90%. Causes of anemia in cancer patients include metabolic disorders and nutrition, chronic disease, kidney disorders, blood loss, decreased production due to bone marrow disease, peripheral destruction due to autoimmune disorders, drug-induced red blood cell aplasia, and chemotherapy-induced anaemia.[11-13] Chemotherapy can cause anaemia through inhibitory mechanisms in normal haematopoiesis and on the action of cytokines. Chemotherapy agents cause anaemia directly by interfering with haematopoiesis, including the synthesis of red blood cell precursors in the bone marrow.[14] The nephrotoxic effect of certain cytotoxic agents (which contain platinum) can also cause anaemia by decreasing erythropoietin production. Platinum based regimen, known as a cause of anaemia due to its toxic effects on bone marrow and kidneys.[15-20]

Table 1. Distribution of nutritional status by age group

Age	Nutritional Status				*p*
	No Malnutrition		Malnutrition		
≤ 30 th	1	2.1%	2	4.2%	0.595
31-50 th	16	33.3%	10	20.8%	
≥ 51 th	10	20.8%	9	18.8%	

Table 2. Distribution of nutritional status based on parity

Parity	Nutritional Status				*p*
	No Malnutrition		Malnutrition		
Nullipara	8	16.7%	7	14.5%	0.514
Multiparous	19	39.6%	14	29.2%	

Table 3. Distribution of nutritional status by stage

Stage	Nutritional Status				*p*
	No Malnutrition		Malnutrition		
Early stage	13	27.1%	10	20.8%	0.601
Advance stage	14	29.2%	11	22.9%	

Table 4. Relationship of hematological side effects after adjuvant chemotherapy with nutritional status

Hematological Side Effects	Nutritional Status				*p*
	No Malnutrition		Malnutrition		
Normal HB	5	10.4 %	3	6.3 %	0.002
Mild Anemia	18	37.5 %	6	12.5 %	
Moderate Anemia	2	4.2 %	12	25.0 %	
Severe Anemia	2	4.2 %	0	0	
Normal Leukocytes	24	50 %	18	37.5 %	0.675
Mild Leukopenia	2	4.2 %	1	2.1 %	
Moderate Leukopenia	1	2.1 %	2	4.2 %	
Normal Platelets	25	52.1 %	20	41.7 %	0.415
Mild Thrombocytopenia	1	2.1 %	0	0	
Moderate Thrombocytopenia	1	2.1 %	0	0	
Severe Thrombocytopenia	0	0	1	2.1 %	

CONCLUSION

There was an increase in the number of malnutrition with the use of NRI compared to BMI in ovarian cancer patients who underwent surgery and continued with adjuvant chemotherapy. In addition, there was also a significant correlation between nutritional status calculated using NRI and side effects of anemia in ovarian cancer patients who received chemotherapy adjuvant, but there was no significant correlation between leukopenia side effects and thrombocytopenia in ovarian cancer patients who received chemotherapy adjuvant.

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