Pharmacogenetics of antiemetics in Indonesian cancer patients

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Impact of chemotherapy induced nausea and vomiting on quality of life in Indonesian patients with gynecological cancer

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ABSTRACT

Background: Quality of Life (QoL) has become a major outcome in the treatment of patients with cancer. This study is aimed at examining the impact of chemotherapy-induced nausea and vomiting on QoL of patients with gynecological cancer in Indonesia.

Methods: . Chemotherapy-naive patients with gynecological cancer, who were treated with cisplatin at a dosage ≥ 50 mg/m^2 as monotherapy or as part of combination chemotherapy regimens, were recruited in the Oncology Department, Dr. Sardjito Hospital, Yogyakarta, Indonesia. QoL was assessed by using the Indonesian version of EORTC QLQ-C30 and SF-36, administered immediately before and on day 5 after chemotherapy administration. Patients used a daily diary to record nausea and vomiting over 5 days after chemotherapy.

Results: Most (74.9%) of the 179 patients experienced delayed emesis during the 5 days after chemotherapy despite prophylactic use of antiemetics. The delayed nausea and emesis caused significant negative impact on patients' QoL. Nausea in the delayed phase caused negative effects on patients' QoL.

Conclusion: Patients reported negative impact on QoL of delayed emesis after chemotherapy. Poor prophylaxis of patients' nausea and vomiting after chemotherapy interferes with patients' QoL. Medical and behavioral interventions may help to alleviate the negative consequences of chemotherapeutic treatment in patients with gynecological cancers treated with suboptimal antiemetics.

INTRODUCTION

In recent decades, quality of life (QoL) has increasingly become an important outcome in the treatment of patients with cancer. In QoL research, the impact of the illness itself and the cancer treatments are assessed from the patients' perspective. One of the factors most seriously impacting patients' QoL during cancer treatment is chemotherapy-induced nausea and vomiting (CINV), especially when it is inadequately treated by antiemetic drugs.[1] Patients may experience acute or delayed CINV during cancer treatment. Acute CINV is defined as nausea and vomiting episodes which persist during the first 24 hours after chemotherapy administration.[2] Delayed CINV starts after the first 24 hours following chemotherapeutic treatment and may persist up to 120 hours.[3] Patients who experience both acute and delayed CINV have worse QoL compared with patients with delayed CINV only, or without acute and delayed CINV.[1] By using an appropriate prophylactic antiemetic regimen, the incidence of CINV can be substantially reduced. However, despite the availability of highly effective antiemetic drugs, about 20-30% of the patients treated with highly emetogenic regimens still experience nausea and vomiting. This is caused by the presence of some risk factors, such as gender, age and individual susceptibility.[4] Health professionals often underestimate the incidence and prevalence of CINV.[5]

Most gynecological cancer types are treated with highly emetogenic chemotherapeutics, such as cisplatin, carboplatin, paclitaxel and cyclophosphamid when paclitaxel is not available.[6] These drugs are reported to cause emesis in more than 90% of patients without prophylactic use of antiemetics[7] and may seriously impact QoL. In addition to CINV, the psychological distress after cancer diagnosis, especially issues concerning femininity, body image, sexuality and reproduction also have been demonstrated to result in a decrease of the patients' QoL.[5,8]

The incidence of cervical cancer in Indonesia is 13.7 per 100,000 women.[9] Despite this high incidence, information about the patients' QoL is still very limited. Therefore, we undertook this study to assess the QoL in gynecological cancer patients after treatment with highly emetogenic chemotherapeutics, using the European Organization for Research and Treatment (EORTC) for Cancer of Quality of Life Questionnaire (EORTC QLQ-C30) as a disease specific instrument and the Short Form-36 questionnaire (SF-36) as a generic instrument for QOL or functional status. Patients' QoL baseline condition was also determined to know the change of patients' QoL after treatment with chemotherapeutics. In addition, we addressed the impact of delayed CINV on these patients' QoL.

PATIENTS AND METHODS

Patients

The study sample consisted of chemotherapy-naive patients with cervical cancer (n = 120), ovarian cancer (n = 51), uterine cancer (n = 8) and vulvar cancer (n = 7) in the Oncology Department of Dr. Sardjito Hospital, Yogyakarta, Indonesia. They were treated with cisplatin at a dosage ≥ 50 mg/m^2 as monotherapy or in combination chemotherapy regimens. Patients with all diagnoses of gynecological cancer and limited to pelvic or advanced stage of cancer were allowed to be included. Patients were referred by the general practitioners to the Dr. Sardjito hospital, Yogyakarta after the diagnosis was made. The staging procedures consisted of physical examination by a gynecologist and limited imaging when appropriate. Patients in the surgery consideration were treated according to the medical standard in Indonesia.

According to the standard of prophylactic antiemetic drug in the hospital, all patients were treated in the outpatient clinic by 8 mg intravenous ondansetron, and 8 mg intravenous dexamethasone 1 hour before cisplatin administration as a prophylactic antiemetic regimen. All patients were also given oral metoclopramide 10 mg, three times a day, from day 2 to day 5, to prevent delayed emesis.

Patients aged ≥ 18 years old with a Karnofsky Index ≥ 50% were included. Patients with nausea or vomiting 24 hours before chemotherapy, use of other antiemetics than ondansetron and dexamethasone, use of benzodiazepines or neuroleptics, treatment with radiotherapy within 24 hours before the start of chemotherapy and the use of opioids within the previous 2 weeks were excluded.

Patients' socio-demographic data were determined from their medical records. All patients gave informed consent. Data collection on demographics and baseline conditions was completed before administration of the chemotherapeutic drugs. Patients filled out the questionnaires EORTC QLQ-C30 and SF-36 one to four hours before chemotherapy, and on day 5 after chemotherapy administration at the hospital. Not all of the patients could fill in the questionnaires by themselves, and needed researcher assistance to explain some questions, i.e. the questions about general health and general QoL in EORTC QLQ-C30. Patients were also asked to fill in a daily diary record to score the degree of nausea and the vomiting frequency during the 4 days after chemotherapy. The study was approved by the local ethics committee of the Medical Faculty, Universitas Gadjah Mada, Yogyakarta.

Measurements

EORTC QLQ-C30

We used the EORTC QLQ-C30 questionnaire which is available in a validated Indonesian translation.[10] This original questionnaire was developed by the EORTC for patients with all cancer types. The EORTC QLQ-C30 covers basic important personal dimensions in cancer patients, in the physical, psychological and social domains. Furthermore, this questionnaire also covers cancer symptoms or cancer treatment related symptoms such as nausea, vomiting, dyspnea, appetite loss, diarrhea, constipation, insomnia as well as financial impact. The questionnaire has been used extensively in many countries to assess QoL of cancer in patients in their respective countries.[11] The normative data of Dutch population in female subjects was used as reference group (n = 796).[12] We used the Dutch population as the normative data in this study because the normative data of EORTC QLQ-C30 in Indonesian population are not available. The characteristics of Dutch subjects who filled in EORTC QLQ-C30 questionnaire were female respondents (n = 796) and the mean of aged (± SD) was 50.8 ± 15. Around 63% subjects reported the health problems as follow; heart disease, hypertension, asthma/chronic obstructive pulmonary disease, diabetes, depression and joint disease.

SF-36

The SF-36 is a generic instrument which can, therefore, be used in the general population and any group of patients with any illness as a generic QoL-instrument.[13] The SF-36 has QoL-dimensions similar to the EORTC QLQ-C30, that is, physical, emotional/mental, social, pain, and vitality/energy. In previous studies which compared the SF-36 and EORTC QLQ-C30 in patients with cancer, they were found to be satisfactory psychometric instruments in assessing consequences of cancer on the physical, emotional, social, pain, and energy dimensions of the questionnaire.[14] The normative data from Dutch population with age of 45-54 years old was used as reference data in this study (n = 180).[15] We used the Dutch population as the reference because of the collaboration study between the institutions in Indonesia and Netherlands and the normative data of SF-36 in Indonesia population are not available.

Delayed emesis

Delayed emesis was defined as delayed nausea and vomiting, as had to be reported by the patients in their diaries. Delayed nausea was measured by the Nausea Visual Analog Scale (NVAS) using a severity nausea scale of 0-100.[16] Zero on the scale represents 'no nausea' and a higher score represents 'more severe delayed nausea'. Patients were asked to

indicate the number on the NVAS once daily, over a 4 days period after chemotherapy. The frequency of delayed vomiting was defined by asking patients to fill in a daily diary record of vomiting frequency. The vomiting episode was defined as single vomiting, and the next vomiting episode was defined one minute after the previous vomiting episode.[16] The delayed emesis was dichotomized into "response" and "no response" based on patient's daily diary record. Patients were grouped into "response" if they did not experience nausea on 0 to 25 scores and did not vomit during 4 days after chemotherapy. Patients were grouped into "no response" if they experienced nausea and vomiting during the 4 days after chemotherapy.[16]

Statistical analysis

Raw QoL-scores were transformed into function scales which ranging from 0-100. On the EORTC QLQ-C30, higher scales scores on the dimensions indicate better function, i.e. better QoL. Higher scores in symptoms indicate more severe symptoms, i.e. lower QoL. Symptoms scores are assessed with the EORTC QLQ-C30, while dimension scores of the functioning are measured with both EORTC QLQ-C30 and SF-36. Higher scores on the SF-36 indicate better QoL, except for fatigue and bodily pain where higher scores indicate more severe symptoms.

Descriptive data are presented as means and standard deviations (SDs). The differences of patients' QoL before and after chemotherapeutic treatment were analyzed using Student's *T*-test. The differences in functions and scales between the two groups of delayed emesis were defined by independent *T*-test. $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics are summarized in Table 6.1. Of the 186 female cancer patients, 64.5% had cervical cancer, 27.4% had ovarian cancer, 4.3% had uterine cancer and 3.8% patients were diagnosed with vulva cancer. The mean age of patients was 48.3 ± 19.8 years. Most of the patients had graduated from high school (34.4%) while 32.3% of patients did not have formal education. Comorbidity was present in 15.6% of patients with one disease and 0.5% of patients with two diseases.

The available cytostatic for the patients in this hospital were cisplatin, cyclophosphamid, doxorubicin and 5FU. In the cervical cancer group, most of the patients who had limited pelvic cervical cancer (73.3%) were treated with cisplatin as single agent or in combination with 5-fluorouracil, although this is not a standard schedule. The dose of cisplatin as single agent was 70 mg/m^2 every 3 weeks, while the dose of cisplatin was 50 mg/m^2 in

Table 6.1 Patient characteristics

Patients characteristics		
Age (*n* = 181)	48.3 (mean)	19.8 (SD)
Education (*n* = 181)	Number	%
No education	60	32.3
Elementary school	50	26.9
High school	64	34.4
Bachelor/Diploma	12	6.5
Type of gynaecological cancer (*n* = 186)	Number	%
Cervical cancer	120	64.5
Ovarian cancer	51	27.4
Uterine cancer	8	4.3
Vulva cancer	7	3.8
Comorbidity (*n* = 186)	Number	%
None	156	83.9
1 disease	29	15.6
2 diseases	1	0.5
Stage of cervical cancer (*n* = 120)	Number	%
Limited to pelvic	88	73.3
Advanced stage	32	26.7
Stage of ovarian cancer (*n* = 50*)	Number	%
Limited to pelvic	31	62.0
Advanced stage	19	38.0
Stage of uterine cancer (*n* = 13*)	Number	%
Limited to pelvic	2	25.0
Advanced stage	3	37.0
Stage of vulva cancer	Number	%
Limited to pelvic	1	14.3
Advanced stage	6	85.7

* Missing data lead to some minor differences in some of the categories.

combination with 500 mg/m^2 of 5-fluorouracil every week. In the ovarian cancer group limited stage (62.0%) the treatment consisted of 500 mg/m^2 of cyclophosphamide, 50 mg/m^2 of adriamycin and 50 mg/m^2 of cisplatin every 3 weeks.

The baseline QoL scores of all subjects are listed in Table 6.2. We compared the baseline QoL in this data with the reference studies.[12,15] For this comparison, we have relied on a publication,[12] for which the raw data were not available for us. As a result is was not possible to adjust this comparison for confounding factors with a multivariate analysis. In the EORTC QLQ-C30, the functions score of this present study in both of the questionnaires were lower than those in reference studies, except for emotional function and cognitive function. Meanwhile, the symptoms scores such as pain, fatigue, nausea and vomiting, sleeping difficulty, appetite loss and constipation were higher than those of reference studies.

Table 6.2 Comparison of baseline patients' quality of life in this study and the reference studies

	Baseline of this study (Mean ± SD)	Baseline of the reference data (Mean ± SD) [12;15]	*P* value
EORTC QLQ-C30	*n* = 186	*n* = 796	
General QoL	60 ± 15	77 ± 18	**< 0.001**
Physical function	77 ± 20	89 ± 17	**< 0.001**
Role function	68 ± 25	87 ± 22	**< 0.001**
Emotional function	94 ± 12	88 ± 17	**0.004**
Cognitive function	95 ± 10	92 ± 16	**< 0.001**
Social function	72 ± 23	93 ± 18	**< 0.001**
Pain	33 ± 25	18 ± 24	**< 0.001**
Fatigue	25 ± 21	20 ± 21	**< 0.005**
Nausea vomiting	5 ± 13	3.9 ± 13	0.300
Dyspnea	5 ± 14	7.6 ± 18	**< 0.001**
Sleeping difficulty	32 ± 30	17 ± 26	**< 0.001**
Appetite loss	18 ± 25	4.4 ± 14	**< 0.001**
Constipation	13 ± 24	6.5 ± 17	**< 0.001**
Diarrhea	4 ± 26	3.8 ± 14	0.942
Financial difficulty	48 ± 48	3.6 ± 13	**< 0.001**
SF-36	*n* = 186	*n* = 180	
General health perceptions	52.9 ± 15.2	71.6 ± 23.0	**< 0.001**
Physical function	51.1 ± 30.6	79.9 ± 24.7	**< 0.001**
Physical role functioning	30.0 ± 40.9	78.9 ± 37.0	**< 0.001**
Emotional role functioning	32.8 ± 43.5	83.6 ± 33.1	**< 0.001**
Mental health	63.2 ± 22.8	76.7 ± 19.6	**< 0.001**
Social function	54.1 ± 22.0	86.1 ± 21.8	**< 0.001**
Bodily pain	58.2 ± 27.5	80.5 ± 26.7	**< 0.001**
Fatigue	61.2 ± 18.9	67.5 ± 20.3	**0.002**
Health change	42.8 ± 28.7	51.9 ± 19.8	**< 0.001**

Values are means (SD). The bold *P* values show the significant differences of baseline QoL scores between this study and the reference studies.

The significant differences of function scores were shown by all functions and symptoms, except for emotional function, nausea and vomiting and diarrhea ($P < 0.001$). Moreover, the Indonesian cancer patients faced higher financial difficulty than the Dutch population. In the SF-36, the Indonesian cancer patients showed significantly lower functions and symptoms than those of reference study ($P < 0.05$).

Seven patients died in this study during the delayed phase, due to their cancer. Most patients (74.9%) experienced delayed emesis in the 4 days following chemotherapy, that is, a response to the attempt to prevent nausea and vomiting. The patients' functions in the baseline and post chemotherapy based on the patients' response are presented in Figure 6.1. At baseline, no significant differences between the response group and no response groups were found for any of the QoL domains and symptoms scale.

On the EORTC QLQ-C30, the patients' functions did not change much or even deteriorated after the chemotherapy. Fatigue was experienced by both response group and no response group patients (Figure 6.1). Meanwhile, in the SF-36, general health perceptions, emotional function and social function were improved after chemotherapy. Figure 6.2 shows the patients' symptoms at baseline and post chemotherapy based on the response and no response groups. This figure shows that the non-response patients experienced more severe dyspnea, sleeping difficulty, appetite loss, and constipation after chemotherapy than at baseline.

The impact of delayed emesis on QoL dimensions in patients with and those without a response is presented in Table 6.3. Significant differences between the two groups in

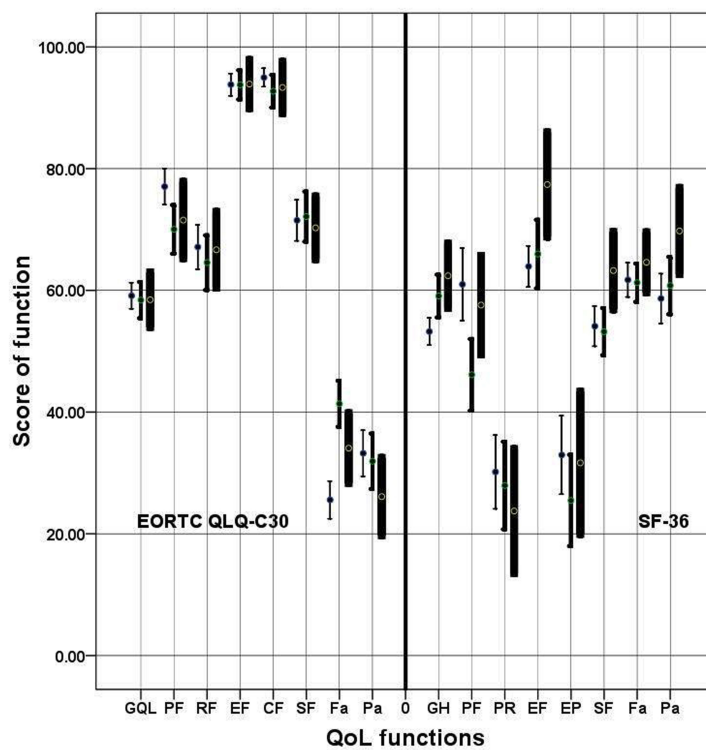

Figure 6.1 Patients' scores on the EORTC QLQ-C30 and SF-36 at baseline and post-chemotherapy in responders and non-responders. GQL, General QoL; PF, Physical Function; RF, Role Function; EF, Emotional Function; CF, Cognitive Function; SF, Social Function; Fa, Fatigue; Pa, Pain; GH, General Health; PR, Physical Role; EP, Emotional Problem.

Group:
Baseline
Post chemotherapy-no response
Post chemotherapy-response group

symptoms, such as fatigue, nausea, vomiting, and appetite loss were found on the EORTC QLQ-C30 questionnaire. The "no response" patients experienced more severe symptoms than "response" patients in whom the attempted prevention of nausea and vomiting was effective, according to the diary data. Significant differences between the two groups on QoL dimensions, such as physical function, mental function, social function and bodily

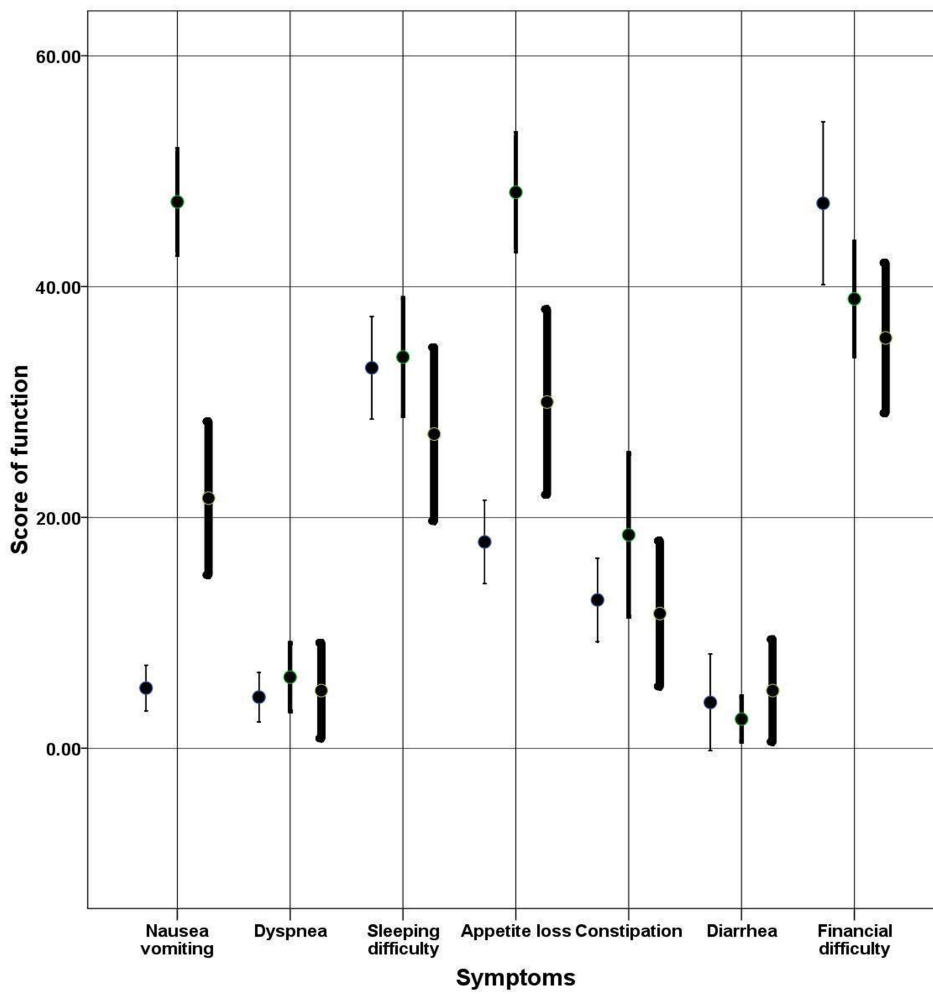

Figure 6.2 Patients' symptoms on the EORTC QLQ-C30 at baseline and post chemotherapy, for responders and non-responders.

Group:
Baseline
Post chemotherapy-no response
Post chemotherapy-response group

pain were also found using the SF-36 questionnaire. The dimensions score show that "no response" patients had lower QoL than "response" patients.

This study also found that both the response and no response groups showed the score deterioration in most of the dimensions and experienced worse symptoms compared to the baseline score (Table 6.3). Other factors which could have a negative impact on patients' QoL are patients' characteristics such as comorbidity, cancer diagnosis and stage of cancer. Meanwhile, only comorbidity showed significant impact on the physical function, pain and fatigue symptoms (data are not presented).

Table 6.3 Mean and standard deviation (SD) of QoL functions 5 days after chemotherapy, based on delayed emesis

	Response (Mean ± SD) *n* = 45	Non response (Mean ± SD) *n* = 134	*P* value
EORTC QLQ-C30			
General QoL	58.4 ± 17.5	58.4 ± 16.4	0.979
Physical function	71.6 ± 24.3	70.0 ± 22.1	0.673
Role function	66.6 ± 24.2	64.5 ± 24.8	0.590
Emotional function	93.9 ± 15.3	93.7 ± 13.2	0.956
Cognitive function	93.3 ± 16.3	92.7 ± 14.7	0.799
Social function	70.3 ± 19.9	72.1 ± 22.7	0.592
Pain	26.1 ± 24.6	31.9 ± 25.1	0.142
Fatigue	34.1 ± 22.2	41.3 ± 20.9	**0.032**
Nausea vomiting	21.7 ± 25.8	47.3 ± 25.2	**<0.001**
Dyspnea	5.0 ± 16.0	6.2 ± 16.2	0.650
Sleeping difficulty	27.2 ± 29.1	33.9 ± 28.2	0.140
Appetite loss	30.0 ± 31.1	48.2 ± 28.0	**<0.001**
Constipation	11.7 ± 24.4	18.5 ± 38.9	0.218
Diarrhea	5.0 ± 17.2	5.0 ± 34.6	0.993
Financial difficulty	35.6 ± 25.2	38.9 ± 27.2	0.423
SF-36			
General health perceptions	62.4 ± 20.5	59.1 ± 19.3	0.121
Physical function	57.6 ± 31.4	46.1 ± 32.4	**0.025**
Physical role function	23.8 ± 39.4	27.9 ± 39.6	0.504
Emotional role function	31.7 ± 45.3	25.5 ± 41.3	0.362
Mental health	77.4 ± 33.1	65.9 ± 30.9	**0.024**
Social function	63.3 ± 24.6	53.2 ± 21.3	**0.005**
Bodily pain	69.8 ± 27.4	60.8 ± 25.9	**0.034**
Fatigue	64.6 ± 19.1	61.3 ± 17.4	0.241
Health change	57.9 ± 33.1	51.1 ± 24.9	0.287

Values are means (SD). Significant score differences between the response and no-response groups are indicated in bold.

DISCUSSION

Our results show that, despite optimal initial prophylactic use of antiemetics followed by suboptimal prophylaxis for delayed nausea and emesis, most patients with gynecological cancer experience delayed emesis. We have to take into account that the standard of prophylactic antiemetic drugs which is used at our hospital is suboptimal. Despite this shortcoming we decided to study the relationship of CINV and QoL.

A previous study showed that around 70% of patients receiving chemotherapy in a community hospital experienced delayed emesis.[17] The present study shows a similar percentage of subjects experiencing delayed emesis (i.e., 74.9%). All patients were treated by a standard antiemetic regimen consisting of ondansetron and dexamethason one hour before the cisplatin treatment. Due to the cost of further ondansetron with dexamethason and certainly apepritant, suboptimal therapy with oral metoclopramide was prescribed for delayed emesis/vomiting. Based on the international guidelines, ondansetron or ganisetron in combination with dexamethasone on day 2 to day 5 should be given after highly emetogenic chemotherapy to prevent delayed emesis.[7] All of our patients were treated with metoclopramide over 5 days, after cisplatin treatment. Only 34.3% patients had complete response in the delayed phase. Poor control of patients' symptoms after chemotherapy interfered in our study with patients' QoL. In another study the metoclopramide efficacy was increased significantly by the augmentation of dexamethasone.[18]

The delayed emesis in our patient sample led to a significant negative impact on the patients' QoL. Significant impact was illustrated by more severe symptoms, such as fatigue, nausea, vomiting, appetite loss and pain after chemotherapy. Interestingly, the patients who did not experience delayed emesis also showed a deterioration of QoL. The scores of the various QoL-dimensions in EORTC QLQ-C30 questionnaire were lower than those in reference groups before the chemotherapy treatment. The symptom scores were also higher than those in the reference groups. This probably indicates that Indonesian gynecologic cancer patients have lower QoL and experience more severe symptoms than the same groups in the Netherlands before start of chemotherapy, possibly related to the suboptimal treatment of delayed nausea/emesis. A recent study in France suggested that the deterioration of physical function, role function and general health could be a reason for impaired QoL in newly diagnosed cancer patients.[19]

The present study showed that delayed emesis affects patients' symptoms such as fatigue, appetite loss and bodily pain. The higher score of the functions in the response group and the significant differences of function scores between the group of patients with 'response' and the 'no response' group indicate that delayed emesis interferes with patients' daily

function. Both 'response' and 'no response' groups showed that CINV interferes with patients' QoL. These findings are similar to other studies in cancer patients treated with moderately to highly emetogenic chemotherapy, despite the use of antiemetic. In addition, acute CINV affects patients' QoL even for the patients who do not experience nausea or vomiting during the delayed phase.[20] The patients' comorbidity should be considered as well as a factor which can impact on physical function, pain and fatigue.

In general, patients' QoL was decreased in our study after chemotherapy compared to baseline. These findings are similar to another study in community oncology setting across the US which revealed that chemotherapy-induced nausea and vomiting significantly interferes with patients' QoL.[1] Our study included cancer patients who received their first chemotherapy course with various emetogenic chemotherapy schedules.

General health perception, emotional and social function were maintained. This could be explained by the role of family and neighborhood support. One characteristic of the Indonesian society, especially in the rural area, is that many people come to the patient's house to give psychological support when the patient comes back from the hospital. This finding is supported by Noonan,[20] who reported that patients' QoL was not only affected by the symptoms of cancer and side effect of treatment, but also by the psychosocial condition, such as family support.The study on the survivorship in cancer patients suggested that the ability to return to family, social and work activities was an essential part of survivorship.[21]

Another study which used FLIE (Functional Living Index of Emesis) as the QoL instrument to study the relationship of CINV and patients' QoL, revealed that the score on FLIE after chemotherapy decreased significantly in the range of 21.6%-24.4%. Patients with CINV also had a decrease of health utility in the range of 15%-6.9%.[22] In addition, it has been reported that both acute and delayed emesis have significant impact on patients' daily functioning. Furthermore, it is frequently under-reported and untreated, since the patients experience these symptoms after they have left the hospital.[1] In our hospital a similar situation exists as patients leave hospital on average 4 hours after the chemotherapy has been given.

Different health care providers in the Western world have variously predicted the incidence rates of CINV and their prediction in prescription of antiemetics has also varied. For example, in patients receiving highly emetogenic chemotherapy, the use of 5-hydroxytriptamine receptor antagonists and dexamethasone as antiemetics led to an underestimation by the health providers in predicting delayed emesis.[23] In contrast, the use of aprepitant in combination with dexamethasone and 5-hydroxytriptamine receptor antagonists led to health care providers' overestimation in predicting delayed

CINV. Furthermore, it has been suggested that the health care providers increase their appreciation of delayed CINV incidence by using structured patients-reported outcome instruments.[5]

On the basis of the results in the present study, we also recommend that the health care providers in Indonesia should closely monitor delayed emesis and prescribe an appropriate antiemetic prophylaxis.

The results of our study indicate that poor control of delayed emesis in cancer patients treated by highly emetogenic chemotherapy unnecessarily reduces the patients' QoL. Thus, appropriately potent antiemetics should be used to prevent delayed emesis. In clinical practice, the oncologist who prescribes chemotherapy in combination with suboptimal chemotherapy, should be aware of delayed CINV, since the delayed emesis adversely affects patients after they have left the hospital. Furthermore, the delayed emesis should be closely monitored to improve the patients' QoL and patients' adherence in following the next cycles of chemotherapy. Cognitive-behavioural interventions, counseling and supportive therapy seem to be additional promising strategies to improve gynecological cancer patients' QoL and their survivorship.[1,21]

Conclusion

Patients with gynecological cancer in our study experienced severe symptoms, such as fatigue, nausea, vomiting, appetite loss and pain after chemotherapy despite adequate prophylactic use of antiemetics for acute nausea and vomiting but with insufficient prophylactic antiemetic therapy for chronic nausea and vomiting. These symptoms affected other domains as shown in both the EORTC QLQ-C30 and the SF-36 questionnaires.

Poor control of patients' chronic nausea and vomiting after chemotherapy has a negative impact on patients' QoL.

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