

## **Nausea, Vomiting and Retching of Patients with Cervical Cancer undergoing Chemotherapy in Bali, Indonesia**

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**Background:** Nausea, vomiting and retching (NVR) was the frequently reported and troublesome adverse effect for patients receiving chemotherapy.

**Purpose:** This study is a part of a larger study which aims to describe the NVR symptom experience in cervical cancer patients undergoing chemotherapy in Bali, Indonesia, and examine relationships with individual's risk factors.

**Method:** Sixty-six patients with stage II and III cervical cancer receiving Paxus (Paclitaxel)-Cisplatin at the second or the third cycle were enrolled. NVR was measured by the Index of Nausea, Vomiting and Retching (INVR) at the second day of their chemotherapy. This current study included only patients with age ranged between 32 to 65 years (M = 47.15, SD = 9.64, min-max age 35 – 65 years).

**Result:** The result showed that the NVR score was at a moderate level. Younger subjects (age 32-50 years old) reported significantly higher NVR scores than that of older subjects (age 51-65 years old) ( $t = 2.76, p = .007$ ). The subjects with higher anxiety scores reported significantly higher NVR scores than those with lower anxiety scores ( $t = -2.41, p = .019$ ). Subjects who had experience in motion sickness had significantly higher NVR scores (M = 12.69, SD = 2.60) than those who did not (M = 9.23, SD = 2.86) and the difference was statistically significant ( $t = 4.98, p < .01$ ). Meanwhile, no significant difference was found between subjects who reported their expectation to have nausea and those who did not ( $t = 0.08, p = .94$ ).

**Conclusion:** The findings provide valuable information regarding NVR and the individual risk factors among patients with cervical cancer undergoing chemotherapy. Nurses should assess the anxiety level and a history of motion sickness of patients planned for chemotherapy and offer preventive interventions to prevent and control NVR occurrence and its distress.

**Keywords:** cervical cancer, chemotherapy, nausea, vomiting and retching

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## **Background**

Cervical cancer is the most common cancer in women in Indonesia (Tjindarbumi & Mangunkusumo, 2002; Parkin, Bray, Ferlay & Pisani, 2005), and becomes the second type of cancer that kills women after breast cancer (Domingo et al., 2008). Few data are available describing the prevalence of cervical cancer in Indonesia. Since Indonesia does not have an established cancer registry, Department of Health assumes cancer incidence to be 100 per 100,000 people. Iswara, Suwiyoga, Mayura and Artha (2004) reported that cervical cancer represented approximately three-quarters of the gynecologic cancers. Cases of cancer in Bali have been found to be 29,696 cases; 55 percent of which is cervical cancer (Bali Provincial Health Office, 2005). From the registration record of one tertiary hospital in Bali, it is known that the number of patients with cervical cancer have been increasing over the years. There were 804 cases of cervical cancer in 2005, 1,554 cases in 2006, and the highest rate was 2,026 cases in 2007.

Chemotherapy is one of cancer treatments that can destroy cancerous cells and prevent metastasis, however it has various side effects such as nausea, vomiting and retching. These side effects are distressing symptoms for patients with cancer, especially those who are receiving chemotherapy (Bender, McDaniel, Murphy-Ende, Pickett & Rittenberg, 2002; Rhodes & McDaniel, 2001), and can potentially lead to patient's refusal to continue with the most effective chemotherapy (Hesketh, 2000). Cohen, de Moor, Eisenberg, Ming and Hu's study (2007) found that 38% of patients who received a new chemotherapy regimen developed acute nausea and vomiting, and 64% had delayed nausea and vomiting that highly related to having in the previous cycle. Liao et al. (2005) suggests that good control of acute chemotherapy-induced nausea and vomiting, particularly during the initial treatment received by chemotherapy-naïve patients, has a positive impact on the control of delayed nausea and vomiting.

The incidence and severity of nausea, vomiting and retching in patients receiving chemotherapy vary, depending on the type and dose of chemotherapy, combination of medication, and individual characteristics (Grunberg, 2004; Smeltzer, Bare, Hinkle & Cheever, 2008). These occur quite frequently under various conditions and can be triggered by different inputs or combinations of input mechanisms (Shelke, Mustian & Morrow, 2004). These unpleasant sensations can appear, either as a result of treatment or a disease itself and significantly affect quality of life of patients and compliance with therapy (Rhodes & McDaniel, 2001). This study presents the findings based on 66 patients with cervical cancer with regard to the level of nausea, vomiting, and retching and discusses the individual's risk factors related to NVR.

## **Objectives**

The objectives of this study were: (1) to describe the level of NVR experience among cervical cancer patients undergoing chemotherapy in Bali, Indonesia, and (2) to examine relationships between individual's risk factors and experience of NVR among cervical cancer patients undergoing chemotherapy in Bali, Indonesia.

## **Methods**

### *Setting*

The study was conducted at a gynecology ward, of a tertiary and referral hospital in eastern part of Indonesia, Bali. This ward is third class care consists of 6-8 beds, separated by a curtain from each other. It provides services for the poor patients or the patients who use health insurance for poor people (*ASKESKIN*).

### *Sample*

Sixty six (66) patients with cervical cancer receiving chemotherapy were recruited. The inclusion criteria included: age 30 years old or above, being at stage II and III of cervical cancer, being at the cycle 2 and 3 of chemotherapy: Paxus-Cisplatin regimen, having nausea/vomiting in their previous cycle, having anxiety at mild to moderate level and no current chronic psychiatric condition.

### *Instrumentations*

A set of questionnaires was used to collect the following data: subjects' characteristics, level of anxiety and nausea, vomiting and retching. The level of anxiety was measured by using the Visual Analogue Scale-Anxiety (VAS-A).

The VAS-A is a horizontal line, 100 mm in length. Patients were advised to mark on a line that represents their current level of anxiety. The VAS-A score was determined by measuring in millimeters from the left hand end of the line to the point that the patient marked. The scores on this VAS-A were categorized into four levels: no anxiety (0), mild anxiety (1-25), moderate anxiety (26-50), severe anxiety (51-75), and worst anxiety (76-100) (Billhult, Bergbom & Stener-Victorin, 2007).

The Index of Nausea, Vomiting and Retching (INVR) developed by Rhodes was used to measure nausea, vomiting and retching. The INVR is an eight-item self-report tool. Each item was assigned a number based on a predefined scoring algorithm. A numeric value to each response was ranged from 0, the least amount of distress, to 4, the most/worst distress. Total symptom experience from nausea, vomiting and retching was calculated by summing the patient's responses to each of the 8 items on the INVR. The range of scores was ranged from 0 to 32. The score of 0 indicated none NVR, 1-8 indicated mild NVR, 9-16 indicated moderate NVR, 17-24 indicated severe NVR, and 24-32 indicated worst NVR (Rhodhes &

McDaniel, 2001).

### *Data collection*

At the second day of each subject's chemotherapy administration, the eligible subjects were approached by the nurse working in the study ward. After they indicated their interest to participate in the study, the primary researcher or the research assistant introduced herself, informed about the study protocol, and obtained an informed consent. They were then asked to respond to the questionnaires described above. For the subjects who were unable to read or had vision problems, the primary researcher or the research assistant read to them verbatim.

### *Data Analysis*

Both descriptive statistics and inferential statistics were used in this study. Descriptive statistics were used to describe the demographic characteristics, health-related characteristics and nausea and vomiting experience. Independent t-test was used for examining the contribution of individual risk factors (age, anxiety level, history of motion sickness, patient's expectation to have nausea, and experience in receiving other complementary therapy) to the current experience of NVR. The assumptions of normality and homogeneity of variance were examined prior to the analyses and revealed no violation in all datasets.

### *Ethical Consideration*

This study was approved by the Ethics Committee of Faculty of Nursing, Prince of Songkla University, Thailand and also granted for ethical clearance by the Research and Development Division, of a study hospital in Bali - Indonesia. The subjects received all necessary information related to study concerning human right issues. They were told that their identities would be kept secret. All the data were stored in a confidential manner and destroyed after the completion of the study. They could ask questions about this study and

had the right to withdraw from the study at any time without any consequences.

## Results

### *The Subject's Characteristics*

Sixty-six women with cervical cancer undergoing chemotherapy were recruited from gynecological ward of a tertiary hospital. The age ranged between 32 to 65 years old with the mean of 47 years. The majority of them were married and Hindu holders. About 53% of subjects had elementary school education and approximately 47% worked as farmers (Table 1).

Table 1

*General Demographic Characteristics of the Group (N = 66)*

| <b>Characteristics</b>                                | <b>n</b> | <b>%</b> |
|---|----------|----------|
| Age (M = 47.15, SD = 9.64, min-max age 32 – 65 years) |          |          |
| Younger age (32-50 years)                             | 39       | 59       |
| Older age (51-65 years)                               | 27       | 41       |
| Marital status  |          |          |
| Married   | 58       | 88       |
| Widowed   | 8        | 12       |
| Religion  |          |          |
| Hindu   | 54       | 82       |
| Non-Hindu<br>(Buddhist/Muslim)                        | 12       | 18       |
| Educational level                                     |          |          |
| Elementary school                                     | 35       | 53       |
| Junior high school                                    | 16       | 24       |
| High school   | 13       | 20       |
| No education  | 2        | 3        |
| Occupation  |          |          |
| Farmer  | 31       | 47       |
| Private employee                                      | 22       | 33       |
| Housewife   | 13       | 20       |

Considering the subjects' health-related characteristics, about 39% subjects had experience in motion sickness (Table 2). Only one subject had consumed alcohol and more than three-quarters expected that they might have nausea (86%). Majority of the subjects had

moderate level of anxiety with the mean anxiety score of 35.5 (SD = 10.50, min-max 13 – 50). Only one subject had experienced of receiving foot massage and less than a quarter of them (17%) had no experience of receiving any complementary therapies. More than half of subjects were in the second cycle of chemotherapy (53%) and all subjects did not have co-morbid disease.

Table 2

*General Health-Related Characteristics of the Group (N = 66)*

| <b>Characteristics</b>                                   | <b>n</b> | <b>%</b> |
|--|----------|----------|
| Experience in motion sickness                            |          |          |
| Yes  | 26       | 39       |
| No   | 40       | 61       |
| Experience of alcohol consumption                        |          |          |
| Yes  | 1        | 2        |
| No   | 65       | 98       |
| Expectation of nausea                                    |          |          |
| Yes  | 57       | 86       |
| No   | 9        | 14       |
| Anxiety score<br>(M = 35.5, SD = 10.50, min-max 13 – 50) |          |          |
| Mild (10-25)   | 10       | 15       |
| Moderate (26-50)   | 56       | 85       |
| Experience of receiving foot massage therapy             |          |          |
| Yes  | 1        | 2        |
| No   | 65       | 98       |
| Experience of receiving complementary therapy            |          |          |
| Yes  | 11       | 17       |
| No   | 55       | 83       |
| Cycle of Chemotherapy                                    |          |          |
| 2  | 35       | 53       |
| 3  | 31       | 47       |
| Stage of Cancer  |          |          |
| II   | 26       | 39       |
| III  | 40       | 61       |

*Nausea, Vomiting and Retching in Cervical Cancer Patients Undergoing Chemotherapy*

The patients with cervical cancer undergoing chemotherapy participating in this study reported having moderate NVR experience (Table 3).

Table 3.

*Mean, Standard deviation, and Level of Symptom Experience of NVR (N = 66)*

| Subscales              | Items on Scale | Potential Range of Scores | Min-Max scores | Mean         | SD          | Level           |
|------------------------|----------------|---------------------------|----------------|--------------|-------------|-----------------|
| <b>NVR Experience</b>  |                |                           |                |              |             |                 |
| Nausea experience      | 4, 5, 7        | 0-12                      | 4-10           | 7.67         | 1.47        |                 |
| Vomiting experience    | 1, 3, 6        | 0-12                      | 0-6            | 2.44         | 2.41        |                 |
| Retching experience    | 2, 8           | 0-8                       | 0-3            | 0.48         | 0.88        |                 |
| <b>Total NVR Score</b> |                | <b>0-32</b>               | <b>4-16</b>    | <b>10.59</b> | <b>3.23</b> | <b>Moderate</b> |

*The Relationship of Individual Risk Factors and NVR*

Independent t-Test was performed to examine whether each individual risk factors contributed to the NVR scores (Table 4). The findings revealed that younger subjects (age 32-50 years old) reported significantly higher NVR scores than those of older subjects (age 51-65 years old) ( $t = 2.76, p = .007$ ). This result indicates that the older they were, the lower the level of nausea, vomiting, and retching they felt. Meanwhile, the subjects with higher anxiety scores reported significantly higher NVR scores ( $t = -2.41, p = .019$ ). These findings demonstrate that the more anxiety they were, the worse NVR they experienced. This study also revealed that the subjects who had experience in motion sickness had significantly higher of the NVR scores ( $M = 12.69, SD = 2.60$ ) than that who did not ( $M = 9.23, SD = 2.86$ ) and the difference was statistically significant ( $t = 4.98, p = .00$ ). Surprisingly, there was no significant difference of subjects who reported their expectation to have nausea and those who did not ( $t = 0.08, p = .94$ ). Similarly, no significantly difference also found in the subjects who had experience in receiving other complementary therapy and those who did not ( $t = -1.60, p = .11$ ).



Table 4

*Comparison of Individual Risk Factors and NVR Score using Independent t-Test (N = 66)*

| Variables   | N  | %  | M     | SD    | t     | p value |
|---|----|----|-------|-------|-------|---------|
| Age   |    |    |       |       | 2.76  | .007    |
| Young age (32-50 yr)                                | 39 | 59 | 11.46 | 3.08  |       |         |
| Old age (51-65)                                     | 27 | 41 | 9.33  | 3.08  |       |         |
| Anxiety   |    |    |       |       | -2.41 | .019    |
| Mild (1 - 25)                                       | 10 | 15 | 8.40  | 2.989 |       |         |
| Moderate ( 26 - 50)                                 | 56 | 85 | 10.98 | 3.136 |       |         |
| Experience in motion sickness                       |    |    |       |       | -4.98 | .000    |
| Yes   | 26 | 39 | 12.69 | 2.60  |       |         |
| No  | 40 | 61 | 9.23  | 2.86  |       |         |
| Expectation of nausea                               |    |    |       |       | 0.08  | .940    |
| Yes   | 57 | 86 | 10.58 | 3.31  |       |         |
| No  | 9  | 14 | 10.67 | 2.87  |       |         |
| Experience of receiving other complementary therapy |    |    |       |       | -1.60 | .114    |
| Yes   | 11 | 17 | 12.00 | 3.63  |       |         |
| No  | 55 | 83 | 10.31 | 3.10  |       |         |

## Discussion

In this study, patients received cisplatin agent that is one of the high risk emetogenic agents. The results showed that the NVR experience among cervical cancer patients undergoing chemotherapy in Bali, Indonesia was at a moderate level. There are several identified factors that might contribute to these results. Firstly, the cycle of chemotherapy might contribute to the severity of NVR symptoms. This current study had involved the patients receiving chemotherapy on the second cycle and the third cycle. The NVR symptoms were usually more severe on the following cycle and anticipatory nausea and vomiting (ANV) may develop (McRonald & Fleisher, 2005), particularly in the fourth cycle (Roscoe, Morrow, Aapro, Molassiotis & Oler, 2010), and was a significant predictor by cycle five

(Watson et al. as cited in Hickok et al., 2001). A possible explanation for the moderate level of the NVR scores could be due to the relatively high number of patients with cycle 2 of chemotherapy. Thus, the NVR scores might be less severe.

The second factor is regarded to the combination of chemotherapy treatments. A previous study found that in the combined therapy (radiation and chemotherapy), subjects reported more symptom of distress than chemotherapy alone (Oh, 2004). Patients receiving a combined therapy of radiation therapy and chemotherapy experienced significantly higher level of symptom occurrence than those receiving chemotherapy only (Hur et al., 2002). This may suggest that the combination of chemotherapy is an important factor contributing to the symptoms experience of NVR. This present study assessed patients who received chemotherapy only and this might be contributed to the severity of NVR symptom.

Thirdly, considering the severity of the disease, the stage of cancer might be another factor that contributes to NVR. Patients with cervical cancer were suffered from several symptoms as a result of their disease or the side effects of cancer treatments. The potential causes of NVR in cancer patients are numerous, especially in those with advanced or metastatic disease (Rhodes & McDaniel, 2001). As cervical cancer progresses into more advanced stages, symptoms begin to appear (Yarbro, Wujcik & Gobel, 2011). Molassiotis, Yung, Yam, Chan and Mok (2002) stated that late stage of disease was a predictor of acute nausea and vomiting. A study conducted by Oh (2004) found that symptom experience was significantly higher in patients with advanced stage (Stages III and IV) than patients in early stage group. This study involved the patients at stage II and III of cervical cancer without co-morbidity disease. Therefore, the stage of disease is suspected to contribute to the moderate level of NVR.

Another factor could be related to beliefs and custom. The Balinese believe that all illnesses, both the physical and mental illnesses have specific causes. They believe western

concepts to be true within the context of certain illnesses. They also believe that illness and misfortune may result from laws of karmic cause and effect (Hobart, as cited in Arriaga, 2010). Therefore, in seeking a treatment for the disease, they combine the medical treatment and some ritual prayer that they believed in. It makes them believe that the god will give whatever is the best for their family or the ill person. Therefore, the symptoms perceived will be lower and will resulting in the experience of the NVR. Nevertheless, research on the symptom experience of side effect of the cancer intervention based on cultural background in Indonesia, to our knowledge, virtually absent.

Regarding individual risk factors, the findings of this study revealed that age, anxiety and experience in motion sickness correlated to the NVR scores. This finding demonstrated that older aged patients (51-65 years old) tended to tolerate chemotherapy better than younger patients (age 32-50 years old). This may relate to patients' response to the antiemetic therapy. A study conducted by Perez (as cited in Noonan, 2005) found that older patients (> 50 years) have better response to antiemetic therapy compared to the younger patients (< 50 years). Similar to the previous study, it was found that younger adult patients (< 50 years old) had greater NVR than older adult patients (Watson, Meyer, Thomson & Osofsky, as cited in Aapro Molassiotis & Olver, 2005).

Anxiety is a significant psychological predictor of chemotherapy-induced nausea and vomiting. This study showed that subjects with higher anxiety scores reported having significantly higher NVR scores. Similar to Adrykowski and Gregg's study (as cited in Hawthorn, 1995), they found state anxiety is significantly related to both severity and incidence of nausea. Moreover, anxiety can be exacerbated by a prior history of nausea and vomiting associated with chemotherapy (Schnell, 2003).

This study also found that experience in motion sickness had relationship with NVR scores. The result revealed that subjects who had experience in motion sickness had

significantly higher NVR scores than the subjects who did not have. The finding of this current study is consistent with study from Schnell, (2003). They found that patients with a history of motion sickness may have a lower threshold to nausea, vomiting and retching than the rest of the population.

In addition, expectation was an important factor that contributes to NVR. Several studies stated that patients' expectation of NVR may potentiate their experience of these effects (Feyer et al., 2005; Liao et al., 2005; Montgomery & Bovbjerg, 2003) and can predict either the occurrence or the severity of common side effect such as NVR (Morrow, 1989). However, in this study, we found that patient expectation did not correlate with NVR scores. Similar result with previous study that investigated the effect of an expectancy manipulation designed to reduce nausea expectancy on chemotherapy-induced nausea (Shelke et al., 2008). They found that changing nausea expectancies possibility does not change occurrence of nausea. The discrepancies found between the expectation of NVR and NVR scores suggest that patients did not have accurate pretreatment expectations.

Considering the experience of receiving other complementary therapy, the findings indicated that most patients preferred to use pharmacological therapies alone rather than combined with non-pharmacological therapies. This condition may be due to a lack of information regarding the use of complementary therapies in order to alleviate symptoms of chemotherapy side effects. Moreover, studies on complementary therapies in Indonesia, particularly Bali, are limited.

Finally, there is a fairly wide variation in the individual patient's susceptibility to the development of NVR, thus there is a reasonably wide variation in the control of NVR. Adequate control of NVR is not often predictable within an individual patient. Some patients are virtually incapacitated with NVR from typically well-tolerated chemotherapeutic agents, while, others require only minimal anti-emetic intervention for virtually complete control.

Therefore, nurses should be vigilant in assessing this distressing symptom, and considering to patients risk factors with individually seeking.

### **Conclusions**

In conclusion, symptom experience of NVR among cervical cancer patients receiving chemotherapy in Bali, Indonesia was at a moderate level. Age, anxiety and experience in motion sickness were individual risk factors that contributed to NVR. Individual risk factors are essential and statistically significantly related to the patients' experience of nausea, vomiting and retching.

### **Recommendations**

Nurses should consider individual risk factors related to nausea, vomiting and retching induced chemotherapy. Further study regarding to NVR in a different stage of cancer and different cycles of chemotherapy are needed. Another study regarding nursing intervention for reducing NVR in cervical cancer patients had conducted and the results will be discussed in the other article.

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