Breast cancer is the most common form of cancer and a common cause of death among women worldwide (Bray, McCarron, & Parkin, 2004; Shih, Wan, & Chan, 2009). In Sweden, the median age at diagnosis is 64 years and less than five percent of those diagnosed are younger than 40 years (Bergman, Jaresand, & Johansson, 2010). Common treatments include surgery, endocrine treatment, antibodies, chemotherapy, and radiation therapy (Abeloff et al., 2008). Chemotherapy and radiotherapy often are associated with varying degrees of side effects. The most common acute side effects related to chemotherapy are nausea, vomiting, and decreased production of white blood cells (Hassan & Yusoff, 2010). On occasion, those side effects interrupt the implementation of the treatment and can be triggered by underlying symptoms of anxiety, depression, and poor adherence to prescribed antiemetics, which may have cumulative effects on the incidence and severity of nausea and vomiting. That also can negatively affect the social perspective and, therefore, women’s well-being. Women receiving chemotherapy can experience stress if their personal economy is affected, and the whole family often is involved in the treatment. In addition, nausea and vomiting related to chemotherapy can lead to anorexia, metabolic problems, gastric irritation, and problems with the esophagus. Those effects can, in turn, impair cognitive and physical status and lead to isolation; in addition, they are particularly harmful to the patient’s quality of life during treatment (Hesketh, 2005; Hilarius et al., 2012; Molassiotis, Stricker, Eaby, Velders, & Coventry, 2008).

Different degrees of nausea and vomiting can be triggered depending on which type of chemotherapy is being used (Hesketh, 2005). Nausea and vomiting can be acute, delayed, or conditioned (Hilarius et al., 2012; Molassiotis et al., 2008). The intensity and frequency of chemotherapy-related nausea and vomiting are helpful signs to determine how serious these side effects are (Badger, Braden, & Mishel, 2001). The absence of disease is important for health-related quality of life, but the feeling...
of complete physical, mental, and social well-being actually determines quality of life (Hesketh, 2005). A woman’s age (younger than 50 years) is a well-known predictor of chemotherapy-induced nausea and vomiting (Liau et al., 2005). Regular exercise and high consumption of alcohol decrease the risk for nausea and vomiting, and morning sickness during prior pregnancies increases the risk (Hesketh, 2005; Liau et al., 2005; Shih et al., 2009). In the current study, well-being in relation to treatment was considered crucial for changes in patient quality of life over time. The purpose of the current study was to describe how nausea, vomiting, and well-being vary during the first 10 days after chemotherapy for women with breast cancer.

Methods

This pilot study had a repeated-measurements design, took place during 10 days in 2012, and was carried out in an outpatient oncology clinic in a county hospital serving 320,000 individuals in southern Sweden. The study is a part of a larger ongoing study on the side effects of chemotherapy. The Regional Ethical Review Board in Linköping approved the study (Dnr 2010/1531-31, December 2010). The women were informed about the study and the significances of their participation, and they could withdraw at any time (World Medical Association, 2013). The participants’ identities were not stored on electronic media.

Participants

Thirty-nine women were included in the study. Inclusion criteria for the study were being a woman treated for breast cancer with first-line chemotherapy using the FEC (fluorouracil, epirubicin, and cyclophosphamide) regimen, which is classified as a high to medium emetogenic regimen. Women with no knowledge of the Swedish language, previous treatment with IV chemotherapy, or neurologic or psychological disorders such as extreme anxiety were excluded.

In connection with their first chemotherapy treatment, 50 women were informed about the study by the first author of this article. Interested women were given additional verbal and written information about the study and how to use the visual analog scale (VAS). In total, 39 women (78%) were willing to participate and signed a consent form. Eleven refused to participate for a variety of reasons, including an overload of information that resulted in stress.

| TABLE 1. Distribution of Nausea and Vomiting Severity by Age (N = 39) |
|-----------------------------|-----------------------------|
| Variable                    | 50 Years or Younger (n = 14) | Older Than 50 Years (n = 25) |
| No nausea                   | 1                           | 5                           |
| Acute nausea                | 9                           | 6                           |
| Delayed nausea              | 4                           | 14                          |
| Vomiting*                   | 1                           | 5                           |

*Six participants had vomiting in addition to reported nausea.

Measurement

Daily self-measurements were conducted for 10 days with the help of a structured diary developed to record nausea, vomiting, and well-being in a Swedish national quality register database (Börjeson, 2009). The diary provided information about the number of vomiting episodes, how often the women felt nauseated, their estimated well-being, and variations during the day. The diary included closed questions where the intensity of nausea was estimated morning and evening using a scale with four alternatives: none, mild, moderate, and severe nausea. The women also documented any vomiting episodes. The estimation of well-being had four options: very good, good, poor, or very poor. This was documented every morning and evening. In the last part of the diary, patients were given instructions for antiemetic medication for the first four days. On day 10 after chemotherapy treatment, a structured telephone follow-up was used to obtain a self-estimated degree of nausea using a VAS scale ranging from 0 (no nausea) to 10 (worst nausea). The VAS is an instrument for measuring a quality or effect believed to exist at a given moment that cannot easily be measured directly (Boogaarts, Vanacker, Seidel, Albert, & Bardiau, 2000). In addition, the women were asked to indicate which of the 10 days they considered the worst day for nausea and vomiting.

Data Analysis

Thirty-nine diaries, each with 10 days’ worth of self-reported nausea, vomiting, and well-being data, were used for the analysis. Of the 10 days analyzed, the evening of the first day measured acute nausea after chemotherapy and was considered the baseline. To describe the delayed nausea, the mornings of day three and day five were selected as follow-up days. These days were selected because the first week after treatment is considered the most significant in terms of these side effects (Booth et al., 2007; Shih et al., 2009). In the analysis, the women were divided into two groups (aged 50 years or younger and aged older than 50 years) according to age, as age is regarded as an important independent factor for nausea and vomiting in the literature (Hesketh, 2005; Shih et al., 2009). That also was done because the oncology department where the study was conducted administers an additional antiemetic to women aged 50 years or younger.

The method used in the current study is based on an analytical method (Avdic & Svensson, 2010; Svensson, 2005, 2007). The method analyzes the presence of systematic changes in terms of both position (relative position [RP], which varies between −1 and +1) and concentration (relative concentration [RC], which also varies between −1 and +1). If the direction of the ordered categorical measurement scale ranges from “strongly agree” to “strongly disagree,” a result closer to +1 means an improvement, and a result closer to −1 indicates a change to the worse. If the scale is in the reversed order, a reversed interpretation is used.

This method analyzes the occurrence of individual differences by studying individual changes in range (rank variation [RV], which varies between 0 and +1), which gives a measurement of the heterogeneity of the changed pattern relative to the change in the group that could be expected if it was homogeneous. In addition, a measurement of the proportion that has not changed (percent agreement [PA]) was included. If PA is less than 100% and RC and/or RP is high while the RV is low, a homogeneous
change in pattern has occurred. However, if a high value of RV occurs, it indicates the presence of individual differences (heterogeneity) from the group of common change patterns. The confidence interval used is 95%. If the frequency of RC or RP contains zero, this will not reject the null hypothesis; no change has occurred. The same applies if PA is close to 100% (Svensson, 2005, 2007). In the analysis, statistics such as medians, as well as figures and tables, have been used to describe the material (Altman, Machin, Bryant, & Gardner, 2000).

Results

Thirty-nine women were included in the study. Participants ranged in age from 34–79 years (median = 60), with 14 aged 50 years or younger and 25 older than 50 years. The majority were nonsmokers (n = 32) and married or cohabiting (n = 30). Twenty-five participants were actively working and 14 were retired. In addition, body mass index scores ranged from 18–36 (median = 60).

Nausea

Thirty-three (85%) of the women experienced nausea, albeit to different extents, with both acute and delayed nausea reported (see Table 1). When comparing the evening of day one (baseline), the morning of day three, and the morning of day five (follow-up), individual variations were obvious: 23 women did not feel nauseated during the first evening but, in comparison, 19 women felt no nausea on the morning of day three. Estimations of nausea during the fifth day varied. Of the 24 women who experienced nausea on the evening of day one, 15 remained nausea-free, 8 had mild nausea, and 1 experienced moderate nausea on the morning of day five. The change in nausea between baseline and follow-up days exhibited no uniform pattern of change in any direction, as determined by the low values of RC and RP (see Table 2). Some patients estimated more nausea, some felt better. The value of the RV between baseline and day three suggests specific individual change patterns; however, that does not persist in the change between baseline and day five.

The telephone follow-up on day 10 following treatment revealed the day women experienced their worst episode of nausea (see Figure 1). The day assessed as the worst was the same as the day they felt ill, experienced nausea, vomited, or felt bad for any other reason. This also was defined by the VAS scale estimates related to nausea and vomiting. The VAS scale measured the nausea estimated to be the worst during the 10 days documented (see Figure 2).

Vomiting

The study shows that six of 39 (15%) women experienced vomiting associated with the chemotherapy. Five of those women were older than 50 years. A marked variation was observed in which days participants reported vomiting, with one woman reporting vomiting on the first three days (one episode each day) and five women each vomiting one day in the study period (days one, two, three, five, and nine).

Well-Being

The chemotherapy treatment affected the women’s well-being and varied from bad to good and vice-versa depending on what time of day the nausea occurred, but that was independent of age. The individual differences that occurred between baseline and follow-up days were obvious. Of the 20 women who estimated well-being as good on baseline, 15 retained that estimate (good) on follow-up days. Among the 13 women who had a low (bad or very bad) estimate regarding well-being on baseline, the well-being estimates on the morning of day three varied. Five still felt bad, five felt good, and one estimated her well-being to be very good. Two who judged themselves as feeling very bad had changed their estimates to good. The results show that more than half of the women experienced improved well-being from day one to day three or five.

| TABLE 2. Estimated Nausea and Well-Being From Baseline to Days 3 and 5 |
|---------------------------------|---------|-------|-------|---------|
| Variable                        | PA (%)  | RP    | RC    | RV      |
| Nausea baseline to day 3        | 44      | -0.0519 | 0.175 | 0.1645  |
| Nausea baseline to day 5        | 62      | -0.0007 | 0.084 | 0.0623  |
| Well-being baseline to day 3    | 59      | -0.10717| 0     | 0.1078  |
| Well-being baseline to day 5    | 37      | -0.142 | 0     | 0.226   |
| PA—percent agreement; RC—relative concentration; RP—relative position; RV—rank variation |

FIGURE 1. Patient Estimation of Worst Day of Nausea (N = 39)
The analysis of the estimates of well-being shows a somewhat more heterogeneous pattern of change than for nausea. The pattern of change is neither homogeneous nor does it move in any certain direction.

Discussion

In this pilot study, individual variation of nausea, vomiting, and well-being related to chemotherapy treatment—regardless of age—was found. A special problem regarding chemotherapy-related nausea and vomiting was the experience of delayed nausea when standard drugs occasionally failed to prevent the symptoms. This was confirmed in a prior study, which concluded that even when the standard treatment for nausea was given before the chemotherapy, it was not always enough to control nausea and vomiting related to chemotherapy (Shih et al., 2009). It also has been indicated that younger women are more vulnerable to nausea and vomiting (Roscoe et al., 2010). Previous studies determined that the older women are and the more illnesses they have, the harder it can be to maintain a normal life (Browall, Persson, Ahlberg, Karlsson, & Danielson, 2009; Mkanta, Chumble, Richard, & Kobb, 2007). However, older women, as opposed to their younger counterparts, might have life experiences such as other diseases and coping strategies built in that can leave them better equipped to handle a cancer diagnosis.

Thirty-three women experienced nausea, with six of them also vomiting. The small number of women who vomited does not mean that the problem was of less importance. On the contrary, this is an important part of the results. Despite advanced drugs used to prevent chemotherapy-related nausea and vomiting, vomiting was still a fact for some. In younger women (aged 50 years or younger), acute nausea occurred in nine participants. Among the women older than 50 years, the results were the opposite, with six women experiencing acute nausea. Delayed nausea was predominantly difficult in the older group and occurred in 14 women.

Notably, the younger age group was treated with additional drugs to prevent nausea and vomiting, which may have contributed to the differences in nausea and vomiting observed between the younger and older women. That can also, to a lesser extent, explain the variation regarding well-being. The assessment of the worst day and the VAS scale assessment of nausea and vomiting showed variations. These variations are also an indication of how inconvenient the nausea and vomiting is, related to chemotherapy, which affects their well-being.

The study revealed that most women estimated chemotherapy-related nausea and vomiting with great variety. Some women reacted in a unique way and did not follow the expected pattern in terms of acute nausea, delayed nausea, and vomiting consistent with the previous study (Roscoe et al., 2010). Standardized procedures often are in place for managing these symptoms in healthcare systems, but the results of this pilot study point to the appeal of a more individualized approach to meet antiemetic needs and to better care for those women who do not follow the expected pattern. In addition, health care is, for the most part, focused on pharmacologic methods (Mulders, Vingerhoets, & Breed, 2008). Because evidence exists that nonpharmacologic approaches can affect nausea and vomiting in a positive manner, these could be used as a complement to conventional pharmacologic treatments (Navari & Camp-Sorrell, 2010; Roscoe et al., 2006).

In the current study, well-being was found to be dependent on the absence of nausea and vomiting, a result supported by an earlier study (Hassan & Yusoff, 2010). However, nausea is not the only problem affecting the well-being of these women (Mulders et al., 2008), as they can have difficulties controlling their life situation. The feeling of having a serious disease that the individual cannot influence, as well as the expected side effects of the treatment, have been shown to decrease well-being (Evangelista & Santos, 2012). Another study showed that women's well-being is affected by the diagnosis itself (Salonen, Kellokumpu-Lehtinen, Tarkka, Koivisto, & Kaunonen, 2011), quite apart from well-being related to the chemotherapy treatment and to the side effects mentioned earlier. Women who are treated for breast cancer need to be seen and cared for with a holistic perspective. The current study shows that significant individual variations for nausea and vomiting occur both in intensity and over time in women treated for breast cancer with chemotherapy; that result also applies to well-being. Personalized treatment of nausea and vomiting related to chemotherapy is, therefore, an important step for healthcare providers in improving patient well-being and quality of life.

Implications for Practice

- Encourage patients to use a diary after every treatment to compare the impact of treatments on daily life.
- Consider patients’ previous experience with nausea when choosing an antiemetic treatment.
- Have the attending nurse call patients before every treatment to determine the patients’ situation, allowing upcoming antiemetic treatment to be adjusted accordingly.

The results of this study imply that careful monitoring of each patient after a chemotherapy course and prior to the following

![Visual Analog Scale Score](image-url)
course would be very helpful in optimizing the care of women with breast cancer receiving emetogenic chemotherapy. Because of large, individual variations in nausea and vomiting postchemotherapy, the use of a personalized approach to the treatment of nausea and vomiting is warranted.

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References


Hassan, B.A., & Yusoff, Z.B. (2010). Negative impact of chemotherapy on breast cancer patients QOL—Utility of antiemetic treat-


