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Toxicities, complications, and clinical encounters during intraperitoneal chemotherapy in 17 women with ovarian cancer

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A B S T R A C T

Purpose of the research: Intraperitoneal (IP) chemotherapy is a viable and superior treatment to standard intravenous (IV) chemotherapy in women with small volume residual ovarian cancer following optimal debulking. Despite this clinical advantage, widespread adoption of the treatment regimen has been hampered by concerns related to toxicities and complications. The purpose of this descriptive study was to describe nursing implications related to toxicities, complications and clinical encounters in 17 women with ovarian cancer who received IP chemotherapy.

Methods and sample: Women with ovarian cancer who received IP chemotherapy at one NCI-designated comprehensive cancer center were accrued. Data related to IP chemotherapy summary, clinical encounters and admissions were obtained through comprehensive chart audits.

Key results: Common treatment-related toxicities included nausea and vomiting, fatigue, hypomagnesia, pain, neuropathy, anemia, and constipation. Reasons for dose-modifications were multi-factorial, and were primarily related to catheter complications and chemotherapy toxicities. The number of clinical encounters was high, and they were primarily related to admissions for inpatient IP chemotherapy and follow-up clinic visits.

Conclusions: Treatment-related toxicities and complications were common in women with ovarian cancer who received IP chemotherapy. Use of IP chemotherapy results in multiple clinical encounters, such as outpatient clinic visits and inpatient admissions. Nursing is a critical part of the interdisciplinary approach in caring for women treated with IP chemotherapy. Interdisciplinary teams with high levels of knowledge and skills related to IP chemotherapy administration are needed to manage treatment-related toxicities and complications, and support multiple clinical encounters during treatment.

Introduction

In the United States, an estimated 22,280 women will be diagnosed with ovarian cancer in 2012 (Siegel et al., 2012). Despite the relatively modest incidence, ovarian cancer is highly aggressive. Most women are diagnosed with advanced disease, and approximately 79% present with regional or metastatic disease (Howlander et al., 2011). The reported five-year survival rate is 26.9% for distant (metastasized) disease (Howlander et al., 2011). Over the years, combined intraperitoneal (IP) and intravenous (IV) chemotherapy regimens have been explored as a viable treatment approach for women with optimally debulked stage III ovarian cancer. Approximately 20–30% of all women with ovarian cancer are appropriate candidates for IP chemotherapy (Armstrong et al., 2006).

The median progression-free survival rate in the pivotal phase 3 trial that compared IV chemotherapy with IV/IP combined treatment in patients with stage III ovarian cancer (Gynecologic Oncology Group – GOG 172) was 5.5 months, with an overall survival advantage of 16 months, both favoring the IV/IP combined regimen (Armstrong et al., 2006). Despite the observed therapeutic advantages for the combined IV/IP chemotherapy regimen, grade 3 and 4 toxicities as well as complications were common (Armstrong et al., 2006; Jaaback et al., 2011). These toxicities and complications

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pose a significant challenge for health-care professionals, including oncology nurses, to sustain optimal overall well-being of women during and after treatment. The purpose of this descriptive study was to describe nursing implications related to toxicities, complications and clinical encounters in a small cohort of women with ovarian cancer who received combined IP/IV chemotherapy.

Background

Findings from several randomized phase III clinical trials have clearly established that IP chemotherapy is superior to standard IV chemotherapy in the treatment of advanced epithelial ovarian cancer with small volume residual disease. A major obstacle to the widespread adoption of IP chemotherapy is the support needed to manage treatment-related toxicities and complications (Markman and Walker, 2006; Trimble et al., 2011). Rothenberg et al. reported that 96% of women who received IP chemotherapy reported at least one of the following grade 3 or 4 toxicities: neutropenia (79%), nausea (50%), vomiting (34%), and fatigue (24%). Side effects were also a common reason for treatment discontinuation (Rothenberg et al., 2003). In the GOG 172 study, 58% of women on the IP arm did not complete the six cycles of treatment because of toxicities (Armstrong et al., 2006). All categories of systemic toxicities, which included grade 3 and 4 fatigue and pain, were more common in the IP-treated group (Armstrong et al., 2006). Common post-treatment side effects included nausea and vomiting, constipation, diarrhea, and fatigue (Anderson and Hacker, 2008; Ryan and Duggan, 2010).

Some pain and discomfort is expected with infusion of up to two liters of fluid into the abdominal cavity, and reported rates of pain and discomfort can be as high as 85.7% (Ryan and Duggan, 2010). Varying degrees of pain during IP treatment have been reported, with 24.5% of women reporting mild pain that was relieved by opioids and did not cause any limitations in daily activity (Almadrones, 2007). In contrast, 11% of women reported severe pain during the infusion requiring opioids and treatment discontinuation (Almadrones, 2007). The GOG 172 study reported that abdominal symptoms were significantly worse in the IP arm during treatment and 3–6 weeks after treatment, but were similar 12 months after treatment (Armstrong et al., 2006). Other chemotherapy-related toxicities that are specific to the agents used in IP infusions (cisplatin and paclitaxel) include neurotoxicity, anorexia, alopecia, and tinnitus (Hydzik, 2007; Lowe et al., 2007; Ryan and Duggan, 2010). In the GOG 172 study, neurotoxicity was worse in the IP arm 3–6 weeks after treatment and remained increased 12 months after treatment (Armstrong et al., 2006).

Catheter and infusion-related complications are also common reasons for treatment discontinuation. Catheter-related complications include access device blockage, internal kinking of the catheter, port infections, catheter migration, bowel perforation, rectal fistula, bowel adhesions, retrograde flow of fluid into port pocket, fluid leakage from port septum and port access difficulty (Armstrong et al., 2006; Echarri et al., 2011; Helm, 2012; Lesnock et al., 2010; Robinson and Beyer, 2010). Complications that commonly arise during IP infusions include pain, burning sensations and peritonitis (Naumann et al., 2009; Ryan and Duggan, 2010). Post-infusion abdominal distention results in bloating, pressure, and discomfort that may not dissipate until 48 h after IP administration and/or after IP fluids are absorbed (Marin et al., 2007; Ryan and Duggan, 2010). Approximately 34% of patients in the GOG 172 study experienced catheter-related complications (Armstrong et al., 2006). Fully implanted IP access device complications occur at an overall rate of 6.8% to 40.5%, and are primarily responsible for the failure to complete planned IP chemotherapy in 1.9% to 2.6% of patients (Helm, 2012). Overall rates for superficial and deep infections can be as high as 20.5%, and rates for catheter obstructions vary from 2.1% to 22% (Helm, 2012). In the GOG 172 study, leakage was a reason for treatment discontinuation for 12.5% of patients (Armstrong et al., 2006).

The amount of resources used to implement IP chemotherapy is also a relevant topic of discussion, particularly when national health care expenditures are forecast to increase in the coming years. Although studies have explored the feasibility of IP chemotherapy administration in outpatient settings (Berry et al., 2009), it has traditionally been given partially in hospital settings. It is expected that expenditures for inpatient treatments are higher compared with outpatient treatments. A GOG study explored the cost effectiveness of IP compared with IV chemotherapy for women with stage III ovarian cancer. The cost effectiveness model incorporated toxicities, costs of adverse events, caregiver costs, charges associated with serious adverse events and hospitalizations. Findings suggest that costs for IP chemotherapy were higher than IV chemotherapy, and that the cost appears to be related to inpatient treatment (Havrilesky et al., 2008). In outpatient settings, treatments were estimated to be more cost effective, if aggressive supportive measures (i.e. scheduled hydration and granulocyte colony-stimulating factors) were given (Berry et al., 2009; Havrilesky et al., 2008).

Overall, although evidence suggests that IP chemotherapy has an overall survival advantage compared to standard IV therapy, this advantage is achieved at the expense of significantly higher rates of treatment-related toxicities, complications, reduced quality of life (QOL) during treatment, and potentially higher resource use based on cost. The administration of IP chemotherapy requires extra time, space, and resources than are typically required for IV administration. As the adoption of IP chemotherapy into standard practice for women with ovarian cancer increases worldwide, it is critical to understand women's experiences related to toxicities and complications during IP chemotherapy, and to describe the amount of health care resources utilized by patients during treatment. Explorations of women's experiences in receiving IP chemotherapy for the treatment of ovarian cancer can expand this understanding.

Materials and methods

The study design and protocol were reviewed and approved by the Institutional Review Board prior to study initiation. Women with ovarian cancer who were undergoing IP chemotherapy treatment, had a prognosis of 6 months or greater, and were 18 years or older were eligible to participate in the study. All participants provided informed consent prior to enrollment. Seventeen women with ovarian cancer who received IP chemotherapy were recruited from the Surgical and Medical Oncology ambulatory clinics of one NCI-designated comprehensive cancer center. Data related to the IP chemotherapy summary and clinical encounters (ambulatory encounters and hospital admissions) were collected for each patient using chart audit forms developed by the investigators. Data were collected during IP chemotherapy and 6–12 months following IP treatment in an attempt to describe each patient's experience. All patients received combined IV/IP chemotherapy using the modified Armstrong protocol (day 1 inpatient IV paclitaxel at 135 mg/m^2 over 24 h; day 2 inpatient IP cisplatin at 75–100 mg/m^2 over 1 h; day 8 outpatient IP paclitaxel 60 mg/m^2) given every 3 weeks for a total of six planned cycles. Each patient was followed throughout the planned six cycles of IP chemotherapy or one month following treatment discontinuation.

Instruments

Basic demographic data obtained for patients included age, race/ethnicity, education, marital status, co-morbidities, employment,