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Clinical Trials Research: Challenges of Patient Education and Informed Consent

Case Study

B.R. is an 83-year-old Norwegian woman with stage III papillary serous ovarian cancer diagnosed after she presented with a two-month history of abdominal pain and bloating. An ultrasound followed by paracentesis revealed a moderate to large amount of ascitic fluid, and cytology was positive for adenocarcinoma. An abdominal computed tomography scan demonstrated extensive peritoneal carcinomatosis, extensive ascites, a heterogeneous nodule of the left adrenal gland, and trace right pleural effusion. Cancer antigen-125 (CA-125) initially was elevated to 71 u/ml (normal < 35 u/ml) and rose to 7,399 u/ml preoperatively.

B.R. underwent an exploratory laparotomy with total abdominal hysterectomy and bilateral salpingo-oophorectomy, including omentectomy and appendectomy. Pathology revealed high-grade adenocarcinoma. On postoperative day four, B.R. was started on single-agent carboplatin (Paraplatin®, Bristol-Myers Squibb, Princeton, NJ) for a total of four doses followed by docetaxel (Taxotere®, Aventis Pharmaceuticals Inc., Bridgewater, NJ) for a total of five doses. After six cycles of chemotherapy, her CA-125 normalized to 10 u/ml but began to elevate during the next cycle. A computed tomography scan was ordered and confirmed progressive disease in the pelvis. At this time, B.R. was offered continued conventional chemotherapy or participation in a clinical trial (i.e., a phase II, open-label, multicenter study for patients with advanced, refractory, or recurrent ovarian cancer).

B.R. is a single, retired, master's-prepared teacher and librarian who resides alone in her home. She is proud of her independence and cares for herself, including cooking, cleaning, shopping, and engaging in an active social life. She enjoys participating in a weekly puzzle club, going to museums, and attending luncheons with friends.

When questioned about participation in a clinical trial, B.R. initially responded positively. She was confident in her physician's advice that a clinical trial was a good treatment option and hoped that she would be cured. However, after reading the informed consent, B.R. was shocked with the stated inclusion criteria: "advanced ovarian cancer that continues to grow despite prior treatment." B.R. was distressed, stating that she did not realize the gravity of her illness until then. On further inquiry, B.R. articulated her understanding of clinical trials as "the thing to do with a rising CA-125" and that she was somewhat aware when presented with the option of a trial that the study drug would not "get rid of the tumor."

As part of initially educating B.R. about clinical trials research, the nurse investigated B.R.'s personal goals for participating, which included her hope to help science and herself. However, she expressed barriers to participation such as doubt about the treatment's effectiveness and the nuisance of visiting the cancer center for frequent blood draws. During B.R.'s participation in the clinical trial, she appreciated the extra attention she felt she received as a patient. Psychologically, she dealt with the challenges and side effects of treatment by maintaining her social relationships "to keep her mind busy and on other things." Unfortunately, B.R. left the study because of progressive disease. At follow-up, she told a nurse that she was scared and "went to pieces, calling another nurse for a sleeping pill" because she was unable to sleep at night as a result of her anxiety. However, she continued to express hope that she would be cancer free in the future and always would trust her doctor's judgment.

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Clinical Problem Solving

Responding to this clinical interview by Associate Editor Nancy Jo Bush, RN, MN, MA, AOCN®, is Aran Levine, RN, MSN, OCN®, clinical nurse II in the Bone Marrow Transplant Unit at the University of California, Los Angeles, Medical Center.

What information regarding clinical trials research is best communicated to educate patients prior to signing an informed consent form?

Oncology nurses play a vital role in the support and education of patients enrolled in clinical trials, beginning by informing patients that clinical trials are designed to answer questions related to the safest and most effective treatments for cancer (Albrecht, Blanchard, Ruckdeschel, Coovert, & Strongbow, 1999; Lee, 2004a). Nurses who directly educate patients during the informed consent process must be knowledgeable about all components of consent, as outlined by the National Cancer Institute (Erikson & Kuck, 2001), including the risks and benefits of treatment as well as confidentiality and compensation for any injuries incurred. Patients must understand that their participation is voluntary and that their consent can be withdrawn at any time without retribution (Erikson & Kuck).

Nurses should be familiar with the types of clinical trials that are conducted to investigate conventional and complementary and alternative medicine treatments (Lee, 2004a) (see Table 1). Prior to signing an informed consent, patients should be informed about the study's application to their situation, the terminology related to clinical trials, and the study phase involved. With the proper educational preparation, nurses can avoid a scenario similar to B.R.'s. Being in the presence of a patient who expresses shock or distress when reading an informed consent form can be difficult for any nurse.

The solutions offered to the clinical problems posed in this column are the opinions of the authors and do not represent the opinions or recommendations of the Oncology Nursing Society, the Oncology Nursing Forum, *or the editorial staff. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the* Oncology Nursing Forum *or the Oncology Nursing Society.)*

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Table 1. Types of Clinical Trials

Type of Trial	Outcome Criteria
Prevention	Identify a new drug or treatment intervention that reduces the risk of developing cancer.
Screening	Identify a tool to detect cancer in people who do not have symptoms of the disease.
Diagnostic	Identify effective tests or procedures that discover cancer at an early stage.
Treatment	Identify new drugs, vaccines, or interventions that are effective in cancer treatment.
Supportive care	Identify symptom management and therapies that improve quality of life.
Genetic	Identify the role of genetic makeup that affects the risk, detection, and diagnosis of cancer and the response to treatment.

Note. From "Clinical Trials in Cancer Part I. Biomedical, Complementary, and Alternative Medicine: Finding Active Trials and Results of Closed Trials" by C.O. Lee, 2004, *Clinical Journal of Oncology Nursing, 8,* p. 532. Copyright 2004 by the Oncology Nursing Society. Adapted with permission.

What ethical principles guide professionals when accruing patients for clinical trials research and obtaining informed consent?

In the case study, B.R.'s initial understanding of her physician's suggestion to enroll in a clinical trial was altered significantly after she read the informed consent. This case study reflects an underlying challenge for professionals involved in patient education, accrual, and informed consent: The patient's perception and the doctor's perception often differ regarding the information presented and how the patient perceives and interprets that information (Cox, 2000). Patients such as B.R. frequently are hopeful that a clinical trial drug or intervention will be curative even when told otherwise.

Specific inclusion criteria are outlined for every clinical trial, and a patient must meet the criteria before the option of participation is presented to them. The purpose of the study, the patient's right to refuse participation, the researcher's role and responsibilities, and the possible risks and benefits must be disclosed completely to patients (Polit & Beck, 2004). Patients have the right to make an informed and voluntary decision to participate without the fear of incurring prejudicial treatment if they opt to decline. Self-determination includes a patient's right to terminate participation at any time during a study without penalty. Patients' right to full study disclosure and to make a personal decision without coercion are the two major ethical principles on which informed consent is based (Polit & Beck). According to federal regulations, a valid informed consent is key to ethical research and demands that information be disclosed and understood (Flory & Emanuel, 2004).

Patients decide to enroll in clinical trials for many different reasons (Halpern, 2002; Lee, 2004b), including confidence and trust in a physician's recommendation and the belief that a physician would not suggest a clinical trial if it was not in their best interest to participate (Cox, 2000). Patients are more likely to enroll when a physician presents information in a supportive, patient-centered, reflective, and responsive manner (Cox). Encouragement from family and friends also may influence patients' decision as well as their own desire for altruism. B.R. expressed "helping science" as a personal benefit of participation in the clinical trial. Researchers must be aware of patients' perceptions that the study drug or treatment may offer hope for cure versus control and must understand how participation may impact patients' survival or quality of life. Patient perceptions of the personal risks and benefits of participation can be investigated by allowing patients the privacy, confidentiality, and time to ask questions in a safe and nonjudgmental environment. Finally, clinicians who are in the dual role of patient care and trial investigator need to be cognizant that their professional agenda does not bias the integrity of the process of informed consent. The inclusion of an individual not directly involved in the study may be helpful in obtaining consent (Loh, Butow, Brown, & Boyle, 2002). A paradox arises when professionals are pressured to enroll patients in a clinical trial to increase sample size while not being biased when disclosing trial information to patients.

What nursing interventions would have identified B.R.'s misunderstanding of her participation in the clinical trial and provided emotional support at the time of advancing disease and withdrawal from the trial?

Even nurses not directly involved in the research process of education and informed consent play an important role in identifying patients' understanding of and participation in their healthcare decisions. Providing patients with the information necessary to make informed decisions creates empowerment and reduces feelings of helplessness and hopelessness, even in the face of advanced disease. If a patient communicates any misinterpretation or misconception related to the decision to participate in clinical research to a direct care provider, the provider is accountable to educate the patient to the best of his or her knowledge and report these findings to the research nurse or principal investigator. B.R.'s need for clarification and understanding regarding the application of the clinical trial to her disease stage was most likely evident prior to reading the informed consent. The nurse at the bedside is in a unique position to assess the educational and psychosocial needs of patients on a continual basis, including understanding of the response to current and prospective treatment options.

In the literature, researchers, clinicians, and patients have offered numerous suggestions regarding interventions to improve the educational and informed consent needs of patients deciding whether to enroll in a clinical trial (Lee, 2004b). Full disclosure of a clinical trial is established on the basic principle of education—presenting information in accordance with each patient's level of knowledge and learning needs (Erikson, 2001). This includes meeting the cognitive, affective, and psychomotor skills of patients (Erikson). Many patients with cancer are not aware of nonstandard treatments, the unproven nature of the drug or treatment being investigated, and the uncertainty of possible risks and benefits (Joffe, Cook, Cleary, Clark, & Weeks, 2001).

The process of disclosure and informed consent inherently involves complex language and detailed information that may lead to patient confusion and misinterpretation. Perhaps this caused B.R.'s inconsistent emotional responses. A patient's educational level and knowledge base, as well as language barriers (i.e., when patients speak a language other than English), can lead to decreased understanding of informed consent. Using language and medical terms understood by the patient and providing professional courtesy ensure the ethical principle of respect for human dignity. Demonstrating respect also encompasses the principle of self-determination, supports patients in actively participating in decisions regarding their health care, and encourages a sense of autonomy (Brown, Butow, Butt, Moore, & Tattersall, 2004).

On average, additional clinical time is necessary to adequately educate and accrue trial participants. Also, most patients take several days to consider enrolling in a clinical trial. Patients who had appropriate time to consider their treatment options and those who had a nurse present to answer questions and provide support were more knowledgeable and prepared than patients who did not. In addition, patients who read the informed consent had a greater level of knowledge regarding their participation (Joffe et al., 2001).

Patients' affective response to informed consent must be considered. Some patients value knowing all of the medical information and possible risks and benefits, whereas others may want minimal information (e.g., the most common side effects) (Schain, 1994).

Clinical Highlights: Clinical Trials Research

Clinical trial: Designed to answer questions related to the safest and most effective treatments for cancer, clinical trials can focus on prevention, screening, diagnostics, treatment, supportive care, or genetics.

Randomization: Patients are randomly assigned to treatment groups by chance alone. A randomized clinical trial involves at least one test group and one control group. Random assignment of patients to each group minimizes the differences among groups with specific characteristics, allowing for better comparisons of treatment outcomes (Esper & Knoop, 2005).

Double blind: This is an experimental treatment in which neither the patient nor the professionals administering the test know who is in the experimental group or control group. This testing procedure is designed to eliminate bias (Esper & Knoop, 2005).

Informed consent: This principle of ethics requires researchers to inform patients of the possible risks and benefits of treatment and to ensure that patients are participating on a voluntary basis.

Phase I: These trials are conducted to determine the dosing strength and safety of a new drug by identifying the maximum tolerated dose in humans and describing the pharmacokinetics of the drug. To determine a safe dosage, drugs are administered at the lowest level of safety for humans and escalated with caution until a defined toxicity end point is reached (Goh, 2000). During this phase, the drug or treatment is tested in a small population of patients and often the trial does not include a control group (Esper & Knoop, 2005; Polit & Beck, 2004).

Phase II: Based on the findings determined in phase I trials, the goal of phase II is to evaluate the activity of a new drug or effectiveness of a treatment intervention against specific tumor types. Often considered the pilot test (Polit & Beck, 2004), a phase II trial aims to determine drug or treatment schedules, toxicities, and symptom management (Erikson & Kuck, 2001).

Phase III: The goals of phase III are to test and compare the effectiveness of a new drug or treatment intervention against standard therapy. This is the experimental phase of a trial involving random assignment of patients to a control or experimental group. Outcome criteria include the evaluation of the response rate and duration of response as well as side effects and impact on quality of life (Erikson & Kuck, 2001).

Phase IV: After a new drug or treatment has been adopted, the goal of phase IV is to identify the role of this newly established intervention in the adjuvant or curative setting (Erikson & Kuck, 2001). At this stage, researchers also identify long-term consequences of the drug or intervention related to side effects, symptom management, and quality-of-life issues (Polit & Beck, 2004).

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Enrolling and managing patients in clinical trials can be challenging for all members of the healthcare team. From patient educator to principal investigator, oncology nurses assume many different roles in clinical trials research. All involved in educating patients during the informed consent process must be knowledgeable about the ethical principle of beneficence (i.e., patient safety and freedom from harm) (Polit & Beck, 2004). This includes providing unbiased information when offering a clinical trial and being aware of conflicting agendas and patient misconceptions.

Oncology clinical trials can offer hope, but it must be realistic. A major component of realistic hope is that patients clearly understand that, regardless of their treatment choice, they will continue to have the physical and emotional support they need. Wherever oncology nurses find themselves on the continuum of clinical trials research, they play a valuable role as patient advocates. When B.R. told her nurse that she went off of the study protocol because of progressive disease and that she was scared, the focus of her care changed from clinical trial participation to palliation. This translated into needed reassurance from her physician and nurses that she would not be abandoned.

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