

Therapeutic Misconceptions and Misestimations in Oncology: A Clinical Trial Nurse's Guide

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Therapeutic misconceptions and misestimations occur frequently in oncology clinical trials and can potentially compromise informed consent. Despite the increased awareness of these issues in medical literature, many practitioners and nurses continue to be unfamiliar with these concepts. This article will define therapeutic misconceptions and misestimations, explore contributing factors, and explain how they can be prevented by clinical trial nurses.

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Digital Object Identifier: 10.1188/13.CJON.486-489

A clinical trial nurse (CTN) has been asked to assist with the informed consent process for Mrs. S to participate in a clinical trial. Mrs. S recently was diagnosed with stage IV breast cancer. The physician has introduced and briefly described the trial to the patient. The CTN enters the room and sits down with the emotional patient and her family and asks what Mrs. S has been told about the trial. Mrs. S cries, states that she needs chemotherapy, and says that this treatment would be the best thing for her right now. The CTN questions her again by asking, "Why do you feel this is your best treatment option?" Mrs. S answers, "I know the doctor wouldn't offer me anything he didn't feel was best for me." The CTN replies, "I think you may have misunderstood some important facts about this option. Why don't we start over and allow me to explain what this trial entails and how it may differ from your other treatment options."

Mrs. S's belief that her physician would only offer treatments that will provide the best care is a symptom of therapeutic misconception. Therapeutic misconceptions happen frequently within oncology clinical

trials (Appelbaum & Lidz, 2008a). In a study of participants who enrolled in phase I oncology clinical trials, more than 68% of participants were experiencing a therapeutic misconception and 94% suffered from therapeutic misestimations (Pentz et al., 2012). When a therapeutic misconception occurs in a current or potential research participant, the informed consent may be compromised (Appelbaum & Lidz, 2008a). CTNs who understand therapeutic misconceptions and misestimations can prevent these from occurring by advocating for research participants, thereby increasing patients' understanding of the informed consent and trial.

Definitions

The term *therapeutic misconception* was first described by Appelbaum, Roth, and Lidz (1982). They reported that this phenomenon exists when research participants believe the care they receive on a clinical trial is based on their needs and is designed to benefit them personally (Appelbaum et al., 1982). This, however, is actually the basis of clinical care (Appelbaum & Lidz, 2008a), whereas the goal

of a clinical trial is to obtain generalizable knowledge to benefit future patients (Grady & Edgerly, 2009; Lawrence, 2008). Clinical, or personalized, care is medical care given to a patient designed specifically for that individual and tailored to their particular needs (Appelbaum & Lidz, 2008a). Care received through clinical trials may be structured, and the specific protocol may not allow adjustments in the regimen or specific medications given for side effects, which is contrary to clinical care (Appelbaum & Lidz, 2008a).

The concept of therapeutic misconception was first seen in randomized, controlled placebo trials and, over time, has been generalized to other forms of trials (Kimmelman, 2007). During the 30 years since this concept was first defined, many articles have been written and published within medical journals attempting to further refine this idea. Despite this, Appelbaum and Lidz (2008b) stated that little effort has been made in preventing therapeutic misconception from occurring.

Therapeutic misestimation is a related concept that differs in that the participant has failed to fully understand the estimated risks or benefits involved with the research (Hornig & Grady, 2003). When misestimations occur, patients may believe that a greater chance of personal benefit exists than what trial coordinators expect, or may fail to appreciate additional risks from trial participation. This occurs in phase I trials when the goals are safety, identifying toxicities, and determining maximum tolerated dose. For phase I trials, efficacy is not a primary outcome, and fewer than 5% of phase I oncology clinical trials involving an experimental medication have proven to provide benefit (Daugherty, 1999).

Therapeutic misconceptions and misestimations have the potential to negatively

impact informed consent. Therapeutic misconceptions should rarely be accepted, because understanding how research differs from personal care is a necessary component for an autonomous assessment of the trial (Horng & Grady, 2003). According to Horng and Grady (2003), therapeutic misestimations can be allowed because complete understanding of the probability of risks and benefits may not be required for an independent decision about participation.

Identifying therapeutic misconceptions or misestimations with research patients may not be straightforward. Markman (2006) discussed how the design of some phase I oncology studies may actually provide a therapeutic intent to the participants. One example is when treatments that are currently U.S. Food and Drug Administration (FDA) approved as single-agent treatments are tested in combination with each other. Another example is when investigational agents are added to the standard of care regimen (Markman, 2006). Gaining benefit from these trials would be expected only to the extent anticipated from each single agent or the standard of care regimen (Markman, 2006). Clinical trial nurses should be familiar with the protocol along with standard treatment options that are currently available to the patient outside the trial setting. This should be verbalized and put in writing for patients so they can make a thorough assessment of benefits.

Literature Review

Although therapeutic misconceptions and misestimations are common, many nurses and medical practitioners are unaware of these concepts. CTNs commonly assist with informed consent and should be able to identify therapeutic misconceptions and misestimations. In an author-conducted survey of 3 CTNs, 18 direct care nurses, and 4 medical practitioners in a rural oncology clinic that provides clinical trials, 24 (96%) were unfamiliar with the concept of therapeutic misconception.

A review of the CINAHL® database revealed few nursing articles discussing therapeutic misconception and misestimation. Even fewer discuss how to prevent these from occurring.

The majority of existing literature regarding these topics is currently found in

medical and law journals. However, many nursing and medical journal articles do address evaluation and comprehension of the informed consent (Cohn & Larson, 2007). These works will be used to address the issue of preventing therapeutic misconception and misestimation, and fill this gap in the current nursing literature.

Informed Consent Process

The informed consent process is where individual autonomy is honored by providing potential participants with the information needed to make an educated decision about clinical trial participation (Twomey, 2008). Although the principal investigator is responsible for this task (FDA, 2012a), it may be delegated to a CTN (Poston & Buescher, 2010). Barrett (2005) noted multiple articles that suggest nurses assisting with the informed consent process can enhance patient comprehension. Twomey (2008) explained that nurses' responsibilities to the research participant include verifying knowledge and understanding of the risks involved with the research.

The Oncology Nursing Society ([ONS], 2010) supports this role for a CTN and has developed competencies relating to the informed consent process. CTNs should be knowledgeable of the current guidelines and regulations that govern informed consent and ensure that the process is compliant with those guidelines. These include the FDA (2012b) elements of informed consent, the U.S Department of Health and Human Services ([HHS], 2010) general requirements for informed consent, and the International Conference on Harmonisation ([ICH], 1996) good clinical practice guidelines (see Figure 1), as well as institutional, sponsor, and investigational review board guidelines. The informed consent process does not end with the consent form being signed. As new information becomes available about a trial, all participants need to be educated and given the opportunity to continue or decline additional participation (ONS, 2010).

Contributing Factors

Emotions

The emotional status of the patient and family is one obstacle to an effective informed consent process that may

International Conference on Harmonisation

- ▶ Guideline for Good Clinical Practice <http://bit.ly/rndBWm>

U.S. Department of Health and Human Services

- ▶ General requirements for informed consent <http://1.usa.gov/Vw3CJG>

U.S. Food and Drug Administration

- ▶ Elements of informed consent <http://1.usa.gov/15G3cQD>

FIGURE 1. Federal and International Guidelines for Informed Consent

lead to a therapeutic misconception or misestimation. In the opening scenario, Mrs. S was recently diagnosed with stage IV cancer and was emotional. Intense feelings such as fear and hope may influence how a person processes risks and benefits (Glannon, 2006) and can have an impact on trial participation. CTNs need to be aware of these emotions and advocate for their patients by allowing them time to cope with these emotions before asking for their decision about trial participation.

Motives

Participant motives also should be assessed and explored (National Institutes of Health, 2009). When motives such as personal medical benefit are expressed as the primary or only reason for participating, the CTN should reevaluate participant understanding of the trial. This evaluation may come in the form of an interactive questionnaire to include the purpose of the trial, the risks involved, and any expected benefits. Hartnett (2011) examined use of the Informed Consent Evaluation Feedback Tool as a questionnaire given to patients prior to the informed consent discussion. This tool assists patients in understanding key elements of a trial and how the trial differs from other care options, as well as helps the potential participants in formulating questions.

Patient Perception of Care

Another factor that contributes to therapeutic misconception may be patients' previous thoughts about medicine and their physician. Many patients have

learned through experience that physicians are to provide individualized care, which can lead to the thought that clinical trials are in the best interest of the patient (Appelbaum & Lidz, 2008a). Stellato, Scholl, and Jester (2012) discussed this, stating “a potential research opportunity can be interpreted as a physician-advised prescription” (p. 139). CTNs should ensure the patients are aware of treatment options available to them outside of the trial. If the patient is unsure of other options, the principal investigator should be brought back in to answer these questions. Appelbaum and Lidz (2008a) also suggested providing a one-page summary describing the trial and how it differs from personal care. Morin et al. (2002) suggested that, when the patient’s regular physician is the research investigator, another team member, such as a CTN, should provide education and obtain informed consent. This facilitates understanding and reduces role confusion.

Media

Media and advertisements also can contribute to therapeutic misconception and misestimation as facilities providing clinical trials are commonly depicted as providing superior care (Appelbaum & Lidz, 2008a). Many specific clinical trial advertisements attempt to attract participants, appealing to their specific need or medical problem, and referring to the research as treatment for their illness (Miller, 2008). One survey showed that 52% of people felt they would participate in a research study to obtain the best medical care (Appelbaum & Lidz, 2008a). Prospective trial participants should understand that care provided on a clinical trial has not yet been proven as “best care.”

Terminology

Terminology can lead to a therapeutic misconception or misestimation. Consent forms do not always use terms that are easily equatable with the experimental nature of the trial (Appelbaum & Lidz, 2008a); common clinical terminology such as efficacy, random, and double-blinded are not typically understood by the lay population, and “treatment” often is used to describe the trial itself (Instone, Mueller, & Gilbert, 2008; Waggoner & Mayo, 1995).

Therapeutic Misconception in Research Staff

Instone et al. (2008) noted that therapeutic misconceptions and misestimations can occur within investigators and CTNs. They explain that (although no published data confirm this), during a review of the informed consent process for clinical trials at their facility, staff members frequently used “treatment” and “treatment trials” when explaining placebo control trials (Instone et al., 2008). Exploring this was not the original aim of their research; however, this was noticed frequently, which suggests nurses may believe these trials provide participants with benefit (Instone et al., 2008). The authors also noted that oncologists may fall victim to therapeutic misconception from a desire to do something for patients with limited or no treatment options left (Instone et al., 2008). Joffe and Weeks (2002) conducted a survey of oncologists of varying subspecialties and found that 13%–38% of them enrolled patients into clinical trials to obtain “state-of-the-art treatment.” When investigators or members of the research staff hold these beliefs and present trials in this manner, therapeutic misconceptions and misestimations may occur in participants (Cohn & Larson, 2007).

Nursing Standards and the Informed Consent Process

The American Nurses Association ([ANA], 2010) standards of practice can assist CTNs with prevention of therapeutic misconceptions and misestimations. Although CTN interactions with patients prior to the consenting process may be limited or nonexistent, the nursing process can still be followed. An assumption that can be made about most potential research participants is they do not possess all the information needed to make a participation decision, or a misunderstanding could occur regarding the information that has been previously presented to them. This assumption leads to a nursing diagnosis of knowledge deficit related to a lack of information or a misinterpretation of information. If participants proceed through the informed consent process and continue to have a knowledge deficit, a therapeutic misconception or misestimation may result.

A general care plan can be developed and used with all potential research participants as a guide for preventing therapeutic misconceptions and misestimations. The evaluation phase of the nursing process for this diagnosis will be instrumental in assessing for a therapeutic misconception or misestimation. Lindegger et al. (2006) suggested using open-ended questions, a process known as reflective education, so patients can paraphrase the consent information in their own words. This method allows CTNs to assess their ability to convey content. If a gap in understanding exists, CTNs should assess how their teaching approach can be adjusted to meet the patient’s and family’s learning needs. Appelbaum and Lidz (2008a) suggested using quizzes to assess for comprehension of the trial and to assess for the key elements of a therapeutic misconceptions or misestimation.

Other nursing standards that assist with preventing therapeutic misconception and misestimation include Standard 11 Communication, Standard 13 Collaboration, and Standard 14 Professional Practice Evaluation (ANA, 2010). CTNs should evaluate participant-preferred communication and learning styles so these can be incorporated into the informed consent process to aid understanding.

Conclusion

The informed consent may be compromised by the presence of therapeutic misconception or misestimation. Through understanding of what these are and knowing the common factors that contribute to them, CTNs may be able to tailor the education provided in the informed consent process to prevent these phenomena from occurring. Prevention of therapeutic misconceptions and misestimations are important because their presence may negate the informed consent and may lead to increased dropout rates and poorer satisfaction with the trial experience (Appelbaum & Lidz, 2008a). Because much of the current literature surrounding the prevention of therapeutic misconception is based on assessing comprehension of the consent and re-educating the patient, additional research is needed to assess the effectiveness of implementing these strategies.

Case Study Follow-Up

The CTN met with Mrs. S, who was much more relaxed than she was at their previous meeting one week prior. After questions were answered, Mrs. S stated, “I think I want to be in this trial. I know the medicine I may get has not been proven to help people like me, but I would like the chance to get it. I also realize that my doctor will be following a protocol that may dictate specific aspects of my care and this may be different than what he normally would do.” The CTN responded, “You seem to have a much better understanding of what this clinical trial is about.” Mrs. S agreed and signed the informed consent document.

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