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Participation in Clinical Research: Perspectives of Adult Patients and Parents of Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation

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A B S T R A C T

Despite major improvements over the past several decades, many patients undergoing hematopoietic stem cell transplantations (HSCT) continue to suffer from significant treatment-related morbidity and mortality. Clinical research studies (trials) have been integral to advancing the standard of care in HSCT. However, 1 of the biggest challenges with clinical trials is the low participation rate. Although barriers to participation in cancer clinical trials have been previously explored, studies specific to HSCT are lacking. The current study was undertaken to examine the knowledge, attitudes, and perceptions of HSCT patients regarding clinical trials. As members of focus groups, participants responded to open-ended questions that assessed factors influencing decision-making about HSCT clinical trials. Suggestions for improvements in the recruitment process were also solicited among participants. Seventeen adult HSCT patients and 6 parents of pediatric HSCT patients participated in the study. The median age was 56 years (range, 18 to 70) and 44 years (range, 28 to 54) for adult patients and parents, respectively. Participants universally indicated that too much information was provided within the informed consents and they were intimidated by the medical and legal language. Despite the large amount of information provided to them at the time of study enrollment, the participants had limited knowledge retention and recall of study details. Nevertheless, participants reported overall positive experiences with clinical trial participation and many would readily choose to participate again. A common concern among participants was the uncertainty of study outcome and general lack of feedback about results at the end of the study. Participants suggested that investigators provide more condensed and easier to understand informed consents and follow-up of study findings. These findings could be used to help guide the development of improved consent documents and enhanced participation in research studies, thereby affecting the future design of HSCT research protocols.

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a high-risk medical procedure that is utilized worldwide as therapy for many malignant and nonmalignant hematologic diseases [1,2]. The number of autologous and allogeneic transplantations performed continues to rise [3], particularly as outcomes have significantly improved over the past few decades [4]. Clinical research has played an important role in advances of standard of care seen in HSCT patients over time [5,6], which has led to improved supportive care, better understanding of disease risks, and newer treatment approaches [4]. Nonetheless, efficacy is still limited by short- and long-term treatment-related complications [1]. Clinical research remains crucial in guiding more effective diagnostic and treatment options [7].

Clinical research has been broadly defined by the Institute of Medicine to "include all studies intended to produce knowledge valuable to understanding the prevention, diagnosis, prognosis, treatment, or cure of human disease" [8]. The translation of basic science advances into human applications provides the opportunity to test hypothesis-driven questions, investigate new therapies, and evaluate outcomes in efforts to improve overall health care [9]. However, 1 of the biggest challenges is that very few patients enter

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clinical research studies (trials). For example, only 3% of US adults with cancer participate in clinical trials [7,10]. Barriers to enrollment in patients undergoing HSCT are additionally magnified because of the small pool of patients undergoing transplantations at most centers and the substantial heterogeneity of diseases treated, donor and recipient characteristics, and sources of hematopoietic stem cells, as well as heterogeneity of transplantation techniques [5]. The consequences of poor recruitment or slower than anticipated enrollment into clinical research studies include premature closure, underpowered results, lack of generalizability, and wasted resources [11]. Although studies have explored barriers to participation in cancer clinical trials, identifying common themes across studies has been challenging [12]. Further, studies specific to HSCT are lacking [5]. Gaps in knowledge remain regarding patient-centered perspectives in HSCT clinical trials. Moreover, relatively little has been published on how to recruit patients for HSCT clinical trials.

Given the growing importance of patient engagement in clinical and translational research [13,14], we sought to identify knowledge, attitudes, and perceptions of participation in clinical research studies among adult HSCT patients and parents of pediatric HSCT patients. The purpose of our study was to examine patient-centered barriers, facilitators, and motivations regarding clinical research studies to develop a questionnaire targeted at the HSCT population. By investigating patient-centered attitudes and perceptions, the new information gained may improve the future design of HSCT clinical research protocols and improve participation into HSCT clinical trials.

METHODS

Empirical Setting

A distinguishing feature of the University of Michigan blood and marrow transplantation (BMT) program is the integration of the adult and pediatric BMT units to promote clinical and translational research. The inpatient and outpatient units for the adult and pediatric BMT programs are located in the Children's and Women's Hospital. The adult and pediatric BMT programs have over 6000 annual outpatient visits, evaluate over 400 new HSCT patients, and perform approximately 250 HSCT each year (200 adult HSCT and 50 pediatric HSCT). This includes approximately 70 allogeneic HLA-identical sibling donor and 70 unrelated donor HSCT. It is standard practice for HSCT-eligible patients to consent to usual care procedures concurrently with as many clinical research studies as possible, including sample repository, ancillary, supportive care, and intervention studies, before admission to the BMT unit.

Focus Group Recruitment

We sought participants who had recently undergone autologous or allogeneic HSCT. Adult post-HSCT patients (age $\geq$18 years) and parents of pediatric post-HSCT patients (age $<$18 years) were eligible to participate in the focus groups. Patients were not required to have previously enrolled in a specific clinical trial. Inclusion criteria required ability to speak and read proficiently in English and ability to travel off-site to a facility on the University of Michigan main campus. Participants were recruited in the outpatient setting through institutional review board–approved flyers posted in the BMT program waiting rooms or attached to patient clipboards during clinic check-in. BMT physicians, advanced practice extenders, and staff assisted with recruitment.

Interested patients/parents were instructed to call a telephone number and sign-up for 1 of 3 focus groups (FG1, FG2, and FG3). After answering a short screening questionnaire over the phone, participants received an information package, including a cover letter confirming their participation, a map with driving directions to the focus group location, and a consent form via mail or e-mail. Participants received a telephone call reminder on the day before the scheduled focus group.

Participants of FG1 and FG2 received $50 as compensation for participation. To encourage participation among parents for FG3, compensation was increased to $100. Participants were reimbursed for metered parking during the time of the focus group. The study was approved by the University of Michigan Medical School's institutional review board (HUM00078723: "Attitudes and perceptions of participation in BMT clinical trials").

Focus Groups

Three focus groups were conducted between September and October 2013. Upon arrival to the focus group site, participants signed the consent form and filled out a brief questionnaire that collected information on sociodemographic and clinical characteristics. No patient identifiers were retained. Each focus group lasted approximately 90 minutes and was audio/video-recorded with consent provided by the participants.

A trained focus group moderator with a background in public health and an assistant moderator with a background in survey methodology, neither affiliated with the BMT program, moderated all 3 focus groups. Researchers from the BMT program attended the sessions and observed the discussions behind a 1-way mirror. Before initiating the study, a focus group guide was developed by the study investigators, who included experts in HSCT and survey methodology, through a literature review on studies about motives for cancer clinical research participation and through the conduct of semi-structured qualitative interviews with BMT physicians, advanced practice extenders (eg, nurse practitioners and physician assistants), nurse coordinators, social workers, nutritionists, pharmacists, and nurses. The moderators used the guide to cover questions on the following: (1) free associations with the term "clinical trial," which was used interchangeably with "clinical research studies," (2) perceptions of information flow (ie, process of recruitment) regarding HSCT trials, (3) the decision-making process for participation in an HSCT clinical trial, (4) general reasons for and against participation in clinical trials, (5) personal experiences with clinical trials, and (6) suggestions for changes in the HSCT clinical trial process at the University of Michigan Health System (Table 1 provides

Table 1
Moderator Guide Questions

Free associations with term "clinical trial"
When you hear the word, "clinical trial" what is the first thing that comes to your mind?
Perceptions of information flow regarding HSCT clinical trials
Now I'd like you to think back to the time when you had the bone marrow transplantation at the University of Michigan, or your child had the bone marrow transplantation. Who presented the trial to you, who talked to you about the trial?*
How many trials were you offered, or presented? What kind of trials were you offered?
When the person talked to you about the trial, whether it was the doctor or the clinical coordinator, what did they say about it? What information did they give you?
Did anyone have the feeling that they were given too much information, or not enough information?
After learning about the BMT trial, or the trials that you participated in, did you actively look for more information about it?
Decision-making process for participation in an HSCT clinical trial
Do you remember your first thoughts when you heard about the BMT trial at the U of M Hospital?
When it came to making a decision whether to participate in the BMT trial or not, did you make the decision alone, or did someone else influence or talk with you before you made the decision?
Reasons for and against participation in clinical trials
What are reasons to participate in a clinical trial?
What are reasons not to participate in a clinical trial?
Personal experiences with clinical trials
Now thinking back to the BMT trial that you participated in at the U of M hospital, what were your experiences with these BMT trials?
Looking back and comparing your expectations before the start of the trial with what actually happened during the trial, to what extent were your expectations met. Was there anything that happened that was different than you were expecting?
Thinking back to the overall experience that you had with the clinical trial, as part of your BMT at the U of M hospital, if you would have to make the decision about participating in a clinical trial again, how willing would you be to participate in the same trial again?
Now imagine that a good friend or close relative comes to you tomorrow and tells you that he or she was offered to participate in a clinical trial as part of a BMT. What would you say to him or her?
Suggestion for changes in the HSCT clinical trial process at the University of Michigan Health System
Thinking back to the BMT trials at the UM hospital. Is there anything that you would like to change?

* To facilitate patients' and parents' understanding in the focus groups, the more colloquial terms "bone marrow transplantation" and "BMT" were used instead of "hematopoietic stem cell transplantations" and "HSCT."