European Journal of Oncology Nursing 18 (2014) 140–144

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Adherence to outpatient oral medication regimens in adolescent hematopoietic stem cell transplant recipients

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Keywords:
Adolescent
Adherence
Hematopoietic stem cell transplantation

A B S T R A C T

Purpose: Hematopoietic stem cell transplantation (HSCT) is an increasingly utilized treatment option for adolescents with many life-threatening diagnoses. Suboptimal adherence may result in compromised treatment effectiveness and increased risk of adverse medical outcomes.
Method: This study examined adherence patterns in six adolescents (ages 12–18) who had undergone HSCT. Demographic and clinical information were obtained from caregivers and via chart review. Electronic pill bottles (Medical Event Monitors, MEMS™) were used to track medication adherence. Daily, weekly, and monthly adherence as well as medication interruptions (periods of ≥24 h between doses) were calculated.
Results: Participants took 73% of doses (SD = 13%) and demonstrated perfect adherence on 56% of days (SD = 18%, Range = 34–88%). Average monthly adherence ranged from 40 to 91% and decreased over time. Participants demonstrated at least two [M(SD) = 4.20(2.28)] medication interruptions. Individual adherence patterns included high sustained adherence, variable adherence, and delayed non-adherence.
Conclusions: Overall, participants struggled to adhere to medication schedules, taking less than three-quarters of prescribed doses and demonstrating perfect adherence on fewer than four out of seven days per week. Adherence rates are similar to those observed in other pediatric populations and demonstrate the importance of routinely assessing adherence in adolescents who have undergone HSCT.

Introduction

Driven by advances in research and clinical trials, hematopoietic stem cell transplantation (HSCT), a treatment once considered more beneficial for younger children, is now considered an effective treatment option for adolescents with oncological, hematological, and immunological diseases (Dini et al., 2011; Savaşan and Abella, 2005). Between 2008 and 2010, approximately a third of pediatric HSCT recipients were between 10 and 19 years of age (National Marrow Donor Program, 2013). While survival rates for adolescents who have undergone HSCT have significantly improved, three year survival rates demonstrate wide variability and range from approximately 35–93% depending on the diagnosis (National Marrow Donor Program, 2012). In addition to numerous medical factors, adherence, or the "extent to which a person's behavior (i.e., taking medications) coincides with medical or health advice", is a modifiable factor that likely accounts for variation in these outcomes (Haynes et al., 1979).

Following HSCT, adolescents and their caregivers must manage a complex treatment regimen. This regimen often includes the administration of numerous intravenous and/or oral medications with different dosing schedules and frequent dosing changes. In addition, adolescents and their caregivers are often asked to attend three to four clinic appointments each week and abide by activity restrictions (i.e., avoiding crowded places). As more complex medical regimens are associated with poorer adherence, individuals who must adhere to the post-HSCT regimen are at risk for non-adherence (Coleman et al., 2012).

Within this at-risk population, non-adherence may be particularly problematic for adolescents. Across numerous medical conditions, including many for which HSCT is the treatment of choice, adolescents demonstrate the highest rates of non-adherence (Butow et al., 2010; Pritchard et al., 2006). Rates of non-adherence among adolescents with cancer, for example, range from 27 to 63% (Butow et al., 2010). If rates of non-adherence in adolescents who have undergone HSCT are similar to those demonstrated by other populations, a significant proportion of

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1462-3889/$ – see front matter
http://dx.doi.org/10.1016/j.ejon.2013.11.007

adolescents may be receiving sub-therapeutic doses of medication, compromising treatment effectiveness and placing them at increased risk for treatment failure and premature death (Pai and Drotar, 2010). Given these significant health implications and the modifiable nature of non-adherence, it is important to understand the prevalence of non-adherence in adolescent HSCT recipients.

The only investigation of adherence in HSCT recipients to date indicated that 40% of adolescents evidenced significant difficulty adhering to their oral antibiotic regimen during hospitalization (Phipps and DeCuir-Whalley, 1990). While qualitative findings suggest similar difficulties are present following discharge (Cooke et al., 2011), studies have not yet examined adherence during this difficult transition. Conceptualization of the post-HSCT regimen within the developmental framework of adolescence, however, suggests that adherence following discharge may be particularly problematic.

Following discharge, normative developmental goals of adolescence collide with the demands of the post-HSCT treatment regimen. Adolescents negotiate increasing independence and new social roles, resulting in unpredictable schedules, decreased parental supervision, increased parent-child conflict, and increased time away from home. In other adolescent chronic illness populations, these normative transitions increase the likelihood that adolescents will forget or choose to forgo treatment tasks (Butow et al., 2010; Pritchard et al., 2006). For example, it is normative for adolescents to place increased importance on peer relationships, making the social acceptance and enjoyment of engaging in social activities far more reinforcing than following a restrictive medical regimen.

Key barriers to adherence (i.e., conflict with caregivers, psychological disorders) also increase during adolescence (Kyngäs et al., 2000). The more barriers faced by adolescents with a chronic condition, the higher the rates of non-adherence (Bregnballe et al., 2011; Gray et al., 2012). As a result of these risk factors, it is likely that rates of non-adherence in adolescent HSCT recipients following discharge may be even higher than the rate of 40% demonstrated during hospitalization (Phipps and DeCuir-Whalley, 1990).

Understanding medication non-adherence in this at-risk population is essential for determining methods to promote adherence to a daunting treatment regimen. The aims of this study were to be the first to describe individual and cohort-level patterns of oral medication adherence over a six- to nine-month period. We hypothesized that adherence would be similar to previously published oral medication adherence rates for adolescents with solid organ transplants or cancer (Butow et al., 2010; Dobbels et al., 2010).

Materials and methods

Participants and procedures

Data for this study are from a larger project examining adherence in pediatric HSCT recipients (Pai et al., 2011). Ninety-one of the 119 eligible participants agreed to participate (76% recruitment rate). The retention rate for the larger study was 99%.

The eight participants (ages 12–18 years) in the current study were recipients of a HSCT, prescribed oral medication, living with a caregiver, and fluent in English. Exclusion criteria included significant cognitive deficits (in the patient or both caregivers) and a medical status that precluded questionnaire completion.

Caregivers completed a questionnaire and were provided with an electronic pill bottle for use following discharge. Data were downloaded from pill bottles at four time points (1-, 3-, 6-, and 9-months). All procedures were approved by the Institutional Review Board and appropriate consent and assent were obtained.

Measures

Caregivers provided demographic information. Date of transplant, hospitalizations, and changes in medications were obtained via chart review. Medication adherence was assessed using Medication Event Monitors (MEMS™), an electronic pill bottle that time-stamps each bottle opening. Participants were asked to use MEMS™ devices to store and administer their medication for the nine-month study period. Medications stored in the MEMS bottles at baseline included: Cyclosporine ($n = 3$), Fluconazole ($n = 1$), Acyclovir ($n = 1$), and Voriconazole ($n = 1$). When prescriptions were changed, participants were instructed to change the medications stored in the MEMS™ bottle. All participants evidenced at least one change in monitored medication during the course of the study, and at study completion, medications in the MEMS™ bottles included: Acyclovir ($n = 3$), Prograf ($n = 2$), and Bactrim ($n = 1$).

Analyses

Two participants were excluded from analyses (loss of device, $n = 1$; discontinued use of device within 40 days, $n = 1$), resulting in a final sample of six participants. A-priori decision rules were applied to account for times when medications were not being dispensed from the bottle. Periods during which a patient was hospitalized, in the emergency room, or having a medication "held" by the medical team were coded as "non-monitored." Data were also coded as "non-monitored" if families reported they were no longer using the MEMS™ bottle.

Table 1
Demographic and clinical characteristics.

	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5	Participant 6
Adolescent						
Gender	Male	Female	Female	Male	Male	Male
Age at transplant, yrs	12	13	13	16	16	13
Diagnosis	Supratentorial primitive neuroectodermal tumors	Acute Lymphoblastic Leukemia	Fanconi Anemia	Pre-B Cell Acute Lymphoblastic Leukemia	X-linked Lymphoproliferative Disease	Acute Myeloid Leukemia
Race	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian
Ethnicity	Non-Hispanic	Non-Hispanic	Hispanic	Non-Hispanic	Non-Hispanic	Non-Hispanic
Caregivers						
Primary caregiver	Mother	Mother	Mother	Mother	Mother	Mother
Marital status	Married	Married	Married	Married	Married	Married
Family						
Income	>$100,000	–[a]	$20,000–$29,999	>$100,000	$40,000–$49,999	>$100,000
Household size	6	4	3	4	4	5

[a] Participant 2 chose not to answer this question.