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Original article

Headache types, related morbidity, and quality of life in survivors of childhood acute lymphoblastic leukemia: A prospective cross sectional study

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ABSTRACT

Background: Increased headache prevalence was recently reported in survivors of childhood ALL. Headache sub types, related morbidity, and effect on quality of life has not been reported thus far.

Objective: To study headache prevalence and type, related disability, and quality of life in a cohort of childhood acute lymphoblastic leukemia (ALL) survivors.

Methods: Childhood ALL survivors in at least 1-year of remission and 5 years from diagnosis completed questionnaires and were evaluated by a neurologist. Disability was evaluated with Pediatric Migraine Disability Assessment scale and the Short Form-36 Health Survey assessed quality of life.

Results: Thirty nine of 72 (54%) females and 37 of 90 (41%) males reported headaches. Median time from ALL diagnosis to first headache was 5.2 years and median age at headache onset was 10.1 years in 76 participants with headache. Migraine headaches were diagnosed in 51 (31%) and episodic tension-type headaches in 49 (30%); migraine and tension-type headaches co-existed in 24 (15%) and 18 (11%) participants had chronic daily headaches. Fatigue was associated with migraine headache while hypertension and female gender associated with tension type headache. Headache-related disability was mild in 22 (29%), moderate in 7 (9%), and severe in 5 (7%) survivors, and was absent in the remaining 42 (55%) survivors with headache. Both migraine and tension type headaches associated

Abbreviations: ALL, acute lymphoblastic leukemia; CCSS, childhood cancer survivor study; PedMIDAS, Pediatric Migraine Disability Assessment scale; SF-36, the medical outcome survey short form-36.

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with reduced mental component scores, while headache related disability associated with a reduced physical component scores.

Conclusions: Headaches are common in ALL survivors but only a minority has significant disability or impairment of quality of life.

1. Introduction

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy and 3000–4000 children are diagnosed with ALL every year.[1] Development of more effective therapy, and advances in supportive care have substantially improved the outcomes of children with ALL, with cure rates of >85% even without the use of radiation therapy.[2] Nevertheless, all children with ALL are treated with potentially neurotoxic drugs, both intravenous and intrathecal.

As the survival rates for children treated for ALL increase, recognition, prevention and optimal management of late toxicities of therapy becomes even more important. Late effects of therapy for childhood leukemia include both neurotoxicity and psychosocial effects.[3] Neurologic complications may include leukemic involvement of the leptomeninges and brain parenchyma, white matter lesions, small-vessel calcifications, cerebrovascular disorders, secondary tumors, and infections.[4–6] Late neurologic outcomes among 4151 adult survivors of childhood ALL were recently reported by the Childhood Cancer Survivor Study (CCSS) and headache was the most common neurologic condition (cumulative incidence of 21% at 20 years).[7] Utilization of a self-reported questionnaire and lack of direct physician input prevented CCSS investigators from qualifying different headache syndromes. Additionally, the headache-related disability and association with quality of life could not be explored.

The primary aim of our study was to prospectively evaluate the neurologic symptoms and signs in a large cohort of ALL survivors. Secondary aims included studying risk factors for neurologic symptoms, assessing disability associated with neurologic symptoms, and effect on health related quality of life. In this paper we report results on headache and related morbidity in long-term ALL survivors.

2. Methods

2.1. Participants

Children treated at St. Jude Children's Research Hospital (St. Jude) are followed after completion of therapy for at least 10 years and at least until 18 years of age. This prospective cross sectional study was approved by the Institutional Review Board. Study eligibility required cancer to be in remission for a year, treatment on institutional protocol, and at least five years from their original ALL diagnosis. Survivors were recruited during their routine annual follow-up visits. All participants were English speaking and did not have pre-existing neurologic disorder which could have affected study results. Written informed consent was obtained from participants when 18 years of age or older, and from the parents or guardians when younger, with assent from the child participant as appropriate.

About 432 potential participants visited the institution from December 2005 to October 2008. Of these, 260 could be invited to participate based on the availability of study personnel and coordination of patient schedules and 232 agreed to participate. However, 58 could not be scheduled due to participant's or physician's schedule (Fig. 1). Thus, 162 (80%) of 202 available survivors could be enrolled over a three year period. As reported previously,[8] there were no statistically significant differences in demographic or treatment variables between 162 participants and 270 non-participants.

2.2. Study measures

2.2.1. Headache diagnosis

After enrollment, a trained study personnel administered the questionnaire, with the patient serving as the primary respondent and a parent corroborating information when needed. This was followed by a face to face interview and

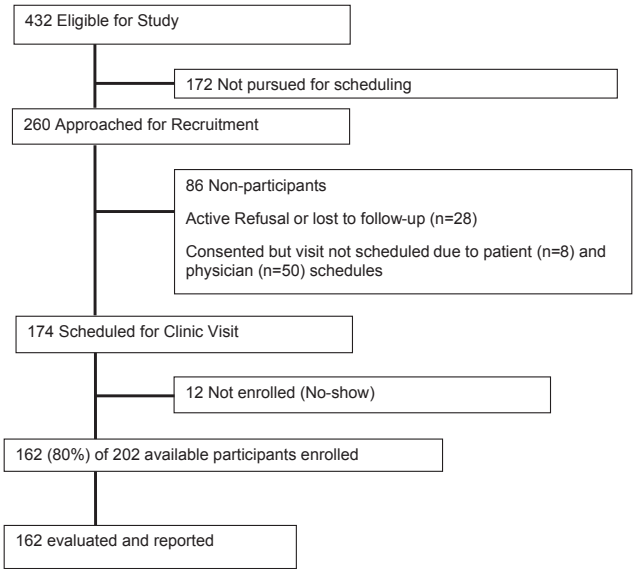

Fig. 1 – Recruitment and participation of patients Consort diagram of accrual of patients based on eligibility with inclusion criteria for recruitment. The actual evaluable participants are those who agreed to participate, did not have scheduling conflicts, or who did not miss their appointments.