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Disturbed Sleep in Pediatric Patients With Leukemia: The Potential Role of *Interleukin-6* (–174GC) and *Tumor Necrosis Factor* (–308GA) Polymorphism

Kelly Vallance, MD, MPH, MS, Jie Yang, PhD, Jiang Li, PhD, Valerie McLaughlin Crabtree, PhD, Pamela S. Hinds, PhD, RN, FAAN, and Belinda N. Mandrell, PhD, RN

Pediatric patients with cancer have rated disrupted sleep and fatigue as two of the most distressing symptoms related to their illness and treatment (Hinds et al., 1999; Hinds, Hockenberry, Gattuso, et al., 2007). These disturbances can persist for years after treatment for acute lymphoblastic leukemia (ALL), with as many as 50% of ALL survivors reporting sleep problems more than 10 years after completion of anticancer therapy (Meeske, Siegel, Globe, Mack, & Bernstein, 2005). Sleep disturbances in patients with cancer are common but often are undiagnosed or assumed to be a tolerable side effect of cancer or its treatment (Rosen, Shor, & Geller, 2008). Several studies have demonstrated poor sleep efficiency in pediatric patients undergoing cancer treatment, with an average sleep efficiency of 84% in patients with ALL who were in their home environment and 72% in patients with acute myelogenous leukemia or solid tumors who were in a hospital environment (Hinds, Hockenberry, Gattuso, et al., 2007; Hinds, Hockenberry, Rai, Zhang, Razzouk, Cremer, et al., 2007; Hinds, Hockenberry, Rai, Zhang, Razzouk, McCarthy, et al., 2007). Hinds, Hockenberry, Gattuso, et al. (2007) documented poor sleep quality and high levels of fatigue in children and adolescents at home during continuation chemotherapy for ALL. The study found that these patients stayed in bed longer, had poorer sleep efficiency, and had more nocturnal awakenings than cohorts of healthy children and adolescents. Given the detrimental effects of poor sleep on the immune system and cognitive development, the authors of this current article believe that decreased sleep quality is a crucial area to explore in pediatric patients with cancer. Therefore, the authors proposed a biobehavioral model of disrupted sleep in that genetic variability of selected inflammatory mediators might predict at-risk pediatric

Purpose/Objectives: To explore an association between sleep quality in children and adolescents undergoing therapy for acute lymphoblastic leukemia (ALL) and polymorphisms in two proinflammatory cytokines, interleukin-6 (IL-6) and tumor necrosis factor (TNF).

Design: Retrospective exploratory analysis using data from a multi-institutional prospective study comparing objective sleep measures by actigraphy over 10 days with retrospective genotyping of *IL-6* (–174GC) and *TNF* (–308GA).

Setting: Pediatric oncology centers in the southeastern and southwestern United States and in Canada.

Sample: 88 children or adolescents with ALL.

Methods: Secondary analysis of 88 patients (ages 5–18) with sleep quality measured by actigraphy over 10 days in their home environment and retrospective DNA genotyping.

Main Research Variables: Sleep variables and genotype.

Findings: *IL-6* promoter (–174G>C) C allele was associated with fewer total daily sleep minutes ($p = 0.028$) and fewer daily nap minutes ($p < 0.01$). Patients with the *TNF* genotype AA had 28.2 more minutes of wake after sleep onset ($p = 0.015$), 3.4 more nocturnal wake episodes ($p = 0.026$), and a 5% lower sleep efficiency rate ($p = 0.03$) than their GA genotype counterparts.

Conclusions: Patients with the *TNF* (–308G>A) or *IL-6* (–174G>C) polymorphisms demonstrated disturbed sleep. This study is the first to find a relationship between these two cytokines and disturbed sleep in children and adolescents with cancer.

Implications for Nursing: Disturbed sleep among pediatric patients with cancer is multifactorial and includes interactions among environment, medications, and genotype. Additional research should explore serum proinflammatory cytokine levels and the influence of mood and worry on sleep.

patients with cancer. The study framework was the Human Response Model, which integrates biopsychological factors, individual characteristics that may or may