A Pilot Study of the Association Between Sleep Disturbance in Children With Liver Transplants and Parent and Family Health-Related Quality of Life

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Objective To investigate the relationship between sleep disturbance in children with liver transplants and parent and family health-related quality of life (HRQOL). Method 47 parents of children with liver transplants completed measures of child sleep and family HRQOL. Relationships between sleep and HRQOL and differences in HRQOL between groups with scores above and below the cutoff on a pediatric sleep measure were examined. Results Parents endorsed higher rates of sleep-related breathing disorder (SRBD) and restless legs syndrome and periodic limb movements during sleep (RLS/PLMS) and lower HRQOL compared with published data. Significant correlations were found between SRBD and RLS/PLMS and lower HRQOL compared with published data. Significant group differences in HRQOL were found between groups above and below the cutoff for behavior problems and RLS/PLMS. Conclusion There are significant relationships between symptoms of SRBD and RLS/PLMS in children with liver transplants and family HRQOL. Behavior problems may account for these strong relationships.

Key words behavior problems; organ transplantation; parents; quality of life; sleep.

Research focusing on the health-related quality of life (HRQOL) of children with liver transplants has increased in the past decade in an effort to improve long-term functional outcomes (Alonso et al., 2003, 2013; Anthony, Pollock Barziv, & Ng, 2010; Devine et al., 2011). Children and adolescents with liver transplants have lower reported HRQOL and greater emotional, social, cognitive, and behavioral difficulties compared with children who are healthy or have other chronic illness, including type 1 diabetes and cardiac disease (Alonso et al., 2010; Bucuvalas et al., 2003; Fredericks, Lopez, Magee, Shieck, & Opipari-Arrigan, 2007; Limbers et al., 2011). Child HRQOL has important implications for parent and family functioning. When impaired, family functioning has been linked with low HRQOL in children and adolescents with liver transplants (Alonso et al., 2010; Devine et al., 2011; Taylor, Franck, Gibson, Donaldson, & Dhawan, 2009).

Parents play a vital role in managing the health-care needs of children and adolescents with liver transplants (Devine et al., 2011). Strong relationships have been found between the psychosocial functioning of parents and the cognitive, language, motor, and social development
of children with liver transplants (Posfay-Barbe, Barbe, Wetterwald, Belli, & McLin, 2013). In addition, family disruption and poorer family cohesion have been linked to medication nonadherence and lower parent and child well-being (Fredericks et al., 2007, 2012). Caring for a child with a chronic health condition requires higher-order skills such as organization, communication, monitoring, problem solving, and coping (Fredericks, 2012). Yet, parents of children and adolescents with liver transplants endorse greater parenting stress, emotional disturbances, and disruption to family activities compared with the general population (Alonso et al., 2003; Bucuvalas et al., 2003; Denny et al., 2012; Sundaram, Landgraf, Neighbors, Cohn, & Alonso, 2007). It is important to identify factors that affect the functioning of these families to promote better care and development of children with liver transplants.

Increased attention has been placed on the impact of sleep problems on parent and family functioning in healthy and chronically ill children (Meltzer & Montgomery-Downs, 2011; Meltzer & Moore, 2008). Sleep disruption in children with chronic illness has been linked with parental reports of diminished health and marital dissatisfaction (Cottrell & Khan, 2005), increased daytime sleepiness, fatigue, anxiety, and depression, and decreased sleep quantity and quality (Boerger, Hart, Owens, Streisand, & Spirito, 2007; Monaghan, 2012). Chronic partial sleep deprivation in parents adversely affects parents’ cognitive performance, communication, and executive functioning (Meltzer & Mindell, 2006; Plessow, Kiesel, Petzold, & Kirschbaum, 2011), all of which are important skills for parents providing medical care to their children.

In a previous study conducted as part of a larger investigation of HRQOL and sleep in children with liver transplants, we found that children and adolescents with liver transplants have higher reported rates of symptoms indicative of restless legs syndrome and periodic limb movements during sleep (RLS/PLMS; e.g., urge to move legs at night, pain in legs, waking multiple times per night, getting out of bed), sleep disordered breathing (e.g., snoring, difficulty breathing during sleep, daytime sleepiness), and daytime behavior problems related to sleep difficulties (e.g., inattention and/or hyperactivity, impulsivity, difficulty with organization) relative to a general pediatric population (Fredericks et al., 2012). These sleep problems accounted for a significant amount of the variance in the children’s HRQOL. Given the critical role parents have in relation to health management and development of children with liver transplants and the important implications both child HRQOL and sleep have for parent and family functioning, it is important to investigate further the impact sleep problems in this population may have on the HRQOL of parents and families of children and adolescents with liver transplants.

The relationship between sleep disturbance, behavioral difficulties related to sleep problems, and parent and family HRQOL among pediatric liver transplant recipients and their families is an area that is not fully understood. It may be that these relationships are similar to those observed in other pediatric populations, wherein the alleviation of child sleep disturbances had a broad impact on family life, including improvement in parent sleep, mood, marital satisfaction, and family HRQOL (Eckerberg, 2004; Hiscock & Wake, 2002; Meltzer & Mindell, 2007; Mindell & Durand, 1993). Child sleep disturbance is a modifiable condition that, if found to have a significant association with parent and family HRQOL, provides a target for treatment that could lead to meaningful improvements in parent and family functioning, and ultimately the health and well-being of children and adolescents with liver transplants.

The overall objective of this pilot study was to examine the relationship between sleep in children and adolescents with liver transplants and parent and family HRQOL as part of a cross-sectional examination of sleep disturbances and HRQOL in pediatric liver transplant recipients. The specific aims were to (a) determine the association between sleep problems in children and adolescents with liver transplants and parent and family HRQOL, and (b) examine differences in parent and family HRQOL between groups above and below the cutoff on a pediatric sleep measure.

**Method**

**Participants**

Participants consisted of 47 parents/guardians of children and adolescents with liver transplants. The parents/guardians were selected from a subset of a sample of children and adolescents with liver transplants reported previously (Fredericks et al., 2012). Parents were identified through their child’s electronic medical record and deemed eligible for participation if their child was between the ages of 2 and 17 years and >6 months after liver transplantation. Children and their parents were recruited from the Pediatric Liver Transplant Clinic at our institution. One parent participated per child and family, and 87% of the respondents were mothers. Mean age of children was 10.9 years (SD = 4.6), and mean time since transplant was 6.2 years (SD = 3.9). Twenty-six children (56%) were female. Fifty-five percent of the children were European American, 30% were African American, 4% were Asian, 4% were
Hispanic, and 2% were American Indian. Fifty-one percent of the children had biliary atresia. Twenty-one percent of the children were actively taking steroids, and 64, 23, and 13% were taking 1, 2, and 3 immunosuppressant medications, respectively.

Procedures
This pilot study was approved by the institutional review board. After their child’s appointment in the Pediatric Liver Transplant Clinic, parents were recruited to participate in a study investigating sleep and quality of life in pediatric liver transplant recipients. Informed consent was obtained and parents completed instruments assessing symptoms associated with pediatric sleep disorders and HRQOL. Medical and demographic information were gathered from the child’s electronic medical record.

Measures
PedsQL™ Family Impact Module
The PedsQL™ Family Impact Module (FIM; Varni, Sherman, Burwinkle, Dickinson, & Dixon, 2004) was used to assess parent and family HRQOL. The FIM is a 36-item parent report measure of the impact of pediatric chronic health conditions on parent and family functioning across eight domains: Physical, emotional, social, and cognitive functioning; communication, worry, family daily activities, and family relationships. It yields three summary scores: The Total score, Parent HRQOL Summary score, and Family Functioning Summary score. Items consist of Likert-type response choices that are reverse scored and converted linearly into a scale of 0–100. Higher scores reflect better HRQOL. This is a valid and reliable measure of HRQOL for parents and families of children with complex health conditions (Varni et al., 2004), chronic pain (Jastrowski Mano, Khan, Ladwig, & Weisman, 2011), sickle cell disease (Panepinto, Hoffmann, & Pajewski, 2009), children undergoing chemotherapy (Scarpelli et al., 2008), and a community sample (Medrano, Berlin, & Davies, 2013).

Pediatric Sleep Questionnaire
Because of the high frequency of children with liver transplants who reported to our pediatric liver transplant clinic with sleep-related breathing disorder (SRBD) and/or RLS/PLMS symptoms, the Pediatric Sleep Questionnaire (PSQ) was selected as the pediatric sleep measure in the current study. The PSQ is a validated parent report measure of sleep disturbance for children aged 2–18 years (Chervin, Hedger, Dillon, & Pituch, 2000). Items are answered as “yes” = 1, “no” = 0, or “don’t know” (scored as missing). Scores reflect the mean response of nonmissing items. A cutoff score of 0.33, indicating that 33% of rated items were positive, is considered to be a positive screen for clinically significant sleep disturbances (Chervin et al., 2000; Chervin & Hedger, 2001). The PSQ yields a 22-item SRBD Index that consists of three subscales: Snoring (nighttime breathing difficulties), Sleepiness (excessive daytime sleepiness), and Behavior (inattentive—hyperactive, impulsive, and disorganized behaviors related to sleep problems and characteristic of attention-deficit/hyperactivity disorder [ADHD]; Chervin et al., 2002). The PSQ also includes a 6-item subscale assessing symptoms of RLS/PLMS. The PSQ subscales have good reliability and validity compared with polysomnography (PSG; Chervin & Hedger, 2001; Chervin et al., 2000, 2006, 2007), and the PSQ is categorized as a “well-established” pediatric sleep measure based on criteria instituted by the American Psychological Association Division 54 Evidence-Based Assessment Task Force (Lewandowski, Toliver-Sokol, & Palermo, 2011).

Health Status Variables
Variables indicative of the child’s health for the year before participation in the study were obtained, including time since transplantation, number of immunosuppressant medications, liver function test results (total bilirubin [TBili], aspartate phosphatase [AST], alanine aminotransferase [ALT]), and number of acute cellular rejection episodes.

Data Analyses
Descriptive statistics (i.e., M, SD, percentages) were calculated for demographic variables, health status variables, and scores on the PSQ and FIM. Because of the categorical nature of the PSQ data, Spearman’s rho correlation analyses were conducted to examine the relationships between child sleep problems and parent and family HRQOL. First, age, health status variables (described above), subscales of the PSQ and the primary FIM indices (FIM Total Scale, Parent HRQOL Summary, and Family Functioning Summary) were entered into the initial correlational analysis to identify potential covariates. No significant correlations were found. For the primary analyses, (a) a correlational analysis was conducted between the PSQ and FIM scales; and (b) independent sample t-tests were used to examine group differences in FIM scores between children above and below cutoff scores on the PSQ (0.33). To control for multiple comparisons, a more stringent cutoff value of 0.01 was used to determine significance. Analyses were conducted using SPSS (IBM Corp. Released 2011. IBM SPSS Statistics, Version 20.0. Armonk, NY: IBM Corp.).
Results

Descriptive Analyses

Descriptive data for the PSQ and FIM are displayed in Table I. A substantial proportion of parents endorsed scores above the cutoff on PSQ scales. Approximately 45 and 40% of the parents rated his/her child above the cutoff score for SRBD and sleepiness symptoms, respectively. Nearly 30% of the parent ratings exceeded the cutoff for the RLS/PLMS subscale. The mean Behavior score was almost twice the cutoff score, with ~75% of parents rating his/her child above the cutoff for behavior problems related to sleep disruption. Parent ratings of HRQOL were similar across all three summary scales.

Correlational Analyses

Relationships Between Sleep and Parent and Family HRQOL

There were no significant relationships between measures of health status or demographic variables and summary scales on the FIM. All three summary scores on the FIM had significant, negative correlations with the SRBD and RLS/PLMS scales on the PSQ, and the Family Functioning Summary was negatively correlated with the Behavior subscale (Table II).

Between-Group Comparisons

As shown in Table III, parents of children and adolescents with scores above the cutoff on the RLS/PLMS and Behavior scales on the PSQ endorsed significantly lower HRQOL as compared with parents whose children had scores below the cutoff on the PSQ scales.

Discussion

This pilot study examined the association between sleep disturbances as measured by the PSQ among children and adolescents with liver transplants and family HRQOL. Results are consistent with previous literature linking child sleep disturbance with impaired parent and family functioning (Boergers et al., 2007; Monaghan, 2012) and extend the literature by connecting sleep disturbance in children and adolescents with liver transplants to lower parent and family HRQOL (Alonso et al., 2003; Bucuvalas et al., 2003). In the current study, parents reported significantly lower HRQOL, particularly when behavioral difficulties associated with sleep problems are present. This suggests that the high rates of inattention, hyperactivity, and executive functioning difficulties in children and adolescents with liver transplants (Kaller, Langguth, Ganschow, Nashan, & Schulz, 2010; Sorensen et al., 2011) may account for the link between child sleep problems and family HRQOL found in this study.

Multiple health-related factors may contribute to the high rates of SRBD and RLS/PLMS reported in this population. With respect to liver disease, physical illness that impairs brain functioning (e.g., hepatic encephalopathy) has been speculated to affect neurological development in children with liver transplants (Sorensen et al., 2011). Acute pediatric steroid use and immunosuppressive therapy have also been linked with sleep disturbance and difficulties with behavior and executive functioning (Kemper, Sparta, Laube, Miozzari, & Neuhaus, 2003; Mrakotsky et al., 2013; Reichenspurner, 2005). The relationship between child sleep problems and steroid use was previously reported, and no significant associations were observed (Fredericks et al., 2012). However, a larger sample would need to be examined to better understand the impact of
steroid use on sleep in this population. Results of the current study suggest that the sleep problems and associated behavioral difficulties in this population are less likely to be due to current health-related factors. However, it is also noted that the majority of the children were taking one immunosuppressant agent, indicating medical stability. Finally, strong associations have been observed between symptoms of ADHD and sleep disorders in children (Cassoff, Wiebe, & Gruber, 2012), and longitudinal research has linked early sleep disruption with the development of ADHD in later childhood (Chervin, Ruzicka, Archbold, & Dillon, 2005). It is also possible that subclinical encephalopathy goes unrecognized or is difficult to measure in infants and young children with severe liver disease. The high rates of SRBD and RLS/PLMS reported in the current study likely contribute to the high rates of behavior problems found to be related to HRQOL in this pilot study.

Although the etiology of sleep problems reported in the current study is unknown, physiological and environmental factors may contribute to this finding. Over half of the children in this pilot study had biliary atresia, a congenital liver disease presenting in infancy. Thus, a substantial proportion of the parents have managed the symptoms accompanying their child’s chronic illness since infancy. Maternal stress and emotional difficulties associated with having a young child with a chronic illness and managing distress during the night can further exacerbate child sleep problems (Meltzer & Montgomery-Downs, 2011). Additionally, high rates of RLS have been found in adults with liver transplants, implicating comorbid disease (e.g., diabetes) and antidopaminergic medications (i.e., antidepressants, antihistamines) as factors influencing RLS symptoms (Franco, Syed, Franco, Saeian, & Farhan, 2013). The pathophysiology of RLS in children and adolescents with liver transplants has yet to be studied, but low iron stores and dopamine deficiency have been speculated as mechanisms through which pediatric RLS develops (Picchietti & Picchietti, 2010). It should be noted that the nature of sleep difficulties changes across development, and there was a wide age range within the current sample. Sleep difficulties as measured by the PSQ were not related to child age in this preliminary study.

The results of this pilot study should be interpreted in light of the following limitations. The cross-sectional design and statistical analyses used in this study prevent the ability to infer causation between sleep problems and parent and family HRQOL. Generalizability and statistical power are also limited by the small sample size obtained from a single center. Despite lower power, several significant relationships were found using more conservative criteria for statistical significance. Therefore, it is possible that additional significant comparisons would be found with a larger sample size. Child sleep was also measured using one subjective parent-reported measure yet to be validated with this population. Relatedly, validated measures of adolescent-reported sleep and objective measures of sleep were not used in this preliminary study. Furthermore, although the Behavior subscale on the PSQ specifically targets daytime behavior problems related to night-time sleep difficulties (e.g., inattention, hyperactivity, impulsivity), this study did not use an empirically validated global measure of child behavioral functioning. The relatively low internal reliability for the RLS/PLMS subscale suggests that results may vary across studies, and further examination of the PSQ is required with a

Table II. Spearman Rank Correlations Between Child Sleep (PSQ) and Parent and Family HRQOL (FIM)

<table>
<thead>
<tr>
<th></th>
<th>FIM Total Scale</th>
<th>Parent HRQOL Summary</th>
<th>Family Functioning Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRBD Index</td>
<td>−0.42*</td>
<td>−0.37*</td>
<td>−0.42*</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>−0.20</td>
<td>−0.22</td>
<td>−0.17</td>
</tr>
<tr>
<td>Behavior</td>
<td>−0.33</td>
<td>−0.23</td>
<td>−0.37*</td>
</tr>
<tr>
<td>RLS/PLMS</td>
<td>−0.41*</td>
<td>−0.38*</td>
<td>−0.39*</td>
</tr>
<tr>
<td></td>
<td>0.004</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note. Bold values indicate significant results.
*p < .01.

Table III. Comparison of Scores on the FIM Among Children Above and Below the Cutoff (0.33) on the PSQ

<table>
<thead>
<tr>
<th></th>
<th>SRBD</th>
<th>Sleepiness</th>
<th>Behavior</th>
<th>RLS/PLMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>FIM Total Scale</td>
<td>69.63*</td>
<td>76.12*</td>
<td>68.40*</td>
<td>76.49</td>
</tr>
<tr>
<td>Parent HRQOL Summary</td>
<td>68.35*</td>
<td>76.27</td>
<td>67.64*</td>
<td>76.19</td>
</tr>
<tr>
<td>Family Functioning Summary</td>
<td>68.69*</td>
<td>75.99</td>
<td>66.14*</td>
<td>77.20</td>
</tr>
</tbody>
</table>

Note. Bold values indicate significant results.
*p < .01.
larger sample of pediatric transplant recipients. Finally, other factors associated with child sleep problems and family HRQOL (e.g., child self-report of sleep problems, parent sleep patterns) were not measured in this study.

Results of this pilot study suggest that further evaluation of sleep disturbance in children and adolescents with liver transplants and family HRQOL is warranted. The relationship between parent and family HRQOL and primary symptoms that comprise SRBD (e.g., snoring, excessive daytime sleepiness, daytime behavior problems) should be explored in future research. Additionally, sleep problems in liver transplant recipients should be assessed using objective measures, such as iron studies as an indicator of risk for RLS/PLMS (Picchietti & Picchietti, 2010), and PSG and actigraphy for measures of breathing problems and movement during sleep, respectively (Sadeh, 2011). Longitudinal, multicenter studies are needed to investigate causal relationships between sleep problems, behavior problems, and child, parent, and family HRQOL. Additional variables should be included in future investigations to determine the extent to which these variables explain differences in parent and family HRQOL. These variables should include comprehensive measures of children’s emotional, behavioral, and executive functioning, health-related variables (e.g., medication, history of hepatic encephalopathy), child and adolescent self-report of sleep difficulties, and other parent-related variables (e.g., demographics, sleep patterns).

The results of this pilot study provide preliminary evidence that high rates of sleep disturbances in children and adolescents with liver transplants may be one factor impacting parent and family HRQOL in this population. Given the significant reduction in behavior problems linked with alleviation of sleep problems (Marcus et al., 2013), sleep should be assessed more ubiquitously in children and adolescents with liver transplants to address modifiable variables that can lead to improvements in behavior problems associated with sleep difficulties, and child, parent, and family HRQOL.

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**Conflicts of interest:** None declared.

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