Anxiety Measures Predict Health-Related Quality of Life in Children and Adolescents with Cyclic Vomiting Syndrome

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Objective To evaluate the relationship between anxiety and health-related quality of life (HRQoL) in children and adolescents with cyclic vomiting syndrome (CVS).

Study design Forty children aged 8-18 years diagnosed with CVS and 40 parents completed the Screen for Child Anxiety Related Emotional Disorders (SCARED) and the child and parent forms of the Pediatric Quality of Life Generic Core Scale, a measure of HRQoL.

Results Eleven of the 40 children (27%) by self-report and 6 of 40 (15%) by parent-proxy report met the clinical cutoff for an anxiety disorder on the SCARED. Parent and child SCARED ratings were moderately correlated (intraclass correlation coefficient 0.68; $P < .001$). Child-rated HRQoL (mean ± SD, 74.3 ± 15.2) and parent-rated HRQoL (mean, 72.1 ± 14.6) were lower than healthy norms ($P < .001$). Disease severity (mean duration of CVS episodes, 3 ± 2.4 days), annual frequency of CVS episodes (mean, 8.2 ± 15.3), chronicity of CVS (mean, 5.8 ± 3.4 years), and delay in diagnosis (mean, 2.4 ± 1.9 years) were not associated with child-reported HRQoL; however, child SCARED scores accounted for approximately 50% of the variance in child-reported HRQoL (adjusted $R^2 = 0.49$; df = 1, 38; $P < .001$).

Conclusion Children and adolescents with CVS appear to be at increased risk for anxiety. Anxiety symptoms are a stronger predictor of HRQoL than disease characteristics in children and adolescents with CVS. Assessment and treatment of anxiety in children and adolescents with CVS may have a positive impact on HRQoL. *(J Pediatr 2015;167:633-8)*.

Cyclic vomiting syndrome (CVS) is a functional gastrointestinal disorder characterized by recurring, stereotypic episodes of high intensity vomiting lasting for hours to days, often accompanied by symptoms of unrelenting nausea, retching, and severe abdominal pain.[1] Between episodes, patients are typically healthy and resume normal activities.[1] CVS is diagnosed based on the consensus criteria developed by an international multidisciplinary committee.[2] Typically an extensive diagnostic evaluation is conducted to exclude other serious medical causes that can mimic its presentation, including intestinal malrotation, hydronephrosis, metabolic disorders, and increased intracranial pressure.

Health-related quality of life (HRQoL) in children with CVS is low compared with that in children with irritable bowel syndrome and healthy peers, and similar to that in children with organic gastrointestinal disorders.[3] This situation is similar to that of children with functional abdominal pain, who have lower HRQoL compared with healthy children and similar HRQoL as children with inflammatory bowel disease and gastroesophageal reflux.[4] Anxiety is associated with CVS[5,6] and other pediatric functional gastrointestinal disorders, including functional abdominal pain[7-9] and nausea-predominant dyspepsia.[10] Preliminary research indicates that anxiety can have a significant impact on HRQoL in children with such medical conditions as chronic pain[11] and epilepsy.[12]

To date, no published study has evaluated the relationship between anxiety and HRQoL in pediatric CVS. The aim of the present study was to evaluate the relationship between child self-reports and parent-proxy reports of the child's anxiety symptoms and disease characteristics and HRQoL in a cross-sectional study.

Methods

Children were recruited from a specialty clinic for CVS at a children's hospital. Those aged 8-18 years who met the international consensus criteria for CVS[2] were invited to participate. Diagnostic criteria included: (1) recurrent severe, discrete episodes of vomiting; (2) normal health between episodes; (3) duration of vomiting of hours

CBT	Cognitive behavioral therapy
CVS	Cyclic vomiting syndrome
HRQoL	Health-related quality of life
ICC	Intraclass correlation coefficient
PedsQL	Pediatric Quality of Life Generic Core Scale
SCARED	Screen for Child Anxiety Related Emotional Disorders

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to days; and (4) no apparent cause of vomiting, as well as supportive criteria that the episodes be stereotypical and self-limited. Children who were not English speakers or who had other major medical or developmental disorders were excluded. Demographic and medical information was collected by parent interview and review of the medical record.

Anxiety

Anxiety symptoms were assessed with the Screen for Child Anxiety Related Emotional Disorders (SCARED; http://psychiatry.pitt.edu/research/tools-research/assessment-instruments).[13] This 41-item questionnaire, based on the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* criteria for anxiety disorders in children, is validated for use in children aged 8 years and older. The SCARED screens for symptoms associated with specific anxiety disorders, as well as for behaviors, such as school avoidance, that are common across anxiety disorders in children. Total SCARED scores range from 0 to 82, with a score of ≥25 indicative of clinically significant anxiety symptoms. Both the child self-report and parent-proxy versions of the SCARED were used. The total SCARED scores were used to evaluate the relationship of anxiety symptoms to child- and parent-rated HRQoL in the child participants.

HRQoL

Children aged 8-18 years completed the age-appropriate Pediatric Quality of Life Generic Core Scale (PedsQL),[14] a 23-item measure that yields a total HRQoL score and subscale scores of physical-, emotional-, social-, and school-related quality of life, as well as a composite psychosocial measure comprising the emotional, social, and school subscales. The PedsQL 4.0 versions for children (aged 8-12 years) and adolescents (aged 13-18 years) were used. Both the total HRQoL and the subscale scores range from 0 to 100, with higher scores indicating better HRQoL.

Parents completed the age-appropriate PedsQL for their child or adolescent. The PedsQL inventories are validated instruments with satisfactory internal reliability,[15,16] including for those with CVS.[3]

Comparison group data were derived from a study by Varni et al,[17] which included a healthy control group and caregivers. The hospital's Institutional Review Board approved this study. Parents and children provided written consent/assent before participating.

Statistical Analyses

Data analyses were performed with SPSS version 22.0 (IBM, Armonk, New York). The Cronbach α was used to evaluate the internal reliability of the PedsQL and the SCARED in the study sample. Intraclass correlation coefficients (ICCs) were used to evaluate agreement between parent and child reports of anxiety symptoms and HRQoL. ICC values were interpreted as follows: 0.40, poor agreement; 0.41-0.60, moderate agreement; 0.61-0.80 good agreement; and 0.81 and higher, excellent agreement. The *t* test was used to examine differences in HRQoL between children with CVS and their parents' proxy reports of HRQoL and published norms for healthy controls. Effect sizes were calculated using the Cohen *d*, with 0.20 indicating a small effect, 0.50 indicating a moderate effect, and 0.80 indicating a large effect. Stepwise multiple linear regression was used to examine associations among child self-reported and parent-proxy–reported anxiety symptoms, CVS characteristics, and HRQoL. Missing data for any dependent variable were excluded from the analyses. The significance level was set at $P = .01$ to control for type 1 error.

Results

Of the 68 eligible families with CVS, 58 were enrolled in the study (85%). Data analyses were performed for the 40 families with complete data (**Figure**; available at www.jpeds.com). There were no differences between the families who did not enroll or did not complete the questionnaires in terms of child age, sex, or ethnicity. Parents completed the parent-proxy version of the SCARED, and 40 children completed the self-report version of the SCARED. Forty children completed the age-appropriate self-report version of the PedsQL (8-12 years, n = 20; 13-18 years, n = 20), and 40 parents completed the age-appropriate PedsQL for their child. Characteristics of the study sample are summarized in **Table I** (available at www.jpeds.com).

Comorbid Conditions

Nine children had a comorbid functional gastrointestinal disorder, including 3 with constipation (7%), 2 with abdominal migraine (5%), and 1 with irritable bowel syndrome (2%). Other medical conditions in the study group included allergies (n = 6; 15%), asthma (n = 4; 10%), postural orthostatic tachycardia syndrome (n = 3; 7%), and others (n = 2; 5%). Information on functional gastrointestinal symptoms, such as abdominal pain and nausea, was not gathered, owing to the overlap of such symptoms with CVS. Eight children had a history of 1 or more psychiatric diagnoses, including attention deficit hyperactivity disorder (n = 5; 12%), anxiety disorder (n = 3; 7%), and depression (n = 2; 5%). One child was receiving a selective serotonin reuptake inhibitor, but did not have a specific psychiatric diagnosis. Information on concurrent psychotherapy was not gathered.

Medications

A majority of the children were receiving 1 or more medications for CVS (n = 26; 65%), including amitriptyline in 17 (42%), propranolol in 11 (27%), L-carnitine and/or coenzyme Q_{10} in 10 (25%), cyproheptadine in 4 (10%), and others in 2 (5%). One subject was using marijuana for symptom control. Twenty-six children (65%) were prescribed an abortive medication (eg, antiemetic, sedative, analgesic) to