

Health-Related Quality of Life is Associated with Hemoglobin Level in Children with Sickle Cell Anemia

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Abstract

Purpose: Pediatric health quality of life (HQOL) refers to a child's physical, emotional, and social well being. HQOL is often compromised in persons with sickle cell anemia (SCA). The purpose of this study was to compare HQOL with hemoglobin in children with SCA.

Methods: In a pilot study looking at energy expenditure in children with SCA, we measured subjects' QOL using the PedsQL survey and compared it to their hemoglobin (Hb) levels at baseline.

Results: Twenty-five subjects, all with HbSS, completed the instrument. Their mean age (standard deviation) was 11.4 (3.25) years and 52% were male. Their mean Hb level was 8.4 (1.2) g/dL. Higher scores in social functioning ($R=0.63$, $p=0.0001$) and school functioning ($R=0.40$, $p=0.05$) were significantly associated with higher Hb levels. **Conclusions:** We conclude that Hb level is related to HQOL and that treatments aimed at improving Hb may help to improve overall HQOL.

Keywords: Hemoglobin; Sickle cell; Children; Health related quality of life

Background

Pediatric health quality of life (HQOL) refers to a child's or parent's assessment of the child's physical, emotional, and social well-being [1]. A good HQOL is important for a child with a chronic condition, such as sickle cell disease, where the likelihood of a cure is small. Moreover, measures to improve HQOL are very important.

Children with sickle cell anemia (SCA) who experience recurring pain have a seven-fold increased risk of not attending school [2]. Both pain and absence from school are considered to be highly disruptive of social and recreational activities. Thomas et al. [3] found that children with SCA report negative effects on their physical, psychological, social and well-being. In their study, children with lower hemoglobin (Hb) levels experienced decreased energy and were often fatigued, which affected activities of daily living and led to an inability to develop social relationships with peers. Thus, having SCA can adversely influence the HQOL of children with this condition in multiple domains [4].

Thornburg et al. [5] found that patients on HU had significantly higher median scores on the Peds QL 4.0 and physical functioning scores that were significantly higher than those not receiving HU. Additionally, children who came into the emergency room (ER) had HQOL compared using the same tool upon ER entrance and 7-days post discharge [6]. This study found that HQOL score medians were significantly lower in the ER than 7-days post discharge.

Generic and disease-specific HQOL instruments that measure both parent and patient perspectives related to a child's HQOL have now been tested in clinical trials and found to be feasible and to yield reliable and valid findings in the clinical care setting [7]. Varni et al. (1999) [8] developed a pediatric generic HQOL instrument for children with chronic health conditions that measures well-being and physical, emotional, social, and school functioning using the patient self-report and/or parental report and thus has usefulness in documenting

self-reports of children with SCA. Panepinto et al. [9] looked at the performance of the PesQL 4.0 survey and determined that it is reliable and valid in the SC population.

Interventions to reduce or prevent SCA-related pain are likely to positively affect the HQOL of a child with SCA. Oral supplementation with the amino acid glutamine given to adults with SCA has been associated with prevention of pain episodes and improved energy and activity levels [10,11]. HU in children has been shown to increase HQOL in one study [5].

We conducted a pilot study in which energy expenditure was measured before and after treatment [11]. A sub-analysis of patients, who entered the study, was performed to examine the relationship of Hb to HQOL at baseline. The purpose of this sub-analysis was to compare HQOL variables with Hb levels in children with SCA to determine if there was a relationship between them.

Methods

Participants

Inclusion criteria for this energy expenditure study were: active patients, who were 5-18 years old, had a diagnosis of Hb SS and weighed at least 15 kg. Subjects were excluded if they were receiving hydroxyurea or another anti-sickling agent, chronic transfusion,

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Received July 17, 2012; **Accepted** August 28, 2012; **Published** August 30, 2012

Citation: Williams-Hooker R, Olivi S, Smeltzer MP, Wang WC (2012) Health-Related Quality of Life is Associated with Hemoglobin Level in Children with Sickle Cell Anemia. J Blood Disorders Transf 3:129. doi:10.4172/2155-9864.1000129

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or nutrition supplements; had a history of poor compliance with treatment; had renal or liver dysfunction; or were pregnant or breastfeeding. Patients on this study were not receiving any treatment for SCA and were relatively well, at the time of this study. They were asked to participate in the energy study by their physicians; therefore this was a convenience sample of subjects. No patients who were approached refused the study.

Quality of life instrument

Subjects completed the PedsQL questionnaire (Pediatric Quality of Life Inventory, Version 3.0)[8]. The instrument contained 30 questions that had a Likert response format with higher scores indicating higher QOL. Age-specific versions (for ages 5-7 years, 8-12 years, and 13-18 years) from the PedsQL 3.0 inventory were utilized. The questions were grouped into six domains: physical, emotional, social, school, well-being, and overall health. The questionnaire, which took approximately 10 minutes to complete, was a self-completed questionnaire that was given to the subjects and parents separately. The nurse read the questions to any subject who was not able to read well. All questions had answers such as never, sometimes, and always, which were given a score of 1-5, with 5 being the best possible health state and 1 being the worst. Although, Panepinto et al. [9] evaluated a newer version (4.0) than that of the survey used (3.0), the same questions were used, thus we also compared our work to the normative data Panepinto presented.

Study design/Data collection

Quality of life measurement was performed before starting treatment, baseline. Subjects had laboratory studies (complete blood count, chemistry panel and serum amino acid quantitation) and completed the PedsQL instrument at the same clinic visit. All study data were collected by the same research nurse.

Statistical analysis

The PedQL responses and Hb values were first assessed for their distributions using the Shapiro Wilk test. Descriptive statistics were then applied to those same responses. Spearman's Rank-Order correlation coefficient was used to compare HQOL and Hb levels, and

exact p-values reported. Median PedQL responses were compared between age groups using the Kruskal-Wallis test with exact p-values. PedsQL mean scores from our SCA cohort were compared with published mean scores from both well and chronically ill children using the two sample t-test. P values were not calculated for physical functioning due to departures from normality. All p values were reported in an exploratory manner and no adjustments were made for multiple comparisons.

This study was approved by the St. Jude Children's Research Hospital Institutional Review Board and all patients/parents signed assent/consent.

Results

Subjects were recruited from the St. Jude Sickle Cell Center. Twenty five patients completed the instrument and lab studies. The subjects had a mean age (standard deviation) of 11.35 (3.25) years; 13 (52%) were male. Their mean Hb level was 8.4 (1.2) g/dl; the median Hb level was 8.1 g/dl. Subjects with higher scores in social functioning and school functioning had significantly higher Hb levels (Table 1). When HQOL variables were examined by age group (5-7 years, 8-12 years, 13-18 years), no significant differences were found.

In addition, when compared with normative data, our cohort with SCA had significantly lower mean QOL scores than those of healthy children in the domains of emotional, social, and school functioning (p-values<0.01). However, when these subjects were compared to a normative sample of children with other chronic health conditions [e.g., asthma, diabetes, attention deficit hyperactivity disorder (ADHD), depression], no significant differences were observed (Table 2) [12].

Discussion

The purpose of this study was to look at factors that might influence HQOL in children with SCA. This was done as part of an energy expenditure study [11]. For this report, we compared Hb and age to HQOL data at baseline. We observed an association of lower Hb levels with lower HQOL scores in two categories: school functioning and social functioning. In the general population, it has been reported

QOL Variable	N	Height Z-Score		Weight Z-Score		Hemoglobin	
			P-Value	Correlation	P-Value		P-Value
Physical Functioning	24-25	0.20	0.34	0.17	0.43	0.30	0.14
Emotional Functioning	24-25	0.37	0.07	0.17	0.43	0.35	0.09
Social Functioning	24-25	0.33	0.12	0.29	0.17	0.63	0.001
School Functioning	24-25	0.35	0.10	0.28	0.18	0.40	0.050
Well Being	23-24	0.14	0.53	0.09	0.68	0.04	0.87
General Health	23-24	0.07	0.74	-0.02	0.93	-0.15	0.47
Hemoglobin	24-25	0.58	0.004	0.61	0.002	---	---

Table 1: Association Results (Spearman's Rank-Order Correlation).

Variable	SCD Patients			Normative Data-Healthy Sample*				Normative Data-Chronic Health Condition*			
	N	Mean	Std. Dev.	N	Mean	Std. Dev.	P-Value	N	Mean	Std. Dev.	P-Value
Physical Functioning	25	70.39	18.70	5070	87.77	13.12	NA**	574	79.47	17.07	NA**
Emotional Functioning	25	68.2	19.57	5068	79.21	18.02	0.002	573	69.32	21.36	0.80
Social Functioning	25	74.6	18.65	5056	84.97	16.71	0.002	572	76.36	21.57	0.69
School Functioning	25	65.2	17.88	5026	81.31	16.09	<0.001	568	68.27	19.05	0.43
Well Being	25	84.57	15.31								
General Health	25	70.83	28.23								

*Normative Values based on Varni 2003

**Physical Functioning sample data is not normally distributed thus no statistical comparison could be made with the normative sample

Table 2: Comparison between SCD Patients and Normative: Data T-Test Comparing SCD vs. Normative Groups.

that low Hb levels contribute to decreased attention span in school and poor academic performance. Halterman et al. [13] compared healthy and iron deficient children and found that those who were healthy and answered positively to the school functioning questions were able to keep up with their school work, remember things, and pay attention in class, thus promoting better school performance. In preliminary work in adult SCA patients, Vichinsky et al. [14] found that Hb was a significant independent predictor of verbal IQ, performance IQ (PIQ), processing speed index (PSI), and math and executive function. Low Hb, older age, and low hippocampal volume (on MRI of the brain) were all predictors of neuropsychological dysfunction; suggesting a link between anemia, loss of neurons, and cognitive impairment. It is probable that impairment earlier in life contributed to decreased school performance, which subsequently limited adult functioning, such as in employment.

Two other studies of children with SCA found that HQOL improved on HU and 7-days after discharge from ER admission [5,6]. Younger children (5-7 years) in our study reported a higher QOL on all but one variable (general health) when compared to the assessments of their parents. Perhaps younger children have not experienced as much illness as older children and, therefore, rate themselves as functioning better. Interestingly, when compared with other children with a chronic disease (e.g., asthma, diabetes, ADHD, depression), our subjects did not have poorer QOL scores [12].

When compared to the normative data (Table 2), it is important that our subjects scored lower than children who did not have a chronic disease, thus stressing the need for treatments that can help these children. Hydroxyurea (HU) has been shown to increase Hb levels and perhaps to increase growth [15]. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) Trial found that daily oral hydroxyurea reduced the frequency of painful crises, episodes of acute chest syndrome and hospitalizations, and the total number of units of blood transfused in SCA patients [16]. Ballas et al. [17] assessed HQOL of patients enrolled in this trial and found that those who responded to HU therapy had improved social function, pain recall, and general health perception. Our data and others, also indicates potential benefit from therapeutic interventions (such as admission for pain and HU) that increase Hb levels and thereby may result in improved HQOL as well as a better medical condition.

Conclusions/Contributions to the Literature

Patients with (SCA) as young as five years of age are willing to participate in HQOL studies. Better HQOL is associated with higher Hb levels in the school and social functioning domains. We conclude that children with SCA have a better HQOL when Hb levels are higher. Therefore, treatment options such as HU and chronic transfusion that result in higher Hb levels may help improve overall HQOL, an additional benefit worth considering. Studies which compare therapeutic interventions should assess their effect on HQOL. Due to the fact that HQOL has been shown to decrease with increasing age, treatment methods which target younger children who have not developed chronic complications of SCA may enhance long-term quality of life.

Acknowledgment

This research was supported in part by the Charles E. Culpepper Foundation and the American Lebanese Syrian Associated Charities.

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