

Factors Affecting Quality of Life in Patients with Pediatric Leukemia during Induction Chemotherapy.

Eman D. El Desouky¹, Maissa K. Noaman¹, Lobna M. Shalaby², Sanna Y. Shaaban³, Inas A. Elattar¹

¹Biostatistics and Cancer Epidemiology, ²Pediatric Oncology Department, National Cancer Institute, Cairo University, Egypt. ³Pediatrics Nutrition, Faculty of medicine, Ain Shams University, Egypt.

Received: April 2016 Accepted: June 2016

Abstract

Objectives: The aim of this study is to describe quality of life (QoL), identify predictors of worse QoL and examine QoL changes from diagnosis and the end of induction chemotherapy in acute leukemia pediatric patients. **Methods:** A prospective study was conducted, including 105 newly diagnosed leukemic patients aged from 2 to 17 years at pediatric department, National Cancer Institute, Cairo University. Parents were interviewed to complete QoL assessment questionnaire using the PedsQL 4.0 Acute Cancer Module. Older children (more than 13 years) were interviewed using the same questionnaire version. **Results:** Patients had an overall score of a median 39 (range 25–64) that changed by the end of induction (median 41.7, range 0–75). Pain and hurt reported a median score of 12 (range 0-100) at diagnosis and by the end of induction, median score was 75 (range 50-100). Both scores were statistically significant being improved by therapy. Both Cognitive Problems and Perceived Physical Appearance worsen by end of induction. Girls and older children had worse QoL. **Conclusions:** Girls and older children had worse QoL. Cognitive Problems and Perceived Physical Appearance deteriorate by therapy. Chemotherapy regimens for childhood leukemia are lengthy with medications administered over 2.5–3.5 years, and thus future efforts should focus on longitudinal studies that describe QoL over time within individual patients.

Key words: *Pediatric leukemia, quality of life, induction chemotherapy*

Corresponding author: Eman D. El Desouky, e-mail: dr.emandesouky@yahoo.com

Introduction

Leukemia is the most common type of childhood cancer. It accounted for 30% of all cancers diagnosed in children younger than 15 years.¹ Within this population, acute lymphoblastic leukemia (ALL) occurred around five times more frequently than acute myeloid leukemia (AML). It accounted for approximately 78% of all childhood Leukemias, while AML accounted for about 19 % of the childhood Leukemias². Survival rates have improved dramatically over the latter

course of the 20th century for most forms of childhood cancers including leukemia³. Now that the majority of pediatric patients survive their cancer, quality-of-life measurement is progressively recognized as an important method of evaluating the effect of treatment interventions and understanding the short and long-term morbidity⁴⁻⁵.

Outcomes for children with leukemia have continued to improve over time, and currently, almost 80% of children with

ALL are cured of their disease with primarily outpatient chemotherapy.⁶ For AML, the 5-year survival rate increased from less than 20% to 68% for children younger than 15 years and from less than 20% to 57% for adolescents aged 15 to 19 years⁷.

Because cure rates have increased, more importance has been placed on reducing toxicities of therapy, improving quality of life (QoL) during treatment and minimizing long-term effects of therapy⁸.

A systematic review has examined measurement of QoL for children with ALL. Most research has focused on survivorship and much less on the period during ongoing treatment⁽⁹⁾. Few studies have focused exclusively on acute myeloid leukemia (AML) QoL¹⁰.

Although the outlook for survival is now optimistic for children with Leukemia, facing a life threatening condition can be strongly difficult for children and their parents. Family life becomes interrupted and the child, parents and other family members are disparate with a lengthy treatment regime and possible side effects. In the initial and intermediary treatment phase, patients can experience unpleasant physical side effects such as nausea and vomiting, mucositis, fatigue, bleeding and infection¹¹.

Recognition of the adverse effects of treatment for ALL has resulted in a growth of interest in quality of life (QOL) assessment of children. In health care, the concept of QOL, often used interchangeably with the term 'health related QOL' is generally understood as a multi-dimensional construct concerning an individual's awareness of the impact of illness and treatment on his/her health, wellbeing or functioning in relation to physical, psychological, and social aspects of life¹². QOL is now considered an important outcome measure for children

with cancers not just in the long term effects but also during courses of active treatment.

The present study's objectives were to describe QoL in children with Leukemia at diagnosis, identify predictors of reduced QoL and to describe how QoL changes by the end of induction.

Patients and Methods

Patients

After IRB approval to conduct this prospective study, 105 leukemic children patients were only eligible if they were at least 2 years of age (lower limit for instrument availability) to 17 years from pediatric department at the National Cancer Institute, Cairo University were recruited in a consecutive fashion in the period from October 2013 to June 2014 with additional follow up for 3 months from the last patient recruited. An informed consent was obtained from parents of those children and an additional informed assent was obtained from children above 7 years old.

Methods

Patients were approached for participation to complete an interview based questionnaire about child QoL. Data tools were general assessment sheet and QoL questionnaire. The general assessment sheet included demographic information, socioeconomic status evaluated by Al Shakhs¹³ familial socioeconomic status scale (SES) for hospitalized patients, information on diagnosis and treatment. Anthropometric parameters, such as body weight and height were measured. Some parameters like weight for age and height for age were calculated and inferred in accordance with the Egyptian growth percentile charts. Malnutrition definition of every single parameter was done based on American Society for Parenteral and Enteral Nutrition (ASPEN) being less than

10th percentile for Weight for age, height for age and less than 5th percentile for BMI.

Outcomes

Quality of life was assessed by the 27-item PedsQL 4.0 Acute Cancer Module, which is a copyrighted material available at www.pedsq.org and a multidimensional instrument that is reliable and valid in children with cancer. The questionnaire assesses the following eight dimensions: pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication. The cultural, linguistic validation process consists of 3 steps: forward translation, backward translation, and patient testing. In the first step, the instruments were translated from the English version to the Arabic version. It was done independently by two translators, native Arabic speakers, and bilingual in English language. The second step, the Arabic version was translated back to English version. It was done independently by two professional translators; native English speakers, and bilingual in Arabic language. In this step, in order to detect any misunderstandings, mistranslations or inaccuracies in the intermediary forward version of the questionnaire, a comparison between the backward versions with the original version was assessed. Finally, to determine whether the translation (instructions, items and response choices) was acceptable, understood the way it was supposed to, or the language used was simple and appropriate, the translated questionnaire was tested in 5 cancer families, both in children and their families. All PedsQL™ translations were conducted in close ongoing collaboration with Mapi Research Institute, Research Institute in Lyon, France and with Dr. James W. Varni in 2012.

It is available for children aged: 5–7, 8–12 and 13–18 years old; as well as for the guardians of children aged: 2–4, 5–7, 8–12 and 13–18 years old. The scale has five Likert response options: never, almost never, sometimes, often and almost always. To simplify the interpretation, all Likert scales were converted to 0 – 100. Higher scores indicate a higher HRQOL.

Statistics

Children with impaired QoL was defined as those with a QoL score at least two standard deviations below the age-specific population mean; these values were derived using data from a PedsQL database⁽¹⁴⁾ and comparisons between poor and good QoL were analyzed with χ^2 (chi square) test and Fisher's exact test when appropriate for categorical variables. Comparisons between the 2 groups with respect to normally distributed numeric variables were done using the t-test. Non normally distributed numeric variables were compared by Mann-Whitney test. To compare QoL score in children between diagnosis and end of induction therapy, the Wilcoxon signed rank test was used. All Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 21. All tests of significance were two sided, and statistical significance was defined as $p < 0.05$.

Results

Patients' criteria: One hundred and five patients (105) were studied 60 of them were boys (57.1%) with median age 5 years When divided by age groups, 42 (40%) were 2–4 years, 18 (17.1%) were 5–7 years, 15 (14.3 %) were 8–12 years and 30 (28.6 %) were ≥ 13 years of age. 64.8% were acute lymphocytic leukemia (ALL). The Demographic characteristics, type of disease, are presented in Table 1

PedsQol score changes: Table 2 describes the PedsQL scores initially and at the end of induction. Overall score was slightly improved from 39.4 ranged from 25 to 64.6 at diagnosis to 41.7 ranged from 0 to 75 at end of induction. Pain and hurt score was significantly improved. However, cognitive problems, perceived physical appearance were deteriorated by therapy.

Factors affecting quality of life: Eighty two patients (78.1%) were identified to have poor quality of life. Table 3 and 4 are showing the factors in relation to QoL status in patients. Children with older age has poor quality of life as shown in Table 3, median age was 7 years compared to 3 years in good quality of life group. Females have worse QOL as compared to male (88.9% compared to 70%). No other factors like SES, diagnosis, weight and other nutritional related symptoms showed significant relation in this study.

Discussion

We have described QoL for 105 children with leukemia in first remission during active treatment. Our findings are concordant with others who have found that QoL scores are lower in children receiving treatment for ALL compared to children with ALL 12 months off therapy¹⁵ and lower compared to healthy children.¹⁶⁻¹⁸ These findings are also concordant with qualitative studies of children receiving treatment for ALL that have noted problems with fatigue, detrimental effects of disease and treatment on physical activities as well as difficulties with social interactions.^{19, 20}

The second objective was to describe predictors of poor QoL during treatment for leukemic patients. Our results revealed that older children and girls had worse QoL and this was concordant with others^{18,19}.

Our third objective was to describe how QoL changes during different phases of therapy. We found very similar QoL scores across different time of assessment for many aspects of QoL. We also found that cognitive functioning worsened over time. This finding is not intuitive because children on maintenance therapy should be integrating better into the school environment over time. Further research is warranted to determine whether this finding is replicated in other studies and if so, whether interventions could be targeted to improve cognitive functioning. Perceived physical appearance worsened over time. This finding might be due to side effect of therapy. However; further research is needed to know how to support patients to overcome this hindering concept from being active.

Our study demonstrated that pain and hurt and total score has improved by end of induction therapy. An Indonesia study also had similar findings they also found that pain and hurt, procedural anxiety and communication were better during maintenance phases of treatment compared to phases preceding maintenance.²⁰

Although this study was a longitudinal prospective study, limitations of the sample size should be considered and further larger studies should be conducted. This study is concerned with patients in active treatment which is lacking in the published data, however; more follow up is needed to assess different phases in treatment. More information on the natural history of HRQL during all phases of treatment and survival is needed.

In conclusion, we have described QoL in children with leukemia and found that age and gender predicted QoL. Future efforts should focus on longitudinal studies that describe QoL over time within individual patients both during and after completion of therapy.

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Table (1): Demographic characteristics and type of disease in studied patients (n=105).

		Number	Percent
Age (yrs.)	Median (range)	5 (2-17)	
Age groups	2-4	42	40.0
	5-7	18	17.1
	8-12	15	14.3
	13-18	30	28.6
Gender	Male	60	57.1
	Female	45	42.9
	M/F Ratio	1.3/1	
Diagnosis	ALL	68	64.8
	AML	37	35.2
Residence	Urban	48	45.7
	Rural	57	54.3

ALL: Acute Lymphoblastic Leukemia, AML: Acute Myeloplasic Leukemia

Table (2): Summary scores of pedsQol at diagnosis and at the end of induction.

Average score of	At diagnosis			End of induction			p value
	Median	Min.	Max.	Median	Min.	Max.	
Pain and hurt	12.5	0	100	75	50	100	<0.001
Nausea problems	43.75	0	87.5	43.8	0	81.3	0.252
Procedural anxiety	0	0	58.3	0	0	58.3	0.495
Treatment anxiety	50	0	100	50	0	100	0.864
Worry	16.7	0	50	16.7	0	50	0.481
Cognitive Problems	56.3	10	100	50	0	100	<0.001
Perceived Physical Appearance	41.7	8.3	66.7	25	0	66.7	<0.001
Communication	66.7	41.7	100	75	0	100	0.902
Total Score	39.4	25	64.6	41.7	0	75.0	<0.001

Table (3): Demographic characteristics, type of disease and laboratory parameters in children with poor and good QoL.

		HRQOL				P value
		Poor (n=82)		Good (n=23)		
		N	%	N	%	
Age (years)	Median(range)	7 (1.8-17)		3 (2.0-17.0)		0.001
Gender	Male	42	70.0	18	30.0	0.021
	Female	40	88.9	5	11.1	
SES	≤Average	44	80.0	11	20.0	0.621
	>Average	38	76.0	12	24.0	
Diagnosis	ALL	54	79.4	14	20.6	0.658
	AML	28	75.7	9	24.3	
Hg (mg/dl)	Mean± SD	8.9±1.5		9.3±1.5		0.306
Albumin (g/dl)	Mean± SD	3.5±0.5		3.6±0.5		0.776
Creatinine(mg/dl)	Mean± SD	0.4±0.2		0.4±0.2		0.744
WBCs (10)³	Median (range)	13.1 (0.9-80.0)		11.8 (1.2-81.4)		0.951
Urea (mg/dl)	Median (range)	21 (6-90)		18 (3-105)		0.148

SES: Socio Economic Status

Table (4): Anthropometry and nutrition related symptoms in children with poor and good Qol

		HRQOL				P value
		Poor (n=82)		Good (n=23)		
		N	%	N	%	
Weight for age	≤10 th percentile	30	75.0	10	25.0	0.547
	>10 th percentile	52	80.0	13	20.0	
Height for age	≤10 th percentile	27	81.8	6	18.2	0.532
	>10 th percentile	55	76.4	17	23.6	
BMI for age	≤5 th percentile	27	75.0	9	25.0	0.580
	>5 th percentile	55	79.7	14	20.3	
Weight loss during induction	No	53	79.1	14	20.9	0.741
	Yes	29	76.3	9	23.7	
Vomiting	No	12	92.3	1	7.7	0.186
	Yes	70	76.1	22	23.9	
Diarrhea	No	50	75.8	16	24.2	0.451
	Yes	32	82.1	7	17.9	
Nausea	No	31	75.6	10	24.4	0.622
	Yes	51	79.7	13	20.3	
Constipation	No	70	79.5	18	20.5	0.414
	Yes	12	70.6	5	29.4	
Dysphagia	No	53	73.6	19	26.4	0.101
	Yes	29	87.9	4	12.1	
Poor appetite	No	28	77.8	8	22.2	0.955
	Yes	54	78.3	15	21.7	
Mucositis	No	24	82.8	5	17.2	0.475
	Yes	58	76.3	18	23.7	