European Journal of Cancer 40 (2004) 1031–1034

European Journal of Cancer

www.ejconline.com

# Longitudinal assessment of nutritional status in children treated for acute lymphoblastic leukaemia in Cuba

A. González[a,*], L. Cortina[b], P. González[c], C. González[d], T. García[e], E.G. de Svarch[f]

[a] *Instituto de Hematología e Inmunología, Apartado 8070, Ciudad de La Habana, Cuba CP 10800, Havana, Cuba*

[b] *Instituto de Hematología e Inmunología, Havana, Cuba*

[c] *Hospital Pediátrico "William Soler", Havana, Cuba*

[d] *Instituto Sup. Ciencias Médicas Fac. "Julio Trigo", Havana, Cuba*

[e] *Instituto de Hematología e Inmunología, Havana, Cuba*

[f] *Instituto de Hematología e Inmunología, Havana, Cuba*

Received 19 May 2003; received in revised form 3 December 2003; accepted 5 December 2003

**Abstract**

Malnutrition has a deleterious effect on the results of therapy for malignant diseases in childhood. The impact of radiotherapy on growth is well known but the impact of cytotoxic drugs on nutritional status is more controversial. The purpose of this study was to determine the nutritional status of a cohort of children treated for acute lymphoblastic leukaemia (ALL) in Cuba. The study involved 49 children admitted to a single center and treated with a Berlin–Frankfurt–Munster-based protocol. Nutritional assessment included measurements of height, weight, body mass index and skin-fold thickness, made at diagnosis, after the intensive phase of treatment and at the end of therapy. Z-scores were used for height and comparison of percentiles for the rest of the variables. All the patients were above the third percentile in all the measurements. There were no statistically significant differences between the results at diagnosis, after intensive therapy and at the end of treatment. Although the sample was small, there was no demonstrable effect of chemotherapy on nutritional status in this Cuban paediatric population, in contrast to that reported in children with ALL in other developing countries.



*Keywords:* Nutritional status; Childhood acute lymphoblastic leukaemia

## 1. Introduction

One of the major advances in paediatric oncology has been in the treatment of acute lymphoblastic leukaemia (ALL), with the most important cooperative groups reporting overall survival rates around 80% at 5 years [1]. Several factors have contributed to this achievement, among them a better understanding of the biology of the disease, more intensive therapies and improvement in supportive care. In this last aspect it is very important to assess nutritional status properly at diagnosis, during therapy and even after the completion of treatment [2]. Cranial radiotherapy affects the final height of the child [3,4] but chemotherapy and the disease itself could compromise nutritional status, and if the patient is undernourished at diagnosis or fails to maintain an adequate nutritional balance during therapy, survival will be compromised, as reported in studies from elsewhere in Latin America [5,6].

Nutritional anthropometry remains the most practical and useful method for the assessment of nutritional status, particularly during childhood. In this paper we describe a longitudinal anthropometric study in a cohort of children with ALL from a single centre in Cuba.

## 2. Patients and methods

This study began in September 1992 and finished in December 1996. During that period 62 children with newly diagnosed ALL were admitted to the paediatric

* Corresponding author. Tel.: +53-7-578268, 544214; fax: +53-7-442334.

*E-mail address:* ihidir@hemato.sld.cu (A. González).

0959-8049/$ - see front matter © 2004 Published by Elsevier Ltd.
doi:10.1016/j.ejca.2003.12.025

clinic of Instituto de Hematología e Inmunología (IHI) in Havana. All the patients were treated with protocol 1-LLA-90 of the Grupo Latinoamericano de Tratamiento de Hemopatías Malignas (GLATHEM), a Berlin–Frankfurt–Munster (BFM)-based protocol in which cranial radiotherapy was given to the minority of the patients [7]. The dose of prednisone was 40 mg/m$^2$ daily during the month of remission induction and dexamethasone 10 mg/m$^2$ daily for 3 weeks before the end of the intensive phase. The prednisone-equivalent dose of steroid for the entire treatment was 3 g/m$^2$. The study sample comprised 49 children only, who were assessed at diagnosis, after the intensive phase of treatment and at the end of therapy. None of them received radiotherapy. Of the remaining 13 patients, seven died during the study period and the rest were excluded because they continued therapy in other centres nearer to their home town and not all the measurements were made by the same person. There were 23 girls and 26 boys with a mean age of 6 years (ranging from 1 to 11 years for the girls and 2 to 15 years for the boys).

The following measurements were performed:

- Height: using a Harpender stadiometer with the results expressed in centimetres (cm).
- Weight: using a spring balance SMIC model (China) with the results expressed in kilograms (kg).
- Skin-fold thickness: using a Holtain LTD fat caliper for measuring tricipital, subscapular and suprailiac skin folds with the results expressed in millimetres (mm).

All the measurements were obtained by conventional techniques [8] and always by the same person.

Data processing was done by the *SPSS-PC*, version 3.1 [9]. Mean and S.D. of all quantitative variables were calculated. For height the Z-score was applied. This method allows a direct comparison between the measurements obtained and the national reference values. For weight and skin folds it was not possible to apply the Z-score method because neither measure has national values expressed as means and S.D., nor are their values normally distributed.

As an additional measure of the nutritional status of the patients, the body mass index (BMI) was determined from the formula $\text{BMI} = \text{WT}/\text{HT}^2$ where WT = weight in kg and HT = height in metres.

National means and S.D. for height were obtained from the 1972 Cuban national study of growth and development [10]. To compare the Z-scores the paired-samples I-test was applied. For comparing weight and skin folds each patient was classified for sex and age in the percentiles according to the national study [10]. A scale of eight percentile channels was used with the limits of the 3rd, 10th, 25th, 50th, 75th, 90th and 97th percentile. The Wilcoxon signed-rank test was applied to the percentilar channels to assess changes in these measurements before, during and after therapy.

The BMI was evaluated in a similar way to weight and skin folds. For all the variables a 5% significance level was chosen.

## 3. Results

In all patients the three sequential measurements of all the study variables (height, weight, skin folds and BMI) were above the third percentile. In the evaluation of height, as is shown in Table 1(a,b), there were no differences in the whole group or between sexes. A comparison between weight percentile channels at diagnosis and after the intensive phase of treatment showed that 39.3% of the patients had experienced an increase in weight by the second measurement (Table 2); this was more pronounced in boys but was not statistically significant. Comparison of weight measurements at diagnosis with those taken at the end of therapy yielded similar results (Table 2).

Table 1
(a) Height by sex at diagnosis, after the intensive phase and at the end of therapy. (b) Comparison of height by sex at diagnosis, after the intensive phase and at the end of therapy

| (a) | Female ($n=23$) | | Male ($n=26$) | |
|---|---|---|---|---|
| | Mean ($Z$) | SEM | Mean ($Z$) | SEM |
| At diagnosis | 0.12 | 0.26 | 0.38 | 0.23 |
| After intensive phase | 0.21 | 0.28 | 0.41 | 0.28 |
| End of treatment | 0.35 | 0.29 | 0.49 | 0.25 |
| (b) | Female | | Male | |
| | $t$ | $P$ | $t$ | $P$ |
| Diagnosis versus intensive phase | 0.70 | 0.50 | 0.15 | 0.88 |
| Diagnosis versus end of treatment | 1.36 | 0.20 | 0.63 | 0.54 |

$Z$, height $Z$-score. $t$, percentile of paired $t$.

Table 2
Comparison of weight at diagnosis, after the intensive phase and at the end of treatment

| | Diagnosis versus intensive phase | | Diagnosis versus end of therapy | |
|---|---|---|---|---|
| | Female | Male | Female | Male |
| Positive ranks | 10 | 5 | 10 | 6 |
| Negative ranks | 7 | 12 | 6 | 11 |
| Ties | 6 | 9 | 7 | 9 |
| Total | 23 | 26 | 23 | 26 |
| $Z_p$ | 0.39 | 1.07 | 0.31 | 0.62 |
| $P$ = asymp. sig. (2-tailed) | 0.69 | 0.28 | 0.76 | 0.53 |

$Z_p$, percentile of standard normal distribution.

Percentile channels for the various skin-fold measures at diagnosis, after intensive therapy and at the conclusion of treatment are shown in Table 3. There were no differences in more than one-third of the children and no differences between the sexes. A similar pattern was observed in the measures of BMI (Table 4).

## 4. Discussion

Malnutrition in children with ALL is not recognised commonly at diagnosis except in developing countries [5,6,11]. However, there are a few reports of this problem in industrialised nations [12,13]. Smith and colleagues [14] have stated that is not enough to measure height and weight for age and weight for height as evidence for undernourishment. When they measured skin folds in 100 children with cancer at diagnosis they found 20% of the patients with values below the third percentile. A more recent study also pointed out the importance of this measure [15]. In all our patients these measurements were above the third percentiles.

Cranial radiotherapy has a negative effect on growth, particularly on final height [3,4]. The effects of chemotherapy alone on nutritional status are less well described. These effects could be related to a decreased rhythm of growth-hormone release [16,17]. Some consider that there is a transient growth retardation during treatment, mainly in the maintenance phase due to the administration of 6-mercaptopurine and methotrexate [18,19]. A tendency to gain weight has been described in patients treated for ALL without radiotherapy, particularly in girls [20]. In our study this weight gain was observed also, but was more obvious in boys.

Evaluation of growth and nutritional status in the general paediatric population is complex because sex differences and puberty prevent a uniform approach [8]. In children with ALL it is even more difficult, due to the effects of the disease and therapy. Some investigators recommend performing nutritional evaluation according to age groups [18,21]. In the present study this analysis was not possible due to the sample size. In spite of that our results could be representative of the national situation in Cuba because IHI is a reference centre that treats one-third of the patients from all over the country.

Table 3
Comparison of percentile values of skin folds at diagnosis, after the intensive phase and at the end of treatment

| | Diagnosis versus intensive phase | | Diagnosis versus end of therapy | |
|---|---|---|---|---|
| | Female | Male | Female | Male |
| **Tricipital** | | | | |
| Positive ranks | 5 | 7 | 4 | 6 |
| Negative ranks | 10 | 11 | 10 | 11 |
| Ties | 8 | 8 | 9 | 9 |
| Total | 23 | 26 | 23 | 26 |
| $Z_p$ | 1.12 | 1.16 | 0.71 | 0.58 |
| $P$ = Asymp. Sig. (2-tailed) | 0.26 | 0.25 | 0.48 | 0.56 |
| **Subscapular** | | | | |
| Positive ranks | 7 | 6 | 6 | 9 |
| Negative ranks | 9 | 10 | 10 | 8 |
| Ties | 7 | 10 | 7 | 9 |
| Total | 23 | 26 | 23 | 26 |
| $Z_p$ | 0.71 | 0.56 | 1.07 | 0.44 |
| $P$ = Asymp. Sig. (2-tailed) | 0.48 | 0.58 | 0.29 | 0.66 |
| **Supra-iliac** | | | | |
| Positive ranks | 10 | 8 | 7 | 11 |
| Negative ranks | 6 | 7 | 7 | 3 |
| Ties | 7 | 11 | 9 | 12 |
| Total | 23 | 26 | 23 | 26 |
| $Z_p$ | 0.53 | 0.18 | 0.25 | 1.18 |
| $P$ = Asymp. Sig. (2-tailed) | 0.59 | 0.86 | 0.80 | 0.24 |

$Z_p$, percentile of standard normal distribution.

Table 4
Comparison of body mass index percentile values at diagnosis, after intensive treatment and at the end of therapy

| | Diagnosis versus intensive phase | | Diagnosis versus end of therapy | |
|---|---|---|---|---|
| | Female | Male | Female | Male |
| Positive ranks | 9 | 8 | 10 | 11 |
| Negative ranks | 6 | 9 | 9 | 6 |
| Ties | 8 | 9 | 4 | 9 |
| Total | 23 | 26 | 23 | 26 |
| $Z_p$ | 1.22 | 0.71 | 0.87 | 0.35 |
| $P$ = Asymp. Sig. (2-tailed) | 0.22 | 0.48 | 0.38 | 0.72 |

$Z_p$, percentile of standard normal distribution.

## 5. Conclusions

An adverse effect of chemotherapy on the nutritional status of patients with ALL was not observed. Although the sample is small, it looks as if growth in the paediatric population with ALL in Cuba has a pattern different to that in most developing countries where malnutrition is commonly found.


## Acknowledgements

We are very grateful to Dr Ronald Barr and Dr Porfirio Hernández for their assistance and review of this paper.


## References


1. Pui C-H. Acute lymphoblastic leukemia in children. *Curr Opin Oncol* 2002, **12**, 3–12.
2. Anon. Nutrition morbidity in children with cancer: mechanisms, measures and management. *Int J Cancer Suppl* 1998, **11**.

3. Sklar C, Mertens A, Walter A, *et al*. Final height after treatment for childhood acute lymphoblastic leukemia: comparison of no cranial irradiation with 1800 and 2400 centigrays of cranial irradiation. *J Pediatr* 1993, **123**, 59–64.
4. Odame I, Reilly JJ, Gibson BES. Patterns of obesity in boys and girls after treatment for acute lymphoblastic leukemia. *Arch Dis Child* 1994, **71**, 747–749.
5. Lobato-Mendízabal E, Ruíz-Argüelles GJ, Marín-López A. Leukemia and nutrition I: Malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukemia. *Leuk Res* 1989, **13**, 899–906.
6. Borato Viana M, Murao M, Ramos G, *et al*. Malnutrition as a prognostic factor in lymphoblastic leukemia: a multivariate analysis. *Arch Dis Child* 1994, **71**, 304–310.
7. Svarch E, González A, Vergara B, *et al*. Tratamiento de la leucemia linfoide aguda (LLA) en el niño. *Sangre* 1993, **38**, 25–30.
8. WHO Working Group. Use and interpretation of anthropometric indicators of nutritional status. *Bull World Health Org* 1986, **64**, 926–941.
9. Nie NH, Hull CH, Jenkins JG, Steinbrenner K, Bent DH. *SPSS: Statistical package for the social sciences*, 2nd Ed. New York, McGraw-Hill, 1975 187–189.
10. Jordán J. Desarrollo humano en Cuba. La Habana: Ed. Científico-Técnica, 1979: 101–106.
11. Gómez-Almaguer D, Ruíz-Argüelles GJ, Ponce de León S. Nutritional status and socio-economic conditions as prognostic factors in the outcome of therapy in childhood acute lymphoblastic leukemia. *Int J Cancer* 1998, **11**(Suppl.), 52–55.
12. Mauer AM, Burgess JB, Donaldson SS, *et al*. Special nutritional needs of children with malignancies: a review. *J Parenteral Enteral Nutr* 1990, **14**, 315–324.
13. Andrassy RJ, Chwals WJ. Nutritional support of the pediatric oncology patient. *Nutrition* 1998, **14**, 124–128.
14. Smith DE, Stevens MCG, Booth IW. Malnutrition at diagnosis of malignancy in childhood: common but mostly missed. *Eur J Pediatr* 1991, **150**, 318–322.
15. Brennan B. Sensitive measures of the nutritional status of children with cancer in hospital and in the field. *Int J Cancer* 1998, **11**(Suppl.), 10–13.
16. Möell C, Garwicz S. Influence of treatment modalities on prepubertal growth in children with acute lymphoblastic leukemia. *Pediatr Hematol Oncol* 1995, **12**, 425–427.
17. Ogilvy-Stuart AL, Shalet SM. Effect of chemotherapy on growth. *Acta Paediatr* 1995, **411**, 52–56.
18. Holm K, Nysom K, Hertz H, *et al*. Normal final height after treatment for acute lymphoblastic leukemia without irradiation. *Acta Paediatr* 1994, **83**, 1287–1290.
19. Groot-Looner JJ, Otten B, Van Hof MA, *et al*. Chemotherapy plays a major role in the inhibition of catch-up growth during maintenance therapy for childhood acute. lymphoblastic leukemia. *Pediatrics* 1995, **96**, 693–695.
20. Warner JT, Gregory JN, Webb DK. Patterns of obesity in boys and girls after treatment for acute lymphoblastic leukaemia. *Arch Dis Child* 1995, **72**, 97–99.
21. Zurlo MG, Terracini B, Balducci D, *et al*. Height of children off therapy after acute lymphoblastic leukemia. *Pediatr Hematol Oncol* 1988, **5**, 187–195.