Assessment of anthropometric indices in children with refractory epilepsy: a case control study

Avaliação dos índices antropométricos em crianças com epilepsia refratária: um estudo caso-controle

Maria Eugênia Goulart Gutheil[1,3], **Magda Lahorgue Nunes**[2,3]

[1] MSc. in Children's Health, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil.
[2] MD., PhD. Professor of Neurology, School of Medicine, PUCRS, Porto Alegre, RS, Brazil.
[3] Division of Neurology (Serviço de Neurologia) and Brain Institute (Instituto do Cérebro – INSCER), PUCRS, Porto Alegre, RS, Brazil.

MEGG was a fellow of the Brazilian Coordination for Improvement of Higher Education Personnel (CAPES).
MLN is a researcher of the Brazilian National Council of Scientific and Technological Development (CNPq).

ABSTRACT

Aims: Although epilepsy is a prevalent disorder during childhood, there is still little knowledge regarding its effects on growth and nutrition of affected patients. The aim of this study was to assess anthropometric indices of children with refractory epilepsy.

Methods: A case control study was carried out by comparing weight, stature and body mass index of 27 children with refractory epilepsy (with only oral nutrition, no swallowing difficulty and no motor limitations) paired (1:1) according to gender and age with children without chronic illnesses. Information regarding type, frequency and time of epileptic seizures, as well as antiepileptic drugs being used, was provided by parents and/or guardians during anthropometric measurements. Statistical analysis was performed using Student's t-test with an established significance level of P less than 0.05.

Results: Children with epilepsy presented lower Z-scores for height-for-age compared to the control group of same age range (P=0.02), however Z-scores for weight-for-age and body mass index for age did not show any significant difference between both groups (P=0.07; P=0.22, respectively).

Conclusions: These data suggest that refractory epilepsy may impair growth during childhood.

KEY WORDS: ANTHROPOMETRY; EPILEPSY; MALNUTRITION; FAILURE TO THRIVE; GROWTH DISORDERS.

RESUMO

Objetivos: Embora a epilepsia seja um distúrbio prevalente na infância, ainda há pouco conhecimento sobre seus efeitos no crescimento e nutrição dos pacientes afetados. O objetivo deste estudo foi avaliar os índices antropométricos de crianças com epilepsia refratária.

Métodos: Foi realizado um estudo caso-controle comparando peso, estatura e índice de massa corporal de 27 crianças com epilepsia refratária, pareadas (1:1) em relação a sexo e idade com crianças sem doenças crônicas. Informações quanto ao tipo, frequência e horário das crises e sobre os fármacos antiepilépticos utilizados foram fornecidas pelos pais e/ou responsáveis durante a aferição das medidas antropométricas. O teste t de Student foi utilizado para a análise estatística com nível de significância estabelecido em P menor do que 0,05.

Resultados: Encontraram-se índices de escore Z para altura/idade menores nas crianças com epilepsia quando comparadas às crianças do grupo controle na mesma faixa etária (p=0,02), enquanto índices de escore Z para peso/idade e índice de massa corporal/idade não apresentaram diferença significativa entre os grupos (P=0,07; P=0,22, respectivamente).

Conclusões: Estes dados sugerem que a epilepsia refratária pode prejudicar o crescimento durante a infância.

DESCRITORES: ANTROPOMETRIA; EPILEPSIA; DESNUTRIÇÃO; INSUFICIÊNCIA DE CRESCIMENTO; TRANSTORNOS DO CRESCIMENTO.

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Endereço para correspondência/Corresponding Author:
Maria Eugênia Goulart Gutheil
Rua Antônio Costa, 11, Ap. 703B
88034-070, Florianópolis, SC, Brazil
Tel.: (+55-48) 9173-4740
E-mail: megutheil@hotmail.com

INTRODUCTION

Malnutrition and epilepsy are prevalent problems in developing countries and studies using animal models suggest a cause-effect relationship between them.[1-3] Growth retardation has been observed in children suffering from epilepsy and it may be more common in untreatable cases. The cause of growth retardation is still not very clear, however it may be a multifactorial one. For instance, frequent seizures reduce child's wake time, causing reduction of total energy intake.[4] Body weight change is an important collateral effect on children in use of certain antiepileptic drugs for long periods of time.[5] Use of antiepileptic drugs may result in loss of appetite, change in cognitive function and also interfere in nutrient absorption.[4]

Childhood and adolescence are critical periods concerning bone mineralization.[6] There is an increased amount of evidence showing that epilepsy may affect bone mass in many ways. Restricted physical activities caused by convulsions, limited physical activities as a result of brain paralysis, often present in symptomatic epileptic patients, as well as drugs used for treatment of seizures, may have a negative effect on bone mineral density.[6-7] Vitamin D deficiency has been increasingly attracting a great deal of attention. Low levels of vitamin D increase the risk of bone mineralization abnormalities and may be associated with poor bone health in epileptic patients.[8] Older antiepileptic drugs may have deleterious effects over bone health as they directly affect cells that are responsible for bone formation and, secondarily, calcium and vitamin D metabolism.[9]

The association of malnutrition with seizures can increase its negative effects over the developing brain.[10] Adverse effects of nutritional status in rodents include changes in neurotransmitter release, reduction of brain size and neuroplasticity alteration.[11] Malnutrition is not considered to be a direct cause of epilepsy although it seems to favor the occurrence of epilepsy or seizures due to many nutritional deficiencies which have a profound and often permanent effect on central nervous system development in early life.[12-13]

Literature review brings no irrefutable evidence that malnutrition itself increases risk of epilepsy and studies that assess epilepsy's influence over nutritional status in children are scarce.[4,12-15] Therefore, the aim of this study was to assess nutritional status of children with refractory epilepsy using anthropometric measurements and correlating weight and height development with clinical variables and epilepsy treatment.

METHODS

A case-control study was carried out with patients from the Outpatient Clinic of Pediatric Neurology and Epilepsy of São Lucas Hospital in Porto Alegre, Rio Grande do Sul state, Brazil (cases) and from the Outpatient Clinic of General Pediatrics of the same institution (controls); data were collected between January and November 2010.

After sample size determination, we selected 27 children with epilepsy from the Outpatient Clinic of Pediatric Neurology and Epilepsy in the 4 to 10 year age group, scoring 7 or higher in Engel's scale for seizure frequency (cutting point for refractory epilepsy),[16] with only oral nutrition and no swallowing difficulty. Patients with motor limitations, those using enteral or parenteral nutrition or ketogenic diet for treating epilepsy, those who could not have their anthropometric measurements taken due to the use of orthopaedic appliances or body abnormalities, and every child whose parents and/or guardian had not authorized their participation in the study were excluded from the sample.

The control group was formed by 27 children within the same age range, who did not have epilepsy and were attending child care in the Outpatient Clinic of General Pediatrics. Children who had any disease that causes significant nutritional impairment (cancer, chronic infections) or metabolic alterations (hyper or hypothyroidism), were on special diets (diabetes, phenylketonuria, celiac disease or lactose intolerance), were using corticosteroids, had degenerative neurological alterations, used enteral or parenteral nutrition, could not have their anthropometric measurements taken due to the use of orthopedics appliances or body abnormalities, or whose parents and/or guardian had not authorized their participation in the study were excluded.

Anthropometric measurements were always taken by the same researcher (MEG) or under her supervision. Weight was obtained with a mechanical platform scale (Indústrias Filizola, Porto Alegre, RS, Brazil) with an attached anthropometer. Patients were positioned barefoot, with an erect posture, feet close together and arms alongside the body, on the center of the scale, wearing the least amount of clothes possible. For the measurement of height, children maintained the erect posture with arms alongside the body and held-up head, looking at a fixed spot on the same level of the eyes, barefoot and feet close together and in parallel.

Measurements were transformed into Z-scores for weight/age (W/A), height/age (H/A) and body mass index (BMI)/age (BMI/A), using World Health Organization (WHO) Anthro Plus software, which is

based on the latest WHO (2005/2007) growth charts.[17] BMI (weight in kg divided by height in m^2) was calculated by the same software.

Information regarding type, frequency and time of seizures, as well as use of antiepileptic drugs was provided by parents and/or guardians during anthropometric measurements.

Data were stored in a data bank using Microsoft Office Excel 2007 software and analyzed using the statistical software SPSS version 17.0. W, H, and BMI of the two groups were compared using Student's t-test, and correlation between kind of treatment (monotherapy or polytherapy) with Z-scores for W/A, H/A and BMI/A was evaluated. ANOVA test was used to analyze correlation of time and type of seizures with the same Z-score indices previously described. Pearson's test was used to analyze correlation between frequency of seizures with Z-scores for H/A, W/A and BMI/A. A statistical significance of $P<0.05$ was considered for all analysis.

The study was approved by the Research Ethics Committee from Pontificia Universidade Católica do Rio Grande do Sul. Guardians of recruited patients gave a written informed consent after receiving explanations regarding the nature and aim of the study.

RESULTS

Twenty-seven children with epilepsy and 27 children without epilepsy were studied, each group containing 19 male and 8 female children. **Table 1** shows the results of anthropometric measurements of the studied sample. Comparison of mean age in months (85.63±20.05 and 82.63±19.66; P=0.58), weight in kg (25.54±6.86 and 27.91±7.69; P=0.23), height in cm (120.88±9.22 and 123.98±12.02; P=0.29) and BMI (17.32±3.43 and 17.92±3.27; P= 0.51) between cases and controls did not show any statistically significant difference.

The results for Z-score assessment of children with and without epilepsy are demonstrated in **Figure 1**. Patients with epilepsy showed Z-scores for H/A that ranged from 2.89 to 1.72, for W/A that ranged from -3.01 to 2.72, and for BMI/A that ranged from -3.45 to 4.12. As for the control group, Z-score indices for H/A ranged from -1.4 to 2.42, for W/A ranged from -1.03 to 6.23 and for BMI/A ranged from -0.76 to 7.5. Comparison of mean Z-scores between cases and controls, using Student's t-test, demonstrated a statistically significant difference when Z-score for H/A was considered (**Table 2**).

Table 1. Results of anthropometric measurements in children with refractory epilepsy (study group) and children without epilepsy or disorders that could impair nutritional status or growth (control group). Sao Lucas Hospital, Porto Alegre, Brazil, January/November 2010.

Variables	Study group N=27				Control group N=27			
	Minimum	Maximum	Mean	Standard deviation	Minimum	Maximum	Mean	Standard deviation
Age (months)	55	131	85,63	20,06	54	121	82,63	19,66
Weight (kg)	16	47,5	25,54	6,86	18,1	41,5	27,92	7,67
Stature (cm)	108	143	120,88	9,22	105	149	123,98	12,03
BMI (kg/m^2)	11,3	24,2	17,32	3,44	14,4	28,4	17,93	3,27

BMI: body mass index.

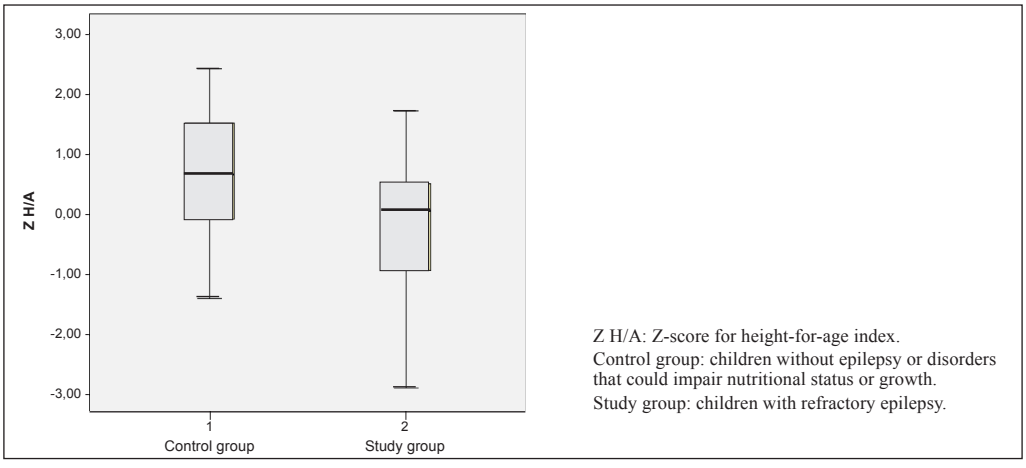

Figure 1. Comparison of height-for-age index between children with refractory epilepsy (study group) and controls. Sao Lucas Hospital, Porto Alegre, Brazil, January/November 2010.

Table 2. Comparison of mean Z-scores for weight-for-age, height-for-age, and body mass index for age between 27 children with refractory epilepsy and 27 children without epilepsy or disorders that could impair nutritional status or growth (control group). Sao Lucas Hospital, Porto Alegre, Brazil, January/November 2010.

Z-score	Children with refractory epilepsy n=27	Control group n=27	P*
Z W/A	0.44±1.48	1.24±1.65	0.07
Z H/A	-0.13±1.14	0.57±1.11	**0.02**
Z BMI/A	0.61±1.74	1.21±1.79	0.22

Data are expressed as mean±standard deviation.
Z W/A: Z-score for weight-for-age; Z H/A: Z-score for height-for-age;
Z BMI/A: Z-score for body mass indez for age.
* Student's t-test; significant if <0.05.

Table 3. Variables related to the disease in 27 children with refractory epilepsy. Sao Lucas Hospital, Porto Alegre, Brazil, January/November 2010.

Variables	n (%)
Type of seizure	
Focal	8 (28.0)
Generalized	17 (64.0)
Focal/Generalized	2 (8.0)
Predominant time of seizures	
Daytime	15 (55.6)
Nighttime	6 (22.2)
No predominant time	6 (22.2)
Therapeutic approach	
Monotherapy	6 (22.2)
Polytherapy	21 (77.8)
Frequency of seizures*	
7 - 8	9 (33.3)
9 - 11	18 (66.7)
Time of disease onset	
5 - 45 months	10 (36.0)
46 - 86 months	12 (44.0)
86 - 118 months	5 (20.0)

* Frequency of seizures according to the Engel scale (reference 16): 7 (1-3 seizures/month), 8 (1-6 seizures/week), 9 (1-3 seizures/day), 10 (4-10 seizures/day) and 11 (>10 seizures/day).

Table 4. Antiepileptic drugs in use by children with refractory epilepsy (n=27). Sao Lucas Hospital, Porto Alegre, Brazil, January/November 2010.

Antiepiletic drugs	n	%
Valproic Acid	15	30
Carbamazepine	13	26
Clobazam	10	20
Fenitoin	1	2
Phenobarbita	1	2
Lamotrigine	3	6
Oxacabazepine	5	10
Topiramate	1	2
Vigabatrine	1	2

Obs.: Out of the 27 children, 21 used polytherapy and the others monotherapy. In addition, four children were using Ritalin and five were using Risperidone simultaneously with antiepileptic drugs.

Table 3 presents variables related to epilepsy. **Table 4** shows the antiepileptic drugs taken by the children during this study. No significant difference was observed in the nutritional status of epileptic children regarding therapeutic approach – mono or polytherapy (W/A Z-score P=0.88; H/A Z-score P=0.78; BMI/A Z-score P=0.85), frequency of seizures (W/A Z-score P=0.69; H/A Z-score p=0.67; BMI/A Z-score P=0.99), time of seizures – daytime, nighttime or no predominant time (W/A Z-score P=0.87; H/A Z-score P=0.98; BMI/A Z-score P=0.74), type of seizures – focal or generalized (W/A Z-score P=0.83; H/A Z-score P=0.68; BMI/A Z-score P=0.75) and duration of disease (W/A Z-score P=0.14; H/A Z-score P=0.57; BMI/A Z-score P=0.20).

DISCUSSION

In this study we have evaluated anthropometric indices in children with epilepsy and have observed a significant decrease on Z-scores for H/A. Crepin et al.,[14] in Africa, observed greater risk of malnutrition in children with epilepsy than in the control group. A study in India has shown association between epilepsy and low BMI.[12] Two other studies carried out in Italy and in the United States showed higher risk of malnutrition in children with refractory epilepsy, the risk being associated with lower energy intake.[4,15] A research carried out in southern Brazil also noticed a tendency to higher incidence of epilepsy in malnourished institutionalized children compared to those with adequate nutrition.[18] The option of using anthropometric indices as indicators for nutritional status is due to the fact that these measurements are a practical resource that must be used by professionals to assess children in clinical interventions, screening and even in nutritional monitoring.[19,20]

Limitations of this study include the fact that no data was collected regarding daily ingestion of calories and proteins. When asked about the regular diet or habits most of the parents were not able to give accurate information. Furthermore, these children were not longitudinally followed, which would have given more information about the effects of epilepsy on nutritional status.

Our study's main results were lower Z-scores for H/A in children with epilepsy compared to healthy children. Epilepsy may coexist with direct and indirect metabolic alterations[21] that interfere with stature growth. Stature is also affected by genetic heritage and we believe that the information of parent's height would be important to evaluate. In the present study, when data was collected, we did not get an accurate information regarding parent´s height because the

majority of the children came to the medical visit only with the mother or other relative that was not able to give the information.

Insufficient height gain has already been observed in children with epilepsy. Stature growth impairment found in these patients might be related to long-term malnutrition, epileptic seizures and antiepileptic drugs.[21,22] Association of epilepsy with psychomotor developmental delay and severe forms of neurological disorders could influence the nutritional status of these children.[23] In the present study, epileptic children showed no significant difference between time of disease exposure and consequent use of antiepileptic drugs regarding Z-scores for H/A. Most patients (78%) were using polytherapy as a therapeutic approach and those in monotherapy had been previously exposed to other drugs.

Tada et al.[21] assessed height in children with epilepsy using Tanner charts and concluded that frequency of seizures had no influence over stature growth. At present, other growth charts (National Center of Health Statistics – NCHS 2000, and World Health Organization – WHO 2005/07) have been proved to have higher accuracy in W/A and H/A assessment. Recent studies that compared charts from WHO 2005 and NCHS 2000 have shown that children with height impairment tend to have a more precocious diagnosis when WHO 2005 was used as reference.[24] It is not known whether children assessed by Tada et al. would be classified in lower percentiles if data were plotted in the WHO 2005/2007 charts.

Hormonal change may also be implicated in stature growth retardation in these children.[25] The relation between epilepsy and the endocrine system has been studied in order to find out whether hormonal changes in epilepsy result from epilepsy itself or from epileptic drugs. Guo et al.[26] pointed out the association between valproate and lamotrigine use for long periods and height deficits, and Kurowski et al.[27] confirmed such association on their patients. Thus, the association between therapeutic approach in epilepsy and height deficit might still be considered a controversial issue.

This study has not found significant difference in weight between children with epilepsy and the control group. Similar finding has been reported by Bertoli et al.[15] with epileptic patients regarding reference charts. Weight measurements have strong clinical value and are used for the indirect evaluation of many chronic diseases as exemplified in metabolic control of diabetic patients.[28] Many studies show the relation between the effects of antiepileptic drugs and body weight.[29,30] These effects depend on the kind of drug used.[12] Weight loss has been mostly associated with the use of topiramate[5,30,31] and felbamate;[29,32] in our study there were no children using felbamate and only one used topiramate.

Possible causes for early malnutrition in the general population, including increase of parents' work day, school level, and/or precarious socio-economical conditions, have been described in literature.[22] Family income can determine the family's diet in terms of quantity and, in some cases, quality.[33] Mother's school level and purchasing power may be the main predictors of a child's nutritional status.[34] In the present study, mother's school level and family/child's diet were not assessed, which might be limiting in a way. In order to control socio-economical bias, we recruited only children who attended public health outpatient facilities. We did not observe any influence of therapeutic approach (mono or polytherapy), frequency of seizures, time of seizures (daytime, nighttime or no predominant time) and type of seizures (focal or generalized) over anthropometric measurements.

Even though our results are limited, since more data on dietary habits, body composition and parent's height were not investigated, the collected anthropometric measurements suggest that refractory epilepsy might impair growth during childhood.

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