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RESEARCH ON POSSIBLE BONE METABOLIC AND FUNCTIONAL IMPAIRMENTS IN CHILDREN WITH CEREBRAL PALSY – PRELIMINARY RESULTS

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The aim of these study was to examine possible changes related to bone metabolism and basic functionality, in cerebral palsy: neuropsychomotor disease generating mobility issues and possibly osteoporosis. We analyzed 2 groups (the first, sub-divided in 2 sub-groups – totally resulting in 3 populations), of children: 5 to 11 years old: ***(1)*** *8 ambulating patients with cerebral palsy (sub-group 1, group 1); (2) 8 non-ambulating patients with cerebral palsy (sub-group 2, group 1); (3) 8 patients with scoliosis (group 2). Evaluating parameters and statistical processing: Functional Independence Measure (FIM) scale, Body Mass Index (BMI)***,** *Thyroid-Stimulating Hormone (TSH), Free Thyroxin (FT_4), urinary calcium and phosphorus concentrations. No significant diferences ($p > 0.05$) between all the lots and groups/ sub-groups, except for FIM (sub-group 1 versus sub-group 2: $p < 0.001$; sub-group 1 + 2 versus group 2: $p < 0.001$; sub-group 2 versus group 2: $p < 0.001$). Parameters' contributivity and correlations (Spearman's rho): values were close to 0 (showing non-correlated items) except for urinary calcium and phosphorus concentrations***,** *(Spearman's rho = 0.61): they are positively correlated, yet (as well) not redundant. Preliminary results, confirm the – predictable – clinical-functional differences between the 2 lots/ sub-groups and the chosen evaluation parameters are appropriate.*

Key words: cerebral palsy, scoliosis, osteoporosis.

INTRODUCTION

The book "The Cerebral Palsies of Childhood" written by William Osler was probably the one which led to the widespread use of the term to describe children with palsy of cerebral origin, as opposite to the other types of palsy (orthopedic palsies, muscular palsies and spinal palsies)[1].

Cerebral palsy (CP) "is a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain".[2] CP is the most known childhood disorder associated with low bone mass.[3]

Osteoporosis is defined as a "systemic skeletal disease characterized by low bone mass, deterioration of the bone tissue microarchitecture, consequent increase in bone fragility, exaggerated susceptibility to suffer fractures".[4] Clinically, there are described osteoporotic syndromes of primary type – including with juvenile ones – and of secondary type – encompassing a wide range of nosologic entities, also many situations that predispose to immbilization, including the lack of gravity (eu)stress for the whole or parts of the skeleton - items found in patients with CP unable to stand and walk[4]. Osteoporosis can be expressed by bone pain (due to micro-fracture/s), height loss; scoliosis or scoliotic attitude and even – by consequent under utilization – decreased muscle mass; also related loss of appetite, may be found. Paraclinically, diagnosis was made through Dual energy X-ray absorptiometry (DEXA), X-ray, CT, laboratory tests, bone biopsy. The most common sites are the spine, femur[5]. Although it is often considered a disease of adulthood, osteoporosis has roots in the childhood. The accumulation of bone mass occurs during childhood and early adulthood, peak bone mass – currently achieved in the early mid age – being determinant of lifetime risk for osteoporosis[6]. Regarding the diagnosis and assessment of osteoporosis in children and adolescents, the phenomenon is less studied than in adults – a normal situation considering that in an alertly demographic aging population, which characterizes the current global society, the involutional osteoporosis is more common than the one in children and adolescents. Consequently, both diagnostic procedures and relationships between bone density and fracture risk, in children, are based on fewer elements of standardization as well as therapeutic modalities; moreover, the term "osteoporosis" itself is recommended to be used cautiously in children[6].

Related to our research, a major path-physiological item – as a risk factor for osteoporosis in children with CP – is the "limitations in sustaining weight" which exists in those incapable of standing and walking. In this respect,

there are points of view asserting that low bone mass could be found at almost all children with spastic tetraplegia and fractures are a well known problem in such children[7]. It is also mentioned in the literature[8], as a potential risk factor for osteoporosis in CP children/ adolescents, the long term use of anticonvulsants/ antidepressants–situations that we have met sporadically in our study as well[6].

The Scoliosis Research Society has defined a medically significant **scoliosis** as "any curve that is 10 degrees or more with or without a rotatory component"[9]. The curvatures greater than 10° are abnormal and may cause significant problems for growing children[10].

Scoliosis can be classified[11] in:

- functional (flexible)
- structural (rigid):
  - congenital
  - idiopathic
  - acquired: degenerative or secondary[9]

MATERIAL AND METHODS

The study was conducted at National Clinic Center for Neuropsychomotor Rehabilitation in Children *"Dr. Nicolae Robanescu"*, Bucharest, studying 2 groups (the first, sub-divided into 2 sub-groups), thus totally resulting in 3 populations of children: 5 to 11 years old (60-132 months), as follows:

- 8 ambulating patients with CP (sub-group 1, group 1)
- 8 non-ambulating patients with CP (sub-group 2, group 1)
- 8 patients with scoliosis – suposed without changes in bone metabolism and basic functionality (group 2)

The evaluating parameters and statistical processing approaches, used in this study, were clinical: Functional Independence Measure (FIM) scale and Body Mass Index (BMI) and respectively, para-clinical: serum Thyroid-Stimulating Hormone (TSH) and Free Thyroxin (FT_4) and respectively, urinary calcium and phosphorus, concentrations.

FIM ™ Scale - The Functional Independence Measure (FIM™)[12] "is the most widely accepted functional assessment measure in use in the rehabilitation community". It consists of 18 items, of which:

- 13 motor tasks grouped into motor subtotal score
- 5 cognitive tasks grouped into cognitive subtotal score

Each item is scored from 1 to 7 based on level of independence, where 1 represents total dependence and 7 indicates complete independence (maximum score is 126).

BMI in children and teens is age – and sex –specific[13], although there are opinions that "BMI is not an exact measure for growing children"[14]. The BMI is measured by weight and height and formula of calculation for children is: weight (kg)/height (m^2)[15].

Inclusion criteria were: disease (CP, scoliosis) and age (5- 11) years old.

Exclusion criteria for the study were: poor nutrition and significantly deviated from the occidental principles of nutrition and malnourished children

Limits of the study: approximatively 23% of parents/ legal caregivers' refused to participate in the study.

Consent of Bioethics Commission - It was obtained from the legal representative for conducting investigations and use of data for scientific aims ensuring the confidentiality required by law. Conducting the study was done with opinion of the Commission for Bioethics from the National Clinic Center for Neuropsychomotor Rehabilitation in Children "Dr. Nicolae Robanescu".

Statistical analysis preliminary included descriptive elements following that depending on method of distribution of the population groups to perform test for parametrical or non-parametrical differentiation and possible correlation test. The digital facility used: Statistical Package for Social Sciences (SPSS) 22. For statistical significance $p < 0.05$ was used.

RESULTS AND DISCUSSIONS

The small number of cases, the lack of normality in populations' distribution, made available for comparative analysis only non-parametric methods: Kruskal-Wallis and median tests (for 3 populations – as afore defined–ambulating, non ambulating, with scoliosis) and, in particular Mann-Whitney (U) test (for 2 groups/sub-groups). There were no significant diferences ($p>0.05$) between all the lots and groups/ sub-groups, except for FIM (sub-group 1 versus sub-group 2: $p<0.001$; sub-groups 1 + 2 versus group 2: $p<0.001$; sub-group 2 versus group 2: $p<0.001$).

In order to evaluate the parameters' contributivity and correlations, Spearman rank correlation coefficient - Spearman's rho – was used. The values were close to 0 (i.e. showing non-correlated items) except for urinary calcium and phosphorus concentrations, where Spearman's rho=0.61; this objectifies that they are positively correlated, yet (as well) not redundant.

Correlations

			IMC	FIM	TSH	F T 4	calciu urinar	fosfor urinar
Spearman's rho	IMC	Correlation Coefficient	1.000	.122	-.129	-.095	.176	.202
		Sig. (2-tailed)		.520	.531	.638	.371	.285
		N	30	30	26	27	28	30
	FIM	Correlation Coefficient	.122	1.000	.006	.262	.273	.312
		Sig. (2-tailed)	.520	.	.977	.186	.159	.094
		N	30	30	26	27	28	30
	TSH	Correlation Coefficient	-.129	.006	1.000	.151	.100	-.234
		Sig. (2-tailed)	.531	.977	.	.443	.636	.250
		N	26	26	26	25	25	26
	F T 4	Correlation Coefficient	-.095	.262	.151	1.000	.300	.146
		Sig. (2-tailed)	.638	.186	.443	.	.137	.469
		N	27	27	25	27	26	27
	calciu urinar	Correlation Coefficient	.176	.273	.100	.300	1.000	.609**
		Sig. (2-tailed)	.371	.159	.636	.137	.	.001
		N	28	28	25	26	28	28
	fosfor urinar	Correlation Coefficient	.202	.312	-.234	.146	.609**	1.000
		Sig. (2-tailed)	.285	.094	.250	.469	.001	.
		N	30	30	26	27	28	30

**. Correlation is significant at the 0.01 level (2-tailed).

Table 1 Sperman'rho correlations

The parents/legal caregivers' refusal to participate in the study led to difficulty of selecting a larger number of patients to become relevant for our research (e.g. refusal of 24 hours urine collection through bladder catheterization and respectively, refusal of investigation with Dual Emission X-ray Absorbtiometry–DEXA– as it is the imagistic gold standard related investigation).

This was a preliminary study and hence, it has been done including in accordance with our initial technical-economical possibilities; yet, for the extended study – within the Doctoral scientific research related endeavor – we have included, in its design, to measure, in the patients approached, urinary hydroxiproline (a widespread, unessential amino acid, which contains important quantities of colagen and which is excreted including in pathological conditions associated with bone resorption[16] (any factor that alters the bone matrix, the healing of fractures, various metabolic connected diseases, including osteoporosis, usually have as a result increases in the concentration of urinary hydroxyproline[16]) and blood vitamin D3 ("a fat-soluble vitamin and it has effects on skeletal health in children"[17]) concentrations, too – considering that the insufficiency of Vitamin D is associated with muscle weakness determining an increased risk of falling in children[18] („Supplementation with vitamin D reduces risk of osteoporotic fracture" [17]).

Accordingly, in the Doctoral scientific research we propose to evaluate MRC[19] 0-5 (Medical Research Council) besides FIM for main movements made by the basic lower limbs muscular groups, basic for ortostatism and gait (as they are in American Spinal Injury Association Impairment Scale - ASIA – Impairment Scale: AIS [20, 21]). There will also be, in the above mentioned extended study, comparatively assessed its blood concentrations, between children who have followed regulary prophylactic/ therapeutic – including admissions – such interventions and who have not. This will entail a standard question, addressed to all the children/ kin within the study, about considering vitamin D3 (the preferred vitamin D for daily supplementation is cholecalciferol[17]), possibly associated with calcium intake – the daily value of calcium is 1,000 mg for children aged 4 years and older [22] – if existing rachitis –"Carential rickets is a general metabolic disease characterized by a disorder of bone mineralization occurred in the growing period in terms of vitamin D deficiency"[23] – antecedents and/or actual concomitant pathology) opportunity/ feed back.

CONCLUSIONS

Caution is required regarding diagnosis and assessment of osteoporosis in children, because there are a limited number of studies compared to the adult population – aspect implied by the fact that in a demographic aging population, which characterizes the current global society, involutional osteoporosis is more common than in children.

Preliminary results obtained, confirm on one hand the predictable clinical-functional difference concerning functionality, between the 2 groups/ subgroups and, on the other, the chosen evaluation parameters are appropriate. This motivates continuing the study with: a higher number of cases, an optimized over 24 hours urine collection and an extended/ advanced further analysis on some newer related biochemical and hormonal markers.

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