EFFECTS OF ENZYME REPLACEMENT THERAPY ON CARDIAC DISEASE IN CHILDREN WITH MUCOPOLYSACCHARIDOSIS TYPE II

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INTRODUCTION

Mucopolysaccharidosis type II (MPS II) is a rare X-linked disorder caused by alterations in the iduronate-2-sulfatase which leads to the accumulation of partially digested glicosaminoglicans (GAGs) in the lysosomes and induces multisystemic alteration (coarse facial features, skeletal dysplasia, hepatosplenomegaly, joint stiffness and contractures, heart, lung, vision and hearing disability, profound neurological decline. Cardiac involvement in MPS type II is variable, consisting in severe cardiac valve disease and ventricular hypertrophy and has a major contribution into the morbidity and mortality of these patients. Enzyme replacement therapy in MPS type II may improve the organ impairment.

AIM OF THE STUDY

The aim of the study was to characterize the cardiac results of enzyme replacement therapy in children with MPS type II.

PATIENTS AND METHODS

Patients

15 patiens with MPS II

Methods

- Doppler echocardiography
  - septal thicknesses
  - posterior wall thicknesses
  - LV dimensions
  - LV function
  - valves thicknesses and function
  - pulmonary hypertension

  → at diagnosis; → after every 6 months of treatment

  Interpretation: - LV dimensions (Z score)
  - valve regurgitation and stenosis (EAE/EAS recommendations)
- Treatment
  - weekly administration of recombinant form of human iduronate 2-sulfatase, dose: 0.5mg/kg, i.v.
  - duration of treatment:
    - 12 months (3 patients)
    - 24 months (7 patients)
    - 36 months (2 patients)
    - 48 months (2 patients)
    - 60 months (1 patient)

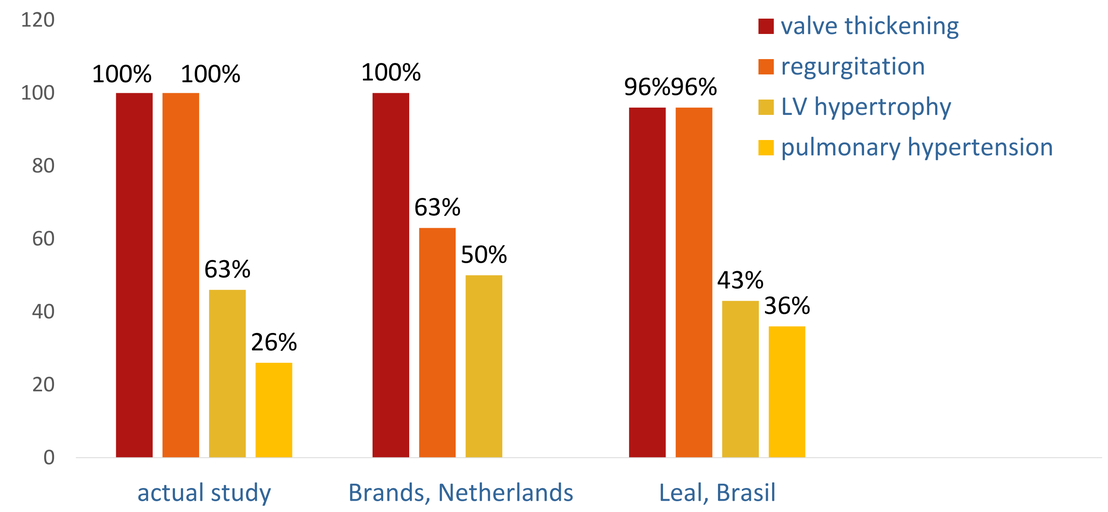
RESULTS

I. Echocardiographic alterations at diagnosis

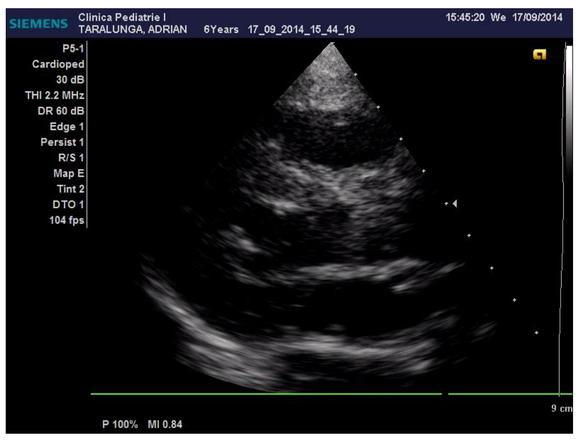
Echocardiographic alterations at diagnosis						
Mitral valve thickening	**Mitral valve regurgitation**	**Aortic valve regurgitation**	**Mitral valve stenosis**	**Aortic valve stenosis**	**Left ventricular hypertrophy**	**Pulmonary hypertension**
15 pt	15 pt	9 pt	2 pt	2 pt	7 pt	4 pt

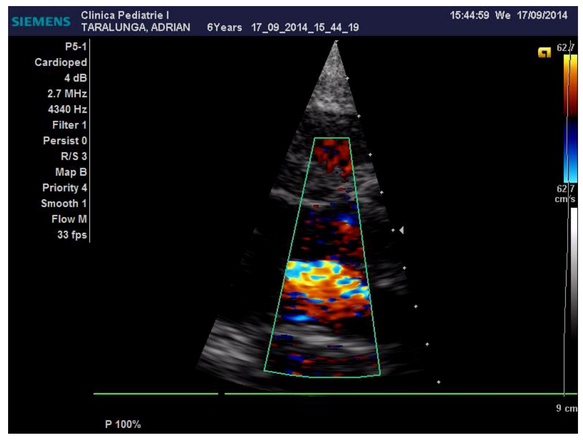
Valvar regurgitation at diagnosis				
Mitral valve regurgitation		**Aortic valve regurgitation**		
Grade I	**Grade II**	**Grade I**	**Grade II**	**Grade III**
10 pt	5 pt	5 pt	3 pt	1 pt

II. Comparison of echocardiographic alterations studies at diagnosis with other studies



No. patients	15	24	29
Age	6.1 years	5.3 years	7 years

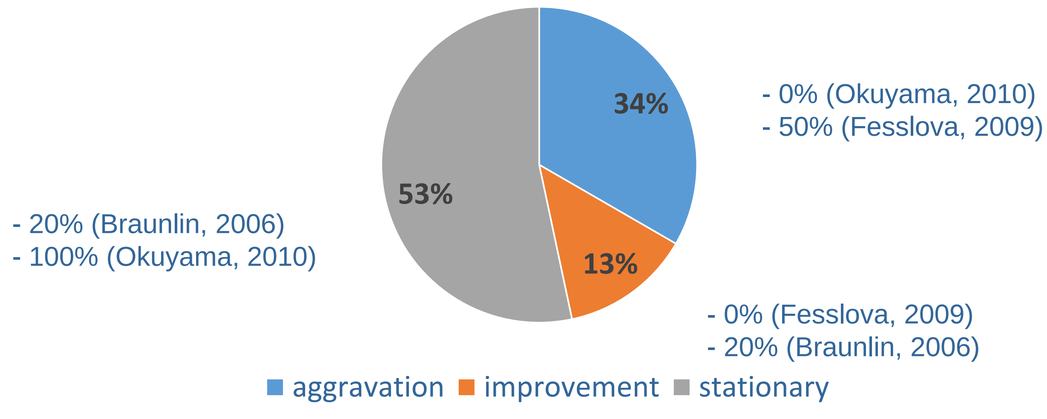




III. Evolution of echocardiographic alterations after treatment

Evolution after treatment	At 12 months		At 24 months	
	Valves abnormalities	LV hypertrophy	Valves abnormalities	LV hypertrophy
Aggravation	13.3%	0	26.6%	0
Improvement	13.3%	14.2	13.3%	14.2%
Stationary	73.3%	85.8	60%	85.8%

IV. Comparison of echocardiographic alterations after treatment with other studies



CONCLUSIONS

Left valves lesions, ventricular hypertrophy, and pulmonary hypertension are the most common findings in children with mucopolysaccharidosis. Enzyme replacement therapy had little effect on cardiac valve disease in children with MPS type II.