

Betatrophin as a new biomarker of Type 1 Diabetes Mellitus in Paediatrics



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INTRODUCTION

- ❖ Type 1 Diabetes Mellitus (DM1) is an autoimmune disease resulting from the destruction of β pancreatic cells.
- ❖ After the diagnosis, up to 80% of patients spontaneously experience partial remission for months.
- ❖ New biomarkers are being studied, such as the betatrophin protein (ANGPTL8) of unknown function, but which could be involved in the evolution of DM1, in this phase of RP and even used as a therapeutic target.

OBJECTIVES

1. Compare betatrophin levels in DM1 patients vs healthy controls
2. Follow up betatrophin levels in DM1 patients in honeymoon phase
3. Evolution of betatrophin levels in DM1 patients during the first 18 months after the onset.
4. Follow up betatrophin levels in a DM1 patient that remains in honeymoon 6 years after the diagnoses

METHODS

- ❖ Observational follow-up study.
- ❖ Plasma was collected from 22 patients with DM1, age at the beginning of the study 9 ± 4.5 (years \pm SD), 50% women, without obesity or other autoimmune disease.
- ❖ Plasma levels of betatrophin (ELISA) were analyzed at debut and after 6, 12 and 18 months of follow-up.
- ❖ Comparison with the levels of 14 healthy non-obese controls of similar ages and with one patient* with DM1 (initial HbA1c of 13.5%, normal weight) who persisted in RP 6 years after diagnosis.
 *This requires low doses of insulin (<0.5 UI / kg / day), has stimulated C-peptide levels of 1.3ng / ml and a HbA1c adjusted for insulin dose (IDDA1c) <9 , which indicates RP. The antibodies (GAD / IA2 / Zn) are repeatedly negative, as well as the MODY study. Typing HLA DR4 / DQ8

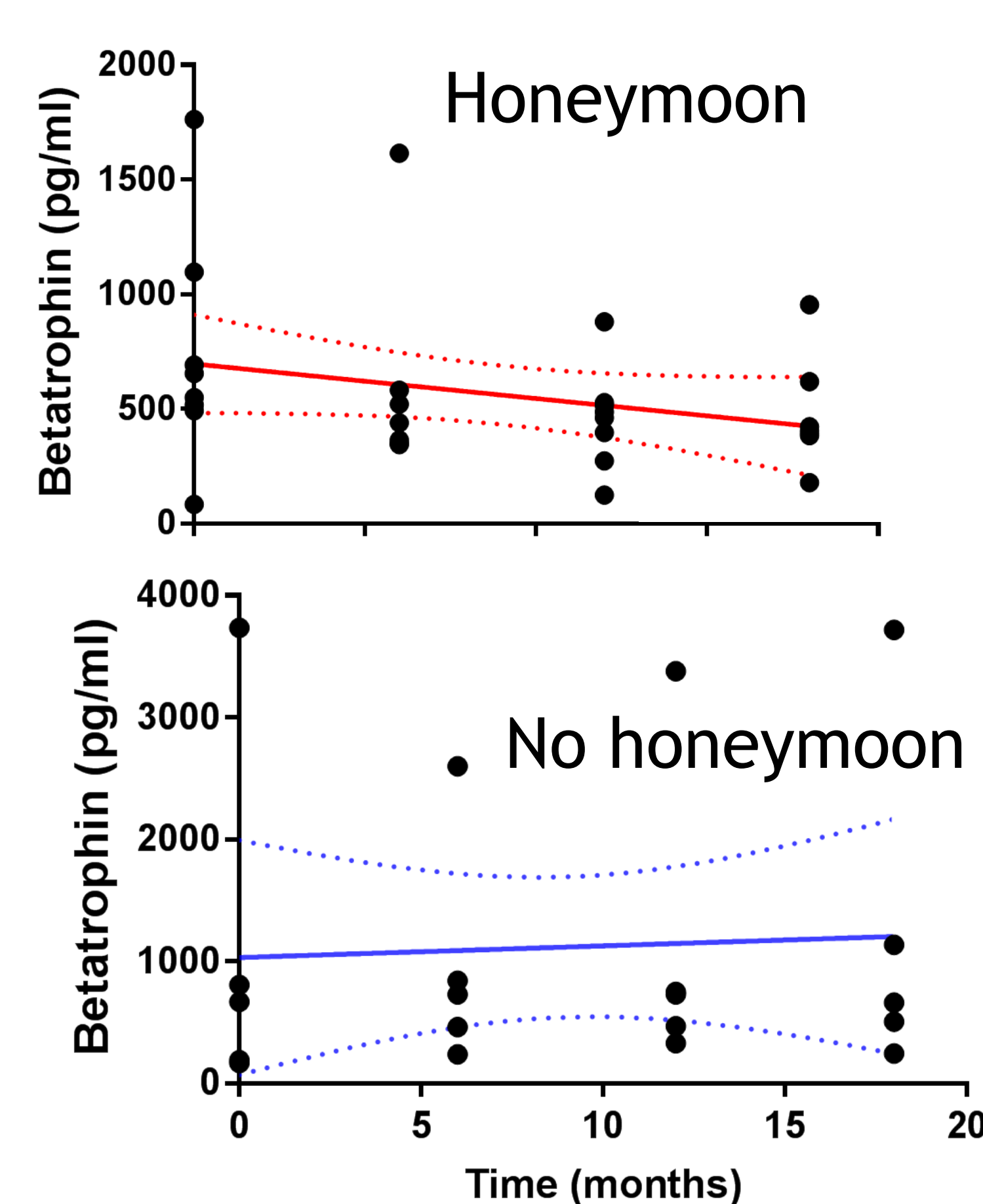
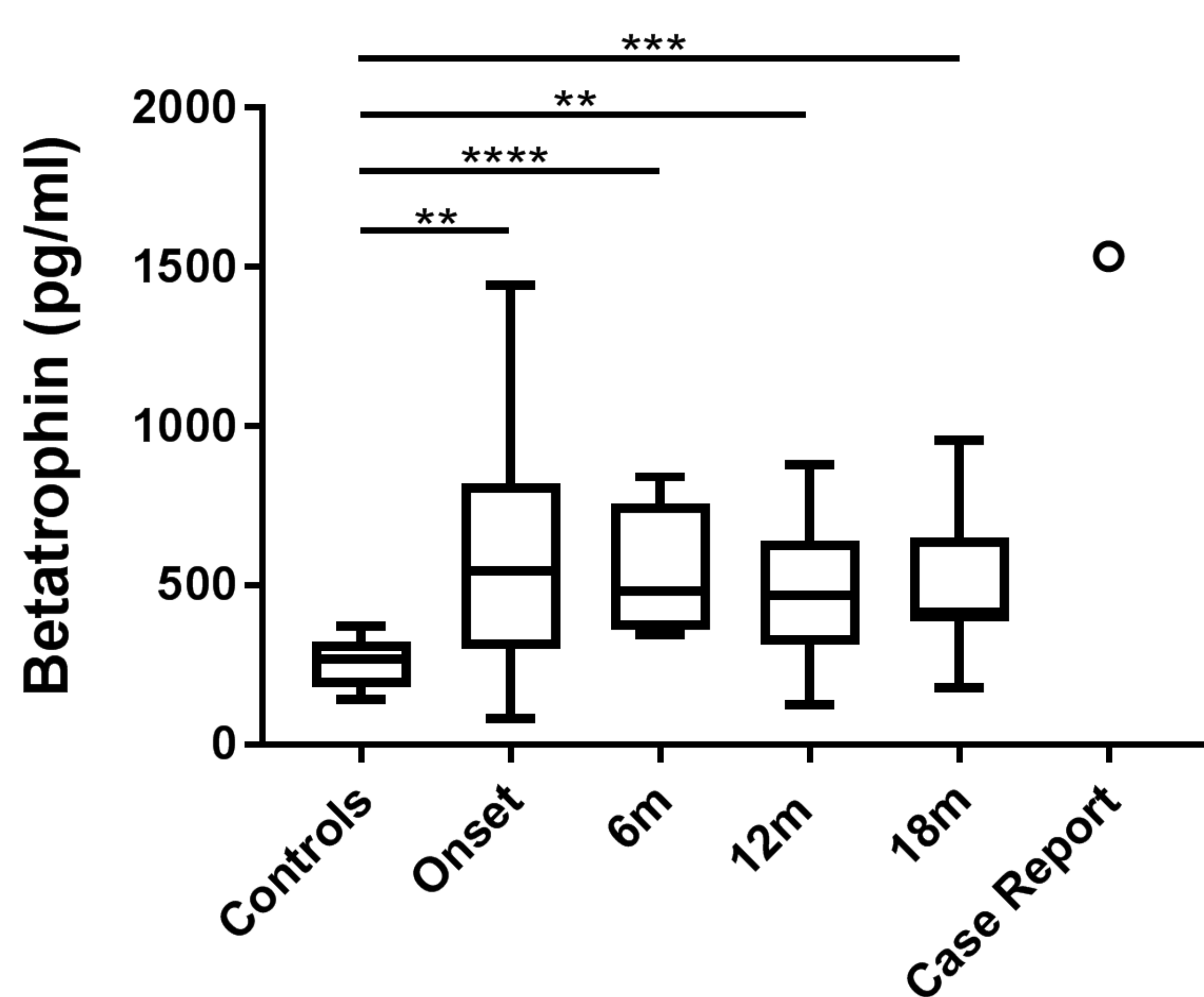
RESULTS

	Control	Onset	6 months	12 months	18 months	Case Report
N	14	22	15	14	13	1
Sex (M/F)	3/11	11/11	8/7	8/6	8/5	F
Age (years, mean \pm DS)	8,09 \pm 3,55	9,09 \pm 4,55	9,59 \pm 4,55	10,09 \pm 4,55	10,59 \pm 4,55	17
BMI (kg/m ²)	19,36 \pm 2,38	17,28 \pm 3,43	18,33 \pm 3,40	18,29 \pm 3,55	17,76 \pm 1,75	20,3
Insulin dose (UI/kg/day)	ND	0,80 \pm 0,40	0,53 \pm 0,20	0,79 \pm 0,70	0,92 \pm 0,72	0,38
HbA1c (%)	ND	11,36 \pm 2,53	7,16 \pm 1,06	7,65 \pm 1,04	7,63 \pm 1,04	5,2
IDAA1C (%)	ND	14,06 \pm 3,44	8,21 \pm 3,21	8,92 \pm 3,47	10,23 \pm 2,73	5
Honeymoon (% patients)	ND	0	8 (53%)	5 (38%)	0	-
C peptide (ng/mL)	ND	0,42 \pm 0,47	ND	ND	ND	1.3
Betatrophin (pg/mL)	258,35	722,78	691,75	687,050	671,59	1535

DM1 first 18 months	
Onset	722.78 pg/mL
6m	691.75 pg/mL
12m	687.05 pg/mL
18m	671.59 pg/mL

Controls VS Cases	
Controls	258.35 pg/mL
Cases	722.78 pg/mL

Case Report	
	1525 pg/mL



CONCLUSIONS

1. Betatrophin levels are increased in paediatric patients with DM1 in comparison with general population
2. Betatrophin levels remain steady in patients with honeymoon within the first 18 months after the onset. Tendency to progressively decrease during the following months.
3. Extremely high levels in a patient with persistent honeymoon (1535 pg/ml)
4. Use of betatrophin as a biomarker of DM1 in Paediatrics
5. Importance of the study of betatrophin during the different phases of the DM1 and relation with autoimmunity and pancreatic reserve in order to determine the potential use as a biomarker.

Fonolleda M, Murillo M, Vazquez F, Bel J, Vives-Pi M. Remission Phase in Paediatric Type 1 Diabetes: New Understanding and Emerging Biomarkers. *Horm Res Paediatr* (2017) 88(5):307-15. doi: 10.1159/000479030
 Murillo M, Fonolleda M, Bosch L, Rodríguez-Fernández S, Vázquez F, Bel J, et al. Sustained spontaneous partial remission in a pediatric patient with type 1 diabetes. *Journal of Clinical and Translational Endocrinology: Case Reports* (2017) 6:11-3. doi: 10.1016/j.jecr.2017.09.001.

