22-26 September 2021

# BLOOD PRESSURE IN GIRLS WITH CENTRAL PRECOCIOUS PUBERTY UNDER GNRH ANALOGUE THERAPY

N. Fisch-Shvalb<sup>a,b</sup>, H. Alfandary-Harani<sup>b,c</sup>, M. Davidovits<sup>b</sup>, N. Shvalb<sup>d</sup>, S. Demol-Eliaza,b, M. Yackobovitch-Gavan<sup>a,e</sup> M. Phillip<sup>a,b</sup>, L. de Vriesa,b

a. The Jesse Z. and Lea Shafer Institute of Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider Children's Medical b. Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. Center of Israel, Petach Tikva, Israel. c. Institute of Nephrology, Schneider Children's Medical Center of Israel, Petach Tikva, Israel. d. Faculty of Engineering, Ariel University, Ariel, Israel. e. Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel







## INTRODUCTION

Case reports show hypertension in children treated with GnRH analogues (GnRH-a) for central precocious puberty (CPP), which resolved upon drug cessation (1-5). These reports and the recent recommendation for monitoring blood pressure in adolescents with gender dysphoria treated with GnRH-a have raised concern regarding the safety of this regimen and the need for close BP monitoring during treatment. However, relevant data on blood pressure are scarce (6).

## **OBJECTIVES**

We aimed to evaluate the rate of elevated BP values among girls presenting with idiopathic CPP or early puberty (puberty onset between 8-9 years), and the change in blood pressure during and after GnRH-a therapy, as well as the association of BP with clinical parameters.

## RESULTS

At baseline, 64 (53%) of the study group and 17 (46%) of the controls had blood pressure values >90th percentile (p=0.57). The mean systolic and diastolic blood pressure percentiles at first measurement under treatment remained unchanged. After treatment cessation, the mean systolic, but not diastolic, blood pressure percentile was lower than baseline (n=47, p=0.006). For the study group, baseline blood pressure >90th percentile was associated with lower birthweight (p=0.014) and a higher BMI-standard deviation score (p=0.01).

	Before treatment (T0)	1 <sup>st</sup> BP under treatment (T1)	Off treatment (T2)	P value
Age, years	7.7 (0.10) <sup>a</sup>	9.2 (0.11) <sup>b</sup>	11.8 (0.15) <sup>c</sup>	< 0.001
Height SDS	0.81 (0.10) <sup>a</sup>	0.99 (0.10) <sup>b</sup>	0.63 (0.12) <sup>a</sup>	< 0.001
BMI SDS	0.90 (0.07)a	1.02 (0.07) <sup>b</sup>	0.92 (0.09)ab	0.030
SBPP	75.4 (2.3) <sup>a</sup>	72.4 (2.4) <sup>a</sup>	59.9 (3.5) <sup>b</sup>	0.006
DBPP	67.9 (2.6) <sup>a</sup>	67.4 (2.6) <sup>a</sup>	58.7 (3.9)b	0.090

	Normal BP at baseline	Abnormal BP at baseline	
	(n=53)	(n=59)	P value
Age at puberty onset, years	7.13 (1.0)	6.9 (1.3)	NS
Birth weight, grams	3108 (485)	2821 (622)	0.01
Preterm (%)	4.4	15.1	NS
Height-SDS	0.77 (1.2)	0.84 (1.0)	NS
BMI-SDS	0.70 (0.8)	1.0 (0.7)	0.01
Thelarche (Tanner 2,3,4) (%)	56, 34, 9	51, 46, 3	NS
BP AAP category:			
Normal	53 (100%)	-	
Elevated	-	16 (27%)	
Stage 1 high BP Stage 2 high BP	-	37 (63%)	
	-	6 (10%)	
Bone age	9.12 (1.4)	9.22 (1.5)	NS
Basal LH (IU/L)	0.65 (0.9)	0.71(0.9)	NS
Stimulated LH (IU/L)	14.0 (14.5)	13.6 (15)	NS
Estradiol (pmol/l)	43.8 (59)	39.2 (47)	NS
DHEAS (mcmol/l)	1.3 (1.0)	1.7 (1.3)	NS
Androstenedione (nmol/l)	2.4 (3.3)	2.1 (1.3)	NS

# METHODS

This is a retrospective longitudinal cohort study in a tertiary paediatric endocrinology institute. Demographic, anthropometric, clinical and laboratory data were collected from electronic files of 112 girls treated with GnRH-a for idiopathic CPP (n=81) or early puberty (n=31), and 37 healthy age-matched pre-pubertal controls. Blood pressure measurements from regular clinic visits were expressed as percentiles adjusted for gender, height and age (7). Data at baseline, under therapy and off-therapy were compared.

#### CONCLUSIONS

At presentation, girls with CPP and early puberty had similar blood pressure values as pre-pubertal controls. Blood pressure did not change during GnRH-a therapy, but the mean systolic blood pressure percentile decreased off-treatment. The stability of mean blood pressure percentile during treatment is reassuring.

#### REFERENCES

precocious puberty. Acta Paediatr Scand. 1988;77:294–8

- Calcaterra V, Mannarino S, Corana G, Codazzi AC, Mazzola A, Brambilla P, et al. Hypertension during therapy with triptorelin in a girl with precocious puberty. Indian J Pediatr. 2013;80:884-5.
- Siomou E, Kosmeri C, Pavlou M, Vlahos AP, Argyropoulou MI, Siamopoulou A. Arterial hypertension during treatment with triptorelin in a child with Williams-Beuren syndrome. *Pediatr Nephrol*. 2014;29:1633–6.
- Palma L, Gaudino R, Cavarzere P, Antoniazzi F. Does the risk of arterial hypertension increase in the course of triptorelin treatment? J Pediatr Endocrinol Metab. 2020 Mar 26;33(3):449-452.
- 4. Klink D, Bokenkamp A, Dekker C, Rotteveel J. Arterial hypertension as a complication of Triptorelin treatment in adolescents with gender dysphoria. Endocrin Metab Int J. 2015;2:1-4. . Sifaki L, Cachat F, Theintz G and Chehade H. Transient Arterial Hypertension Induced by Gonadotropin-
- Releasing Hormone Agonist Treatment for Central Precocious Puberty. Front. Pediatr. 2019;7:74. 6. Liker HR, Barnes KM, Comite F, Hench KD, Loriaux DL, Cutler GB Jr, et al. Blood pressure and body size in
- Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, , et al; subcommittee on screening and management of high blood pressure in children. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics*. 2017 Sep;140(3).

## ACKNOWLEDGEMENTS

The authors wish to thank Pearl Lilos for the statistical analysis.

## CONTACT INFORMATION

Naama Fisch Shvalb MD, Institute for Endocrinology and Diabetes, Schneider Children's Medical Center of Israel,

14 Kaplan Street, Petach Tikva 4920235, Israel.

Tel: +972-3-9259018; Fax: +972-3-9253836;

E-mails: naamafi@gmail.com nammaf@clalit.org.il

