Pubertal induction in girls with hypogonadism: preliminary data of efficacy in patients with/without initial overnight estrogen replacement

G. RODARI[1,2], S. FEDERICI[3,4], L. PERSANI[3,4], M. AROSIO[1,2], M. BONOMI[3,4], C. GIAVOLI[1,2]

1. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy
2. Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy
3. University of Milan Department of Medical Biotechnology and Translational Medicine, Milan, Italy.
4. IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases and Lab. of Endocrine and Metabolic Research, Milan, Italy

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INTRODUCTION

Pubertal induction in girls with hypogonadism through estrogen replacement therapy (ERT) aims at the development of secondary sexual characteristics, cognitive functions, uterine growth and maturation, bone mass accrual and linear growth, **resembling natural puberty**.

To date, the best induction regimen, capable of assuring both **physiological gradual progression through Tanner stages** and effective **uterine development**, is still to be established.

METHODS

Here we present our data regarding **19 prepubertal girls** (age 16.9±2.8 years, range: 11.7-24.8 years, Tanner stage B1 at diagnosis) with hypogonadism:

- **16/19 hypogonadotropic hypogonadism;**
- **3/19 premature ovarian insufficiency.**

They were followed for at least 12 months (range 1.0-4.2 years) of estrogen replacement therapy (ERT) with transdermal 17βoestradiol patches.

Eleven out of 19 patients started with **overnight** ERT for six months (0.07- 0.1 mcg/kg/day). In all patients, ERT was gradually increased every six months.

Progesterone replacement was started in 10 girls at Tanner stage 5 or bleeding occurrence.

Auxological, biochemical (17βoestradiol), pelvic ultrasound and bone age assessment data were collected every 12 months from ERT start.

RESULTS

Mean tempo at Tanner stage B3 was 1.2±0.4 years, being negatively correlated with ERT dose/kg at start (p=0.01).

Mean tempo at Tanner stage B4 was 2.0±0.5 years, being higher in patients with initial overnight ERT (p=0.02).

Mean tempo at Tanner stage B5 or bleeding occurrence was 2.4±0.7 years, being positively correlated with uterine maturation (uterine length > 65 mm, p=0.02).

Mean adult height (AH) was 171.3±6.1 cm (1.24±0.94 SDS WHO), not statistically different from mid-parental height (MPH-AH -0.6±1.4 SDS WHO, p=0.2).

Uterine maturation was achieved by 71% patient at the end of induction, with final uterine length positively correlated with ERT dose/kg at progesterone introduction (p=0.02). No difference was found in uterine length between patients who underwent an initial overnight ERT and others.

	mean	SD	min	max
Chronological age (years)	16.9	2.8	11.7	24.8
Bone Age (years)	13.1	1.9	10.1	18
MPH[1] (SDS)	-0.55	1.44	-2.82	2.59
HT[2] (cm)	161.6	9.7	140	177
HT[2] (SDS)	0.05	1.2	-2.57	1.96
BMI[3] (kg/m²)	20.8	4.0	14.3	27.6
BMI[3] (SDS)	-0.23	1.51	-3.27	+2.15

Tab. 1 Baseline Characteristics of study population
1. MPH: Mid-parental Height; 2. HT: Height; 3. BMI: Body Mass Index
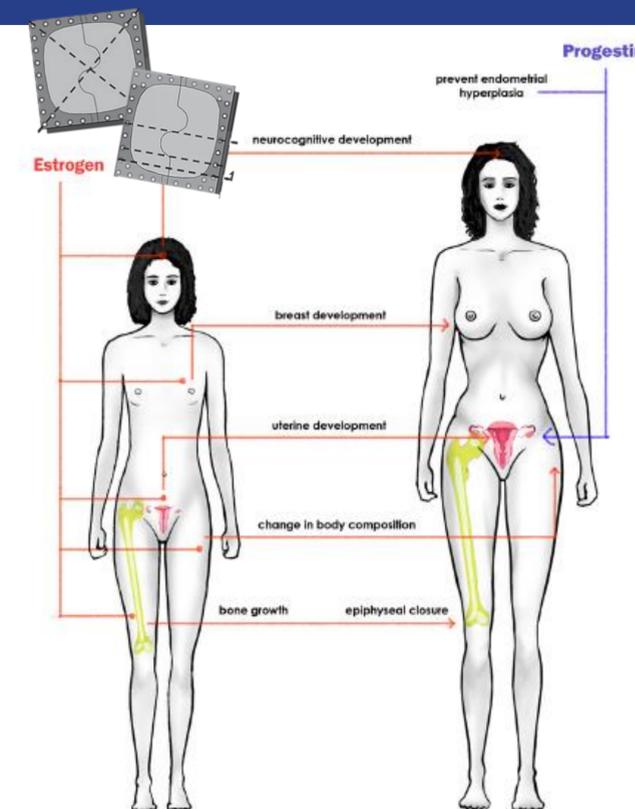
CONCLUSIONS

(i) **Initial overnight ERT assures a gradual pubertal progression,** increasing mean tempo at Tanner stage B4, **along with an adequate uterine maturation**;

(ii) **delaying Tanner stage 5** achievement and bleeding occurrence seems to be beneficial in terms of **uterine maturation.**

Further multicentic data are needed to confirm these evidences and the possible role of initial overnight ERT replacement

CONTACT INFORMATION

Giulia Rodari, MD

Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico; Department of Clinical Sciences and Community Health, University of Milan, Via Francesco Sforza 35, 20122, Milan, Italy.

giulia.rodari@unimi.it; rodarigiulia@gmail.com

Marco Bonomi, Prof.

Dept. of Endocrine and Metabolic Disease, Istituto Auxologico Italiano, Piazzale Brescia 20 - 2019 Milan, Italy

marco.bonomi@unimi.it; m.bonomi@auxologico.it.

REFERENCES

Matthews D et al. Hormone supplementation for pubertal induction in girls. *Arch Dis Child. 2017 Oct;102(10):975-980.*

Ankarberg-Lindgren C et al. Nocturnal application of transdermal estradiol patches produces levels of estradiol that mimic those seen at the onset of spontaneous puberty in girls. *J Clin Endocrinol Metab 2001;86:3039–44.*

Ankarberg-Lindgren C et al. Physiological estrogen replacement therapy for puberty induction in girls: a clinical observational study. *Horm Res Paediatr 2014;81:239–44*

Burt E et al. Reduced uterine volume after induction of puberty in women with hypogonadism. *Clin Endocrinol (Oxf). 2019 Dec;91(6):798-804.*

Estrogen — Progestin — prevent endometrial hyperplasia — neurocognitive development — breast development — uterine development — change in body composition — bone growth — epiphyseal closure