Normalized pubertal tempo of maturation and pubertal height gain in girls with MPHD, using a physiological treatment approach with natural estradiol & GH

Lundberg E[1], Kriström B[1], Holmlund M[1], Albertsson Wikland K[2]

[1]Dep of Clinical Science/Pediatrics, Umeå University, [2]Dep of Physiology/Endocrinology, Institute of Neurosciences and Physiology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden.

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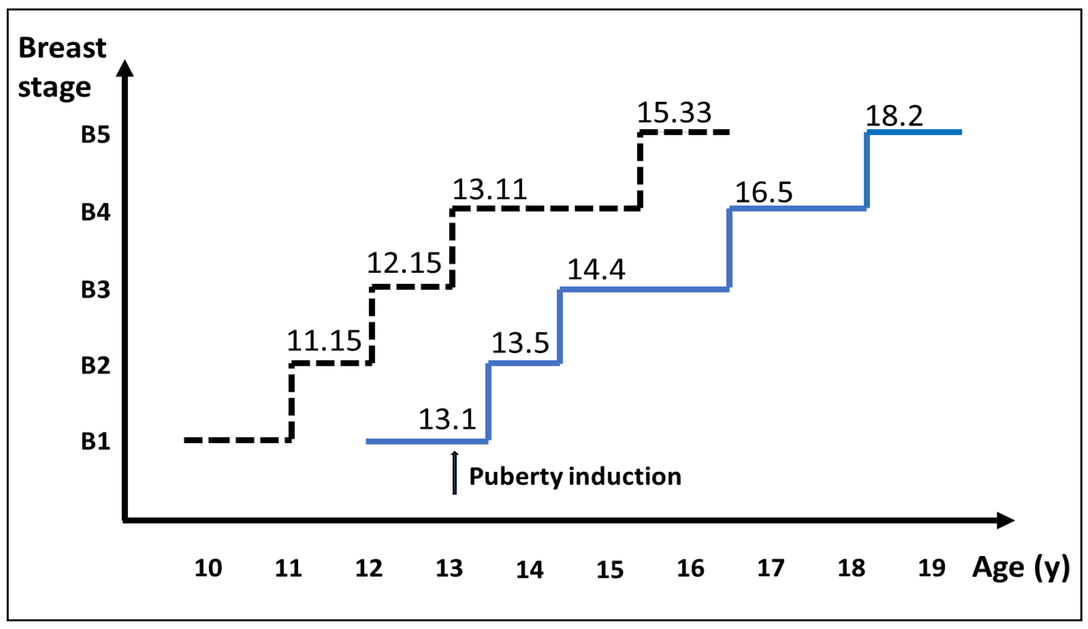
Aim: By mimicking normal pubertal physiology induce breast development, pubertal height gain and increase adult height in children with multiple pituitary hormone deficiencies (MPHD)

Background: Pubertal tempo of breast development on natural sex-steroid replacement therapy in girls with MPHD and pubertal growth spurts on adequate GH-treatment regimens were unknown in 1989 and are still not known.

Study population and treatment: Six girls with organic or idiopathic MPHD with at least one prepubertal year on GH 33µg/kg/day, were randomized to receive GH (Genotropin®) 33 or 67µg/kg/day during puberty. Sex-steroid replacement was 17ß-estradiol patches in slowly increasing doses (5, 10, 12.5, 25, 50µg/day) mimicking the spontaneous pubertal tempo[1]. For this purpose, pharmaceutical 17ß-estradiol patches (Estraderm®) were produced and donated**.**

Results

Breast development in girls with MPHD on therapy vs healthy girls [1]



Breast development in girls with MPHD on therapy. Median age for each breast stage (blue line) compared to normal values according to Tanner[1] (broken line).

Median age and duration of breast stages in girls with MPHD on therapy vs healthy girls[1]

Total (n)	Stage	Age (y)	Range (y)	Mean values Tanner (y)
6	**B2**	13.5	12.9-14.4	11.15
6	**B3**	14.4	13.4-15.6	12.15
6	**B4**	16.5	14.6-17.6	13.11
4	**B5**	18.2	15.6-19.2	15.33
Total (n)	**Interval**	**Duration (y)**	**Range (y)**	**Mean values Tanner (y)**
6	**B2-B3**	1.2	0.8-1.7	0.86
6	**B3-B4**	1.8	0.5-4.0	0.89
4	**B4-B5**	1.5	1.0-3.1	1.96
6	**B2-B4**	3.0	1.7-4.2	1.80
4	**B2-B5**	4.3	2.7-5.5	4.00

Median age and duration of breast stages in girls with MPHD, receiving increasing doses of transdermal estradiol replacement compared to Tanner[1] mean values from healthy girls.

elena.lundberg@umu.se

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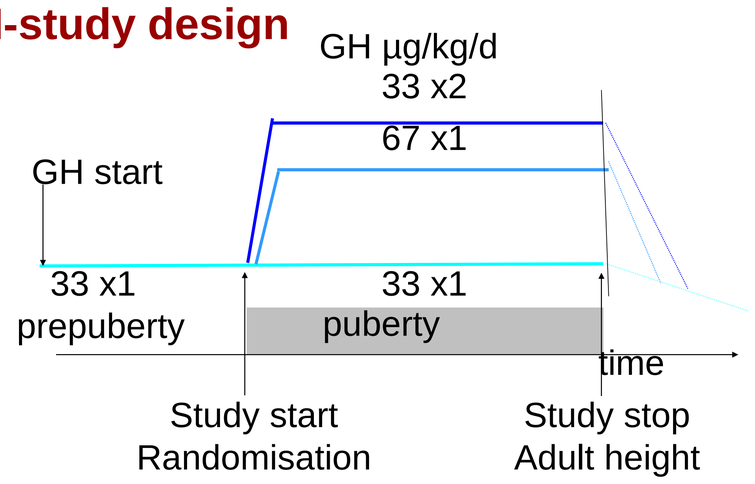
Conclusion

•Tempo of breast development, pubertal growth spurt and adult height can be normalized in MPHD girls by using a physiological substitution therapy with transdermal 17ß-estradiol and adequate GH-doses.

•This allows earlier age for pubertal induction.

GH-study design



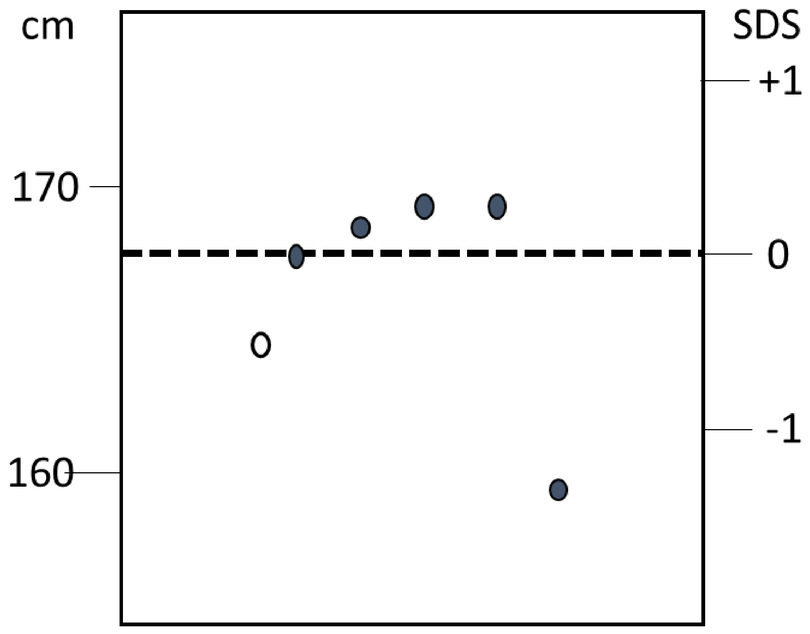
Height methods and outcome

Pubertal height gain was estimated as change from $height_{SDS}$ at start of 17ß-estradiol-replacement (calculated vs prepubertal height reference) to Adult Height.

Pubertal gain in $height_{SDS}$ was median +0.8 (0 to 1.15); in cm 21.1 (11.8-21.6).

AH_{SDS} median 0.075 (-1.33 to 0.31); in cm 168.0 (159.5 to 169.5).

Adult height in girls with MPHD vs mean population height for girls[2]



Filled circles: GH dose 67 µg/kg/day. Open circle: GH 33 µg/kg/day. Mean population height for females in Sweden is 167.7 cm[2] (broken line)

Referenser

[1]Marshall&Tanner, Arch. Dis.Child.1969;44:291-303
[2]Albertsson-Wikland et al Acta Ped 2002;91:739-54