Growth, pubertal course and long-term outcome of 46,XY boys born with atypical genitalia and low birthweight

L. Tack, S. Van der Straaten , S. Riedl, A. Springer, S.F. Ahmed and M. Cools
On behalf of the I-DSD consortium*
* P.M. Holterhus, N. Hornig, M. Niedziela, Z. Kolesinska, F. Barinio, A. Balsamo, S. E. Hannema, A. Nordenström, S. Poyrazoglu, F. Darendeliler, R. Grinspon, F. Aljuraibah, C. Acerini, G. Guaragna-Filho, A. Trevas Maciel-Guerra, G. Guerra-Junior, U. Tonnhofer, M. Hiess and J. Weninger

KEY MESSAGES

- 1/3 SGA boys show incomplete catch-up growth
- No difference in urological outcome between AGA and SGA cases
- SGA boys have higher LH levels during minipuberty, and lower peak testosterone levels post HCG stimulation in childhood

INTRODUCTION

Boys born small for gestational age (SGA) often have undermasculinized genitalia. Little is known about the pubertal development and gonadal function on a longer-term in this specific group of males.

AIMS

To determine the (pubertal) development and long-term urological and endocrine outcome of undermasculinized boys born SGA compared to undervirilized boys born appropriate for gestational age (AGA).

METHODOLOGY

I-DSD Registry:

- Boys with non-specific 46, XY DSD
- Aged ≥2 years at the time of survey
- Twelve participating centers

Analyses:

Secondary use of routinely obtained clinical data and statistical analysis as appropriate.

RESULTS

Patient characteristics

	SGA (n=115)	AGA (n=64)	P-value
EMS first presentation	6,5 (4)	7,25 (3,0)	0,311
EMS last assessment	12 (1,0)	12 (1,1)	0,531
GA: <37 weeks	71/115 (61,7%)	18/64 (28,1%)	<0,001
<33 weeks	*28/115 (24,3%)*	*9/64 (14,1%)*	
Delayed neuromotor development	20/102 (19,6%)	1/53 (1,9%)	<0,001

GA: gestational age

Growth

At 2 years of age:

- 31/104 SGA boys (29.8%) had incomplete or absent catch-up growth

Growth hormone therapy:

- Only 8 cases
- Mean effect : + 1,5 SD length & weight

At last assessment:

- Lower SD-scores for height and weight in SGA boys (both p<0.001) at a median age of 8.0 (SGA) and 7.7 years (AGA)

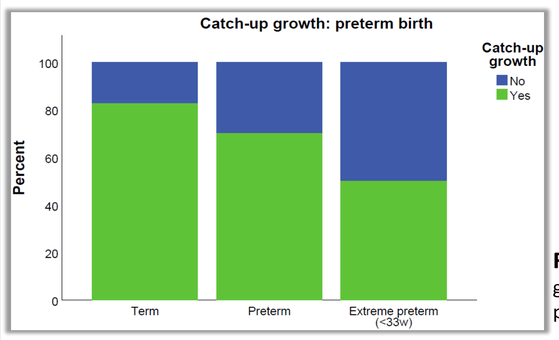

Figure: Less catch-up growth in boys born preterm (p=0,030)

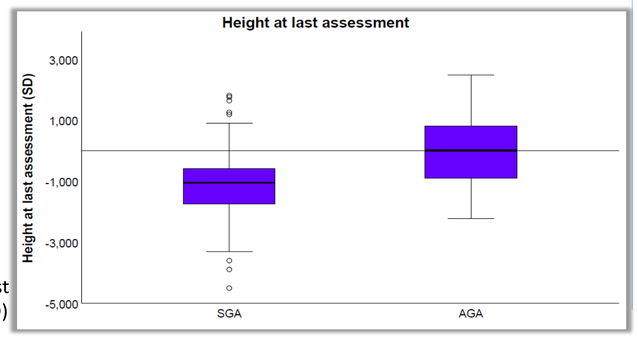

Figure: Height at last assessment(SD)

Urological

Hypospadias repair:

- The number of reinterventions was similar in both groups (1 (2); p=0.836)

EMS:

- At last assessment, nearly all boys had an external masculinization score of 12/12
- Residual hypospadias was the most frequent cause of lower scores in both SGA and AGA boys

Endocrine

Stimulation of penile growth:

- Postnatal or childhood treatment had a good clinical effect in 38/42 (90.5%) SGA and 14/15 (93.3%) AGA boys

Minipuberty/stimulation test:

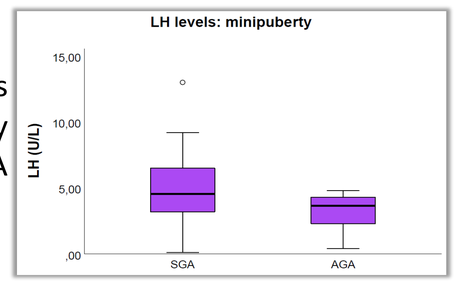

Figure: LH levels during minipuberty were higher in SGA boys (p=0,037)

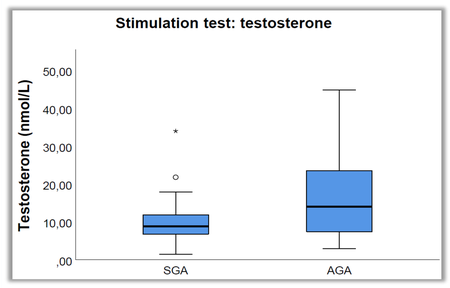

Figure: Peak testosterone levels post stimulation were lower in SGA boys (p=0.040)

Puberty:

- Majority of boys: spontaneous onset and uneventful course of puberty
- At the end of puberty: no difference in sex hormone levels was observed between SGA and AGA boys

CONCLUSION

About one-third of boys with non-specific XY DSD who have SGA show insufficient catch-up growth. The urological outcome and effect of treatments to increase penile size was similar between SGA and AGA cases. Our data suggest a dysfunction of infantile Leydig cells in SGA boys, which does not seem to persist in adult-type Leydig cells. Alternatively, alteration of the hypothalamic-pituitary-gonadal axis during infancy may underlie the hormonal changes found in SGA boys.

FUNDING

Ghent University Hospital, Pediatric Endocrinology & Diabetology (3K12D), Ghent University, BELGIUM – Contact: lloyd.tack@ugent.be, Martine.Cools@ugent.be

58ESPE RFC8-006
Sex differentiation, gonads and gynaecology or sex endocrinology
Lloyd Tack
Poster presented at: ESPE 2019 VIENNA
PosterSessionOnline.com