Altered Thyroid function following Growth Hormone (GH) Initiation in children with Prader-Willi syndrome (PWS)

Musthaffa, Yassmin[1]; Scheermeyer, Elly[2]; Hughes, Ian[3]; Harris, Mark[1]; Crock, Patricia[4]; Leong, Gary[1]

1. *Lady Cilento Children's Hospital, Queensland, Australia*
2. *School of Medicine, University of Queensland*
3. *Mater Research Institute, The University of Queensland, Australia*
4. *John Hunter Children's Hospital, University of Newcastle, NSW*

OBJECTIVE

Growth is optimal in the euthyroid state. Growth Hormone (GH) treatment may perturb the Hypothalamic-Pituitary-Thyroid Axis through both central inhibition of TSH (Thyroid Stimulating Hormone) release and increased peripheral conversion of T4 to T3. Hypothalamic dysfunction is common in PWS, and these children may be at risk of central hypothyroidism following GH treatment.

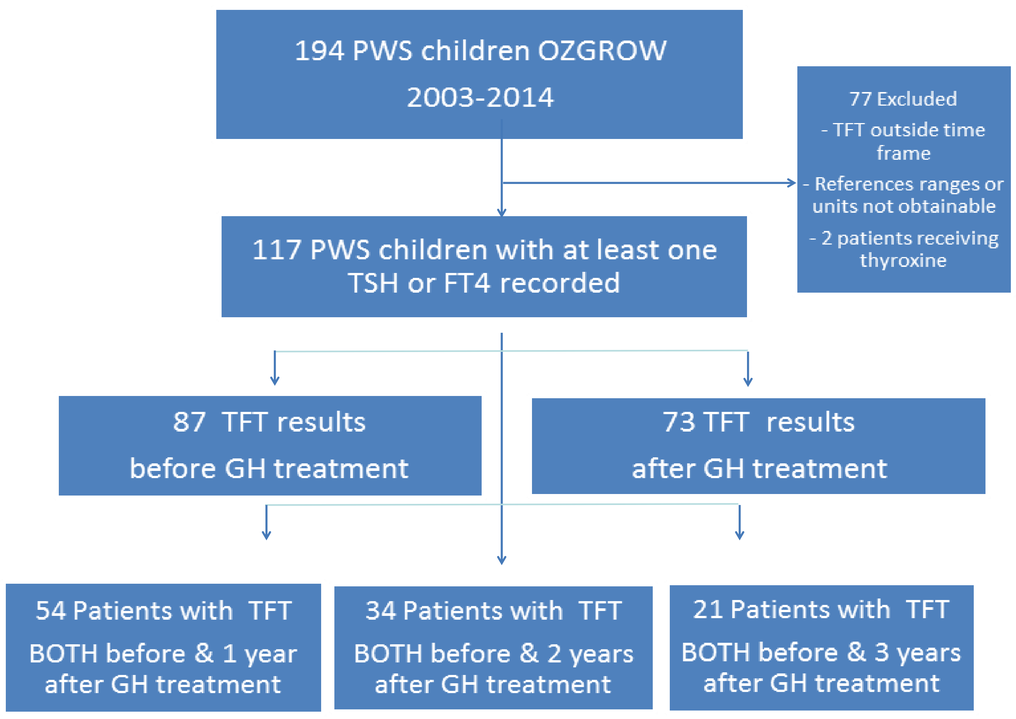
Objective: To assess thyroid function in children with PWS before and after GH treatment.

METHODS AND STATISTICAL ANALYSIS

A retrospective review of children with PWS receiving GH under the national Australian GH programme (OZGROW) between 2003 and 2014 was performed.

FT4 and TSH results were standardized by expressing them as a % of the reference range (RR) using the equation described.

Mean test % were compared to an expected mean of 50% for tests taken one year pre-GH and post-GT using a one-sample t test. We also assessed change in test % for those who had tests before and after GH commencement (Δ%) using a paired t test.



$$x\% = 100\left(\frac{(x-L)}{(U-L)}\right)$$

x = test result
U = Upper limit of RR
L = Lower limit of RR

RESULTS

BASELINE DEMOGRAPHICS AT GH COMMENCMENT	Study participants	OZGROW PWS population	
N	117	194	
Sex (M/F)	1:1	1:1	$\chi^2 = 0.13$
Mean Age (years) (sd)	12.6 (3.8)	7.7 (4.8)	$P = 4.0\times10^{-5}$
Mean Height SDS (sd)	-0.82 (1.2)	-0.5 (2.2)	$P = 0.47$
Mean BMI SDS (sd)	1.28 (1.1)	1.26 (1.2)	$P = 1.0$

Table 1. **MEAN TEST %**

	Baseline	*1st Year of GH*
N	87	73
Mean FT4 (sd)	33.1 (19.2) % [a]	21.7 (17.5)% [a]
Mean TSH (sd)	38.2 (22.7) % [a]	25.4 (22.6)% [a]

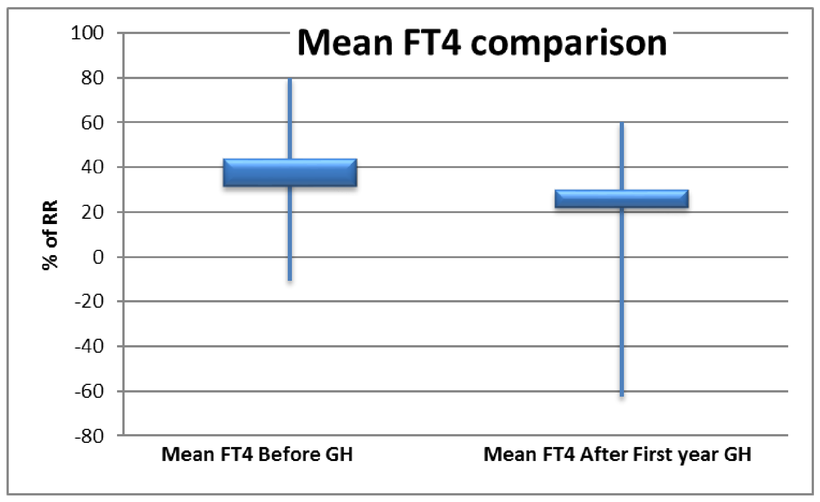
[a] ***p < 0.001***
[b] ***p < 0.01***
[c] ***p < 0.05***

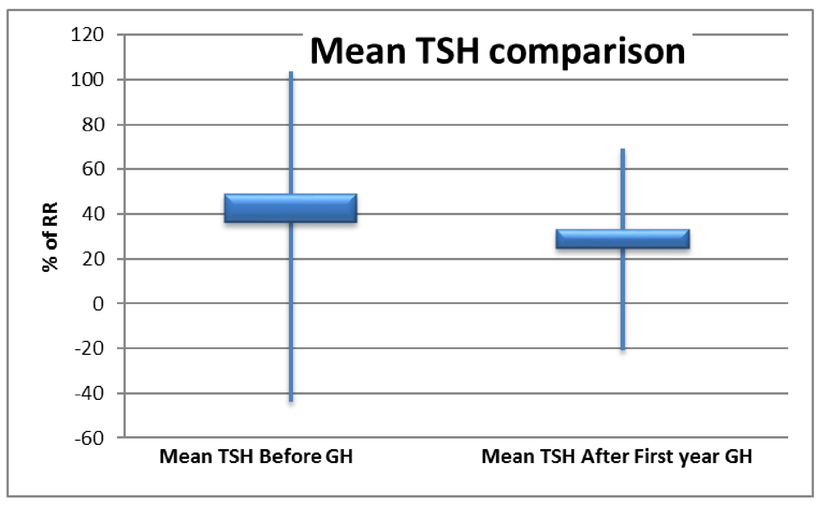
Table 2. **MEAN Δ%**

	1 year post GH	*2 years post GH*	*3 years post GH*
N	54	34	21
FT4 Δ% (sd)	-11.5 (23.0)% [a]	-8.9 (19.3)% [c]	-8.1 (15.5)% [c]
TSH Δ% (sd)	-12.9 (26.5)% [a]	-15.0(18.6)% [a]	-11.4(18.4)% [b]

In the year prior to GH, most FT4 and TSH were in the low normal range while 4 patients had FT4 below the RR (Table 1).

Following GH therapy, FT4 and TSH decreased further. This effect was sustained for 3 years (Table 2).





CONCLUSIONS

FT4 was significantly lower than expected in patients with PWS. This further decreased during GH therapy. Whether these changes have adverse clinical effects on growth is unclear. GH therapy has been suggested to decrease TSH by both a direct central and an indirect peripheral mechanism. Analysis of T3 levels is required to distinguish between these hypotheses and elucidate whether Thyroxine supplementation would be of benefit.

REFERENCES

- *Department of Health and Ageing. Pharmaceutical Benefits Scheme (PBS) Growth Hormone Program. 2015 Available from: http://www.health.gov.au/hgh [accessed 8 Jan 2015].*
- *Swaab, D.F et al. Prader–Willi and the hypothalamus. Acta Paediatrica. Supplementum, 1997 Jan, 423, 50–54*
- *Rose 1995 et al. Thyroid function in non-growth hormone-deficient short children during a placebocontrolled double blind trial of recombinant growth hormone therapy. J Clin Endocrinol Metab. 1995 Jan;80(1):320-324*
- *Portes ES et al. Changes in serum thyroid hormones levels and their mechanisms during long-term growth hormone (GH) replacement therapy in GH deficient children. Clin Endocrinol. 2000 Aug; 53(2):183-189.*
- *Lippe BM et al. Reversible hypothyroidism in growth hormone-deficient children treated with human growth hormone. J Clin Endocrinol Metab. 1975 Apr; 40(4):612-618*
- *Behan LA et al. The interaction between growth hormone and the thyroid axis in hypopituitary patients. Clin Endocrinol. 2011 Aug, 74, 281–288*

55ESPE 814--P1
Syndromes : Mechanisms and Management
Yassmin Musthaffa
DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS 10-12 SEPTEMBER
PosterSessionOnline.com