



TITLE: Human Growth Hormone Treatment for Prader-Willi Syndrome in Adolescent and Adult Patients: Clinical Evidence, Safety, and Guidelines

DATE: 13 February 2012

RESEARCH QUESTIONS

1. What is the clinical evidence for the use of human growth hormone treatment for Prader-Willi syndrome in adolescent and adult patients?
2. What is the clinical safety of human growth hormone treatment for Prader-Willi syndrome in adolescent and adult patients?
3. What are the evidence-based guidelines for the use of human growth hormone treatment for Prader-Willi syndrome in adolescent and adult patients?

KEY MESSAGE

The evidence suggests that, with appropriate control and careful monitoring, human growth hormone treatment is a safe and effective treatment option in adolescent and adult patients with Prader-Willi syndrome.

METHODS

A limited literature search was conducted on key resources including PubMed, EMBASE, The Cochrane Library (2012, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and abbreviated list of major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2007 and January 26, 2012. Internet links were provided, where available.

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The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs), non-randomized studies and evidence-based guidelines.

One meta-analysis, two randomized controlled trials and ten non-randomized studies were identified regarding human growth hormone (hGH) treatment for Prader-Willi syndrome (PWS) in adolescent and adult patients. No health technology assessments and no evidence-based guidelines were identified. Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One meta-analysis¹ demonstrated that hGH therapy for PWS in adult patients led to increased lean body mass and to decreased body adiposity. There was a small increase in fasting glucose levels and a trend towards higher insulin resistance.

Two RCTs and 10 non-randomized studies²⁻¹³ indicated that hGH therapy in adolescent or adult patients with PWS had multiple beneficial effects on body composition and growth and a few negative effects. The observed outcomes included:

- increase in lean body mass^{2,3,4,8,9,11,12,13}
- increase in IGF-1 (Insulin-like Growth Factor 1) levels^{2,3,6,13}
- decrease in body fat mass^{2,4,5,7,8,11,12,13}
- few observed serious adverse events^{2,5,9,10,12}
- observed onset of scoliosis and curve progression was similar to controls³ or did not progress⁶
- improvement in mean height^{3,6,7,9,10}
- increased insulin resistance⁴
- high rate of scoliosis that warrants monitoring by a pediatric orthopedic surgeon⁴
- increase in lung function (peak expiratory flow)⁵
- high incidence of sleep apnoea⁶ and abnormal sleep polygraphy⁷
- increase in agility and physical activity⁸
- normalization of T₃ (Triiodothyronine) levels¹¹
- mildly progressive ankle edema¹¹
- increase in cardiac mass requiring monitoring¹³

No evidence-based guidelines on the use of hGH treatment for PWS in adolescent and adult patients were identified; therefore, no summary of the guidelines has been provided.

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Sanchez-Ortiga R, Klibanski A, Tritos NA. Effects of recombinant human growth hormone therapy in adults with Prader-Willi syndrome: a meta-analysis. *Clin Endocrinol (Oxf)*. 2011 Nov 25.
[PubMed: PM22117629](#)

Randomized Controlled Trials

2. Sode-Carlson R, Farholt S, Rabben KF, Bollerslev J, Schreiner T, Jurik AG, et al. One year of growth hormone treatment in adults with Prader-Willi syndrome improves body composition: results from a randomized, placebo-controlled study. *J Clin Endocrinol Metab*. 2010 Nov;95(11):4943-50.
[PubMed: PM20702523](#)
3. de Lind van Wijngaarden RF, de Klerk LW, Festen DA, Duivenvoorden HJ, Otten BJ, Hokken-Koelega AC. Randomized controlled trial to investigate the effects of growth hormone treatment on scoliosis in children with Prader-Willi syndrome. *J Clin Endocrinol Metab*. 2009 Apr;94(4):1274-80.
[PubMed: PM19158197](#)

Non-Randomized Studies

4. Colmenares A, Pinto G, Taupin P, Giuseppe A, Odent T, Trivin C, et al. Effects on growth and metabolism of growth hormone treatment for 3 years in 36 children with Prader-Willi syndrome. *Horm Res Paediatr*. 2011 Feb;75(2):123-30.
[PubMed: PM20847547](#)
5. Sode-Carlson R, Farholt S, Hoybye C, Bollerslev J, Rabben K, Christiansen JS. Growth hormone treatment for two years is safe and effective in adults with Prader-Willi syndrome [abstract]. *Hormone Research in Paediatrics*. 2011 Oct;76:85.
[PubMed: PM21664161](#)
6. Meehan J, Hoey HMCV. A Comprehensive study of Irish children with Prader Willi syndrome aged 2 to 14 years: demographics, clinical features, laboratory, auxology, polysomnography, quality of life, behaviour and the effects of growth hormone treatment [abstract]. *International Journal of Pediatric Obesity*. 2010;5:60.
7. Sipila I, Sintonen H, Hietanen H, Apajasalo M, Alanne S, Viita A-M, et al. Long-term effects of growth hormone therapy on patients with prader-willi syndrome. *Acta Paediatrica, International Journal of Paediatrics*. 2010 Nov;99(11):1712-8.
[PubMed: PM20545932](#)

8. Gondoni LA, Vismara L, Marzullo P, Vettor R, Liuzzi A, Grugni G. Growth hormone therapy improves exercise capacity in adult patients with Prader-Willi syndrome. *J Endocrinol Invest.* 2008 Sep;31(9):765-72.
[PubMed: PM18997487](#)
9. Lin HY, Lin SP, Tsai LP, Chao MC, Chen MR, Chuang CK, et al. Effects of growth hormone treatment on height, weight, and obesity in Taiwanese patients with Prader-Willi syndrome. *J Chin Med Assoc.* 2008 Jun;71(6):305-9.
[PubMed: PM18567561](#)
10. Lindgren AC, Lindberg A. Growth hormone treatment completely normalizes adult height and improves body composition in Prader-Willi syndrome: experience from KIGS (Pfizer international growth database). *Horm Res.* 2008 Sep;70(3):182-7.
[PubMed: PM18663319](#)
11. Mogul HR, Lee PDK, Whitman BY, Zipf WB, Frey M, Myers S, et al. Growth hormone treatment of adults with Prader-Willi syndrome and growth hormone deficiency improves lean body mass, fractional body fat, and serum triiodothyronine without glucose impairment: Results from the United States multicenter trial. *J Clin Endocrinol Metab.* 2008 Apr;93(4):1238-45.
[PubMed: PM18211968](#)
12. Hoybye C. Five-years growth hormone (GH) treatment in adults with Prader-Willi syndrome. *Acta Paediatrica, International Journal of Paediatrics.* 2007 Mar;96(3):410-3.
[PubMed: PM17407467](#)
13. Marzullo P, Marcassa C, Campini R, Eleuteri E, Minocci A, Sartorio A, et al. Conditional cardiovascular response to growth hormone therapy in adult patients with Prader-Willi syndrome. *J Clin Endocrinol Metab.* 2007 Apr;92(4):1364-71.
[PubMed: PM17264185](#)

Guidelines and Recommendations

No literature identified.

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APPENDIX – FURTHER INFORMATION:

Systematic Reviews - children

14. Takeda A, Cooper K, Bird A, Baxter L, Frampton GK, Gospodarevskaya E, et al. Recombinant human growth hormone for the treatment of growth disorders in children: a systematic review and economic evaluation. *Health Technol Assess*. 2010;14(42):1-237. [PubMed: PM20849734](#)

Randomized Controlled Trials – children

15. Festen DA, Visser TJ, Otten BJ, Wit JM, Duivenvoorden HJ, Hokken-Koelega AC. Thyroid hormone levels in children with Prader-Willi syndrome before and during growth hormone treatment. *Clin Endocrinol (Oxf)*. 2007 Sep;67(3):449-56. [PubMed: PM17716335](#)

Guidelines and Recommendations – children

16. Human growth hormone (Somatropin) for the treatment of growth failure in children [Internet]. London: National Institute for Health and Clinical Excellence; 2010 [cited 2012 Feb 08]. (NICE technology appraisal guidance 188). Available from: <http://www.nice.org.uk/nicemedia/live/12992/48715/48715.pdf>
(-See Section 4.1.11 on Prader-Willi Syndrome, pages 12-15)

Consensus Statements

17. Prader-Willi Syndrome Association. Growth hormone treatment and Prader-Willi syndrome (PW): clinical advisory consensus statement. Sarasota (FL): Prader-Will Syndrome Association USA; 2009. Available from: <http://www.pws.org.nz/assets/pdfs/GH-consensus-statement-w-logo.pdf>