# Long-term histrelin implant shows promise for central precocious puberty

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Long-term subcutaneous histrelin implant therapy is a viable option for patients with central precocious puberty (CPP) who require continuous gonadotropin-releasing hormone analogue (GnRHa) therapy, say researchers.

They found that the implant, which provided controlled delivery of histrelin at an average of 65 µg/day over 12 months, offered sustained suppression of the hypothalamic-pituitary-gonadal (HPG) axis and significantly improved predicted adult height.

They trialled the implant in 36 children, 33 of whom were girls, who following a phase III open-label study of the implant for 12 months were allowed to continue treatment with a new implant for up to 6 years.

Stimulated serum luteinizing hormone (LH) levels were sustained below the predetermined peak pubertal response of 4 mIU/mL in all patients throughout the 72-month evaluation.

The findings were similar for stimulated follicle-stimulating hormone (FSH), with levels sustained below the predetermined 2.5 mIU/mL for the 72 months. Oestradiol and testosterone levels were also consistently in the prepubertal range over the course of the study.

Evidence for recovery of the HPG axis after long-term gonadotropin suppression was seen in eight patients who entered an optional post-treatment phase, with serum LH and FSH concentrations increasing to pubertal levels 6 months after removal of the latest implant and oestradiol and testosterone levels within 12 months.

Auxology assessments also showed signs of normalisation of skeletal maturity relative to patient age. There was a sustained decrease in the ratio of bone age to chronological age, from approximately 1.38 at baseline to 1.12 at month 60, and a significant increase in mean predicted adult height, after excluding boys, from 151.9 cm at baseline to 166.5 cm at month 60, including a 10.7 cm height gain in children who had not received GnHRa therapy prior to the original implant.

The researchers, led by Lawrence Silverman, from Goryeb Children's Hospital in Morristown, New Jersey, USA, note that there was no adverse effect of potent HPG axis suppression on growth, as indicated by sustained decreases in growth velocity standard deviation scores, relative to baseline, to prepubertal growth velocity norms.

Extended-duration GnRHa formulations bring the advantage of continuous suppression of the HPG axis and flexibility regarding medical appointments, say the researchers, but they also note the possible disadvantages including device breakage and difficulties removing the device. Breakages on removal occurred in 22.1% of 113 explants in their study, with 15 patients experiencing at least one breakage. Otherwise, the implants were well-tolerated; mild-to-moderate pain and discomfort at the site of implantation were the treatment-emergent effects most commonly reported in around half the patients over the 72-month period.

"These results indicate that treatment with up to 6 yearly cycles of the histrelin implant may be an option to arrest the progression of CPP", the team concludes in *The Journal of Clinical Endocrinology & Metabolism*.

"Moreover, as a once-yearly treatment, the histrelin implant offers an alternative to conventional depot formulations."

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