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Replacement of male mini-puberty

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No disclosures

Background:

• Hormonal replacement in boys with congenital Hypogonadotropic Hypogonadism remains a challenge.

• Micropenis has been traditionally successfully treated with 3 monthly injections of testosterone enanthate before the age of 2, but when bilateral cryptorchidism coincides, surgery is required.

• But even after a successful surgery, the hypoplastic testes with the deficient proliferation of immature Sertoli cells, due mainly to the lack of the male mini-puberty in the neonatal period as well as the subsequent midinfancy surge in pulsatile gonadotropin secretion, are condemned in azoospermia and the boys in infertility.

Objective and hypotheses:

We investigated whether early postnatal daily injections of the commercially available recombinant LH/FSH preparation (Pergoveris®) could mimic the physiological male mini-puberty and successfully resolve bilateral cryptorchidism, repair micropenis, reinstate normal growth velocity and restore the responses of the Leydig and Sertoli cells.

Method:

Five neonates and infants, all with bilateral cryptorchidism in intra-abdominal position and micropenis ≤ 2 cm, (<-2 SDS) with absence of neonatal male mini-puberty, LH < 0.44, FSH < 0.73 IU/L and undetectable basal Testosterone measured repeatedly from age 15 days up to 3-6 months were treated for 3 months with daily s.c. injections of the recombinant LH 75 + FSH 150 IU preparation (Pergoveris®). Total dose: LH 6,750 and FSH 13,500 IU with monthly follow-up. For all cases approval for the off-label use of Pergoveris was obtained from the National Organisation for Medicines.

Parents were trained and performed the injections.

• Case 1 had CHARGE syndrome diagnosed before choanal atresia.

• Cases 2 and 4 had non syndromic Kallmann syndrome.

• Case 3 had septo-optic dysplasia and

• Case 5 had aplastic pituitary with panhypopituitarism diagnosed in the neonatal ICU before symptomatic hypoglycemia and cholestatic jaundice.

Results:

• In all cases testes descended in scrotal position by the end of the 1st in one, 2nd in two and 3rd month in two patients with a volume between 1.5 and 2.5 ml.

• Penile length increased to a median of 4.5 cm.

• During therapy all infants initiated catch-up growth.

• Median LH from undetectable reached high normal 6.5 IU/L and FSH supranormal levels 88 IU/L.

• Inhibine b and AMH from subnormal, reached high normal levels: median 248 pg/ml and 1025 pmol/L respectively.

• Testosterone increased from undetectable to a median of 2.42 ng/ml.

• In 3 cases with a follow-up of 1-5 yrs testes have slightly regressed to 0.5 -1.5 ml but are still in scrotal position.

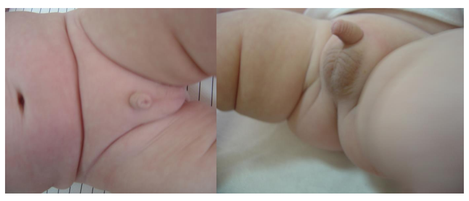
• in one case with septo-otic dysplasia, one of the testes regressed to low inguinal position

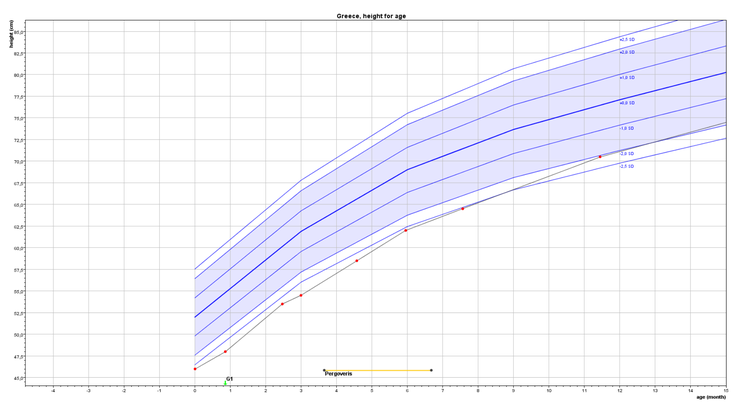
1 year after completion of treatment and was succesfullly operated.

• Case 5 just completed therapy

• None presented any adverse events or reactions

• Ultrasound examination of the testes at the end of therapy was absolutely normal.





Conclusions:

Treatment with daily s.c. injections with the commercially available preparation of LH 75 / FSH 150 IU

- **mimics neonatal male mini puberty repairing micropenis and cryptorchidism and inducing high-normal activation of Leydig and Sertoli cells.**
- **May be as well as beneficial to the brain as to the testes.**
- **Seems to stimulate initiation of catch-up growth**
- **A non-invasive strategy that mimics physiology**
- **Costs less than two surgical operations (real cost 6,100 € / patient for the public health insurance), without being able to measure the cost of an unsuccessful surgery**
- **Even if it proves partially unsuccessful in some cases, the work of the surgeon will be much easier**

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