INFERTILITY IN PWS

A better word is infertile....the word “sterile” has negative connotations. On a purely theoretical level, males with PWS should be able to correct their infertility if they receive gonadotropin replacement or if we knew of a way to restore endogenous gonadotropin secretion. The testicles are generally normal (except in cases of testicular damage due to maldescent and/or surgical damage) However, in practice, it is rather difficult to correct gonadotropin deficiency in males. This is true in other situations of male hypogonadotropic hypogonadism, not only PWS. The reasons for this are complex, but basically have to do with the need for pulsatile gonadotropin secretion, which is difficult to replicate using medications. Some andrology clinics have had limited success using gonadotropin pump therapy in cases of hypogonadotropic hypogonadism, but I am not aware of any attempts in males with PWS. We now also recognize the importance of other hormones, such as inhibin and activin, in the control of male fertility, but I am not aware of any studies specifically looking at these hormones in PWS.

The physiology of gonadotropin secretion and effect in females is different than in males. In general, the regulation of gonadotropin secretion in normal females is somewhat more “loose” than in males. It appears possible to restore at least some cyclic secretion in females with PWS using SSRIs and other agents, although this has not been rigorously studied. Females with other forms of hypogonadotropic hypogonadism can be induced to ovulate with exogenous therapy.

Phillip Lee, M.D.

ESTROGEN THERAPY IN PWS

In my opinion, the primary reason for estrogen therapy in PWS is to prevent osteoporosis. Estrogen (or testosterone in boys) and growth hormone are necessary for normal bone mineralization, particularly during the period of bone-building (e.g. before age 25-30 yr). This particular individual is 28 yo and has apparently never been on estrogens, and the GH status is not reported. Therefore, she is at very high risk for osteoporosis and fractures. As you know, osteoporosis is a very serious and common condition in adults with PWS.

At the very least, she needs to have:

(1) A bone mineral density study (DEXA scan).
(2) if this confirms osteopenia or osteoporosis, then medical therapy is required.
(3) the DEXA scan should be repeated in 6-12 months after institution of therapy and about annually for routine monitoring even if therapy is not started.

In terms of which therapy to use, the recent studies re: HRT are, in my opinion, overblown. The risks for any adverse reaction from HRT are quite low, and the actual numbers of affected individuals in the reported studies is very small., estrogen therapy is not only required for bone maintenance, but also for quality of life, the latter particularly in sexually-active women. The efficacy and risks of HRT in women with PWS have not been specifically studied, but my own professional opinion is that HRT is still a viable and useful option in estrogen-deficient women.

Another option is the use of bisphosphonates (Fosomax, etc.). These medications have a more dramatic effect on bone mineralization than estrogens, but do not have the other beneficial or reported adverse risk profiles of hormonal therapy.

For this particular individual, I would recommend evaluation by an endocrinologist experienced in the care of PWS. The DEXA scan will be a crucial element in the decision-making process.

Dr. Philip Lee

TESTOSTERONE & PWS

1. Can testosterone be used in an adult male to increase the length of the penis?

Testosterone will not significantly affect penile length in a sexually-mature male, e.g. a male who has been previously exposed to full testosterone levels either naturally or via medication for an extended period of time. However, a male with hypogonadism (abnormally low natural testosterone production) who has not received full medical replacement therapy will have a response to testosterone therapy.

2. Does it have beneficial effect on bone density?

Yes, testosterone is thought to increase bone density and bone strength. It is not known whether this is a direct or indirect effect. However, it is interesting that even though women have very low levels of testosterone compared to men, these low natural levels of testosterone appear to have similar bone effects in women.

3. Can aggressiveness be avoided by dosage?

There is no scientific evidence that physiologic (e.g. normal adult) or even supraphysiologic) levels of testosterone cause aggressive (i.e. violent) behavior in humans. Most of the reported associations of testosterone and violent behavior have been anecdotal, scientifically uncontrolled and/or statistically

biased. A well performed study published this year [1] scientifically measured a number of behaviors in both normal and hypogonadal men who received 200 mg of depot testosterone by injection every other week.

Interestingly, in this study, the hypogonadal group self-reported increased levels of verbal aggression, hostility, anger and irritability during testosterone therapy, although the scientific measures of aggressive behavior did not change. Moreover, the normal group who actually had much higher levels testosterone did not have changes in either measured or self-reported aggression. This indicates that the self-perception of increased aggressiveness during therapy might be more related to preceding hormonal status and behavior patterns than to testosterone levels per se. Here is the last paragraph from that study:

"In conclusion, we have found that supraphysiologic levels of T (testosterone) do not lead to significantly increased aggression or mood disturbances. Instead, the inability to control one's behavior when such control is required by a particular situation was found to significantly predict levels of aggression over and above age and T level."

For males with PWS, I recommend normal replacement levels of testosterone using daily patches or gels, combined with specific psychosexual and behavioral counseling as clinically indicated.

Reference:

1. O'Connor DB, Archer J, Hair WM, Wu FCW: Exogenous testosterone, aggression, and mood in eugonadal and hypogonadal men. Physiology and Behavior 75: 557-566, 2002.

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