Growth hormone kinetics in polycystic ovary syndrome

Dear Sir,

Kaltzas et al. (1998), performed an interesting study to determine the effects of gonadotropin-releasing hormone agonist (GnRHa) administration on growth hormone releasing hormone (GHRH) stimulated release in women with polycystic ovary syndrome (PCOS). In both the PCOS and control groups, the growth hormone response to GHRH was significantly smaller after treatment with GnRHa than before treatment, but more so in the PCOS group. This suppression of the growth hormone response to GHRH following GnRHa administration in women with PCOS lead them to ask the clinically relevant question of whether the addition of growth hormone to the gonadotrophin regimen may be needed during ovulation induction with GnRHa in these patients.

It is unfortunate that this was left as an open question as a glance at Homburg et al. (1995) in which we published the results of a randomized, double-blind, placebo controlled trial of adjuvant growth hormone for induction of ovulation with GnRHa and gonadotrophins in PCOS, would have provided the answer. Our study was performed for the very reasons which prompted Kaltzas et al. to ask the question, i.e. women with PCOS have a disturbance of growth hormone kinetics; those who are obese and some of normal weight have lower than normal adult circulating concentrations of growth hormone (Prelevic et al., 1992; Insler et al., 1993; Morales et al., 1996); and a reduced pituitary reserve of growth hormone (Ovesen et al., 1992), usually associated with insulin resistance, hyperinsulinaemia, and a reduction of insulin-like growth factor binding protein-1 (IGF-BP1) serum concentrations (Homburg et al., 1992). Treatment involving GnRHa further reduces pituitary reserves of growth hormone (Word et al., 1990; Kaltzas et al., 1998). Finally, follicular fluid concentrations of IFG-I are decreased in PCOS compared with normally ovulating women when stimulated with gonadotrophins (Volpe et al., 1992).

In our study (Homburg et al., 1995), 30 women with PCOS were given adjuvant growth hormone or placebo during GnRHa/gonadotrophin therapy. Other than a GH-induced increase in serum insulin and IFG-I concentrations, there were no significant differences between the growth hormone and placebo groups in gonadotrophin requirement to attain ovulation, serum oestradiol concentrations, number of growing follicles induced, nor in ovulation or pregnancy rates. We concluded that although growth hormone kinetics are abnormal and growth hormone pituitary reserves are suppressed in women with PCOS receiving GnRHa, the addition of growth hormone to this treatment regimen does not bestow any potential clinical benefit.

These findings however, do not rule out the possible involvement of growth hormone in the pathogenesis of women with PCOS, predominantly in those of normal weight with no insulin resistance and normal insulin levels and who have an increased pituitary secretion and relatively high concentrations of growth hormone (Prelevic et al., 1992). Indeed, these lean women with PCOS were found to have a mean growth hormone pulse amplitude that was elevated by 30% in comparison with lean controls (Morales et al., 1996) when growth hormone was frequently sampled over a 24h period. We have previously proposed that the high ovarian androgen concentrations in non-insulin resistant women with PCOS may be induced by growth hormone in a similar mechanism to that of insulin (Homburg et al., 1996). This theory has gained credence from a series of elegant experiments by Morales et al. (1996) who concluded that the neuroendocrine–metabolic dysregulation in PCOS, in the absence of the confounding influence of obesity, may be viewed as the pathophysiology underlying the ‘authentic’ syndrome and that obesity constitutes a modifier of the syndrome. This intriguing idea adds further spice for those attempting to unravel the pathophysiology and pathogenesis of this fascinating syndrome.

References


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Dear Sir,

We thank Dr Homburg for his interest in our study (Kaltzas et al., 1998). Certainly, the results of the study by Homburg et al. (1995) are interesting and have given an answer to the question of whether growth hormone should be added to the gonadotrophin regimen used in combination with gonadotrophin-releasing hormone (GnRH) agonist for
Letters to the Editor

ovulation induction in women with polycystic ovary syndrome (PCOS). Nevertheless, this does not mean that the problem has been solved completely and that further research is not required. There are several factors that can influence the results of a study, such as the kind of patients selected, i.e. homogeneous groups or not, the number of patients, the dose of drugs, the design of the study (cross-over) etc. In addition, there is continuous research interest in current literature on the role of growth hormone in PCOS.

Our study was not designed to examine whether growth hormone supplementation is required during gonadotrophin induction in women with PCOS, but to investigate further growth hormone secretion during treatment of PCOS patients with a GnRH agonist. The fact that during such a treatment growth hormone reserve was reduced is only a piece of the puzzle of the role of growth hormone in PCOS and as we state in our paper, the physiological importance of this finding is not clear. Certainly, we are aware of the interesting data by Homburg et al. (1995) and have referred to them in previous studies (Messinis and Milingos, 1997). That we did not include their study in our present paper was not done on purpose. There is no doubt that this oversight will not reduce the importance of their data.

References


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