Abstract. This study investigated the stimulatory potential of a superactive gonadotropin releasing hormone analogue in idiopathic oligozoospermia. In a double-blind trial, 19 men were randomized to receive buserelin (D-Ser(TBU)₆-GnRH ethylamide) in one of two dosages or saline, twice weekly, for twelve weeks. Treatment did not lead to a significant increase in serum concentrations of the pituitary gonadotropins or in sperm concentrations. However, in the dosages and schedules investigated, there was no inhibitory effect of the analogue. Further assessment of this approach is suggested.

There is no treatment that stimulates spermatogenesis in patients with idiopathic oligozoospermia. Although this condition is heterogeneous, in a proportion of patients there may be a comparative insensitivity of germ cells to follicle-stimulating hormone. Single doses of long-acting analogues of the gonadotropin releasing hormone cause supraphysiological release of the gonadotropins, while repeated administration leads to down-regulation of the pituitary-gonadal axis (Bergquist et al. 1979a,b). Initially these compounds were applied to patients with hypothalamic hypogonadism in an attempt to induce puberty. These attempts failed, possibly because of the schedule of administration of the analogue which was given on a daily basis (Tharandt et al. 1977). If the long-acting analogues were applied less frequently, on an intermittent basis, their stimulatory properties might be taken advantage of. This study investigated the role of one such analogue, in men with idiopathic oligozoospermia.

Patients and Methods

Patients attending the Joint Infertility Clinic at the London Hospital were entered into study. Male partners of an infertile marriage of greater than 3 years duration having sperm concentration less than 10 millions/ml on two occasions and negative Kibrick tests were invited to participate in the trial which was double-blind, and had been approved by the Hospital Ethical Committee.

Semen analysis was performed after 3 days abstinence from sexual intercourse. Sperm concentrations measured by Makler Chamber and computer-assisted velocity analysis (Holt et al. 1985) were assessed after 3 days abstinence from sexual intercourse. Basal serum concentrations of FSH, LH and testosterone were measured at 8.30 h. Testosterone was assayed using a single antibody radioimmunoassay (assay cross-reactivity was with dehydrotestosterone 28.5% and with androstenedione 2.1% with all other steroids tested < 0.25%; assay sensitivity 0.4 nmol/l, intra-assay precision 5–8%, inter-assay precision 6–8%). LH and FSH were measured by second antibody radioimmunoassay using MRC standards 68/40 and 78/549, respectively (significant cross-reactivity with hCG; assay sensitivity 0.8 U/l for LH and 0.3 U/l for FSH, intra-assay precision 7% and inter-assay precision 10%). Student's t-test was applied to
assess the significance of the changes in seminal analysis and in hormone changes with treatment.

After assessment, patients were randomized to receive either 1 µg of buserelin, 10 µg buserelin or 0.1 ml of normal saline twice weekly for 12 weeks by sc injection. Sperm concentration and computer-assisted sperm velocity together with basal hormone levels, were measured monthly, until 2 months after the completion of treatment. Each patient kept a record of frequency of sexual intercourse during the period of study.

Seven men received the 1 µg regimen, eight the 10 µg buserelin treatment regimen, and four normal saline.

Results

Sperm concentration and mean sperm velocity are detailed in Tables 1 and 2. Mean sperm concentrations increased in both the control group and in the patients receiving the 10 µg buserelin regimen; these changes were not statistically significant. Sperm velocity decreased in the patients receiving the 10 µg buserelin regimen, but this change was not statistically significant. Mean sperm velocity was unaltered by treatment with either the 1 µg regimen or with saline.

Basal serum hormone concentrations are described in Table 3. Before treatment, serum FSH was elevated above the normal range in one man. Neither serum gonadotropins nor testosterone concentrations were affected by treatment. No patient noted any alteration in libido, in either the control or treatment groups.

Discussion

Eight men with idiopathic gonadotropin deficiency were treated by Tharandt et al. (1977) with twice daily injections of 100 µg D-Leu₆-desGly¹⁰ GnRH ethylamide. This resulted in an initial increase in concentration of the gonadotropins which was not sustained, and no stimulation of spermatogenesis. This study may have failed to achieve its aim because of the schedule of administration of the long-acting GnRH analogue. This current randomized study investigated whether administration of a long-acting analogue of GnRH given on a less frequent basis taking advantage of its superagonist properties, could stimulate spermatogenesis in a different group of patients, oligozoospermic men. Nineteen men with

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Normal range 30 micron/s.

Table 1.
Sperm concentration (millions/ml).

Table 2.
Mean sperm velocity (microns/s).
Demonstration of gonadotropin-induced plasma renin activity in human internal spermatic vein

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Abstract. In order to investigate the secretion of renin from the Leydig cells of human testis, plasma renin activity (PRA) in left internal spermatic vein (ISV) and cubital vein (CV) was measured at the time of surgical repair of varicocele in 19 patients aged from 21 to 39 years. Ten of them were given a single i.m. administration of hCG (10 000 IU/m²) 4 days before the operation, whereas the remaining nine were not treated. Although mean PRA levels in CV in treated and non-treated groups were similar (1.25 ± 0.45 and 1.14 ± 0.38 nmol/l per h, respectively), mean PRA level of ISV in the treated group (3.52 ± 0.76 nmol/l per h) was significantly higher than that in the non-treated group (1.30 ± 0.32 nmol/l per h) (P < 0.01); serum testosterone levels in the same ISV were also much higher in the treated than in non-treated group (P < 0.001). These data show the following results; 1) under basal conditions, no release of renin from Leydig cells into testicular blood flow could be observed; 2) after treatment with hCG, the secretion of renin into the ISV seemed to be demonstrable. The present results suggest for the first time the secretion of hCG-induced renin from the human testis in vivo.

Renin, produced in the cortical cells of the kidney, is released into circulation and mediates the first step of angiotensin formation in plasma by cleaving the decapptide angiotensin I (AI) from the prohormone angiotensinogen. AI is further converted into active hormone angiotensin II (AII) by angiotensin-converting enzyme. AII is a potent vasoconstrictor and a stimulator of aldosterone secretion. Thus, it plays a key role in the blood pressure regulation.

Recent reports have shown the existence of renin in the rat testis by immunohistochemical and biochemical methods and also in the human testis by a specific immunohistological method (Parmentier et al. 1983; Naruse et al. 1985). Moreover, it was also found that treatment of cultured Leydig tumour cells with LH/hCG brings about a marked increase in renin activity and biosynthesis of angiotensins (Pandey et al. 1985).

In this study, the secretion of renin from the human Leydig cells into the testicular blood was examined by estimating PRA in left internal spermatic vein (ISV) and cubital vein (CV) in 19 subjects treated with or without hCG.

Patients and Methods

Nineteen patients with left-sided varicocele, aged from 21 to 39 years (mean ± sd, 31.9 ± 2.6 years), were