Comparison of Testosterone, Dihydrotestosterone, Luteinizing Hormone, and Follicle-Stimulating Hormone in Serum after Injection of Testosterone Enanthate or Testosterone Cypionate

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COMPARISON OF TESTOSTERONE, DIHYDROTESTOSTERONE, LUTEINIZING HORMONE, AND FOLLICLE-STIMULATING HORMONE IN SERUM AFTER INJECTION OF TESTOSTERONE ENANTHATE OR TESTOSTERONE CYPIONATE

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Long-acting testosterone esters injected intramuscularly have been used for replacement therapy in male hypogonadism for many years.[1] More recently, testosterone esters applied either as a single entity or in combination with progestational or other gonadotropin-suppressing steroids have also been investigated for control of male fertility.[2] Long-acting testosterone esters have also been applied in eliciting a rebound phenomenon in the treatment of male infertility.[3]

Testosterone enanthate and testosterone cypionate are the most widely used long-acting testosterone esters. It is generally accepted that, for replacement therapy, 200 mg of either of these esters should be injected every 2 to 3 weeks.[1] However, since no comparison of the serum testosterone levels achieved by injection of testosterone enanthate or cypionate in equivalent doses has been reported, it is undecided which of the two esters produces the longer-lasting effects and the more favorable plasma testosterone pattern. To perform this comparison, we analyzed serum testosterone, dihydrotestosterone (DHT), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) concentrations after injection of equal amounts of testosterone given either as enanthate or cypionate to normal men.

SUBJECTS AND METHODS

Subjects. Six healthy men ages 20 to 29 years served as volunteers. After extensive explanation of the purpose of the study and possible risks, each man gave written consent to participate.

Protocol. The study was designed as a crossover study, so that three subjects first received testosterone enanthate, followed 7 weeks later by testosterone cypionate (cyclopentyl propionate). The other three subjects received testosterone cypionate first, and 7 weeks later testosterone enanthate. On the day prior to injection and on the day of the injection blood samples were collected for baseline determinations. Blood samples were obtained daily up to day 6 after the injections and every 2nd day from day 6 to day 26. They were always collected between 12 noon and 1 P.M. The serum was stored at −20° C prior to analysis.

Testosterone Preparations. Commercially available testosterone preparations were used. Testosterone enanthate (194 mg) (Schering AG, Berlin/Bergkamen) and testosterone cypionate (200 mg) (Upjohn Co., Kalamazoo, Mich.) were injected so that the amount of unesterified testosterone was the same in both preparations (140 mg).

Hormone Analysis. Hormone determinations in the serum samples were performed with established radioimmunoassay methods routinely applied in our laboratory. Free unesterified testosterone and DHT were measured by radioimmunoassay after isolation by thin-layer chromatography on silica gel plates.[4] LH was determined with substances kindly provided by the National Institute of Arthritis, Metabolism and Digestive Diseases, Bethesda, Md., and FSH with commercially available reagents (Union Carbide, Düsseldorf). The standard for LH was LER-907; 1 ng of the FSH assay standard preparation was equivalent to 3.3 mIU of the First International Refer-

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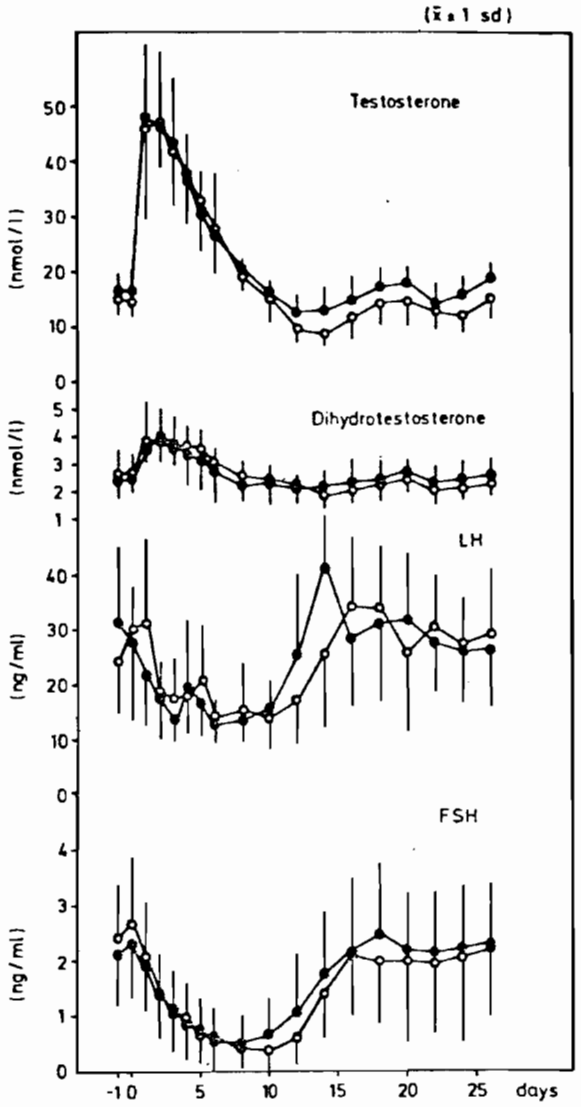

FIG. 1. Effect of 140 mg of testosterone injected either as enanthate (●) or cypionate ester (○) on serum hormone levels of six normal men. To convert testosterone values from nanomoles per liter (SI units) to nanograms per 100 ml the results must be divided by 0.0347; for DHT the factor is 0.0345.

ence Preparation of human pituitary LH and FSH for bioassay (MRC 69/104).

RESULTS

Figure 1 shows the serum hormone levels in six normal men after intramuscular injection of either testosterone enanthate or cypionate. The serum testosterone profiles were identical after both preparations. The concentrations increased sharply, reaching maximal levels 3 times above basal on days 1 and 2 after injection, and decreased gradually thereafter, so that basal levels were reached on day 10. Values continued to fall below basal concentrations on days 12 and 14 ($P < 0.05$) and then returned to basal. DHT showed a significant elevation above basal levels on days 1 to 5. LH concentrations after injection were significantly ($P < 0.05$) suppressed until day 10. LH levels then began to increase while testosterone levels were still below basal. FSH levels were already below basal on day 1 and remained significantly ($P < 0.01$) suppressed until day 14. The lowest concentrations were found between days 6 and 10.

The serum profiles of hormones measured in this study, achieved after the administration of either testosterone enanthate or cypionate, were at no point significantly different from each other.

DISCUSSION

Injection of either testosterone enanthate or testosterone cypionate in equivalent doses yielded identical serum testosterone concentrations both in terms of maximal concentrations and in terms of duration of elevation above basal levels. Maximal and supraphysiologic levels were achieved as early as the 1st day after injection, and these values had returned to basal concentrations on day 10. There were also no differences in the conversion of testosterone to DHT and in the suppression of LH and FSH observed. Thus, both esters show the same pharmacokinetic properties and appear to be equally useful for clinical purposes.

To our knowledge serum testosterone concentrations after the injection of testosterone cypionate have not been reported previously. From urinary excretion of 17-ketosteroids it was previously concluded that testosterone cypionate has a longer-lasting effect than testosterone enanthate.[5] However, the data are based on a study using widely different doses of the two esters.[5] In an earlier study we had investigated serum testosterone and LH concentrations in normal and hypogonadal men after the injection of 250 mg of testosterone enanthate ester.[6] The maximal levels achieved after the administration of 250 mg of testosterone enanthate in the previous study were identical with the levels achieved after the administration of 194 mg of this ester in the present study. After 250 mg of testosterone enanthate, however, elevated levels could be observed for 12 days. Thus, increasing the dose of injected testosterone enanthate from 194 to 250 mg appears not to influence the maximal concentration but rather the duration of the effect. The present data suggest that, when 194 or 200 mg of testosterone enanthate or cypionate are used for substitution therapy in

hypogonadism, the intervals between injections should be closer to 2 weeks than to 3 weeks.

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REFERENCES

1. Paulsen CA: The testes, In Textbook of Endocrinology, Fifth Edition, Edited by RH Williams. Philadelphia, WB Saunders Co, 1974, p 355
2. Patanelli DJ (editor): Hormonal Control of Male Fertility. Bethesda Md, Department of Health, Education and Welfare Publication No (NIH)78-1097, 1978
3. Charny CC, Gordon JA: Testosterone rebound therapy: a neglected modality? Fertil Steril 29:64, 1978
4. Wickings EJ, Nieschlag E: The effect of active immunization with testosterone on pituitary-gonadal feedback in male rhesus monkeys. Biol Reprod 18:607, 1978
5. Hamburger C: Testosterone treatment and 17-ketosteroid excretion. Acta Endocrinol (Kbh) 22:379, 1956
6. Nieschlag E, Cüppers HJ, Wiegelmann W, Wickings EJ: Bioavailability and LH-suppressing effect of different testosterone preparations in normal and hypogonadal men. Horm Res 7:138, 1976