Comparison of finasteride versus flutamide in the treatment of hirsutism

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Abstract

Objective: To compare the effectiveness of finasteride and flutamide in the treatment of hirsutism in patients with polycystic ovary syndrome (PCOS) and with idiopathic hirsutism.

Design: Randomized study.

Patients: One hundred and ten hirsute patients were selected: 64 women with PCOS and 46 with idiopathic hirsutism.

Methods: Patients were assigned randomly to receive 5 mg finasteride once daily or 250 mg of flutamide twice daily, for 12 consecutive months. Hirsutism was evaluated at 12 months of therapy, with the Ferriman–Gallwey score and with measurement of the terminal hair diameters (μm) taken from four different body areas. Blood samples were taken for assessment of endocrine and hematocchemical parameters. Side effects were monitored during the treatment.

Results: Both finasteride and flutamide induced a significant decrease in the hirsutism scores and hair diameters at the end of 12 months. Finasteride reduced the Ferriman–Gallwey score by 31.4% in the PCOS cases and by 34.2% in the idiopathic hirsutism cases, and hair diameter by 27.0–34.1% in PCOS and by 29.6–37.9% in idiopathic hirsutism. Flutamide reduced the Ferriman–Gallwey score by 56.7% in PCOS and by 50.9% in idiopathic hirsutism, and hair diameter by 50.3–60.0% in PCOS and by 47.7–56.5% in idiopathic hirsutism. Flutamide did not induce hormone variations, while finasteride increased testosterone levels by 40% in PCOS and by 60% in idiopathic hirsutism and decreased 3α-androstanediol glucuronide (3α-diolG) by 66.7% in PCOS and by 69.5% in idiopathic hirsutism. No important side effects or changes in the hematocchemical parameters were observed with finasteride, while two patients (3.6%) in the flutamide group expressed abnormal transaminase levels after 6 months of treatment. Dry skin also appeared significantly more with flutamide (67.3%) than with finasteride (23.6%).

Conclusions: Both drugs are effective in the treatment of hirsutism but flutamide is more effective than finasteride.

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Introduction

Hirsutism affects 5–8% of the whole female population of fertile age (1). Seventy to 80% of the hirsute women have hyperandrogenism, while 6–17% have normal androgen levels and regular ovulatory menstrual cycles (2, 3).

Androgen-dependent hirsutism may be caused by abnormalities in the ovaries or in the adrenal glands, by exogenous androgen administration or by a combination of these factors. Sixty-five to 85% of all women with androgen excess have polycystic ovary syndrome (PCOS) or hyperthecosis (4, 5). PCOS is a clinical condition characterized by altered gonadotropin secretion, chronic anovulation, hyperandrogenism and a variety of metabolic effects such as obesity and insulin resistance. Hirsutism is present in 60–83% of women with PCOS (6, 7).

Idiopathic hirsutism is caused by increased sensitivity of the pilosebaceous unit to normal circulating androgen levels presumably caused by increased peripheral 5α-reductase (5α-R) enzyme activity (8).

Numerous studies have documented that in all hirsute women, with or without hyperandrogenism, the 5α-R activity in the skin was steadily elevated (9). 5α-Reductase is therefore a key step in hirsutism. The activity of 5α-R and consequently the formation of dihydrotestosterone (DHT) and 5α-reductase metabolites such as 3α-androstanediol glucuronide (3α-diolG) (10), can be regulated by an increase in the circulating androgenic precursors, as well as genetic factors (11.
endocrine profile compatible with androgen-producing syndrome, evidence of enzymatic adrenal deficiency, informed consent was given. No patients had Cushing’s syndrome of Gynaecological Endocrinology of the University of Brescia, were included in the study, after written informed consent was given. No patients had Cushing’s syndrome, evidence of enzymatic adrenal deficiency, history of drug-induced hyperandrogenism or an endocrine profile compatible with androgen-producing neoplasm or prolactin (PRL) and thyroid disorder. Diagnosis of PCOS was based on clinical and endocrine findings. Oligoamenorrhea was present in 45 (70.7%) patients, while secondary amenorrhea was present in 19 (29.3%). All the 64 patients had anovulatory cycles and hirsutism. The hormonal profile showed high luteinizing hormone (LH) levels (LH: FSH ratio > 2), high levels of total and free testosterone and androstenedione and low sex hormone-binding globulin (SHBG) levels (Table 1). High dehydroepiandrosterone sulfate (DHEAS) levels (mean was 3.5 ± 0.8 μg/ml) were present in 22 patients. Forty-six patients were diagnosed as having idiopathic hirsutism because they had regular ovulatory menstrual cycles, normal serum androgen levels, normal SHBG and 17α-hydroxyprogesterone (17-OHP), both in basal conditions and after the adrenocorticotropin (ACTH) stimulation test, performed during the follicular phase of the cycle. Ovulatory cycles were determined by the midluteal phase plasma progesterone levels (> 4 ng/ml). Hirsutism was always evaluated by the same physician with the Ferriman–Gallwey score (21) and with measurement of the hair diameter. A score greater than 7 is indicative of hirsutism, but only women with a Ferriman–Gallwey score that ranged from 11 to 23 were included in this study.

Hairs were taken from four different parts of the body: face (chin), abdomen (immediately below the umbilicus), anterior midtigh and forearm. Three terminal hairs were cut from each body area at their cutaneous base. Each hair was then fixed on a slide with a transparent resin which solidifies with air, and was covered with another slide. Hair measurement was carried out with a micrometer, applied to an optical microscope (10x magnification), at a constant distance of 0.8 mm from the base. Measurement of the hair diameter from each body area, expressed in micrometers (μm), represented the mean ± S.D. of the measurement of three hairs.

All patients underwent hematoclinical examinations (hemochrom, glycemia, azotemia, creatinemia, electrophoretic protidogram, total and fractional bilirubinemia, transaminases and alkaline phosphatase), SHBG and hormonal assays, including LH, follicle-stimulating hormone (FSH), 17-OHP, androstenedione (A), total (T) and free (FT) testosterone, DHEAS, 3α-diolG and fasting insulin (I). Hormonal assays were assessed in the early follicular phase (5th to 7th day) of a spontaneous menstrual cycle or progestin-induced menstrual bleeding (medroxyprogesterone acetato at a dose of 10 mg/day for 5 days).

During therapy all hirsute women had an interview every 3 months, in order to establish the cause of the menstrual cycles and side effects. Hematoclinical examinations were repeated every 3 months in women treated with flutamide and every 6 months in women with finasteride. Hormone samples were carried out at the start and at the end of the treatment (12th month).

Patients were advised to avoid pregnancy during treatment because of possible male fetus feminization. Sexually active women were advised to use contraception barrier methods (condom) during the study.

Patients of both groups were randomly assigned in a 1:1 ratio to receive either 5 mg/day of finasteride (Prostide, Sigma Tau, Milan, Italy) or 250 mg of flutamide (5a-R1 and 5a-R2), showed that 5a-R2 enzymatic activity is predominant in the urogenital sinus and in genital skin, whereas 5a-R1 is predominant in the central nervous system (only type 1), in pubic skin, in the adult scalp and in the nonsex skin of the normal male, normal women and hirsute patients (14–17). However, the distribution and role of 5a-R1 is less clear.

Finasteride, a member of the 4-azasteroid family of compounds, is more effective against isoenzyme 5a-R type 2 than type 1, but the specificity for the two isoenzymes is incomplete (18). Finasteride blocks the conversion of testosterone to the more potent DHT. Concentrations of DHT fall by 60–80% in men treated with a dose of 5–400 mg (15). The fall in serum DHT is accompanied by a reduction in metabolites of DHT such as 3α-diolG and by a rise in plasma testosterone concentrations. No side effects were reported in the women using finasteride.

Flutamide, a non-steroidal drug, is a pure peripheral androgen antagonist. It is metabolized to 2-hydroxyflutamide, an active metabolite which acts as a competitive inhibitor of the cytoplasmic and nuclear binding of androgens to the receptor (19). The drug does not have a progestogenic or anti-gonadotropic action and thus does not cause menstrual irregularity. The use of flutamide can be associated with liver toxicity with abnormal transaminase levels and cholestatic jaundice (20).

The aim of the present report is to compare the therapeutic efficacy of finasteride and flutamide on hirsutism in women with PCOS and idiopathic hirsutism.

Materials and methods

One hundred and ten hirsute women, between 18 and 29 years of age, of which 64 with PCOS and 46 with idiopathic hirsutism that were referred to the Department of Gynaecological Endocrinology of the University of Brescia, were included in the study, after written informed consent was given. No patients had Cushing’s syndrome, evidence of enzymatic adrenal deficiency, history of drug-induced hyperandrogenism or an endocrine profile compatible with androgen-producing neoplasm or prolactin (PRL) and thyroid disorder.

Diagnosis of PCOS was based on clinical and endocrine findings. Oligoamenorrhea was present in 45 (70.7%) patients, while secondary amenorrhea was present in 19 (29.3%). All the 64 patients had anovulatory cycles and hirsutism. The hormonal profile showed high luteinizing hormone (LH) levels (LH: FSH ratio > 2), high levels of total and free testosterone and androstenedione and low sex hormone-binding globulin (SHBG) levels (Table 1). High dehydroepiandrosterone sulfate (DHEAS) levels (mean was 3.5 ± 0.8 μg/ml) were present in 22 patients.

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Finasteride vs flutamide in treatment of hirsutism

Hormonal assays

Plasma LH, FSH and SHBG levels were determined by immunoradiometric assay method (Radim, Pomezia, Rome, Italy), while the remaining hormones were tested using radioimmunoassay commercial kits from Diagnostic Products Corporation, Los Angeles, CA, USA (17-OHP, A, T, FT); Immunotech, Marseille, France (DHEAS); Medgenix, Brussels, Belgium (I); Diagnostic Systems Laboratories, Webster, TX, USA (3α-diolG).

All samples from each subject were analyzed in duplicate in the same assay.

Conversion factors to SI units are as follows: LH and FSH 1.00: 17-OHP 3.03; A 3.492; T and FT 3.467; DHEAS 2.56; 3α-diolG 2.136; I 7.178; and SHBG 3.44.

Statistical analysis

All values were expressed as mean ± s.d. Student’s paired t-tests were employed to compare mean hormone levels before and after treatment. The percentage of change in hirsutism scores between treatments was tested using a one-way analysis of variance. The statistical analysis of the hair diameters was carried out using the Wilcoxon signed rank test.

Results

The mean age in patients with PCOS and idiopathic hirsutism was respectively 22.9 ± 4.9 and 22.3 ± 5.8 years, and the mean body mass index (BMI) was 23.7 ± 4.1 and 22.4 ± 3.2 kg/m².

Table 1 shows the basal endocrine profile of patients with PCOS, idiopathic hirsutism and that of the control group. In the 64 women with PCOS serum LH levels, 17-OHP, A, T, FT, DHEAS and I were significantly higher than in women with idiopathic hirsutism and in controls, while SHBG levels were significantly lower than in women with idiopathic hirsutism and in controls. The Ferriman–Gallwey score in women with PCOS and idiopathic hirsutism did not present any significant difference compared with the control group, except for plasma levels of 3α-diolG.

Table 2 shows the Ferriman–Gallwey scores and the measurements of hair diameters in women with PCOS, idiopathic hirsutism and in controls. The Ferriman–Gallwey score in women with PCOS and idiopathic hirsutism was respectively 16.2 ± 3.3 and 16.7 ± 3.5. In patients with PCOS and idiopathic hirsutism the hair diameters in each area of the body were significantly higher than those of the controls. Furthermore, women with PCOS had hair diameters significantly higher than idiopathic hirsutism women.

Table 3 shows the hormone profiles in women with PCOS and idiopathic hirsutism in basal conditions and after 12 months of treatment with finasteride and flutamide. In the groups of women treated with flutamide no significant changes in the plasma hormone levels were observed. On the contrary, the treatment...
with finasteride increased T from 1.0 ± 0.2 ng/ml at baseline to 1.4 ± 0.2 ng/ml in PCOS (P < 0.001) and from 0.5 ± 0.1 to 0.8 ± 0.2 ng/ml in idiopathic hirsutism (P < 0.001) and significantly reduced 3α-diolG from 6.0 ± 1.7 ng/ml at baseline to 2.0 ± 0.4 ng/ml and from 5.9 ± 1.2 to 1.8 ± 0.4 ng/ml in PCOS and idiopathic hirsutism respectively.

Table 2 Ferriman–Galloway scores and basal hair diameters (μm) in patients with PCOS, idiopathic hirsutism and in controls. Values are mean ± s.d.

<table>
<thead>
<tr>
<th></th>
<th>PCOS (n = 64)</th>
<th>Idiopathic hirsutism (n = 64)</th>
<th>Controls (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ferriman–Galloway score</strong></td>
<td>16.2 ± 3.3</td>
<td>16.7 ± 3.5</td>
<td>–</td>
</tr>
<tr>
<td><strong>Basal hair diameter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>54.1 ± 5.8†</td>
<td>51.2 ± 5.0*</td>
<td>27.6 ± 1.6</td>
</tr>
<tr>
<td>Abdomen</td>
<td>78.1 ± 7.0‡</td>
<td>74.0 ± 5.6*</td>
<td>35.2 ± 5.1</td>
</tr>
<tr>
<td>Thigh</td>
<td>76.7 ± 5.4‡</td>
<td>73.1 ± 4.9*</td>
<td>33.0 ± 5.3</td>
</tr>
<tr>
<td>Forearm</td>
<td>52.9 ± 4.3‡</td>
<td>49.0 ± 4.7*</td>
<td>26.6 ± 3.5</td>
</tr>
</tbody>
</table>

* P < 0.001, PCOS and idiopathic hirsutism vs controls; † P < 0.01, PCOS vs idiopathic hirsutism; ‡ P < 0.001, PCOS vs idiopathic hirsutism (analysis of variance).

Figure 1 shows the modifications of the Ferriman–Galloway scores after treatment for 12 months with finasteride and flutamide. Finasteride significantly reduced the Ferriman–Galloway scores from 15.9 ± 3.1 at baseline to 10.9 ± 2.6 in PCOS and from 16.1 ± 3.8 to 10.6 ± 3.1 in idiopathic hirsutism; flutamide reduced it from 16.4 ± 3.4 to 7.1 ± 2.5 and from 17.3 ± 3.1 to 8.5 ± 3.3 in PCOS and idiopathic hirsutism respectively (P < 0.001).

Statistical analysis indicated greater effectiveness of flutamide than finasteride in both groups.

Also, the measurements of hair diameters (Table 4) decrease significantly in all patients with both drugs. In PCOS finasteride decreased hair diameters by 27.0–34.1%, flutamide by 50.3–60.0%. In the idiopathic hirsutism group, finasteride decreased it by 29.6–37.9% and flutamide by 47.7–56.5%. Hairs in the abdomen were the most sensitive to both drugs, decreasing with finasteride by 34.1% in PCOS and by 37.9% in idiopathic hirsutism, and with flutamide by 60.0% and by 56.5%. Hairs in the forearm were the least sensitive to antiandrogens; finasteride reduced them by 27.0% in PCOS and by 29.6% in idiopathic hirsutism, flutamide by 50.3% and by 47.7% in PCOS and idiopathic hirsutism respectively. After the hairs in the abdomen, the most sensitive to both drugs were those in the face and in the thighs.

The antiandrogens did not change the menstrual cycles or their alterations in women with PCOS.

Table 3 Plasma hormone levels in PCOS and idiopathic hirsutism before and after 12 months of finasteride and flutamide treatment. Values are mean ± s.d.

<table>
<thead>
<tr>
<th></th>
<th>PCOS (n = 32)</th>
<th>Idiopathic hirsutism (n = 23)</th>
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<tbody>
<tr>
<td><strong>LH (mIU/ml)</strong></td>
<td></td>
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<tr>
<td>Baseline</td>
<td>14.1 ± 3.2</td>
<td>14.6 ± 3.2</td>
</tr>
<tr>
<td>12 months</td>
<td>14.5 ± 2.9</td>
<td>14.4 ± 3.0</td>
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<tr>
<td><strong>FSH (mIU/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>5.3 ± 1.2</td>
<td>5.4 ± 1.3</td>
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<tr>
<td>12 months</td>
<td>5.1 ± 1.3</td>
<td>5.1 ± 1.2</td>
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<tr>
<td><strong>17-OHP (ng/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>1.2 ± 0.4</td>
<td>1.1 ± 0.4</td>
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<tr>
<td>12 months</td>
<td>1.3 ± 0.4</td>
<td>1.1 ± 0.4</td>
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<tr>
<td><strong>A (ng/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>3.5 ± 0.6</td>
<td>3.6 ± 0.6</td>
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<tr>
<td>12 months</td>
<td>3.7 ± 0.3</td>
<td>3.4 ± 0.5</td>
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<tr>
<td><strong>T (ng/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>1.0 ± 0.2</td>
<td>0.9 ± 0.3</td>
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<tr>
<td>12 months</td>
<td>1.4 ± 0.2</td>
<td>0.9 ± 0.2</td>
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<td><strong>FT (pg/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>3.2 ± 0.6</td>
<td>3.5 ± 0.4</td>
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<tr>
<td>12 months</td>
<td>3.5 ± 0.5</td>
<td>3.6 ± 0.5</td>
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<tr>
<td><strong>DHEAS (μg/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>2.9 ± 0.9</td>
<td>2.7 ± 0.8</td>
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<tr>
<td>12 months</td>
<td>2.8 ± 1.0</td>
<td>2.5 ± 0.6</td>
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<tr>
<td><strong>3α-diolG (ng/ml)</strong></td>
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<tr>
<td>Baseline</td>
<td>6.0 ± 1.7</td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td>12 months</td>
<td>2.0 ± 0.4</td>
<td>5.9 ± 1.5</td>
</tr>
<tr>
<td><strong>I (μU/ml)</strong></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>10.3 ± 1.8</td>
<td>10.7 ± 2.1</td>
</tr>
<tr>
<td>12 months</td>
<td>10.1 ± 1.5</td>
<td>10.8 ± 2.0</td>
</tr>
<tr>
<td><strong>SHBG (nmol/l)</strong></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>22.9 ± 6.2</td>
<td>21.8 ± 6.0</td>
</tr>
<tr>
<td>12 months</td>
<td>20.7 ± 5.6</td>
<td>21.0 ± 4.6</td>
</tr>
</tbody>
</table>

* Twelve month values in the flutamide groups refer to 31 patients in PCOS and 21 in idiopathic hirsutism groups.
† P < 0.001 values at 12 months versus baseline (Student’s paired t-test).
Three women in treatment with flutamide dropped out of the study: one from the PCOS and one from the idiopathic hirsutism group after 6 months due to high transaminase levels and one from the idiopathic hirsutism group at 7 months due to nausea and vomiting. Side effects from flutamide were dry skin in 37 patients (67.3%), reduction in libido in nine (16.3%), headache in one (1.8%), gastrointestinal disorders in seven (12.7%) and high transaminase levels in two (3.6%). Dry skin appeared after 2 months from the beginning of the therapy.

**Discussion**

Our randomized study has shown that: (1) both antiandrogens are effective \( P < 0.001 \) in the treatment of hirsutism; (2) flutamide is significantly more effective than finasteride; (3) flutamide does not modify the hormone profile; (4) both antiandrogens do not modify the menstrual cycles in women with idiopathic hirsutism or its irregularity in women with PCOS; (5) flutamide has a high risk/benefit ratio and its chronic administration requires repeated checks on liver function.

Flutamide reduced the Ferriman–Gallwey score and the hair diameter in women with PCOS respectively by 56.7% and by 50.3–60.0% and in women with idiopathic hirsutism by 50.9% and by 47.7–56.5%, whereas finasteride reduced the score and hair diameter by 31.4% and by 27.0–34.1% in PCOS and by 34.2% and by 29.6–37.9% in idiopathic hirsutism. The most sensitive hairs to both drugs were, in decreasing order, those in the abdomen, face, thigh and forearm. This confirms the different androgen sensitivity of hairs in various parts of the body. Our study also showed that at the end of the treatment with flutamide, the Ferriman–Gallwey score decreased to 7.1 ± 2.5 and 8.5 ± 3.3 (very

**Table 4** Hair diameters (μm) and changes (%) in PCOS and idiopathic hirsutism before and after 12 months of finasteride and flutamide treatment. Values are mean ± s.d.

<table>
<thead>
<tr>
<th></th>
<th>PCOS</th>
<th>Idiopathic hirsutism</th>
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<tbody>
<tr>
<td></td>
<td>Finasteride</td>
<td>Flutamide</td>
</tr>
<tr>
<td>Face</td>
<td>54.0 ± 6.0</td>
<td>36.6 ± 5.1†</td>
</tr>
<tr>
<td>Change (%)</td>
<td>32.2</td>
<td>34.1</td>
</tr>
<tr>
<td>Abdomen</td>
<td>77.6 ± 7.1</td>
<td>51.1 ± 5.7†</td>
</tr>
<tr>
<td>Change (%)</td>
<td>34.1</td>
<td>34.1</td>
</tr>
<tr>
<td>Thigh</td>
<td>77.1 ± 5.5</td>
<td>53.2 ± 4.8†</td>
</tr>
<tr>
<td>Change (%)</td>
<td>31.0</td>
<td>31.0</td>
</tr>
<tr>
<td>Forearm</td>
<td>53.0 ± 4.2</td>
<td>38.7 ± 3.5†</td>
</tr>
<tr>
<td>Change (%)</td>
<td>27.0</td>
<td>27.0</td>
</tr>
</tbody>
</table>

* Twelve month values in the flutamide groups refer to 31 patients in PCOS and 21 in idiopathic hirsutism groups.
† \( P < 0.001 \) values at 12 months versus baseline; †† \( P < 0.001 \) flutamide versus finasteride; § \( P < 0.01 \) flutamide versus finasteride (Wilcoxon signed rank test).
mild hirsutism), while the hair diameters are completely normalized (see control group). This discrepancy is to be attributed to the Ferriman–Gallwey score, subjective and semi-quantitative estimation of hirsutism in 12 body areas. In addition, there is variability in the threshold score for hirsutism; in fact, some authors identify as hirsute, women with a Ferriman–Gallwey score > 8.

In the literature, the findings on finasteride and flutamide in hirsutism, nearly all calculated only on the Ferriman–Gallwey score, are controversial. Investigators who used both drugs with the same dosage as ourselves for 6–12 months report that finasteride decreases the Ferriman–Gallwey score from 11% (25) to 63.8% (26) in PCOS and from 10.6% (27) to 63% (28) in idiopathic hirsutism. Findings with flutamide range from 36.4% (29) to 53% (30) in PCOS and from 30.1% (31) to 70.9% (24) in idiopathic hirsutism.

The hormone findings showed that finasteride, a 5α-R2 selective inhibitor, significantly increases the plasma levels of T (by 40% in PCOS and by 60% in idiopathic hirsutism), and reduces a3-diolG (by 66.7% in PCOS and by 69.5% in idiopathic hirsutism), while flutamide did not vary the basal hormone profile. In agreement with our findings, many authors report that flutamide does not significantly modify hormone parameters (29, 32), while other studies show a significant decrease in T and DHEAS, favoring the hypothesis that flutamide may reduce androgen synthesis (inhibiting the 17,20 desmolase adrenal activity) or increase androgen catabolism (24, 33, 34).

All the studies did not show modifications of the menstrual cycles after finasteride or flutamide therapy. Recently De Leo (35) reported that flutamide (500 mg/day for 6 months) in eight hirsute girls with PCOS, ranging in age from 16 to 19 years, was able to reduce the Ferriman–Gallwey score by 63.4% and to completely normalize the menstrual cycles within 3 months. Longitudinal studies documented that hyperandrogenism with high LH levels in adolescence (PCOS-like) is a frequent condition and often spontaneously reversible, indicating a different maturational pathway of the reproductive system (36, 37).

During treatment with flutamide, three patients dropped out of the study: two due to high transaminase levels (3.6%) and one due to nausea and vomiting (1.8%). Flutamide liver toxicity is dose-dependent, so in chronic therapy it is advisable to use the minimum effective doses. Venturoli (23), in fact, using flutamide with a 250 mg daily dose for 12 months obtained a Ferriman–Gallwey score reduction of 55% without transaminase variations, and the absence of side effects.

During treatment with both drugs, we noticed that flutamide induced dry skin in 67.3% of cases while finasteride only in 23.6%. Flutamide, because of its action mechanism, seems to be active in the inhibition of sebum production. Imperato-McGinley (38) has in fact shown how sebum production was depressed in subjects with complete insensitivity to androgen but not in those with congenital deficiency of 5α-R.

The best effectiveness of flutamide on hirsutism must be ascribed to the complete block of androgen actions on target tissues by competitive inhibition of all nuclear binding to the receptors (T and DHT).

The lesser results of finasteride could be due to various factors: (1) the limited action of this drug on 5α-R1, perhaps involved in hirsutism; (2) the increase in T could have per se a direct effect on target tissues; and (3) the inability to decrease DHT production under a threshold value that is ineffective on the pilosebaceous apparatus. In our study the a3-diolG, DHT peripheral metabolite, showed a partial reduction with finasteride.

In conclusion, although both antiandrogens are effective in hirsutism, flutamide actually proves to be a very satisfactory therapeutic regimen in the treatment of hirsutism associated with normal or elevated androgen levels. The high risk/benefit ratio could be reduced by the use of lower doses of this drug (250–375 mg/day).

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