Systematic review of finasteride effect in women with hirsutism

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INTRODUCTION

Hirsutism is the most frequent complaint of women during their reproductive lifetime. It negatively impacts their perception of femininity, wellness, and quality of life. Therefore, antiandrogen therapy is important to mitigate the consequences of such a condition1-3.

Chronic use of antiandrogens, for example, cyproterone, spironolactone, and flutamide, may cause, however, several side effects like hepatotoxicity, depression, anxiety, gastrointestinal dysfunction, and menstrual disorders. These affections may require the discontinuance of long-term treatments4. There are, nevertheless, some authors who have suggested that one of the antiandrogen drugs, i.e., finasteride, exerts a milder effect, making it a promising medication for long-term use2.

Finasteride inhibits 5α-reductase type 2, the action of which competitively inhibits testosterone conversion into dihydrotestosterone (DHT), a potent stimulator of loss of hair from scalp skin follicles but of growth of body hair. Thus, the action of the drug may reduce hirsutism5. Nevertheless, it is necessary to compare the literature data to assess the true effectiveness and safety of finasteride use in the treatment of women with idiopathic hirsutism and polycystic ovary syndrome (PCOS).

METHODS

A systematic review of computer-collected research data was carried out using the Medline and PubMed databases. The keywords used in the search were hirsutism and finasteride.

The review included only randomized clinical trials in which finasteride was used in the treatment of women with hirsutism, idiopathic hirsutism, or related to PCOS scored with the modified Ferriman–Gallwey (F–G) scale6-7. In addition, finasteride action had to be set against that of other antiandrogen medications and/or placebo treatment.

All studies were excluded which were not randomized clinical trials (e.g., nonrandomized clinical trials, case series, case controls, literature review, etc.), which involved women whose hirsutism was brought on by other causes (e.g., steroid-producing tumors, hyperprolactinemia, enzyme deficiency of the adrenal glands, Cushing’s syndrome, and thyroid dysfunction), which compared finasteride with treatments other than oral antiandrogen medications (e.g., cosmetic treatments and GnRH analogs), and which were not in Portuguese, English, or Spanish. This initial screening was followed by reassessment of the remaining studies leading to the exclusion of those with an F–G score lower than 8 and those with unstated causes of hirsutism. Adverse effects resulting from finasteride use were deemed secondary outcomes.

Research was limited to women and covered the years from 1990–2015.

The studies that were selected fell into three categories:
1. comparison of finasteride and placebo and of different finasteride regimens,
2. comparison of finasteride and other medications [i.e., spironolactone, flutamide, and cyproterone acetate (CPA) with ethyln estradiol (EE)], and
3. comparison of finasteride associations and finasteride was associated with in isolation (i.e., spironolactone and CPA with EE).

A total of 75 papers were retrieved from the Medline and PubMed databases. No studies were found before 1990 using the aforementioned descriptors. Figure 1 shows the study flowchart.

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The initial screening left out 55 studies for two main reasons: they were observational studies or literature reviews. A second screening excluded three articles: one for not meeting the hirsutism criteria adopted in this review and the other two for not stating the causes of hirsutism. Our analysis followed the PRISMA Statement for systematic reviews.

**RESULTS**

The results were classified into three categories:

1. comparison of finasteride and placebo and different finasteride regimens (n=4),
2. comparison of finasteride and other medications (i.e., spironolactone, flutamide, and CPA with EE; n=9), and
3. comparison of finasteride associations and finasteride was associated with in isolation (i.e., spironolactone and CPA with EE; n=4).

The two studies in which finasteride was compared with placebo showed that hirsutism improved with finasteride especially after six months of treatment. No improvement was observed in the placebo groups, and no changes in libido were observed in either group. Ciotta et al. reported side effects in both the study group and the placebo group. In the study by Lakryc et al., there were no reports of severe side effects, but four patients dropped out owing to diarrhea and nausea (n=3) and allergic symptoms (n=1). After the third month of treatment, 17% of the total patients from both groups complained about dizziness, and most of them were from the finasteride group.

The comparison of different finasteride dosages is included in Table 1. Bayram et al. found no differences in the final F–G score up to six months of treatment. Thereafter, the larger dose of 5 mg/day produced better results than the smaller dose of 2.5 mg/day. The quantity and intensity of side effects were greater with the dose of 5 mg; the main sequelae were dry skin, reduction in libido, headache, and gastrointestinal dysfunction. It appears that, in a 10-month period, intermittent use of 2.5 mg of finasteride has the same effect as continuous administration of the same dose of the drug on the F–G score but with smaller adverse effects.

**Figure 1.** Flowchart of study selection.
Table 1. Effects of finasteride on hirsutism: comparing finasteride with other drugs.

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of clinical trial</th>
<th>Duration (months)</th>
<th>Treatment</th>
<th>Age (years)</th>
<th>Results</th>
<th>Adverse effects*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong et al.12</td>
<td>Randomized and without placebo</td>
<td>6</td>
<td>Finasteride(^a) (n=9) versus spironolactone(^b) (n=5)</td>
<td>15–40</td>
<td>Finasteride spironolactone</td>
<td>No side effects</td>
</tr>
<tr>
<td>Ciotta et al.21</td>
<td>Randomized single-blind</td>
<td>9</td>
<td>Finasteride(^a) (n=9) versus placebo (n=9)</td>
<td>20.6±0.43</td>
<td>Finasteride&gt;placebo</td>
<td>Headache (n=4) and depression (n=2)</td>
</tr>
<tr>
<td>Lakryc et al.9,α</td>
<td>Randomized double-blind; placebo-controlled</td>
<td>6</td>
<td>Finasteride(^b) (n=12) versus placebo (n=12)</td>
<td>19–40</td>
<td>Finasteride&gt;placebo</td>
<td>No severe adverse effects</td>
</tr>
<tr>
<td>Bayram et al.10</td>
<td>Randomized and without placebo</td>
<td>12</td>
<td>Finasteride 2.5 mg/day (n=29) versus finasteride 5 mg/day (n=27)</td>
<td>18–41</td>
<td>5 mg/day&gt;2.5 mg/day</td>
<td>Continuous intermittent</td>
</tr>
<tr>
<td>Tartagni et al.23</td>
<td>Randomized and without placebo</td>
<td>10</td>
<td>Finasteride 2.5 mg/day (n=19) versus 2.5 mg every three days (n=19)</td>
<td>18–34</td>
<td>Continuous intermittent</td>
<td></td>
</tr>
<tr>
<td>Erenus et. al.14</td>
<td>Randomized and single blind</td>
<td>9</td>
<td>Finasteride(^a) (n=7) versus spironolactone(^b) (n=9)(^x)</td>
<td>21.3±4.6</td>
<td>Finasteride&lt;spironolactone</td>
<td>No side effects</td>
</tr>
<tr>
<td>Falsetti et al.18</td>
<td>Randomized and without placebo</td>
<td>6</td>
<td>Finasteride(^a) (n=22) versus flutamide(^c) (n=22)</td>
<td>22.9±4.9</td>
<td>Finasteride flutamide</td>
<td>Dry skin (n=6), reduction in libido (n=3), and headache (n=2)</td>
</tr>
<tr>
<td>Sahin et al.24</td>
<td>Randomized and without placebo</td>
<td>9</td>
<td>Finasteride(^a) (n=21) versus CPA+EE(^a) (n=21)</td>
<td>21.8±0.97</td>
<td>Finasteride&lt;CPA+EE</td>
<td>No effects</td>
</tr>
<tr>
<td>Falsetti et al.20</td>
<td>Randomized and without placebo</td>
<td>12</td>
<td>Finasteride(^a) (n=55) versus flutamide(^a) (n=52)(^y)</td>
<td>18–29</td>
<td>Finasteride&lt;flutamide</td>
<td>Dry skin (n=13), headache (n=7), and reduction in libido (n=6)</td>
</tr>
</tbody>
</table>

Continue...
Finasteride effect in women with hirsutism

Three studies compared finasteride with spironolactone (Table 1). In all these studies, hirsutism decreased with both drugs from baseline measurements. Wong et al.12 and Moghetti et al.13 reported that finasteride was not superior to spironolactone. However, Erenus et al.14 observed that the change in the percentage of hirsutism score with spironolactone was significantly higher than that with the finasteride treatment (at six months because of poor efficacy of treatment in the Finasteride group, n=3 in the spironolactone group) or inadequate response according to the patient’s opinion and the Ferriman–Gallwey score (n=3 in the spironolactone group). Two patients dropped out in the Flutamide group, one due to nausea and vomiting, and one because of high transaminase levels. Three patients dropped out in the Flutamide group, two because of high transaminase levels after six months, and one at seven months due to nausea and vomiting. Two women (8.7%) in the Flutamide group dropped out of the study at seven months: one (4.3%) because of nausea and vomiting and another (4.3%) because of high transaminase levels. CPA: cyproterone acetate; EE: ethynyl estradiol. Dosages: 5 mg/day of Finasteride; 100 mg/day of spironolactone. 150 mg/day of Flutamide two times. 2 mg/day of CPA plus 35 μg/day of EE on days 5–25. 250 mg/day of Flutamide two times. 25 mg/day of CPA on days 1–10 of the menstrual cycle plus 20 μg of EE every day for 21 days. 25 mg/day of CPA on days 5–14 plus 20 μg/day of EE on days 5–25.

Table 1. Continuation.

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of clinical trial</th>
<th>Duration (months)</th>
<th>Treatment</th>
<th>Age (years)</th>
<th>Results</th>
<th>Adverse effects*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falsetti et al.15</td>
<td>Randomized and without placebo</td>
<td>12</td>
<td>Finasteride (n=23) versus Flutamide (n=21)</td>
<td>18–29</td>
<td>Finasteride &lt; Flutamide</td>
<td>Dry skin (n=5), headache (n=3), and reduction in libido (n=2)</td>
</tr>
<tr>
<td>Fruzetti et al.15</td>
<td>Randomized and without placebo</td>
<td>12</td>
<td>Finasteride (n=14) versus CPA+EE (n=13) versus Flutamide (n=15)</td>
<td>16–29</td>
<td>Finasteride CPA+EE Flutamide</td>
<td>No side effects</td>
</tr>
<tr>
<td>Moghetti et al.13</td>
<td>Randomized, double-blind, and placebo-controlled</td>
<td>6</td>
<td>Finasteride (n=10) versus Spironolactone (n=10) versus Flutamide (n=10) versus Placebo (n=10)</td>
<td>20.4±0.5</td>
<td>Finasteride Spironolactone &gt; Flutamide &gt; Placebo</td>
<td>Finasteride: transient sensation of bloating (n=1)</td>
</tr>
<tr>
<td>Beigi et al.16</td>
<td>Randomized and without placebo</td>
<td>9</td>
<td>Finasteride (n=20) versus CPA+EE (n=20)</td>
<td>16–29</td>
<td>Finasteride CPA+EE</td>
<td>No side effects</td>
</tr>
</tbody>
</table>

*Adverse effects of Finasteride. **Loss of four cases due to allergy (n=1) plus nausea and diarrhea (n=3). Finasteride dosages: 7.5 mg/day; 15 mg/day. *Adverse effects of Finasteride. †Thirteen patients in the Finasteride group and six in the Spironolactone group dropped out of the study at six months because of poor efficacy of treatment (n=13 in the Finasteride group, n=3 in the Spironolactone group) or inadequate response according to the patient’s opinion and the Ferriman–Gallwey score (n=3 in the Spironolactone group). ‡Two patients dropped out in the Flutamide group, one due to nausea and vomiting, and one because of high transaminase levels. §Three patients dropped out in the Flutamide group, two because of high transaminase levels after six months, and one at seven months due to nausea and vomiting. ¶Two women (8.7%) in the Flutamide group dropped out of the study at seven months: one (4.3%) because of nausea and vomiting and another (4.3%) because of high transaminase levels. CPA: Cyproterone acetate; EE: Ethynyl estradiol. Dosages: 5 mg/day of Finasteride. *100 mg/day of Spironolactone. 150 mg/day of Flutamide two times. 2 mg/day of CPA plus 35 μg/day of EE on days 5–25. 250 mg/day of Flutamide two times. 25 mg/day of CPA on days 1–10 of the menstrual cycle plus 20 μg of EE every day for 21 days. 25 mg/day of CPA on days 5–14 plus 20 μg/day of EE on days 5–25.

Table 2 shows a summary of the studies in which Finasteride associated with Spironolactone or with CPA and EE is
compared with these drugs in isolation. In general, the finasteride association achieved a better score on the F–G scale 21,22 . Tartagni et al. 23 showed that the combination of the three drugs (i.e., finasteride + CPA + EE) produced an earlier and more effective result. However, Sahin et al. 24 found that the superior efficacy of the triple association did not manifest so early, not before 12 months. In the study by Tartagni et al., the side effects of the finasteride association (20%) were greater than those of the association without it (10%), and the main complaint was a reduction in libido 23 . The other study did not report any significant effects 24.

Table 2 also shows two more studies of finasteride administered together with spironolactone set against spironolactone alone. Keleştimur et al. 21 compared the F–G scores at baseline and at 12 months, whereas Unlühızarcı et al. 22 contrasted the basal scores to those at six months. In both studies, the association was found to achieve a significantly larger reduction than spironolactone alone. The main side effect was abnormal uterine bleeding, which occurred more frequently with spironolactone used in isolation (50–60.7%) than in association with finasteride (20–47.3%) 21,22.

### DISCUSSION

Hirsutism impacts significantly the quality of life of a woman lowering the perception she has of her femininity. It is a long-term treatment and the drugs required for it have important side effects that may interfere with her sexuality because they reduce her libido 1-3. One such drug is finasteride; it is effective and safe, its side effects are not as marked as those of two other drugs, namely, spironolactone and flutamide, and its interference in sexuality is less 12–14,18–20.

In the studies contrasting finasteride to placebo only, many of the adverse effects (i.e., anxiety, depression, and migraine) that were reported might have been due to the psychic influence of the placebo 8,9 or due to the lack of results with respect to cutaneous hyperandrogenism, which decreases women’s femininity and self-esteem 25.

In one study, finasteride was inferior to spironolactone, but the study was short-term (9 months) and had few participants 14. In some cases, long-term treatments (over two years) are necessary to produce important cosmetic results in women with hirsutism. Nevertheless, the side effects of finasteride were less frequent than those of spironolactone. This drug may act directly on ovarian function, determining menstrual irregularities, which some women find unbearable. Hence, finasteride would have the advantage of not unduly influencing women’s menstrual cycle 6,12,14,18-20.

Although the administration of intermittent or smaller doses of finasteride results in fewer side effects, it cannot be concluded that such doses are just as effective as the customary dosage, given the scarce number of participants and the duration of the study, which is not long-term (over two years) 10,11. Thus, these facts hinder the assessment of the best dosage.

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**Table 2. Effects of finasteride associated with other drugs on hirsutism.**

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of clinical trial</th>
<th>Duration</th>
<th>Treatment</th>
<th>Age (years)</th>
<th>Results</th>
<th>Adverse effects*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tartagni et al. 23</td>
<td>Randomized and single-blind</td>
<td>6</td>
<td>Finasteride+CPA+EE(^a) (n=23) versus CPA+EE(^b) (n=23)</td>
<td>18–35</td>
<td>Finasteride+cyproterone +EE&gt;cyproterone +EE</td>
<td>Lower libido (n=2)</td>
</tr>
<tr>
<td>Sahin et al. 24</td>
<td>Randomized and double-blind</td>
<td>12</td>
<td>Finasteride+CPA+EE(^c) (n=18) versus CPA+EE(^d) (n=16)</td>
<td>27.1±5.8</td>
<td>Finasteride+CPA+EE&gt;CPA+EE</td>
<td>No side effects in either group</td>
</tr>
<tr>
<td>Unlühızarcı et al. 22</td>
<td>Randomized and without placebo</td>
<td>6</td>
<td>Finasteride+spironolactone(^e) (n=16) versus spironolactone(^f) (n=18)</td>
<td>20.4±0.5</td>
<td>Finasteride+spironolactone&gt;spironolactone</td>
<td>Polymenorrhea (n=2)</td>
</tr>
<tr>
<td>Keleştimur et al. 21</td>
<td>Randomized and single-blind</td>
<td>12</td>
<td>Finasteride+spironolactone(^g) (n=33) versus spironolactone(^h) (n=32)</td>
<td>20.9±0.3</td>
<td>Finasteride+spironolactone&gt;spironolactone</td>
<td>Polymenorrhea (n=9)</td>
</tr>
</tbody>
</table>

*Adverse effects of finasteride. CPA: cyproterone acetate; EE: ethynyl estradiol. Dosages: \(^a\)5 mg of finasteride on days 1–14 plus 2 mg/day of CPA plus 35 mcg/day of EE on days 1–21. \(^b\)2 mg/day of CPA plus 35 mcg/day of EE on days 1–21. \(^c\)5 mg of finasteride continuously plus 2 mg of CPA plus 35 mcg/day of EE on days 5–25. \(^d\)2 mg of CPA plus 35 mcg/day of EE on days 5–25. \(^e\)5 mg/day of finasteride plus 100 mg/day of spironolactone. \(^f\)100 mg/day of spironolactone.
Therefore, our review shows the potential benefit of finasteride in the treatment of hirsutism, but further randomized double-blind studies should be conducted not only to overcome the aforementioned limitations but also to assess the influence of finasteride in steroidogenesis.

**AUTHORS’ CONTRIBUTIONS**

**DZG:** Project Administration, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **JMSJ:** Project Administration, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **RSS:** Project Administration, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **ECAV:** Project Administration, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **ECB:** Formal Analysis, Project Administration, Writing – Original Draft, Writing – Review & Editing.

**REFERENCES**


