REVIEW ARTICLE
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Systematic review of finasteride effect in women with hirsutism

José Maria Soares Júnior[1], Daniela Zaros Guimarães[1], Ricardo dos Santos Simões[1], Eduardo Carvalho de Arruda Veiga[1]*, Cristiane Lima Roa[1], Isabel Cristina Espósito Sorpreso[1], Maria Cândida Baracat[1], Edmund Chada Baracat[1]

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 condition[1-3].

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 treatments[4]. 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 use[2].

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 hirsutism[5]. 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) scale[6,7]. 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 ethynyl 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.

[1]Universidade de São Paulo, School of Medicine, Clinic's Hospital, Department of Gynecology – São Paulo (SP), Brazil.
*Corresponding author: eduveiga56@gmail.com
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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.

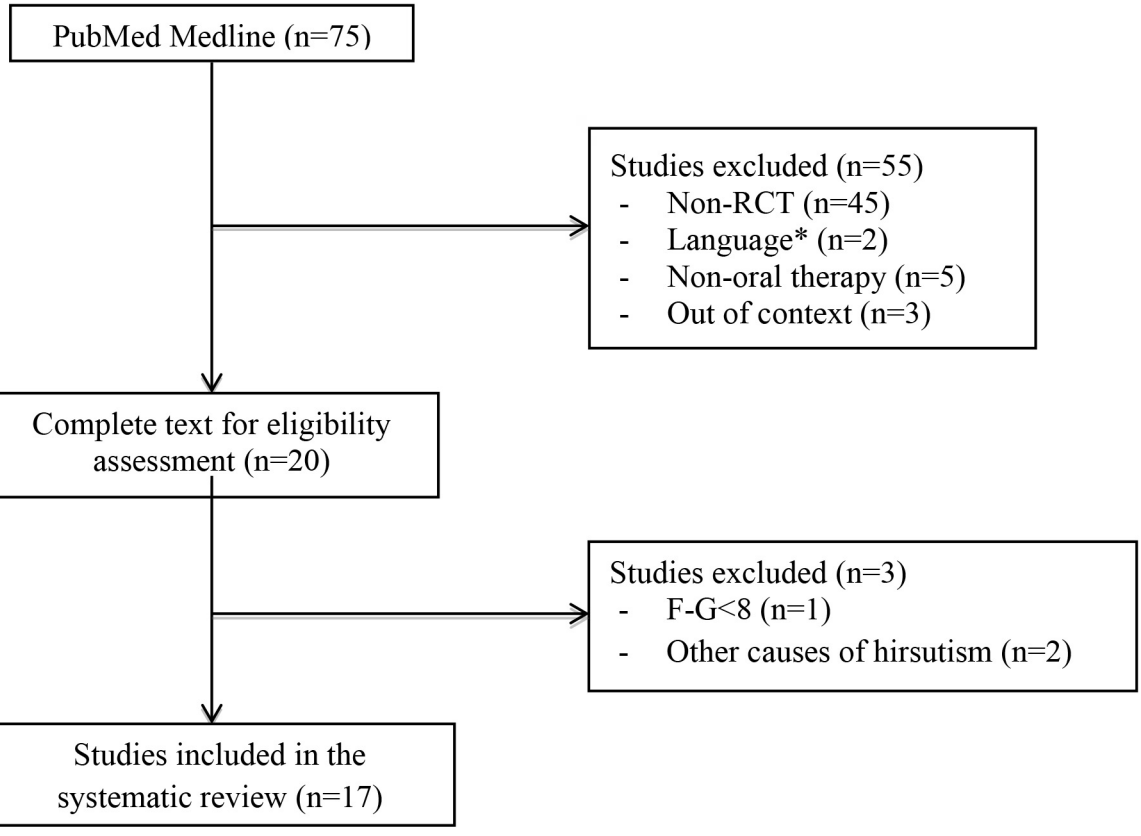
RESULTS

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[8,9], 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.[6] reported side effects in both the study group and the placebo group. In the study by Lakryc et al.[9], 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[10]. 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[11].



RCT: randomized controlled trial; F-G: Ferriman–Gallwey. *Language other than Portuguese, Spanish, and English.

Figure 1. Flowchart of study selection.

Table 1. Effects of finasteride on hirsutism: comparing finasteride with other drugs.

Author	Type of clinical trial	Duration (months)	Treatment	Age (years)	Results	Adverse effects*
Wong et al.[12]	Randomized and without placebo	6	Finasteride[a] (n=9) *versus* spironolactone[b] (n=5)	15–40	Finasteride spironolactone	No side effects
Ciotta et al.[21]	Randomized single-blind	9	Finasteride[a] (n=9) *versus* placebo (n=9)	20.6±0.43	Finasteride>placebo	Headache (n=4) and depression (n=2)
Lakryc et al.[9,α]	Randomized double-blind; placebo-controlled	6	Finasteride[b] (n=12) *versus* placebo (n=12)	19–40	Finasteride>placebo	No severe adverse effects
Bayram et al.[10]	Randomized and without placebo	12	Finasteride 2.5 mg/day (n=29) *versus* finasteride 5 mg/day (n=27)	18–41	5 mg/day>2.5 mg/day	2.5 mg: dry skin (n=1), reduction in libido (n=1), headache (n=2), and gastrointestinal disorders (n=1). 5 mg: dry skin (n=3), reduction in libido (n=4), headache (n=1), and gastrointestinal disorders (n=4)
Tartagni et al.[23]	Randomized and without placebo	10	Finasteride 2.5 mg/day (n=19) versus 2.5 mg every three days (n=19)	18–34	Continuous intermittent	Continuous: small reduction in libido (n=1, 5 months; n=2, 10 months) and mild and transient gastrointestinal discomfort (n=1). Intermittent: no adverse effects
Erenus et. al.[14]	Randomized and single blind	9	Finasteride[a] (n=7) *versus* spironolactone[b] (n=9)[α]	21.3±4.6	Finasteride<spironolactone	No side effects
Falsetti et al.[18]	Randomized and without placebo	6	Finasteride[a] (n=22) *versus* flutamide[c] (n=22)	22.9±4.9	Finasteride flutamide	Dry skin (n=6), reduction in libido (n=3), and headache (n=2)
Sahin et al.[24]	Randomized and without placebo	9	Finasteride[a] (n=21) *versus* CPA+EE[d] (n=21)	21.8±0.97	Finasteride<CPA+EE	No effects
Falsetti et al.[20]	Randomized and without placebo	12	Finasteride[a] (n=55) *versus* flutamide[e] (n=52)[γ]	18–29	Finasteride<flutamide	Dry skin (n=13), headache (n=7), and reduction in libido (n=6)

Continue...

Table 1. Continuation.

Author	Type of clinical trial	Duration (months)	Treatment	Age (years)	Results	Adverse effects*
Falsetti et al.[20]	Randomized and without placebo	12	Finasteride[a] (n=23) *versus* flutamide[e] (n=21)[δ]	18–29	Finasteride<flutamide	Dry skin (n=5), headache (n=3), and reduction in libido (n=2)
Fruzetti et al.[15]	Randomized and without placebo	12	Finasteride[a] (n=14) *versus* CPA+EE[e] (n=13) *versus* flutamide[e] (n=15)	16–29	Finasteride CPA+EE flutamide	No side effects
Moghetti et al.[13]	Randomized, double-blind, and placebo-controlled	6	Finasteride[a] (n=10) *versus* spironolactone[b] (n=10) *versus* flutamide[g] (n=10) *versus* placebo (n=10)	20.4±0.5	Finasteride spironolactone flutamide>placebo	Finasteride: transient sensation of bloating (n=1)
Beigi et al.[16]	Randomized and without placebo	9	Finasteride[a] (n=20) *versus* CPA+EE[h] (n=20)	16–29	Finasteride CPA+EE	No side effects

*Adverse effects of finasteride. [α]Loss of four cases due to allergy (n=1) plus nausea and diarrhea (n=3). Finasteride dosages: [a]7.5 mg/day; [b]5 mg/day. *Adverse effects of finasteride. [α]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). [β]Two patients dropped out in the flutamide group, one due to nausea and vomiting, and one because of high transaminase levels. [γ]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. [δ]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: [a]5 mg/day of finasteride. [b]100 mg/day of spironolactone. [c]150 mg/day of flutamide two times. [d]2 mg/day of CPA plus 35 µg/day of EE on days 5–25. [e]250 mg/day of flutamide two times. [f]25 mg/day of CPA on days 1–10 of the menstrual cycle plus 20 µg of EE every day for 21 days. [g]250 mg/day of flutamide. [h]25 mg/day of CPA on days 5–14 plus 20 µg/day of EE on days 5–25.

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 in the hirsutism score with spironolactone treatment was significantly higher than that with the finasteride treatment (at six and nine months). Despite the significant results, after the sixth month, 19 out of the 40 women in the study comprised initially dropped out because of inadequate responses. Additionally, five patients from the spironolactone group could not be included in the final analysis at nine months owing to irregular uterine bleeding and the need for hormonal contraceptive use.

Neither Wong et al.[12] nor Erenus et al.[14] reported adverse effects of finasteride use. Moghetti et al.[13] reported one patient with a transient sensation of overall bloating. Adverse effects, particularly nausea and abnormal uterine bleeding, were reported with the use of spironolactone[12-14], but Wong et al.[12] did not report any side effects with its use.

Two of the studies comparing finasteride with CPA associated with EE; Table 1) found no significant differences between the groups[15,16]. Sahin et al.[17] showed the CPA+EE association was more effective than finasteride after six months of treatment. No adverse effects were reported during the studies[15-17].

Five studies were reviewed comparing finasteride with flutamide (Table 1). All of them showed a significant reduction in the F–G score with both medications[13,15,18-20]. In three of them, Falsetti et al.[18], Fruzetti et al.[15], and Moghetti et al.[13] did not find any differences between the two treatments. Falsetti et al.[19,20] suggested the superiority of flutamide after 12 months of treatment.

There were more reports of side effects with flutamide, and these were more severe, namely, nausea, vomiting, dry skin, and reduction in libido in three studies[18-20], hyporexia in one[13], and acute hepatitis in another as evidenced by a pronounced increase in transaminases[19]. Two studies reported dropouts because of such effects[19,20]. There was no loss of patients with finasteride, but there were complaints about the reduction in libido (8.7–13.6%), headache (9.1–13%), dry skin (21.7–27.3%)[18,20], and bloating (10%)[13].

Table 2 shows a summary of the studies in which finasteride associated with spironolactone or with CPA and EE is

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

Author	Type of clinical trial	Duration	Treatment	Age (years)	Results	Adverse effects*
Tartagni et al.[23]	Randomized and single-blind	6	Finasteride+CPA+EE[a] (n=23) *versus* CPA+EE[b] (n=23)	18–35	Finasteride+cyproterone +EE>cyproterone+EE	Lower libido (n=2)
Sahin et al.[24]	Randomized and double-blind	12	Finasteride+CPA+EE[c] (n=18)*versus*CPA+EE[d] (n=16)	27.1±5.8	Finasteride+ CPA+EE>CPA+EE	No side effects in either group
Unlühizarci et al.[22]	Randomized and without placebo	6	Finasteride+spironolactone[e] (n=16) *versus* spironolactone[f] (n=18)	20.4±0.5	Finasteride+ spironolactone> spironolactone	Polymenorrhea (n=2)
Kelestimur et al.[21]	Randomized and single-blind	12	Finasteride+spironolactone[e] (n=33) *versus* spironolactone[f] (n=32)	20.9±0.3	Finasteride+ spironolactone> spironolactone	Polymenorrhea (n=9)

*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/day 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.

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 Unlühizarci 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[9-12,14,18-20].

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.

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. **CLR:** Writing – Original Draft, Writing – Review & Editing. **ICES:** Writing – Original Draft, Writing – Review & Editing. **MCPB**: Writing – Original Draft, Writing – Review & Editing. **ECB:** Formal Analysis, Project Administration, Writing – Original Draft, Writing – Review & Editing.

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