Efficacy and Safety of Finasteride Therapy for Androgenetic Alopecia

A Systematic Review

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Context: Androgenetic alopecia is the most common form of alopecia in men.

Objective: To determine the efficacy and safety of finasteride therapy for patients with androgenetic alopecia.

Data Sources: MEDLINE, EMBASE, CINAHL, Cochrane Registers, and LILACS were searched for randomized controlled trials reported in any language that evaluated the efficacy and safety of finasteride therapy in comparison to treatment with placebo in adults with androgenetic alopecia.

Study Selection and Data Extraction: Two reviewers independently evaluated eligibility and collected the data, including assessment of methodological quality (Jadad score). Outcome measures included patient self-assessment, hair count, investigator clinical assessment, global photographic assessment, and adverse effects at short term (≤12 months) and long term (≥24 months). Heterogeneity was explored by testing a priori hypotheses.

Data Synthesis: Twelve studies fulfilled the eligibility criteria (3927 male patients), 10 of which demonstrated a Jadad score of 3 or more. The proportion of patients reporting an improvement in scalp hair was greater with finasteride therapy than with placebo treatment in the short term (relative risk [RR], 1.81 [95% confidence interval (CI), 1.42-2.32]; I^2, 64%) and in the long term (RR, 1.71 [95% CI, 1.15-2.53]; I^2, 16%); both results were considered to have moderate-quality evidence. The number needed to treat for 1 patient to perceive himself as improved was 5.6 (95% CI, 4.6-7.0) in the short term and 3.4 (95% CI, 2.6-5.1) in the long term. Moderate-quality evidence suggested that finasteride therapy increased the mean hair count from baseline in comparison to placebo treatment, expressed as a percentage of the initial count in each individual, at short term (mean difference [MD], 9.42% [95% CI, 7.95%-10.90%]; I^2, 50%) and at long term (MD, 24.3% [95% CI, 17.92%-30.60%]; I^2, 0%). Also, the proportion of patients reported as improved by investigator assessment was greater in the short term (RR, 1.80 [95% CI, 1.43-2.26]; number needed to treat, 3.7 [95% CI, 3.2-4.3]; I^2, 82%) (moderate-quality evidence). Moderate-quality evidence suggested an increase in erectile dysfunction (RR, 2.22 [95% CI, 1.03-4.78]; I^2, 1%; number needed to harm, 82.1 [95% CI, 56-231]) and a possible increase in the risk of any sexual disturbances (RR, 1.39 [95% CI, 0.99-1.95]; I^2, 0%). The risk of discontinuing treatment because of sexual adverse effects was similar to that of placebo (RR, 0.88 [95% CI, 0.51-1.49]; I^2, 5%) (moderate-quality evidence).

Conclusion: Moderate-quality evidence suggests that daily use of oral finasteride increases hair count and improves patient and investigator assessment of hair appearance, while increasing the risk of sexual dysfunction.

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ANDROGENETIC ALOPECIA (AGA) (male pattern hair loss) is the most common form of alopecia in men, affecting 30% of men by the age of 30 years and 50% by the age of 50 years.[1,2] Men who have visible hair loss are perceived as older and less physically and socially attractive.[3-5] Androgenetic alopecia does not occur in men with a genetic deficiency of the type 2 5α-reductase enzyme, which converts testosterone to dihydrotestosterone.[6-9] Finasteride selectively inhibits type 2 5α-reductase enzyme,[10] reduces serum and scalp dihydrotestosterone concentrations by approximately 60% to 70%,[11] and inhibits or reverses miniaturization of hair follicles as demonstrated in scalp biopsy studies.[12,13]

The high prevalence of AGA[14] and its associated psychosocial morbidity have stimulated a huge market for treatments. A systematic review that addresses the efficacy of finasteride therapy has not previously been published (to our knowl-

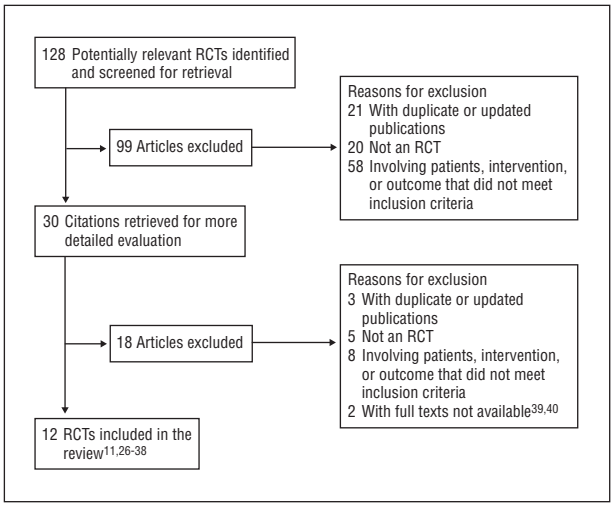

Figure 1. Flow of trials through the selection process. RCT indicates randomized controlled trial.

edge), and controversy remains regarding the adverse effects of finasteride therapy.[15-17] This systematic review addresses the efficacy and safety of finasteride therapy for AGA.

METHODS

ELIGIBILITY CRITERIA

We included all randomized controlled trials (RCTs) that met the following criteria: (1) population—men older than 18 years with AGA; (2) intervention—oral finasteride (1 or 5 mg); (3) comparison—placebo; and (4) outcomes—patient self-assessment, hair count, investigator clinical assessment, global photographic assessment, or adverse effects. We excluded studies that included patients with other causes of alopecia or that used other medications with androgenic or antiandrogenic properties within 3 months of enrollment.

SEARCH STRATEGY

We searched for relevant articles in the following electronic databases: MEDLINE (1966 to December 2009), EMBASE (1980 to December 2009), CINAHL (1982 to December 2009), Cochrane Central Register of Controlled Trials (2009), Cochrane Skin Group Specialized Register (2009), and LILACS (1985 to December 2009). The key terms used were *alopecia*, *hair loss*, *male pattern alopecia*, *male pattern hair loss*, or *hair diseases*; *finasteride*, or different commercial names of finasteride; and *randomized controlled trial*, *controlled clinical trial*, *random allocation*, *drug therapy*, *therapeutics*, *rct*, or *all random*. No language restriction was applied. We reviewed the reference lists of included articles and relevant dermatologic, pharmacologic, and internal medicine textbooks. We also contacted experts in the field and pharmaceutical companies to identify unpublished articles.

DATA COLLECTION

Two of the authors (J.M.M. and M.C.P.) independently reviewed titles and abstracts for eligibility. Subsequently, they assessed the full text of all articles deemed possibly eligible. When disagreement occurred, a third reviewer (H.N.C.) evaluated eligibility. Data from eligible articles were independently abstracted in duplicate by the first 2 authors (J.M.M. and M.C.P.).

RISK OF BIAS ASSESSMENT

The Jadad score[18] (range, 0-5) was used to evaluate the risk of bias associated with each study. The methodological quality was independently abstracted in duplicate by the first 2 authors; reviewers resolved differences by consensus.

OUTCOME MEASURES

The outcome measures included patient self-assessment, hair count, investigator assessment, global photographic assessment, and adverse effects. We abstracted these data from the text or, if necessary, graphic representations. Our analysis considered treatment with finasteride (1 or 5 mg) vs placebo over the short term (≤12 months) and long term (≥24 months), performing a separate analysis for each time frame and using the earliest time point for the short-term outcomes and the latest time point for the long-term outcomes.

EFFICACY ANALYSIS

Patient Self-Assessment

Most studies used validated questionnaires[19] consisting of 6 or 7 questions related to treatment efficacy and to patient satisfaction with appearance of hair. The effect measure that we used to express the results was the proportion of patients who reported improvement in scalp hair from baseline. We considered patients improved if they reported slight, moderate, or great improvement; a positive self-assessment; or being satisfied.

Hair Count

Investigators counted hair using macrophotographic analysis (Canfield method[20]) or manual count of clipped hair in a specific balding area of the scalp (1 cm^2 or 1 sq in in diameter) centered by a dot tattoo. The effect measure we used to report the results was the mean change in hair count from baseline expressed as a percentage of the initial hair count. We took the reports of the mean change in each trial, expressed it as a percentage of the hair count at baseline, and then calculated the difference in the percentages between groups. This effect measure enabled us to pool studies that examined different sizes of balding scalp (1 cm^2 or 1 sq in).

Investigator Assessment

Investigators assessed the change in hair growth using a photograph of the area taken at baseline for reference. Most studies used a standardized 7-point rating scale of hair growth. The effect measure that we used to report the results was the proportion of patients rated by investigators as improved. Improvement was considered to be slightly, moderately, or greatly increased hair growth or any other expression of a positive change.

Global Photographic Assessment

Photographs of a patient's specific balding area were taken with the head in a fixed position. Change in hair growth was assessed by expert panels of dermatologists using the same standardized rating scales as for investigator assessment. The effect measure that we used was the percentage of patients rated by investigators as improved based on analysis of photographs. Improvement was considered as for investigator assessment.

Table 1. Characteristics of Included Studies

Source	Country	Mean Age, y	Severity of Hair Loss[a]/Age at Which It Began, y	Finasteride Dose, mg (No. of Patients Included)	Comparison of Drug and Dose (No. of Patients Included)	Treatment Duration, mo	Follow-up, %[b]	Jadad Score, 0 to 5
Brenner and Matz,[26] 1999	Israel	65	NA	5 (14)	Placebo (14)	24	100	3
Drake et al,[11] 1999	United States, Canada, and Belgium	37	NA	1 (37), 5 (38)	Placebo (67); finasteride, 0.01 mg (37), 0.05 mg (34), and 0.2 mg (36)	1	92.4	3
Finasteride Male Pattern Hair Loss Study Group,[27] 2002[c]	Multinational (United States, Europe, and Asia)	32.5	NWH II-V/24	1 (779)	Placebo (774)	60	86[d]	3
Kawashima et al,[29] 2004	Japan	40	NWH II-V/NA	1 (139)	Placebo (138); finasteride, 0.2 mg (137)	12	95	4
Leavitt et al,[30] 2005	United States	40.5	NWH IV-VI/27.5	1 (40)	Placebo (39)	12	77	3
Leyden et al,[31] 1999	United States	32.5	NWH II-III/25.5	1 (166)	Placebo (160)	12	87	3
Olsen et al,[32] 2006	United States	36.4	NWH III-V/26.1	5 (70)	Placebo (64); dutasteride, 0.05 mg (71), 0.1 mg (72), 0.5 mg (68), and 2.5 mg (71)	6	89	4
Price et al,[34] 2006[e]	United States	31.9	NWH II-III/NA	1 (33)	Placebo (33)	48	83	2
Roberts et al,[35] 1999	United States	30	NWH III-IV/23.2	5 (111)	Placebo (116)	12	76	3
				1 (117)	Placebo (117); finasteride, 0.2 mg (115), and 0.01 mg (117)	6		
Stough et al,[36] 2002	United States	38.4	NWH II-V/27	1 (9)	Placebo (9)	12	100	3
Van Neste et al,[37] 2000	United States, Europe	30	NWH II-V/23.2	1 (106)	Placebo (106)	12	83	2
Whiting et al,[38] 2003	United States	49.9	NWH II-V/34.8	1 (286)	Placebo (138)	24	70	4

Abbreviations: NA, not available; NWH, Norwood-Hamilton scale.

[a] In the studies by Kawashima et al,[29] Roberts et al,[35] Stough et al,[36] and Van Neste et al,[37] more than 50% of patients were NWH II/III. In the studies by the Finasteride Male Pattern Hair Loss Study Group,[27] Olsen et al,[32] and Whiting et al,[38] more than 50% of patients were NWH IV/V.

[b] Mean percentage of patients available for follow-up in both arms (finasteride and controls) of treatment.

[c] Continuation of the study by Kaufman et al,[28] published in 1998.

[d] Sixteen percent (mean, both arms) of patients unavailable for follow-up at 12 months of treatment, 15% at 24 months, 15% at 36 months, 15% at 48 months, and 21% at 60 months.

[e] Continuation of the study by Price et al,[33] published in 2002.

Safety Analysis

We evaluated the occurrence of decreased libido, erectile dysfunction, and ejaculation disorder. We also considered global sexual disturbances as a composite outcome that included the 3 outcomes mentioned above. Also, we assessed the rate of withdrawals attributable to drug-related sexual adverse effects. Studies that reported no withdrawals in either intervention or control groups were not included in the analysis. For crossover trials, we included only data from the first treatment period.

Intention-to-Treat Principle

Wherever possible, we included patients in the arm to which they were randomized, irrespective of compliance.

STATISTICAL ANALYSIS

Descriptive data were expressed in mean values or percentages with their respective standard deviations or 95% confidence intervals (CIs). We used weighted κ to assess agreement between reviewers on the selection of articles for inclusion and on methodological quality. RevMan 5.0 was used for the meta-analysis. We used random-effects models. For continuous data, the effect measure was expressed as the mean difference (MD). For dichotomous data, effect measure was expressed as relative risk (RR). The statistical method used was Mantel-Haenszel. We calculated the risk difference and the number needed to treat (NNT) or to harm (NNH), reporting only those statistically significant (number <0 or >0, with a 95% CI that did not include 0). We estimated baseline risk in un-

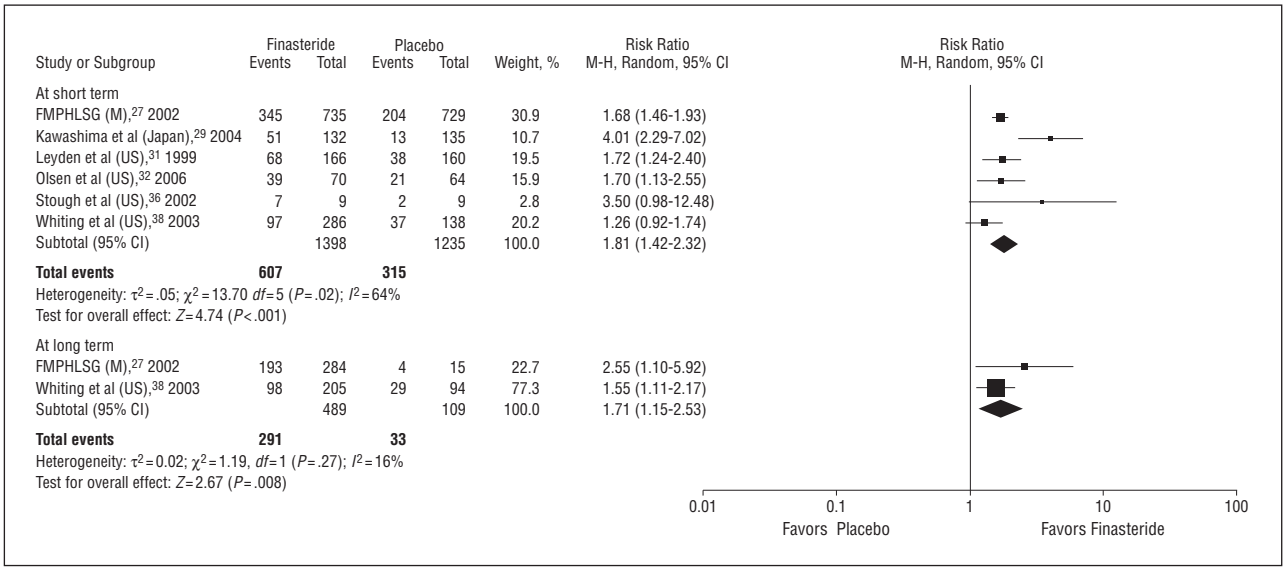

Figure 2. Patient self-assessment (improvement expressed as risk ratio). Finasteride in comparison to placebo at short- and long-term points. CI indicates confidence interval; FMPHLSG, Finasteride Male Pattern Hair Loss Study Group; M, multicentric; M-H, Mantel-Haenszel test; and US, United States.

treated patients from the media control group event rate for all outcomes. We constructed funnel plots to evaluate publication bias.[21,22] To quantify the inconsistency among the pooled estimates, we used the I^2 statistic and the χ^2 test.[23] We examined explanations of heterogeneity irrespective of the I^2 or the P value on the test for heterogeneity. We conducted tests of heterogeneity based on the following prespecified hypotheses. We expected to find bigger effects with higher doses of finasteride, in younger men, in men with less baseline hair loss, in men in whom the hair loss began earlier, when measuring bigger scalp areas, and in studies with lower quality. Our thresholds for these hypotheses were as follows: dose of finasteride (1 mg vs 5 mg); mean age of patients (≤34 years vs >35 years); mean age at which hair loss began (≤30 years vs >30 years); severity of alopecia at baseline according to the Norwood-Hamilton (NWH) scale (less severe, NWH II, NWH III, and NWH II-V, where more than 50% of patients were NWH II/III, vs more severe, NWH IV, NWH V, and NWH II-V, where more than 50% of patients were NWH IV/V); diameter of the area of scalp examined (1 cm^2 vs 1 sq in); and methodological quality (Jadad score ≥3 vs Jadad score <3). Tests for subgroup differences, based on inverse variance, were applied. For safety analysis, we conducted tests of heterogeneity based on a prespecified hypothesis for toxic effects. We expected to find more adverse effects with higher doses of finasteride and with studies of lower quality. Our thresholds for these hypotheses were as for the efficacy analysis.

EVALUATION OF QUALITY OF EVIDENCE

We used the Grading of Recommendations, Assessment, Development, and Evaluation system to evaluate the quality of the evidence.[24,25] We rated the quality of evidence down if the studies suffered from a high risk of bias (study limitations), inconsistency of results (I^2 > 50% and heterogeneity P < .05), indirectness of evidence, imprecision (wide CIs), and reporting bias (asymmetrical funnel plot). We rated 1 level down for each problem, except in the cases in which we did not consider the presence of 2 issues of sufficient seriousness to rate the quality down for each problem.

FUNDING SOURCE

We documented whether or not studies were sponsored by pharmaceutical industries.

RESULTS

We identified 128 possibly relevant articles, of which we selected 12 that fulfilled the eligibility criteria (**Figure 1** and **Table 1**). Agreement on full text review was high (κ, 0.93; 95% CI, 0.85-1.00). Eligible studies enrolled a total of 3927 patients (2152 patients randomized to finasteride therapy, 1 or 5 mg; 1775 patients randomized to treatment with placebo), with a mean age of 37 years.

QUALITY OF STUDIES

Ten (83%) of the 12 trials had a Jadad score of 3 or more (Table 1). Although authors described all trials as randomized, most of them did not report the randomization method. Concealment allocation was only reported in 1 trial (Olsen et al[32]). Most trials reported double blinding, and in many of them the blinding was specified. Most trials described their analysis as "modified intention to treat" and described the reasons for withdrawals. Eleven trials were sponsored by pharmaceutical industries (9 by Merck & Co, 1 by Banyu Pharmaceutical Co, and 1 by GlaxoSmithKline); the remaining trial did not report sponsorship.

PATIENT SELF-ASSESSMENT

Short-term Efficacy

Six trials, involving 2633 patients, compared finasteride therapy (1 or 5 mg) vs placebo treatment. Three trials[31,32,38] presented data at 6 months and the other 3[27-29,36]

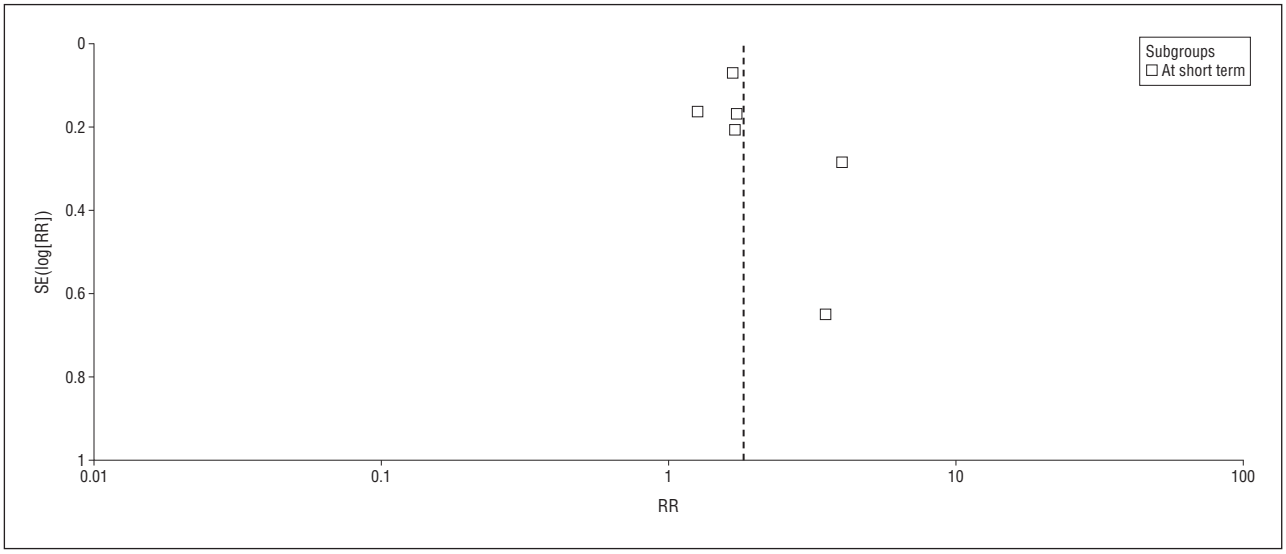

Figure 3. Funnel plot. Patient self-assessment at short term. RR indicates risk ratio; SE, standard error

at 12 months. The meta-analysis showed a higher proportion of patients reporting improvement in self-assessment with finasteride therapy: RR, 1.81 (95% CI, 1.42-2.32); NNT, 5.6 (95% CI, 4.6-7.0); I^2, 64%; $P=.02$ (**Figure 2**). Heterogeneity could not be explained by prespecified hypotheses. In **Figure 3**, the funnel plot showed an asymmetrical shape, raising the possibility of publication bias; we found small trials showing effects that were greater than those of the larger trials, but no small trials showing effects that were smaller than those of the larger trials (the symmetrical distribution that one would expect), suggesting a possible overestimate of the effect of finasteride therapy. Although we considered there to be problems with inconsistency and likelihood of publication bias, we did not consider these issues of sufficient seriousness to rate the quality for each problem down; therefore, we considered the evidence of moderate quality (**Table 2**).

Long-term Efficacy

Two studies[27,38] that involved 598 patients examined patient assessment, Whiting et al[38] at 24 months and the Finasteride Male Pattern Hair Loss Study Group[27,28] at 60 months. The percentage of men with a positive self-assessment was higher in the finasteride group: RR, 1.71 (95% CI, 1.15-2.53); NNT, 3.4 (95% CI, 2.6-5.1); I^2, 16%; $P=.27$ (Figure 2). We considered the evidence of moderate quality because of the likelihood of publication bias (Table 2).

HAIR COUNT

Short-term Efficacy

Eight trials, involving 2763 patients, compared finasteride therapy (1 or 5 mg) with placebo treatment at short term. Seven trials presented data at 6 months[27,30-33,35,37] and 1 trial at 12 months[36] as the earliest time point. Finasteride therapy significantly increased hair count in comparison to placebo (**Figure 4**): MD, 9.42% (95% CI, 7.9%-10.9%). Heterogeneity was significant (I^2, 50%; $P=.05$) and could be explained by the severity of hair loss at baseline (hair count was greater in patients with more severe baseline hair loss; test for subgroup differences, $P<.001$) and by the different sizes of the area measured (hair count was greater when measured in areas of 1 sq in; $P=.009$). The funnel plot appeared asymmetrical. We considered the quality of evidence moderate because of the risk of bias (2 studies[33,37] had a Jadad score <3) and the likelihood of reporting bias (Table 2).

Long-term Efficacy

Two studies[27,34] that involved 388 patients examined hair count at 48 months. Finasteride therapy significantly increased hair count in comparison to placebo treatment (Figure 4): MD, 24.3% (95% CI, 17.92%-30.60%); I^2, 0%; $P=.46$. We considered the quality of evidence moderate because we rated it down by risk of bias (1 study[34] had a Jadad score <3) and likelihood of reporting bias (Table 2).

INVESTIGATOR ASSESSMENT

Short-term Efficacy

Four trials (2501 patients) assessed the proportion of patients rated by the investigators as improved, 1 at 6 months and the other 3 at 12 months. Finasteride therapy (1 mg) was superior to placebo treatment: RR, 1.80 (95% CI, 1.43-2.26); NNT, 3.7 (95% CI, 3.2-4.3); I^2, 82%; $P<.01$. Heterogeneity could not be explained by prespecified hypotheses. The funnel plot showed an asymmetrical shape. Although we considered there to be problems with inconsistency and likelihood of publication bias, we did not consider these issues of sufficient seriousness to rate the quality for each problem down; therefore, we considered the evidence to be of moderate quality (Table 2).

Table 2. Evidence Profile: Finasteride vs Placebo

Outcome	Time Frame	Evidence Profile: Risk of Bias	Precision	Consistency	Directness	Publication Bias	% of MD or RR (95% CI)
Efficacy analysis							
Improvement in patient self-assessment	Short term	No serious limitations	Precise	Inconsistent	Direct	Detected	RR, 1.81 (1.42 to 2.32)
	Long term	No serious limitations	Precise	Consistent	Direct	Detected	RR, 1.71 (1.15 to 2.53)
Hair count	Short term	No serious limitations	Precise	Consistent	Direct	Detected	MD, 9.42% (7.95% to 10.90%)
	Long term	No serious limitations	Precise	Consistent	Direct	Detected	MD, 24.3% (17.92% to 30.60%)
Improvement in investigator assessment	Short term	No serious limitations	Precise	Inconsistent	Direct	Detected	RR, 1.80 (1.43 to 2.26)
Improvement in global photographic assessment	Short term	No serious limitations	Precise	Inconsistent	Direct	Detected	RR, 5.09 (2.27 to 11.40)
	Long term	No serious limitations	Precise	Consistent	Direct	Detected	RR, 10.11 (4.57 to 22.35)
Safety analysis: sexual adverse effects							
Global sexual disturbances	All time points	No serious limitations	Imprecise	Consistent	Direct	Not detected	RR, 1.39 (0.99 to 1.95)
Erectile dysfunction	All time points	No serious limitations	Imprecise	Consistent	Direct	Not detected	RR, 2.22 (1.03 to 4.78)
Decreased libido	All time points	No serious limitations	Imprecise	Consistent	Direct	Not detected	RR, 1.08 (0.67 to 1.76)
Ejaculation dysfunction	All time points	No serious limitations	Imprecise	Consistent	Direct	Not detected	RR, 1.75 (0.79 to 3.88)
Withdrawals because of sexual adverse effects	All time points	No serious limitations	Imprecise	Consistent	Direct	Not detected	RR, 0.88 (0.51 to 1.49)

(continued)

Long-term Efficacy

No studies provided data for long-term efficacy.

GLOBAL PHOTOGRAPHIC ASSESSMENT

Short-term Efficacy

Improvement in global photographic assessment was evaluated in 7 trials (2748 patients) that compared finasteride therapy (1 or 5 mg) and placebo treatment. Two trials reported data at 6 months and 5 trials at 12 months. The proportion of patients rated as having improved hair growth was higher in the finasteride group: RR, 5.09 (95% CI, 2.27-11.40); NNT, 2.5 (95% CI, 2.2-2.9); I^2, 95%; $P<.001$) (**Figure 5**). Heterogeneity could not be explained by prespecified hypotheses. The funnel plot appeared asymmetrical. We considered the quality of evidence as moderate because of inconsistency and reporting bias (Table 2).

Long-term Efficacy

Two trials (719 patients) compared finasteride therapy (1 mg) with placebo treatment, Whiting et al[38] at 24 months and the Finasteride Male Pattern Hair Loss Study Group[27] at 60 months. A higher proportion of patients taking finasteride were rated as improved compared with those using placebo: RR, 10.11 (95% CI, 4.57-22.35); NNT, 2.8 (95% CI, 2.4-3.2); I^2, 0%; $P=.76$ (Figure 5). We considered the quality of evidence as moderate because of the likelihood of publication bias (Table 2).

ADVERSE EFFECTS

Nine studies (3570 patients) were included in the safety analysis.

Global Sexual Disturbances

Finasteride therapy in comparison to treatment with placebo has a tendency to increase the risk of any sexual disturbances (9 trials, 3570 patients): RR, 1.39 (95% CI, 0.99-1.95); I^2, 0%; $P=.85$ (**Figure 6**). We considered the quality of evidence to be moderate because of imprecision (Table 2).

Erectile Dysfunction

Six studies (3110 patients) reported data about erectile dysfunction. When finasteride therapy (1 or 5 mg) was compared with treatment with placebo, finasteride therapy increased the risk of erectile dysfunction: RR, 2.22 (95% CI, 1.03-4.78); NNH, 82.1 (95% CI, 56-231); I^2, 1%; $P=.41$(**Figure 7**). We rated down by imprecision, considering the evidence as moderate quality (Table 2).

Decreased Libido

Six studies (3002 patients) reported data about decreased libido. When finasteride therapy (1 or 5 mg) was

Table 2. Evidence Profile: Finasteride vs Placebo (continued)

Outcome	Time Frame	Summary of Findings[a]	
		Assumed Risk Without Treatment t[b]	Absolute Change With Treatment[c] (95% CI)
Efficacy analysis			
Improvement in patient self-assessment	Short term	26 per 100	20 More per 100 (13 to 27)
	Long term	30 per 100	27 More per 100 (3 to 51)
Hair count	Short term	MD, –1.6%	MD, 9.42% more
	Long term	MD, –16%	MD, 24.26% more
Improvement in investigator assessment	Short term	37 per 100	27 More per 100 (20 to 35)
Improvement in global photographic assessment	Short term	9 per 100	40 More per 100 (34 to 46)
	Long term	4 per 100	36 More per 100 (31 to 42)
Safety analysis: sexual adverse effects			
Global sexual disturbances	All time points	3 per 100	1 More per 100 (–0.1 to 2)
Erectile dysfunction	All time points	<1 per 100	1 More per 100 (0 to 2)
Decreased libido	All time points	2 per 100	0 More per 100 (–1 to 2)
Ejaculation dysfunction	All time points	<1 per 100	1 More per 100 (–1 to 2)
Withdrawals because of sexual adverse effects	All time points	2 per 100	1 Less per 100 (–2 to 1)

Abbreviations: CI, confidence interval; MD, mean difference; RR, relative risk.
[a] The overall quality of evidence was moderate for all outcomes.
[b] Assumed risk without treatment was estimated from the media event rate of the placebo group for each outcome.
[c] Absolute change with treatment was estimated by taking the difference of the risk with treatment and the risk without treatment (placebo).

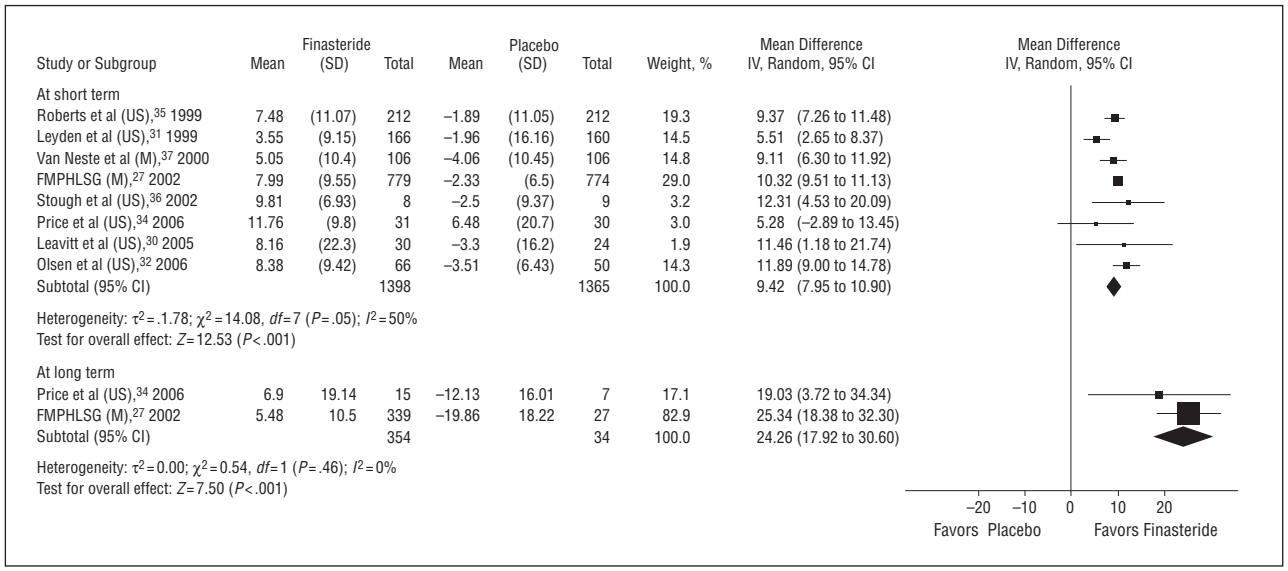

Figure 4. Hair count (percentage of mean difference from baseline). Finasteride in comparison to placebo at short- and long-term points. CI indicates confidence interval; FMPHLSG, Finasteride Male Pattern Hair Loss Study Group; IV, inverse variance; M, multicentric; and US, United States.

compared with treatment with placebo, finasteride therapy did not decrease libido: RR, 1.08 (95% CI, 0.67-1.76); I^2, 0%; $P = .60$. We considered the quality of evidence as moderate because of imprecision (Table 2).

Ejaculation Dysfunction

Four studies (2437 patients) reported data about ejaculation problems. When finasteride therapy (1 or 5 mg) was compared with treatment with placebo, finasteride therapy did not increase the risk of ejaculation problems: RR, 1.75 (95% CI, 0.79-3.88); I^2, 0%; $P = .55$. We considered the quality of evidence as moderate because we rated down by imprecision (Table 2).

Withdrawals Because of Sexual Adverse Events

Five trials (2487 patients) reported discontinuation of treatment because of sexual adverse experiences. The risk of discontinuing treatment because of sexual adverse effects was similar between finasteride therapy (1 or 5 mg) and placebo treatment: RR, 0.88 (95% CI, 0.51-1.49); I^2, 5%; $P = .38$. We considered the quality of evidence as moderate because of imprecision (Table 2).

COMMENT

This meta-analysis of RCTs provides moderate-quality evidence that daily use of oral finasteride increases hair

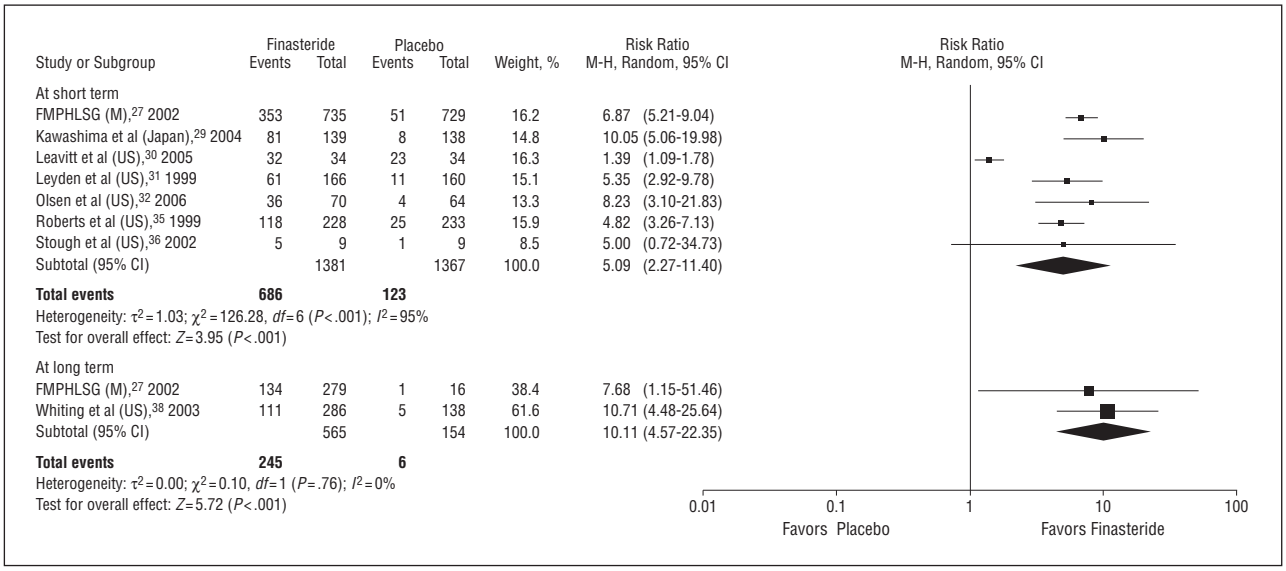

Figure 5. Global photographic assessment (improvement expressed as risk ratio). Finasteride in comparison to placebo at short- and long-term points. CI indicates confidence interval; FMPHLSG, Finasteride Male Pattern Hair Loss Study Group; M, multicentric; M-H, Mantel-Haenszel test; and US, United States.

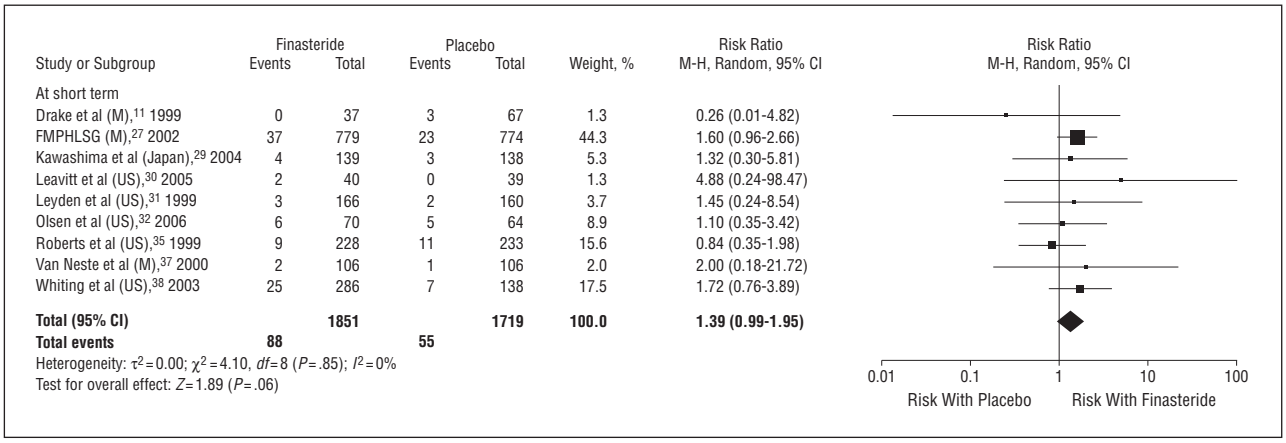

Figure 6. Global sexual disturbances (presence expressed as risk ratio). Finasteride vs placebo at any time point. CI indicates confidence interval; FMPHLSG, Finasteride Male Pattern Hair Loss Study Group; M, multicentric; M-H, Mantel-Haenszel test; and US, United States.

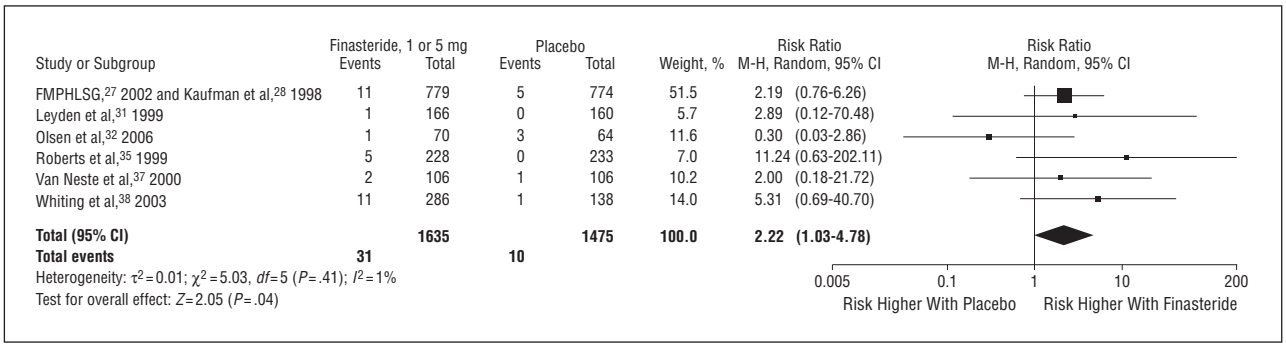

Figure 7. Erectile dysfunction (presence expressed as risk ratio). Finasteride vs placebo at any time point. CI indicates confidence interval; FMPHLSG, Finasteride Male Pattern Hair Loss Study Group; and M-H, Mantel-Haenszel test.

count and improves patient and investigator assessment of hair appearance, while increasing the risk of sexual dysfunction. The available moderate-quality evidence (Table 2) suggests that the use of finasteride almost doubles the probability of patients perceiving improvement in comparison with placebo, with a sustained effect over time. This effect corresponds to an absolute increase of approximately 20% in the short term (NNT, 5.6 [95% CI, 4.6-7.0]) and 30% in the long term (NNT, 3.4 [95% CI, 2.6-5.1]). A similar size effect was found in the improvement in investigator assessment with finasteride therapy in the short term: NNT, 3.7 (95% CI, 3.2-

4.3). With respect to hair count, we observed that finasteride therapy has a tendency to maintain and improve hair count over time during treatment; the longer the treatment, the greater the effect. The relative increase in hair count increase was close to 10% at short term (MD, 9.42% [95% CI, 7.9%-10.9%]), reaching higher values at long term during continuation of treatment (MD, 24.3% [95% CI, 17.9%-30.6%]).

When we explored sources of heterogeneity, hair count was the only outcome in which we found significant subgroup differences based on a prespecified hypothesis. We found that trials including patients with more severe baseline hair loss and assessing larger areas (1 sq in) had a significantly greater increase in hair count. Although we expected that the evaluation of bigger areas would lead to a greater effect, we anticipated that patients with less baseline hair loss would have a greater benefit. We remain skeptical about these apparent subgroup effects[41]: although we planned a small number of a priori hypotheses and the magnitude of these 2 subgroups effects is large, these comparisons were between rather than within studies; the results obtained were not consistent across other important related outcomes; and we do not have indirect evidence to support these differential responses to treatment.

The usual concerns of men taking finasteride involve the sexual adverse effects. The only adverse effect that was significantly more frequent with finasteride therapy in comparison to placebo treatment was erectile dysfunction: moderate-quality evidence suggests an RR of 2.22 (95% CI, 1.03-4.78) with an associated NNH of 82.1 (95% CI, 56-231), suggesting that 1 of every 80 patients treated will experience erectile dysfunction.

We found no significant difference between the use of 1 and 5 mg of finasteride in any of the outcomes, a finding that supports the appropriateness of the current recommended daily dose of 1 mg. The major problems with quality of evidence included imprecision, inconsistency, and likelihood of publication bias (Table 2). The likelihood of publication bias was suggested not only by the asymmetrical funnel plots but also by the fact that all trials were relatively small and almost all were funded by industry sponsors.

STRENGTHS AND WEAKNESS OF THE STUDY

The strengths of our systematic review include (1) explicit, detailed eligibility criteria; (2) a comprehensive search; (3) restriction to RCTs; (4) high levels of agreement on issues requiring judgment; (5) a sophisticated and appropriate statistical analysis; and (6) use of the systematic Grading of Recommendations, Assessment, Development, and Evaluation approach. Our systematic review is limited in that although we included only RCTs, most did not mention randomization methods and concealment allocations, at least in part, because the trials are not recent. In efficacy analysis, merging slight, moderate, and great responses as "improved" may have exaggerated the treatment effect in patient self-assessment, investigator assessment, and global photographic assessment. We do not have high-quality evidence for any of either the benefit or the harm outcomes.

IMPLICATIONS FOR CLINICAL PRACTICE

Men willing to use long-term medication to improve male pattern hair loss should consider that there is moderate-quality evidence suggesting an increase in the absolute likelihood of noticeable improvement of approximately 30% and there is moderate-quality evidence suggesting an absolute increase in the risk of erectile dysfunction of approximately 1.5%.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Mella, Perret, Catalano, and Guyatt. *Acquisition of data:* Mella and Perret. *Analysis and interpretation of data:* Mella, Perret, Manzotti, Catalano, and Guyatt. *Drafting of the manuscript:* Mella, Perret, Catalano, and Guyatt. *Critical revision of the manuscript for important intellectual content:* Mella, Perret, Manzotti, Catalano, and Guyatt.
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Archives Web Quiz Winner

Congratulations to the winner of our July quiz, Nahayat Dashgir, MD, Skin Cancer Institute, Chicago, Illinois. The correct answer to our July challenge was *aggressive angiomyxoma*. For a complete discussion of this case, see the Off-Center Fold section in the August *Archives* (Riemann H, Gaido L, Szajkowski K, Lee LA, Fitzpatrick JE. Recurrent erythematous vulvar nodule on a 33-year-old woman. *Arch Dermatol*. 2010; 146[8]:911-916).

Be sure to visit the *Archives of Dermatology* Web site (http://www.archdermatol.com) to try your hand at the interactive quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the *Archives*. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of *The Art of JAMA II*.