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Original Research Article

Treatment of benign prostatic hyperplasia with finasteride: Evidence from a meta-analysis

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Abstract

Purpose: *To clarify the usefulness and safety of finasteride in the treatment of patients with benign prostatic hyperplasia (BPH) compared to placebo group or controls.*
Methods: *In a meta-analysis, PubMed and Web of Science were searched to include relevant studies. The results were combined with a random effect model. Publication bias was evaluated using Egger regression asymmetry test.*
Results: *Fourteen publications involving 17,364 patients were included in the study. Pooled results indicated that International Prostate Symptom Score (IPSS) in the finasteride group was lower [weighted mean difference (WMD) = -0.77, 95% CI= -0.97 to -0.57] compared to the placebo group. The usefulness of finasteride was higher in total prostate volume (TPV) [WMD= 0.13, 95%CI= 0.00 to 0.26] but lower in serum DHT [WMD= -1.18, 95%CI= -1.51 to -0.86] when compared to the placebo group. Drug-related adverse event was higher in the finasteride treatment group when compared to placebo group [summary RR= 1.95, 95%CI= 1.31-2.90].*
Conclusion: *Finasteride could improve the symptom score (IPSS and TPV) and reduce serum DHT. However, the potential adverse events, especially the drug-related adverse events in Finasteride treatment should be attention.*

Keywords: *Benign prostatic hyperplasia, Finasteride, Meta-analysis*

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INTRODUCTION

In aging men, it is a common disease with benign prostatic hyperplasia (BPH). Urinary tract obstruction and even complete urinary retention often accompanied by prostate enlargement [1]. BPH can lead to bladder outlet obstruction (BOO), incomplete bladder emptying, poor stream and hesitancy. Therefore, it could affect a person's quality of life [2,3]. In some more advanced situations, the risk with enlarged prostates (>30 mL) could increase three fold among men with acute urinary retention (AUR) [4].

Finasteride belongs to the competitive inhibitor of 5a-reductase [5]. Application of this drug in a short period of time resulted in a decrease in serum dihydrotestosterone concentrations, a reduction in the prostate volume, and an

improvement in urinary flow rate [6,7]. While some studies [8-10] reported the effectiveness of finasteride in BPH, others did not find it better than the placebo or control [11]. Thus, the aim of this meta-analysis was to compare the outcomes of the treatment of BPH using finasteride.

METHODS

Search criteria and inclusion criteria

PubMed and Web of Knowledge databases were reached for records as at May 2015. The search utilized the terms 'benign prostatic hypertrophy', 'prostatic hyperplasia', or 'BPH' in combination with 'finasteride' or '5ar inhibitor'. List of references from all full research and review articles retrieved were also used to identify other relevant articles. All the articles and abstracts were reviewed.

Two investigators independently searched and reviewed articles for eligibility using the following inclusion criteria:: (1) written in English; (2) used randomized controlled trials (RCTs) design; (3) exposure of interest was the treatment using finasteride; (4) disease of interest was BPH, and (5) mean and standard deviation (SD) for International Prostate Symptom Score (IPSS), total prostate volume (TPV) (cm^3), peak urinary flow (Q_{max}) (ml/s), serum testosterone (pg/ml) or dihydrotestosterone (DHT) (pg/ml) (or data to calculate them were provided) and the number of adverse events (AE) and withdrawal due to AE were provided.

Data extraction

The following data independently extracted by two authors from studies included: first author's last name, publication years, sample size, age, the methods of treatment, treatment duration, the mean and SD for continuous variables, the numbers of any AE, withdrawal due to AE, drug-related AE, and serious AE for dichotomous variables.

Statistical analysis

Dichotomous data were presented as odds ratios (OR) and 95% confidence interval (95% CI), and continuous parameters were shown as weighted mean difference (WMD) and 95% CI. Pooled treatment effect was determined with a random-effects model, which considers between-study variation [12]. Heterogeneity was assessed by using I^2 statistic [13]. Egger's test was used to assess the publication bias [14]. A sensitivity analysis by exclusion of one study at the time was performed to assess the stability of results and potential sources of heterogeneity [15]. Meta-analysis was performed on STATA version 10.0. The level of significance was defined as p-value ≤ 0.05.

RESULTS

Characteristics of included studies

From the search, 487 publications from PubMed and 582 publications from Web of Knowledge were retrieved. A total of 1031 studies were excluded on review of each of the abstract or title. As shown in Figure 1, another 24 publications were further excluded. Thus, 14 publications [8-11, 16-25] (Table 1) covering 17,364 patients were utilized for this report. When a clinical trial reported different outcomes, we then regarded them as a separate study. There were 11 articles that assessed the relationship between finasteride and placebo for BPH risk, 2 publications assessed the association between finasteride and dutasteride for BPH risk, and 2 studies for finasteride and tamsulosin.

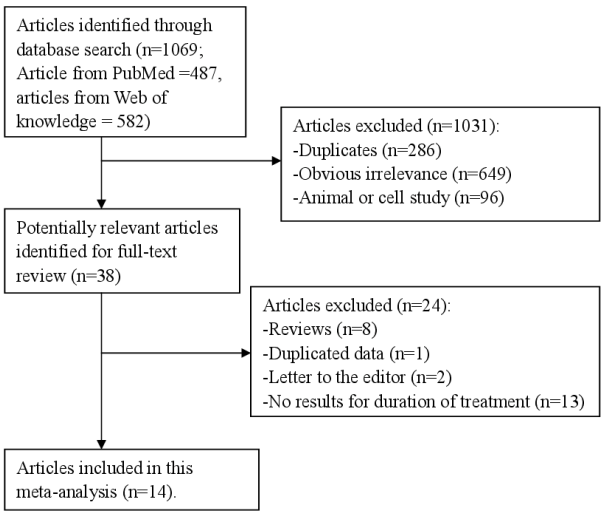

Figure 1: Study flow chart

Efficacy of finasteride interventions

There was only one study that reported the association for IPSS, and a significantly greater reduction in finasteride group than placebo group (WMD= -0.77, 95%CI= -0.97 to -0.57). The relation between finasteride group and placebo for BPH treatment was not significant in Q_{max} (WMD= -0.01, 95% CI= -0.14 to 0.11) (Figure 2). Four studies reported the association for finasteride treatment and TPV, and the association was significant in the treatment of finasteride group than placebo group (WMD= 0.13, 95% CI = 0.00 to 0.26) (Figure 3). The

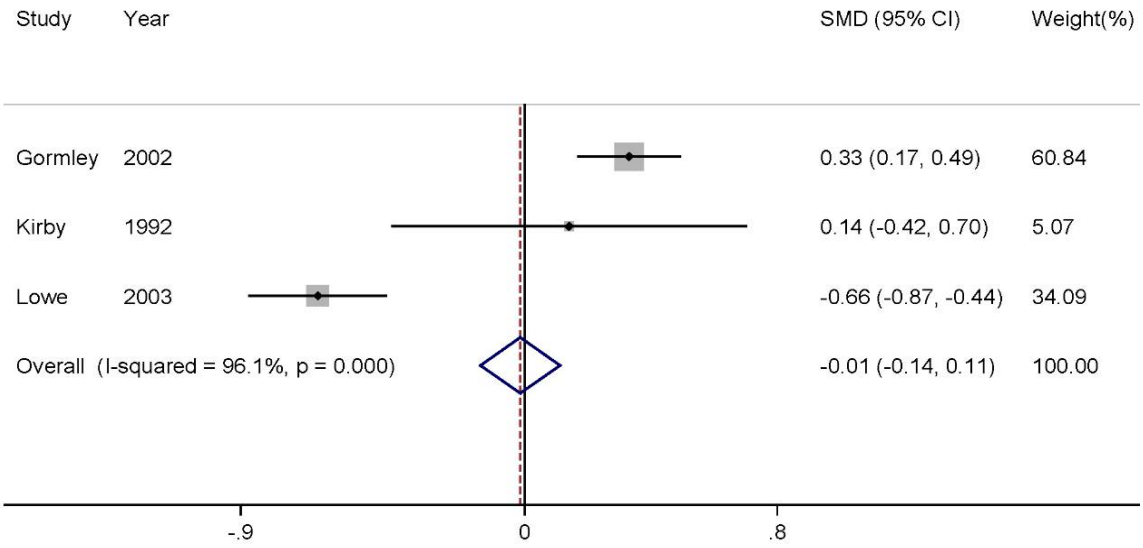

Figure 2: Forest plot and meta-analysis of the treatment for finasteride compared with placebo group with respect to Q_{max}

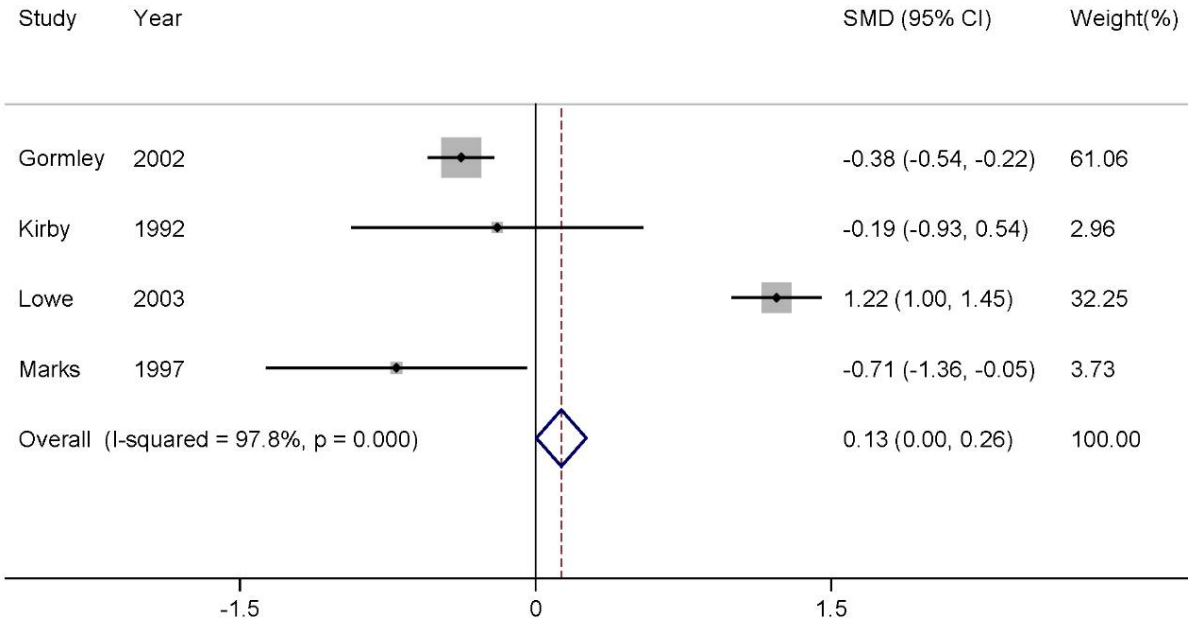

Figure 3: Forest plot and meta-analysis of the treatment for finasteride compared with placebo group with respect to TPV

treatment by finasteride showed a significant reduction association in serum DHT (WMD= -1.18, 95%CI= -1.51 to -0.86) (Figure 4) and increase but not significant in serum testosterone (WMD= 0.19, 95%CI= -0.12 to 0.50) (Figure 5).

In addition, the treatment effects between finasteride group and tamsulosin group showed that no significant association was found in the analyses for IPSS and Q_{max}. The treatment effects of finasteride were supported by a significant increase in serum DHT compared with dutasteride group (WMD= 1.49, 95%CI= 1.07 to 1.91).

Safety of finasteride interventions

There are 6 studies conducted to assess the association of finasteride with AE. Pooled data indicated that there was no significant association in AE in treatment with finasteride than placebo (RR= 1.00, 95%CI= 0.94-1.07) (Figure 6). The association was not significant in withdrawal due to AE for the treatment with finasteride than placebo (RR= 0.98, 95%CI= 0.85-1.14). Pooled data indicated drug-related AE were higher in finasteride group than that in placebo group (RR= 1.95, 95%CI= 1.31-2.90) (Figure 7). No significant association was found in the serious AE (RR= 0.91, 95%CI= 0.80-1.03)

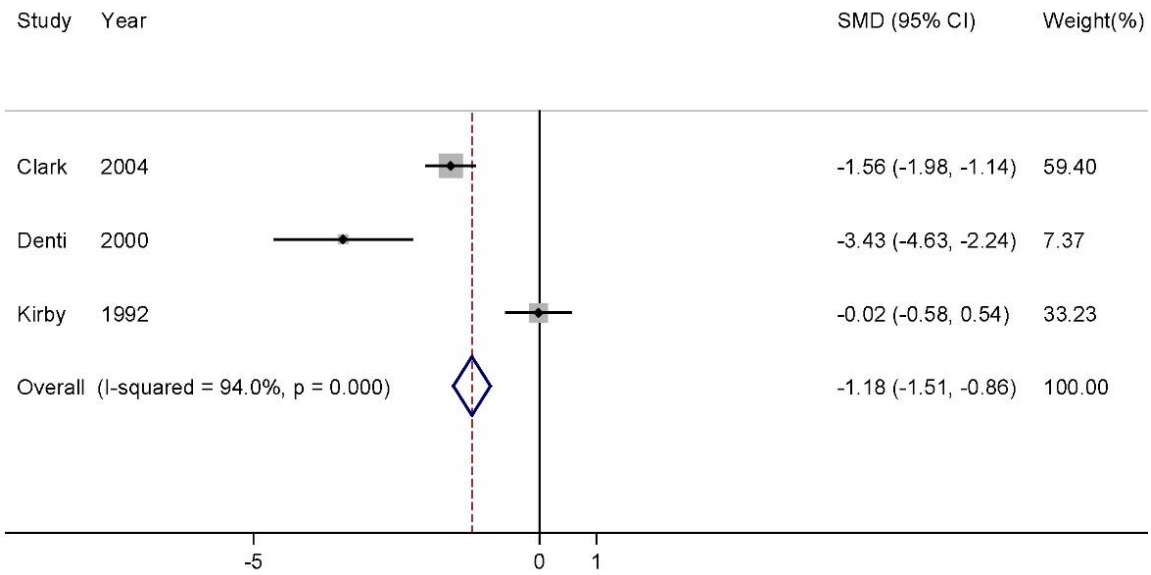

Figure 4: Forest plot and meta-analysis of the treatment for finasteride compared with placebo group with respect to serum DHT.

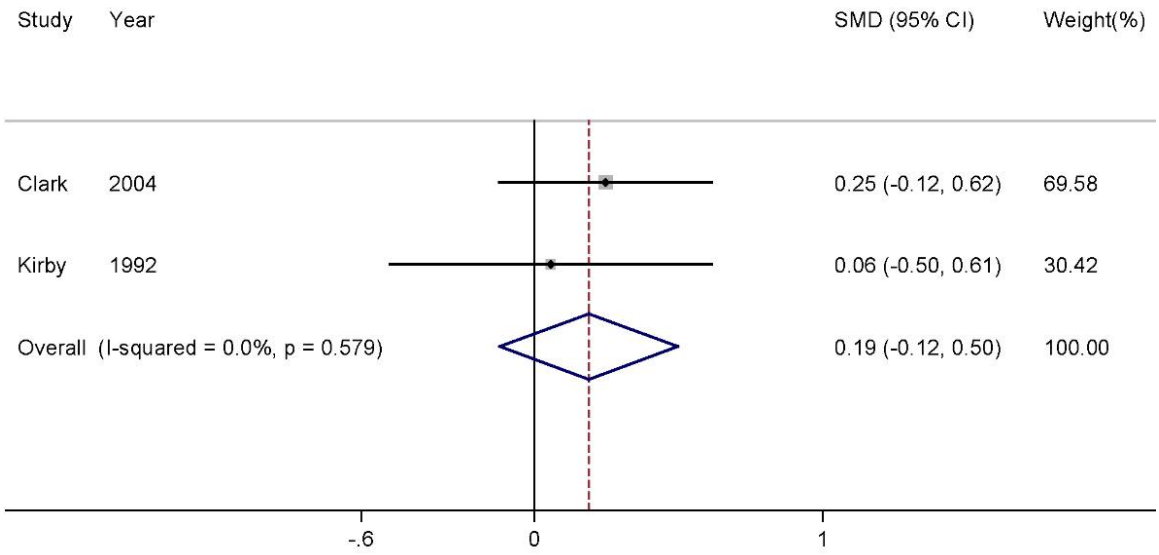

Figure 5: Forest plot and meta-analysis of the treatment for finasteride compared with placebo group with respect to serum testosterone

In addition, withdrawal from finasteride or tamsulosin was not associated with ADE, drug-related adverse events. Similarly, ADE and withdrawal due to adverse events were not significantly associated with the treatment of finasteride compared with dutasteride group.

Sensitivity analysis and publication bias

A sensitivity analysis of the relationship between finasteride group and placebo group was conducted accordingly. However, no apparent effect was found on overall merged results. The potential publication bias assessed by Egger's test (*P*= 0.176) showed no significant publication bias between finasteride group and placebo group for the treatment of BPH was found.

DISCUSSION

Findings from this study demonstrated that finasteride could improve the symptom score of IPSS and TPV. The treatment effect of finasteride had a reduction in serum DHT compared with placebo group. However, drug-related AE reported higher in the finasteride group than in the placebo group. No significant associations were found in other three adverse events group. We also found a greater increased in serum DHT for the efficacy of finasteride than that in dutasteride group.

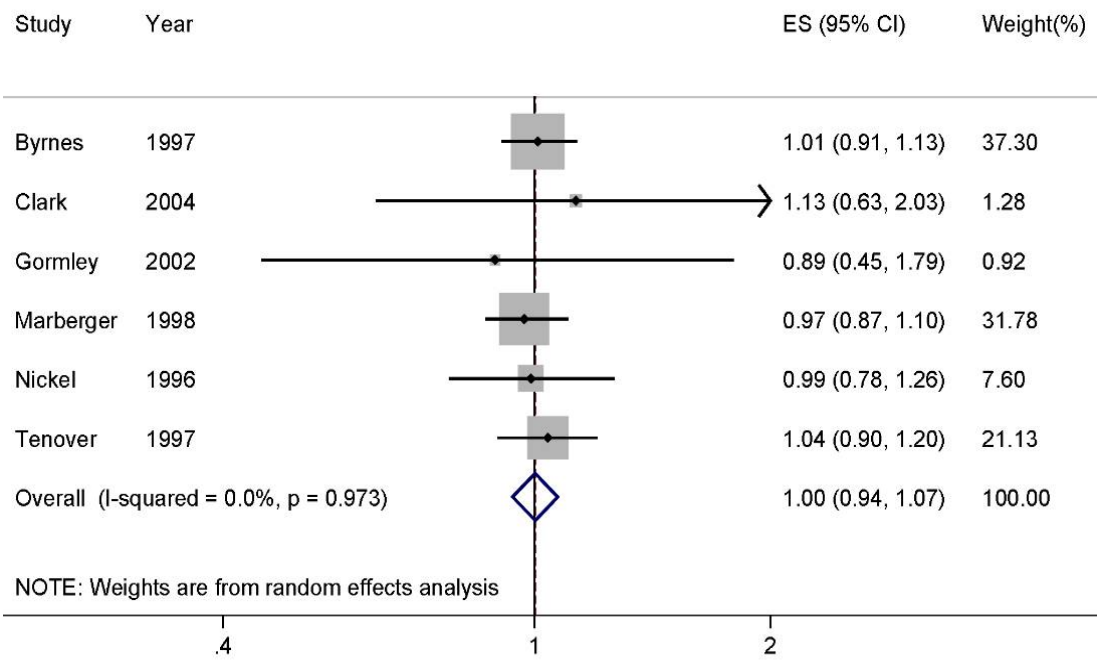

Figure 6: The forest plot of BPH symptoms measured by AE about finasteride compared with placebo group.

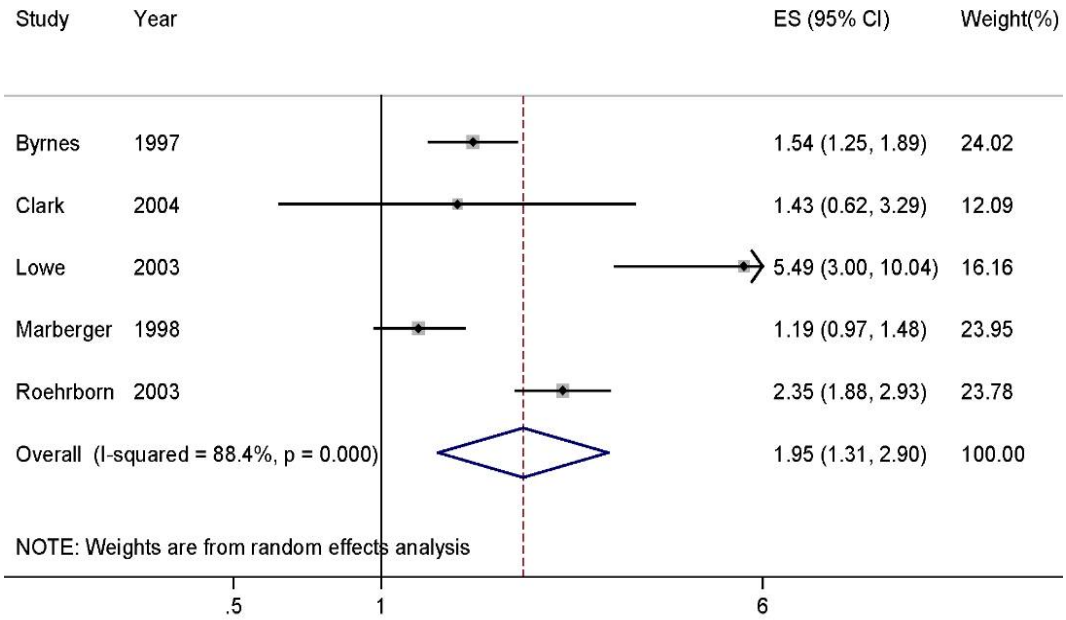

Figure 7: The forest plot of BPH symptoms measured by drug-related adverse events about finasteride compared with placebo group

Several mechanisms have been proposed to explain the possible role of finasteride in the treatment of BPH. Finasteride belongs to 5-alpha reductase inhibitor (5-ARI), which is known to inhibit BPH-related disease progression by blocking 5-alpha reductase (5AR), which converts testosterone to DHT, a hormone responsible for prostate growth. Finasteride is a selective inhibitor of type II 5AR that could reduce the circulating DHT levels by about 70% [26]. The results in our study are similar to the previous meta-analysis of dutasteride treatment in urinary symptoms (IPSS and Q_{max}), TPV, and potential AE [27]. Like finasteride, dutasteride is a 5-ARI and may have the same effect as finasteride in the treatment of BPH.

The major strength in this meta-analysis is the absence of any significant publication bias as demonstrated with the Egger's test. However, the number of articles analysed are limited by our inclusion criteria. In addition, different doses of the drugs (finasteride: once daily (OD): 5 mg, Dutasteride: OD 0.5 mg, Tamsulosin: OD 0.4mg

or 0.2mg) were used in the studies that may lead to between-study heterogeneity. However, a random effect model was used in this report, which assumes that the individual specific effects are uncorrelated with the independent variables. Furthermore, the lack of information on the distribution of clinical and methodological variables can lead to potential sources of heterogeneity or inconsistency in each of the more specific test groups.

CONCLUSION

This study suggests that finasteride improves symptom score (IPSS and TPV) and reduce serum DHT in patients with BPH. However, potential AE, especially drug-related AE should be given special attention in finasteride treatment.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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