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[Intervention Review]

Beta-sitosterols for benign prostatic hyperplasia

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ABSTRACT

Background

Benign prostatic hyperplasia (BPH), nonmalignant enlargement of the prostate, can lead to obstructive and irritative lower urinary tract symptoms (LUTS). The pharmacologic use of plants and herbs (phytotherapy) for the treatment of LUTS associated with BPH has been growing steadily. Phytotherapeutic preparations containing beta-sitosterols, derived from the South African star grass, Hypoxis rooperi, or from species of Pinus and Picea, are available for the treatment of BPH.

Objectives

This systematic review aimed to assess the effects of beta-sitosterols (B-sitosterol) on urinary symptoms and flow measures in men with of benign prostatic hyperplasia (BPH).

Search methods

Trials were searched in computerized general and specialized databases (MEDLINE, EMBASE, Cochrane Library, Phytodok), by checking bibliographies, and by contacting manufacturers and researchers.

Selection criteria

Trials were eligible for inclusion provided they (1) randomized men with BPH to receive B-sitosterol preparations in comparison to placebo or other BPH medications, and (2) included clinical outcomes such as urologic symptom scales, symptoms, or urodynamic measurements.

Data collection and analysis

Information on patients, interventions, and outcomes was extracted by at least two independent reviewers using a standard form. Main outcome measure for comparing the effectiveness of B-sitosterols with placebo and standard BPH medications was the change in urologic symptom scale scores. Secondary outcomes included changes in nocturia as well as urodynamic measures (peak and mean urine flow, residual volume, prostate size). Main outcome measure for side effects was the number of men reporting side effects.

Main results

Five hundred nineteen men from four randomized, placebo-controlled, double-blind trials, (lasting 4 to 26 weeks) were assessed. Three trials used non-glucosidic B-sitosterols and one utilized a preparation that contained 100% B-sitosteryl-B-D-glucoside. B-Sitosterols improved urinary symptom scores and flow measures. The weighted mean difference (WMD) for the IPSS was -4.9 IPSS points (95% CI = -6.3 to -3.5, n = 2 studies). The WMD for peak urine flow was 3.91 mL/s (95% CI = 0.91 to 6.90, n = 4 studies) and the WMD for residual volume was -28.62 mL (95% CI = -41.42 to -15.83, n = 4 studies). The trial using 100% B-sitosteryl-B-D-glucoside (WA184) show improvement in urinary flow measures. B-sitosterols did not significantly reduce prostate size compared to placebo. Withdrawal rates for men assigned to B-sitosterol and placebo were 7.8% and 8.0%, respectively.

Authors' conclusions

The evidence suggests non-glucosidic B-sitosterols improve urinary symptoms and flow measures. Their long term effectiveness, safety and ability to prevent BPH complications are not known.

PLAIN LANGUAGE SUMMARY

Herbal medicines containing beta-sitosterols may help to relieve the urinary symptoms and urinary flow problems caused by an enlarged prostate gland (benign prostatic hyperplasia)

Benign prostatic hyperplasia (BPH), enlargement of the prostate gland, is common in older men. An enlarged prostate can interfere with urination, increasing the frequency and urge, or causing problems emptying the bladder. Both surgery and drugs are used to try to treat BPH. However, using herbal medicines to try to relieve the symptoms of BPH is becoming common. One popular herbal treatment for BPH contains active ingredients called beta-sitosterols. The review found that beta-sitosterol treatments were well tolerated and improved urinary symptoms and flow measures in men with mild to moderate BPH. More research into long-term effects of beta-sitosterols is needed.

BACKGROUND

Benign prostatic hyperplasia (BPH) is a nonmalignant enlargement of the prostate. The enlarging prostate results in the progressive occlusion of the proximal urethra and can lead to obstructive and irritative urinary tract symptoms. The majority of men over the age of 60 are considered to have urinary symptoms attributable to BPH. In the United States treatment of BPH accounts for approximately 1.7 million physician office visits (Guess 1992) and results in more than 300,000 prostatectomies annually (McConnell 1994). Several strategies have been utilized to reduce the symptoms of BPH, including pharmacologic therapies (Oesterling 1995).

The pharmacologic use of plants and herbs (phytotherapy) for the treatment of BPH symptoms has been growing steadily in most countries. Phytotherapeutic agents represent nearly half of the medications dispensed for BPH in Italy (Di Silverio 1993). In Germany and Austria phytotherapies represent over 90% of all drugs prescribed for the treatment of BPH (Buck 1996). Use of phytotherapies in the United States have markedly increased. They are readily available as nonprescription dietary supplements and are often recommended in "natural health food stores or books" for self treatment of BPH symptoms. Nearly a quarter of men seen with previously treated BPH at a university urology clinic for urinary symptoms indicated they had used phytotherapeutic agents (Gerber 1998).

There are about 30 phytotherapeutic compounds utilized for the treatment of BPH including those that contain B-sitosterols (Buck 1996). B-sitosterol is a phytopharmacologic extract containing a mixture of phytosterols, with smaller amounts of other sterols, bonded with glucosides. These phytosterols are commonly derived from the South African star grass, Hypoxis rooperi, or from species of *Pinus* and *Picea*. The purported active constituent is termed B-sitosterol. Additionally, the quantity of B-sitosterol-B-D-glucoside is often reported. The exact mechanism of action of B-sitosterols is not known although it may be related to cholesterol metabolism or anti-inflammatory effects (via interference with prostaglandin metabolism) (Lowe 1996). Despite wide spread use, the clinical efficacy of B-sitosterols to improve BPH symptoms and urody-

namic measures remains unclear. Therefore, we wished to assess the effects of preparations containing B-sitosterols.

OBJECTIVES

The main outcome was the effect of B-sitosterols versus placebo or active control in improving urologic symptom scale scores. Secondary outcomes included changes in peak and mean urine flow, residual urine volume, prostate size and side effects associated with the use of B-sitosterols.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled clinical trials

Types of participants

Men with symptomatic benign prostatic hyperplasia

Types of interventions

Comparison of preparations of B-sitosterols with placebo or medical therapies for BPH with a treatment duration of at least 30 days.

Types of outcome measures

Urologic symptom scores (Boyarsky, American Urologic Association Score, International Prostate Symptom Score (IPSS); Urodynamic measures (defined as change in peak urine flow (measured in mL/s), mean urine flow (measured in ml/sec), residual urine volume (measured in ml), nocturia (measured in times per evening) and changes in prostate size (measured in cc).

Search methods for identification of studies

We searched Medline for 1966 to 1998 using a combination of the March 1996 update of the optimally sensitive search strategy for trials from the Cochrane Collaboration with the MeSH headings "prostatic hyperplasia," "phytosterols," "plant extracts," "sitosterols," "Harzol," "Azuprostat" and "WA184" including all subheadings (Dickersin 1994). A search of Embase, years 1974-1998 (performed in July 1998) was done by using a similar approach. We also searched the private database Phytodok, Munich Germany, and the Cochrane Library, including the database of the Cochrane Prostate Review Group and the Cochrane Field for Complementary Medicine. Reference lists of identified trials and reviews were searched and expert relevant trialists were asked to identify additional published or unpublished trials. There were no language restrictions.

Data collection and analysis

Eligibility:
At least two reviewers independently decide on eligibility.
Extraction:
Data extraction, including study characteristics, was performed independently by two reviewers. Missing or additional information was sought from authors/sponsors. Extracted data was reviewed by the principal reviewer and discrepancies resolved by discussion.
Assessment of methodological quality:
As a measure of overall methodologic study quality we assessed the quality of concealment of treatment allocation according to a scale developed by Schulz (Schulz 1995) assigning 1 to poorest quality and 3 to best quality: 1 = trials in which concealment was inadequate (e.g. such as alternation or reference to case record numbers or to dates of birth); 2 = trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories; and 3 = trials deemed to have taken adequate measures to conceal allocation (e.g. central randomization; numbered or coded bottles or containers; drugs prepared by the pharmacy; serially numbered, opaque, sealed envelopes etc. that contained elements convincing of concealment). Additionally, we assessed whether study participants and investigators were blinded to the treatment provided.
Summarizing results of primary studies:
Outcomes:
The mean urologic symptom scores (IPSS and Boyarsky), peak and mean urine flow (mL/s), residual urine volume (mL), nocturia (times per evening) and prostate size (cc). The number and percent of men reporting specific side effects and/or withdrawing from the study.
Meta-analysis:
A random effects model was used to combine data for all outcomes. For continuous variables, weighted mean differences and their 95% confidence intervals were calculated. The difference between treatment means and their correlated standard error of the difference were calculated using the methods of Lau and Laird (Lau 1996; Laird 1990). Papers reported only the mean values before and after B-sitosterol and control as well as the corresponding standard error of the mean. Because the standard error of the difference between the means (B-sitosterol and control) was not reported, analyses were carried out for 3 different assumed values of correlation (0.25, 0.50, 0.75). This approach was taken in order to test the sensitivity of the results to this unknown parameter. Because there were no statistically significant differences in

the outcomes according to the different correlation coefficients we utilized standard errors of the mean calculated with a correlation coefficient of 0.50. Chi-square tests were used for analysis of bivariate comparisons. Additional sensitivity analyses were performed by excluding the only study that utilized a compound containing 100% B-sitosterol-B-D-glucoside as its B-sitosterol.

RESULTS

Description of studies

The combined search strategies identified 10 reports of trials; four studies met inclusion criteria. All studies were placebo-controlled and included men with mild to moderate symptomatic BPH. Reasons for exclusion included: non-randomized/clinical controlled trials or lacking control groups (Bialluch 1980; Hallwachs 1981; Dorner 1982; Karcher 1982); lack of clinical data (Ebbinghaus 1977); and one was an additional report of a previous publication (Senge 1995). A total of 519 participants were randomized in the four trials. The mean age of participants was 65.4 years and ranged from 34 to 85. Trials lasted between 4 to 26 weeks. The overall rate of dropouts or losses to follow up was 7.9% (41/519).

Studies utilized purified extracts from a variety of plant species. Three studies contained non-glucosidic B-sitosterol, but the dosages ranged from 60 mg/day to 195 mg/ day (Berges 1995; Fischer 1993; Klippel 1997). Two studies utilized a preparation (Azuprostat) that contains at least 70% non-glucosidic B-sitosterol (Fischer 1993; Klippel 1997) and one utilized a preparation with a non-glucosidic B-sitosterol concentration of 50% (Harzol) (Berges 1995). One study utilized a preparation that contained 100% B-sitosteryl-B-D-glucoside (WA184) (Kadow 1986). In the three other trials, the quantity of the B-sitosterol derivative, B-sitosterol-b-D-glucoside was less than 5% of the daily B-sitosterol (Berges 1995; Fischer 1993; Klippel 1997). The mean baseline values for these variables did not differ by treatment and included IPSS score = 15.2 points (n = 377), peak urine flow = 10.2 mL/s (n = 519), residual volume 73.3 mL (n = 519) and prostate size = 49.1 cc (n = 262).

Risk of bias in included studies

Treatment allocation concealment was rated as unclear in three trials (Kadow 1986; Fischer 1993; Klippel 1997) and adequate in one (Berges 1995). All studies were double blinded.

Effects of interventions

Urinary symptoms:

Symptom score results were reported in two studies (Berges 1995; Klippel 1997). The weighted mean difference (WMD) for the IPSS urinary symptom scale scores (scale range = 0 to 35) versus placebo was -4.9 IPSS points (95% confidence interval (CI) = -6.3 to -3.5). The WMD for the Boyarsky quality of life score (scale range = 0 to 27) was -4.5 points (95% CI = -6.0 to -3.0) (Berges 1995).

Subjective evaluation of treatment effects by participants and physicians was reported in one study (Fischer 1993). The weighted risk ratio (RR) for subject evaluation was 8.25 (95% CI = 3.22 to 21.13). The weighted RR for physician evaluation was 11.0 (95% CI = 3.67 to 32.97).

Nocturia:

Nocturia results were reported in 1 study (Fischer 1993). The WMD for was -1.00 times per evening (95% CI = -1.75 to -0.25).

Urinary flow measures and prostate size:

Peak urine flow was reported in four studies (Kadow 1986; Fischer 1993; Berges 1995; Klippel 1997). The WMD for peak urine flow was 3.91 mL/s versus placebo (95% CI = 0.91 to 6.90). With the exclusion of the study that utilized only B-sitosteryl-B-D-glucoside (WA184) (Kadow 1986), the WMD was 5.13 (95% CI = 2.37 to 7.89). The WMD for mean urine flow was 2.60 mL/s (95% CI = 1.30 to 3.90) (Berges 1995). All four studies reported residual volume data (Kadow 1986; Fischer 1993; Berges 1995; Klippel 1997). The WMD was -28.62 mL versus placebo (95% CI = -41.42 to -15.83). Excluding the study that utilized the preparation containing only B-sitosteryl-B-D-glucoside (WA184) (Kadow 1986), the WMD was -29.97 mL (95% CI = -38.27 to -21.66). B-sitosterols did not significantly reduce prostate size compared to placebo (WMD was -6.19, 95% CI = -15.29 to 2.91) (Kadow 1986; Berges 1995).

Adverse effects:

Adverse effects due to B-sitosterol compounds were generally mild in nature and comparable in frequency to placebo. Withdrawal rates were: B-sitosterol 7.8%; Placebo 8.0% (P value = ns). Gastrointestinal side effects were the most common side effects, occurring in 1.6% of men on B-sitosterols and in no men taking placebo. Impotence was reported in 0.5% of men on B-sitosterols. In men randomized to placebo none reported impotence.

DISCUSSION

The available data from this systematic review suggest that B-sitosterols improve urinary symptoms and flow measures, and are associated with few adverse events. Participant baseline characteristics regarding age, prostate volume, peak urine flow and symptom scale score were comparable to previous trials and meta-analyses involving pharmacologic management of BPH (Boyle 1996). The treatment effect size with regard to urologic symptoms and flow are considered clinically relevant and similar to effects reported with other pharmacologic agents in placebo controlled trials (Chapple

1996, Roehrborn 1996). Reported adverse effects were infrequent and mild and the dropout rate was less than 8%.

While all studies used a double-blind method, quality of treatment allocation concealment was deemed adequate in one trial (Berges 1995) and unclear in three (Kadow 1986; Fischer 1993; Klippel 1997). Studies utilized different doses and preparations of B-sitosterol. To date, standardized doses and preparations of B-sitosterols have not been clearly established. Although B-sitosterol is the purported active component, this has not been clearly demonstrated. The only study (Kadow 1986) that used 100% B-sitosteryl-B-D-glucoside (WA184) did not show improvement in urinary flow measures and did not report information on lower urinary tract symptoms. The treatment duration was short with no studies lasting longer than 26 weeks and fewer than 600 men have been evaluated. Therefore, the long term efficacy and safety of B-sitosterols as well as their effectiveness in preventing complications of BPH such as acute urinary retention or the need for surgical interventions is not known.

Only two studies reported results from standardized and validated urologic symptom scales (Berges 1995; Klippel 1997). Secondary outcomes were available from most but not all studies. Combining studies that utilized plant extracts containing different dosages of B-sitosterols may be problematic. However, if an overall quantitative estimate is deemed useful, a random effects model that incorporates between study heterogeneity is appropriate as we have done.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review provides the most complete assessment regarding the effects of B-sitosterols in the treatment of mild to moderate BPH. The available evidence suggests that B-sitosterols are well tolerated and improve urologic symptoms and flow measures. B-sitosterols maybe a useful pharmacologic treatment option for men with mild to moderate BPH, particularly men who would like to avoid or are at increased risk for adverse effects from alpha-blockers or surgical intervention. The long term effectiveness and safety of B-sitosterols and their ability to prevent complications from BPH are not known.

Implications for research

Additional placebo and active-controlled studies (alpha-blockers, 5a-reductase inhibitors and other phytotherapeutic agents such as *Serenoa repens*) are needed. These trials should utilize standardized extracts with known concentrations of B-sitosterols. Future trials should be of sufficient size and duration to detect important differences in outcomes including urologic symptom scale scores (e.g., IPSS), peak and mean urine flow, prostate size, residual urine volume, development of acute urinary retention or need for surgical intervention.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Berges 1995

Methods	Multisite study (8 centres). Randomization: Numbered or coded identical containers administered according to a randomization sequence. Patients blinded: Providers blinded: Lost to follow-up: 5% for secondary outcomes
Participants	Geographic region: Germany Study setting: community n = 200 Age range: 50-80 (inclusion age range) mean: 65.4 Race: White Diagnostic criteria:
Interventions	Control: matching placebo Treatment: Beta-sitosterol* (Harzol) 20 mg t.i.d. (*Beta-sitosterol is the active substance although Harzol contains a variety of phytosterols) Average follow-up: 24 weeks.
Outcomes	Modified Boyarsky score IPSS Symptom Score Quality of Life (points) Peak urine flow (mL/s) Median/mean urine flow (mL/s) Voiding time (s) Bladder residual volume (mL) Prostate volume (mL) Dropouts due to side effects: none
Notes	Exclusions: history of acute urinary retention; prostate cancer; PSA > 10 ng/mL; history of transurethral resection; prostatitis; urinary infection; hematuria; urethral stricture; bladder stones; diabetes; abnormal enzymes; severe cardiopulmonary disease

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Fischer 1993

Methods	Single-site study. Randomization: unclear. Patients blinded: Providers blinded: Lost to follow-up: none
Participants	Geographic region: Germany Study setting: community n = 80 Age range: 34-85 (inclusion age range) mean: 64.0 Race: White Diagnostic criteria: residual urine volumes 100 ml or less; uroflow 20mL/s or less
Interventions	Control: matching placebo Treatment: Beta-sitosterol 65 mg t.i.d. Average follow-up: 4 weeks
Outcomes	Nocturia Uroflow -Peak urine flow (mL/s) Bladder residual volume (mL) Physician and patient overall evaluation Dropouts due to side effects: none
Notes	Exclusions (major): BPH-relevant drugs and drugs which may act on micturition (e.g. estrogens, androgens, corticoids, alpha-blockers, diuretics); cystic calculi; neurogenic micturition difficulties; prostate cancer; history of surgical prostatic or ureteral intervention; urethral stricture or bladder diverticulae

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Kadow 1986

Methods	Single-site study. Randomization: noted but method not described. Patients blinded: Providers blinded: Lost to follow-up: 15%
Participants	Geographic region: UK Study setting: community n = 62 Age range: 53-81 mean: 67.0 Race: White Diagnostic criteria: "prostatism", full urodynamic assessments, Trucut needle biopsy performed to confirm benign hyperplasia

Kadow 1986 (*Continued*)

Interventions	Control: matching placebo Treatment: Beta-sitosterol (WA184) 0.15 mg bid Average follow-up: 24 weeks
Outcomes	Peak urine flow (mL/s) Bladder residual volume (mL) Maximum detrusor pressure at peak flow (cm H2O) Prostate volume (mL) Dropouts due to side effects: none
Notes	Exclusions: prostate cancer; gastrointestinal or hepatobiliary disease; patients in whom overwhelming indications for surgical relief of outflow obstruction existed

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Klippel 1997

Methods	Multisite study (13 centres). Randomization: Numbered or coded identical containers administered according to a randomization sequence. Patients blinded: Providers blinded: Lost to follow-up: 12%
Participants	Geographic region: Germany Study setting: community n = 177 Age range: 50-80 (inclusion age range) mean: 65.4 Race: White Diagnostic criteria: BPH confirmed with DRE. IPSS of at least or > than 6 points. Residual urinary volume 30-150 mL. Peak flow less than/equal to 15 mL/s, at a voiding volume of at least or > than 150 mL
Interventions	Control: matching placebo Treatment: Beta-sitosterol 65 mg bid (derived from species Hypoxis, Pinus or Picea) Average follow-up: 24 weeks
Outcomes	IPSS symptom score (points). Quality of life score (points). Peak urine flow (mL/s) Bladder residual volume (mL) Dropouts due to side effects:

Klippel 1997 (*Continued*)

Notes	Exclusions (major): IPSS < 6 points; Prostate cancer; PSA > 10 ng/mL; bacterial prostatitis; urinary infection; history of acute urinary retention; history of surgical prostatic intervention; need for surgical intervention in case of urethral stricture or bladder diverticulae; bladder stones; IDDM; severe cardiopulmonary disease; concomitant prostatotropic treatment

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	A - Adequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bialluch 1980	Not a randomized controlled trial.
Dorner 1982	Not a randomized controlled trial (field study only).
Ebbinghaus 1977	No urodynamic measures reported.
Hallwachs 1981	Not a randomized controlled trial.
Karcher 1982	Not a randomized controlled trial.
Senge 1995	Duplicate/additional report of a previous publication

DATA AND ANALYSES

Comparison 1. Beta-sitosterol versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptom score/IPSS (points)	2	342	Mean Difference (IV, Random, 95% CI)	-4.91 [-6.29, -3.53]
2 Symptom score/Boyarsky quality of life scale (points)	1	200	Mean Difference (IV, Random, 95% CI)	-4.50 [-6.05, -2.95]
3 Patient overall evaluation of efficacy (rated very good or good).	1	80	Risk Ratio (M-H, Random, 95% CI)	8.25 [3.22, 21.13]
4 Physician overall evaluation of efficacy (rated very good or good).	1	80	Risk Ratio (M-H, Random, 95% CI)	11.00 [3.67, 32.97]
5 Nocturia (times per evening)	1	80	Mean Difference (IV, Random, 95% CI)	-1.00 [-1.75, -0.25]
6 Peak urine flow (mls/s)	4	474	Mean Difference (IV, Random, 95% CI)	3.91 [0.91, 6.90]
7 Peak urine flow (mls/s): sensitivity analysis	3	421	Mean Difference (IV, Random, 95% CI)	5.13 [2.37, 7.89]
8 Residual volume (mls)	4	475	Mean Difference (IV, Random, 95% CI)	-28.62 [-41.42, -15.83]
9 Residual volume (mls): sensitivity analysis	3	422	Mean Difference (IV, Random, 95% CI)	-29.97 [-38.27, -21.66]
10 Prostate size (cc)	2	216	Mean Difference (IV, Random, 95% CI)	-6.19 [-15.29, 2.91]

Analysis 1.1. Comparison 1 Beta-sitosterol versus placebo, Outcome 1 Symptom score/IPSS (points).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 1 Symptom score/IPSS (points)

Study or subgroup	B-sitosterol N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berges 1995	96	7.5 (6.27)	91	12.8 (6.1)		61.0 %	-5.30 [-7.07, -3.53]
Klippel 1997	77	7.8 (7.02)	78	12.1 (7.06)		39.0 %	-4.30 [-6.52, -2.08]
Total (95% CI)	**173**		**169**			**100.0 %**	**-4.91 [-6.29, -3.53]**

Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.48, df = 1 (P = 0.49); I^2 =0.0%

Test for overall effect: Z = 6.95 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Beta-sitosterol versus placebo, Outcome 2 Symptom score/Boyarsky quality of life scale (points).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 2 Symptom score/Boyarsky quality of life scale (points)

Study or subgroup	B-sitosterol N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berges 1995	100	7.7 (5.6)	100	12.2 (5.6)		100.0 %	-4.50 [-6.05, -2.95]
Total (95% CI)	**100**		**100**			**100.0 %**	**-4.50 [-6.05, -2.95]**

Heterogeneity: not applicable

Test for overall effect: Z = 5.68 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Beta-sitosterol versus placebo, Outcome 3 Patient overall evaluation of efficacy (rated very good or good)..

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 3 Patient overall evaluation of efficacy (rated very good or good).

Study or subgroup	B-sitosterol n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fischer 1993	33/40	4/40		100.0 %	8.25 [3.22, 21.13]
Total (95% CI)	**40**	**40**		**100.0 %**	**8.25 [3.22, 21.13]**
Total events: 33 (B-sitosterol), 4 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.40 (P = 0.000011)					
Test for subgroup differences: Not applicable					

Analysis 1.4. Comparison 1 Beta-sitosterol versus placebo, Outcome 4 Physician overall evaluation of efficacy (rated very good or good)..

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 4 Physician overall evaluation of efficacy (rated very good or good).

Study or subgroup	B-sitosterol n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fischer 1993	33/40	3/40		100.0 %	11.00 [3.67, 32.97]
Total (95% CI)	**40**	**40**		**100.0 %**	**11.00 [3.67, 32.97]**
Total events: 33 (B-sitosterol), 3 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.28 (P = 0.000019)					
Test for subgroup differences: Not applicable					

Analysis 1.5. Comparison 1 Beta-sitosterol versus placebo, Outcome 5 Nocturia (times per evening).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

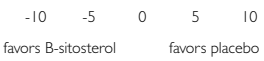
Outcome: 5 Nocturia (times per evening)

Study or subgroup	B-sitosterol N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Fischer 1993	40	1.2 (1.71)	40	2.2 (1.71)		100.0 %	-1.00 [-1.75, -0.25]
Total (95% CI)	**40**		**40**			**100.0 %**	**-1.00 [-1.75, -0.25]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.62 (P = 0.0089)

Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1 Beta-sitosterol versus placebo, Outcome 6 Peak urine flow (mls/s).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

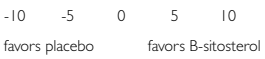
Outcome: 6 Peak urine flow (mls/s)

Study or subgroup	B-sitosterol N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berges 1995	95	15.2 (6.43)	91	11.4 (6.3)		27.1 %	3.80 [1.97, 5.63]
Fischer 1993	40	23.1 (7.08)	40	14.7 (7.08)		22.8 %	8.40 [5.30, 11.50]
Kadow 1986	25	10.75 (3.5)	28	10.37 (3.7)		26.7 %	0.38 [-1.56, 2.32]
Klippel 1997	77	19.4 (9.21)	78	15.7 (9.27)		23.4 %	3.70 [0.79, 6.61]
Total (95% CI)	**237**		**237**			**100.0 %**	**3.91 [0.91, 6.90]**

Heterogeneity: $Tau^2 = 7.75$; $Chi^2 = 19.43$, df = 3 (P = 0.00022); $I^2 = 85\%$

Test for overall effect: Z = 2.56 (P = 0.011)

Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1 Beta-sitosterol versus placebo, Outcome 7 Peak urine flow (mls/s): sensitivity analysis.

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

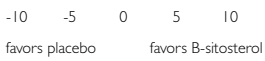
Outcome: 7 Peak urine flow (mls/s): sensitivity analysis

Study or subgroup	B-sitosterol N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berges 1995	95	15.2 (6.43)	91	11.4 (6.3)		39.3 %	3.80 [1.97, 5.63]
Fischer 1993	40	23.1 (7.08)	40	14.7 (7.08)		29.7 %	8.40 [5.30, 11.50]
Klippel 1997	77	19.4 (9.21)	78	15.7 (9.27)		31.1 %	3.70 [0.79, 6.61]
Total (95% CI)	**212**		**209**			**100.0 %**	**5.13 [2.37, 7.89]**

Heterogeneity: $Tau^2 = 4.18$; $Chi^2 = 6.85$, df = 2 (P = 0.03); $I^2 = 71\%$

Test for overall effect: Z = 3.65 (P = 0.00027)

Test for subgroup differences: Not applicable



Analysis 1.8. Comparison 1 Beta-sitosterol versus placebo, Outcome 8 Residual volume (mls).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

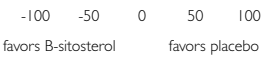
Outcome: 8 Residual volume (mls)

Study or subgroup	N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berges 1995	96	30.4 (43.31)	91	54.3 (42.16)		37.2 %	-23.90 [-36.15, -11.65]
Fischer 1993	40	37.5 (39.4)	40	74.8 (39.4)		27.8 %	-37.30 [-54.57, -20.03]
Kadow 1986	25	144 (125.8)	28	103 (133.13)		3.2 %	41.00 [-28.74, 110.74]
Klippel 1997	77	25.6 (47.3)	78	59.1 (47.6)		31.9 %	-33.50 [-48.44, -18.56]
Total (95% CI)	**238**		**237**			**100.0 %**	**-28.62 [-41.42, -15.83]**

Heterogeneity: $Tau^2 = 75.57$; $Chi^2 = 5.77$, df = 3 (P = 0.12); $I^2 = 48\%$

Test for overall effect: Z = 4.39 (P = 0.000012)

Test for subgroup differences: Not applicable

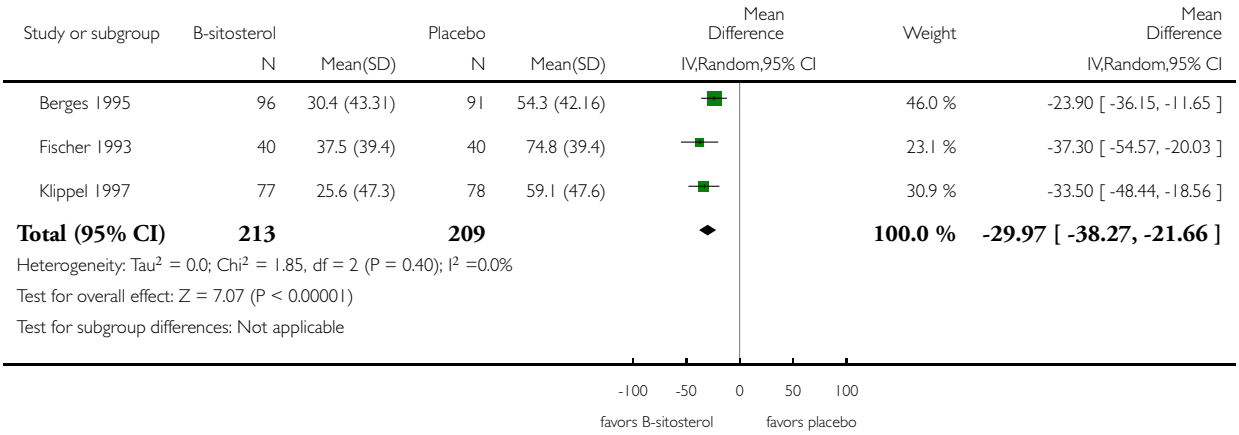


Analysis 1.9. Comparison 1 Beta-sitosterol versus placebo, Outcome 9 Residual volume (mls): sensitivity analysis.

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 9 Residual volume (mls): sensitivity analysis

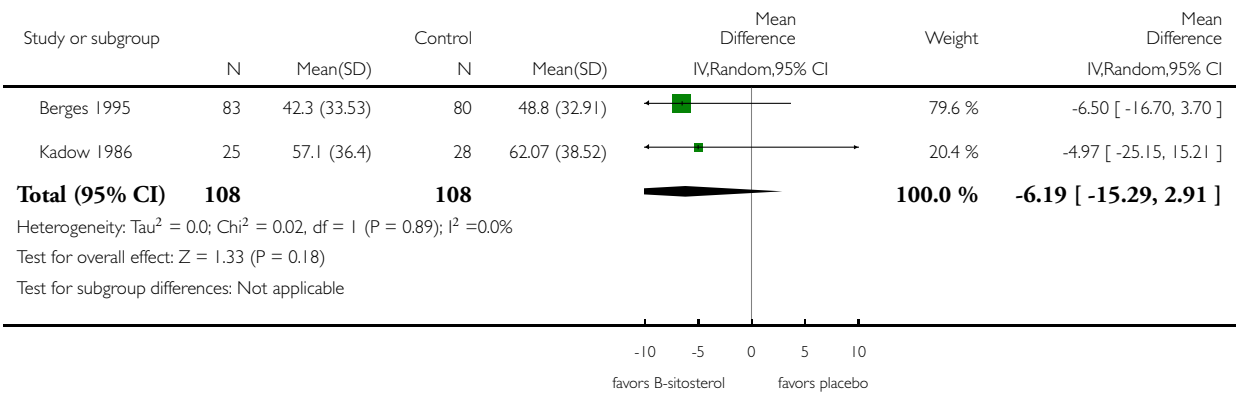


Analysis 1.10. Comparison 1 Beta-sitosterol versus placebo, Outcome 10 Prostate size (cc).

Review: Beta-sitosterols for benign prostatic hyperplasia

Comparison: 1 Beta-sitosterol versus placebo

Outcome: 10 Prostate size (cc)



WHAT'S NEW

Last assessed as up-to-date: 18 May 1999.

Date	Event	Description
30 March 2011	Amended	Primary author has indicated he cannot update the review. Subsequently, it has been withdrawn

HISTORY

Protocol first published: Issue 1, 1998

Review first published: Issue 4, 1999

Date	Event	Description
12 May 2008	Amended	Converted to new review format.
19 May 1999	New citation required and conclusions have changed	Substantive amendment

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Dept. of Veterans Affairs Health Services Research and Development Program, USA.
- Minneapolis/VISN-13 Center for Chronic Diseases Outcomes Research (CCDOR), USA.

External sources

- No sources of support supplied

NOTES

Primary author has indicated he cannot update the review. Subsequently, it has been withdrawn.

INDEX TERMS

Medical Subject Headings (MeSH)

Phytotherapy; Prostatic Hyperplasia [*drug therapy]; Sitosterols [*therapeutic use]; Urodynamics

MeSH check words

Humans; Male