Evidence Is Enough?: A Systematic Review and Network Meta-Analysis of the Efficacy of Tamsulosin 0.2 mg and Tamsulosin 0.4 mg as an Initial Therapeutic Dose in Asian Benign Prostatic Hyperplasia Patients

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Purpose: We compared the efficacy of tamsulosin between 0.2 mg and 0.4 mg in Asian prostatic hyperplasia (BPH) patients using network meta-analysis due to lack of studies with direct comparison.
Methods: The literature search was conducted using the MEDLINE, Embase, and Cochrane Library. Keywords used were "BPH," "tamsulosin," "placebo." Experimental groups were defined as tamsulosin 0.2 mg (Tam 0.2) and 0.4 mg (Tam 0.4) and common control group was defined as placebo for indirect treatment comparison. Mixed treatment comparison was performed including one direct comparison study.
Results: Seven studies met the eligible criteria. Indirect treatment comparison revealed that total International Prostate Symptoms Score (IPSS) and quality of life score of IPSS were not significantly different in Tam 0.2 and Tam 0.4 (P > 0.05). There was no significant difference of maximal flow rate and postvoid residual urine volume in Tam 0.2 and Tam 0.4 (P > 0.05). Mixed treatment comparison including one direct comparison study showed inconsistency (P < 0.001). Therefore, analysis using direct treatment comparison effect sizes of Tam 0.2 vs. placebo and Tam 0.4 vs. placebo was done and there was no significant difference.
Conclusions: Network meta-analysis showed no difference of efficacy between tamsulosin 0.2 mg and 0.4 mg and the evidence of tamsulosin 0.4 mg as initial dose for Asian BPH patient seems to be insufficient. Therefore, initial dose of tamsulosin for Asian BPH patient should be 0.2 mg.

Keywords: Prostatic Hyperplasia; Tamsulosin; Asian; Men; Dose

- *HIGHLIGHTS*
  - Network meta-analysis with mixed treatment comparison showed no significant difference between tamsulosin 0.2 mg and 0.4 mg as initial dose and the result by a study reported better effect of tamsulosin 0.4 mg was inconsistent with previous studies.
  - Therefore, tamsulosin 0.2 mg should be initial standard dose in Asian BPH patients.

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INTRODUCTION

Tamsulosin is an oral medicine commonly used to treat lower urinary tract symptoms (LUTS) of men with benign prostatic hyperplasia (BPH). Generally, the initial treatment dose is different between Asian and Western men with BPH. Tamsulosin 0.2 mg (Tam 0.2) is recommended as the initial dose for Asian men with BPH, while the recommended dose for Western men is tamsulosin 0.4 mg (Tam 0.4) [1]. The difference of initially recommended doses between Asian and Western men with BPH was based on clinical trials meant to evaluate efficacy and adverse effect; therefore, the initial treatment dose was decided as 0.2 mg for Asian men and 0.4 mg for Western men [2]. In Korea as well as in other Asian countries, men experiencing LUTS due to BPH have an improvement of symptoms and effects after initial treatment with Tam 0.2 mg compared with men treated with other types of alpha-blockers [3,4]. Therefore, the general consensus of a standard initial dose of Tam 0.2 in Asian men is a reasonable estimate for the treatment of LUTS due to BPH.

Recently, Kim et al. [5] reported results comparing the efficacy between Tam 0.2 and Tam 0.4 as an initial dose in Korean men with LUTS due to BPH. The investigators noted that Korean men with BPH receiving Tam 0.4 showed significant improvements on the International Prostatic Symptom Score (IPSS) compared with men receiving Tam 0.2 as their initial treatment dose after 12 weeks of medication. This result is different from those of the above researchers who investigated tamsulosin in Asian men with BPH and used Tam 0.2 as the standard dose for initial treatment [1-4]. Therefore, a reassessment of the efficacy and safety of tamsulosin in Asian men with BPH is necessary to clarify this discrepancy between the recent study [5] and the general consensus [1-4]. However, direct comparison studies to compare the efficacy and safety between Tam 0.2 and Tam 0.4 as the initial treatment dose in Asian men with BPH are insufficient.

Therefore, we compared the effect of Tam 0.2 and Tam 0.4 as the initial treatment dose using network meta-amalysis (NMA).

MATERIALS AND METHODS

This systematic review and network meta-analysis was performed according to the standard PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol and the Cochrane Collaboration [6].

Data Sources and Literature Searches

The electronic databases screened were MEDLINE (1966 through January 2016) and Cochrane Library (1993 through January 2016). Medical Subject Headings terms were used. The search formula was Search ("tamsulosin" [Supplementary Concept]) OR "tamsulosin"[tiabkw] OR "YM178" [all]) AND ("Placebos"[Mesh] OR "placebo"[tiabkw]) AND ("Lower Urinary Tract Symptoms"[Mesh] OR "Lower Urinary Tract Symptoms"[tiabkw] OR "LUTS"[tiabkw] OR "benign prostatic hyperplasia"[tiabkw] OR "BPH"[tiabkw]). The searches were no language limitation. The same search formula as for Emtree was adopted for the Embase search. Prospective randomized controlled trials (RCTs) using placebo were included in this analysis.

Selection of Studies

Study inclusion criteria were as follows: (1) Interventions were with placebo, Tam 0.2, and/or Tam 0.4 and no dose escalation study from Tam 0.2 to Tam. (2) Participants were diagnosed with BPH. (3) Randomization, blind method, and intention-to-treat (ITT) analysis were performed in RCTs. Only one article using direct treatment comparison (DTC) between Tam 0.2 and Tam 0.4 [4] did not meet selection criteria. However, we input this article to estimate for mixed treatment comparison (MTC) analysis. Two authors (SJK and ISS) independently screened the titles and abstracts of all articles using predefined inclusion and exclusion criteria. The full-text articles were examined independently by another 2 authors (JWK and YSC) to determine whether they met the inclusion criteria. Then, 2 authors (SJK and ISS) independently extracted data using data extraction forms. Final inclusion was determined by the GRADE evaluation discussion using a point estimation system for each article. References and data for each included study were carefully cross-checked to ensure that no overlapping data was present and to maintain the integrity of the meta-analysis.

Types of Interventions and Outcomes

The experimental group received Tam 0.2 or Tam 0.4 and the control group received placebo. The primary outcome was change in BPH as measured by IPSS. Secondary outcomes included quality of life (QoL), maximal flow rate (Qmax), and postvoided residual (PVR) volume.

Indirect Comparison Analysis and Mixed Comparison Analysis: Assessment of Outcome Findings

We conducted all frequentist meta-analyses using the standard

techniques of random effects meta-analysis of continuous variables using inverse variance as described by Deeks et al. [7]. We extracted data from all RCTs with Tam 0.2 and Tam 0.4 arms. We combined the 3-arm trials of Tam 0.2, Tam 0.4, and placebo to calculate DTC and indirect treatment comparison (ITC) for the 4 outcomes of interest. For MTC analysis, we use only IPSS because QoL, Qmax, and PVR were lack of data. We combined DTC estimate with the ITC estimate using the method described by Song et al. [8]. The MTC method is not appropriate for the present NMA because of the fail to meet the basic assumption of consistency between DTC and ITC. However, we conducted MTC method after ITC analysis to emphasize for our research hypothesis that the effect size between Tam 0.2 and Tam 0.4 will not be different. A 2-sided P-value of 0.05 or lower was considered to be significant. The abovementioned analyses were conducted with STATA ver. 14 (Stata Corp LP, College Station, TX, USA).

Quality Assessment

The risk of bias and methodological quality were evaluated in duplicate using the Cochrane Collaboration tool. We graded each parameter as unclear, low risk of bias, or high risk of bias throughout the grade evaluation meeting with all authors.

Assessment of Potential Publication Bias

Publication bias was explained by Funnel plot. Asymmetry find-ings in funnel plots indicate publication bias, but the shape of the plot in the absence of bias depends on the choice of trial arms.

RESULTS

Study Selection Results

The initial search identified a total of 807 articles from electronic databases (PubMed, 62; Cochrane, 97; Embase, 648) and 8 articles from hand-searching. Thirty-nine excluded studies contained overlapping data in more than one database. Upon more detailed screening, an additional 739 papers were excluded for the following reasons: unmatched outcome (243), letter (18), commentary (15), unrelated topic (290), overlapping (43), abstract only (45), review paper (35), and no randomization (50). After screening the titles and abstracts, 37 studies were determined to be eligible for full text review. Among of them, 29 studies were further eliminated because of no prospective clinical trials, no blinding, and insufficient data. Finally, 7 studies [9-15] met our selection criteria and 1 study [4] using direct treatment comparison between Tam 0.2 and Tam 0.4 was inputted to estimate for MTC analysis (Fig. 1). A systematic review of the 8 studies was conducted to assess detailed experimental differences and subject descriptions (Table 1).

Quality Assessment

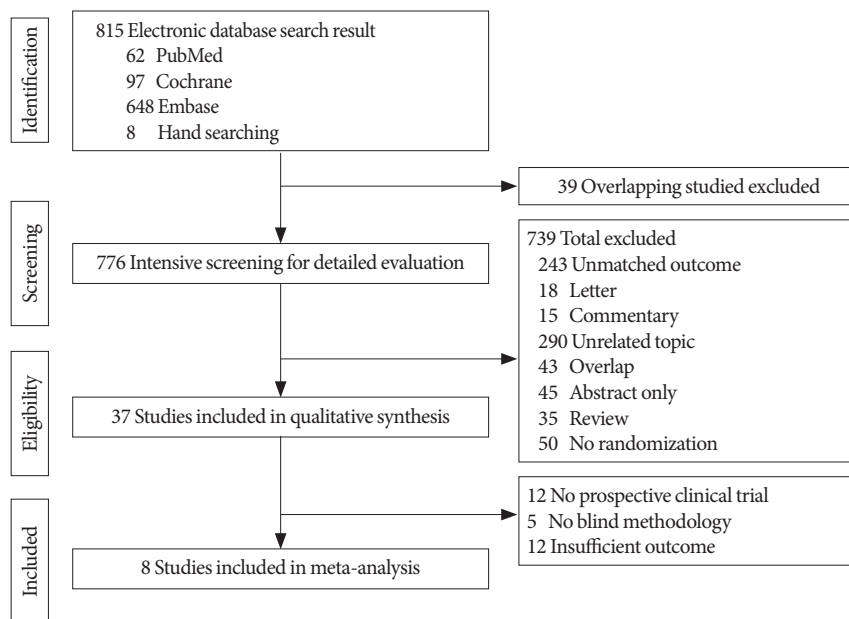Table 2 shows quality assessment of the included studies. All of

Fig. 1. Flowchart of the study selection process.

Table 1. Characteristics of included studies

Study	Intervention, dose (No. of patients)	Country	Mean age (yr)	Baseline IPSS	Study duration (wk)
Nordling 2005 [9]	Placebo (154), Tamsulosin 0.4 mg (158), Finasteride 5 mg (153), Alfuzosin 10 mg (154), Alfuzosin 15 mg (158)	Denmark	64.5	17.6	12
Chapple et al. 2011 [10]	Placebo (190), Tamsulosin 0.4 mg (384), Silodosin 8 mg (381)	UK	65.9	19	12
Narayan et al. 1998 [11]	Placebo (239), Tamsulosin 0.4 mg (248), Tamsulosin 0.8 mg (244)	USA	NA	NA	13
Oelke et al. 2012 [12]	Placebo (172), Tamsulosin 0.4 mg (168), Tadalafil 5 mg (171)	Germany	63.6	17.1	12
Lepor 1998 [13]	Placebo (254), Tamsulosin 0.4 mg (254), Tamsulosin 0.8 mg (247)	USA	NA	19.8	13
Kawabe et al. 2006 [14]	Placebo (89), Tamsulosin 0.2 mg (192), Silodosin 4 mg (175)	Japan	65.6	17	12
Yokoyama et al. 2013 [15]	Placebo (154), Tamsulosin 0.2 mg (152), Tadalafil 2.5 mg (151), Tadalafil 5 mg (155)	Japan	63.1	16.8	12
Kim 2016[a]	Placebo (160), Tamsulosin 0.4 mg (152), Tamsulosin 0.2 mg (159)	Korea	NA	19.9	12

IPSS, International Prostate Symptoms Score; NA, not available.
[a] American Urological Association 2016 abstract, a randomised, double-blind, phase 3 trial in Korean men.

Table 2. The quality assessment of included studies

Study	Random sequence	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Loss of following-up	Intent-to-treat analysis	Selective reporting	Other sources of bias
Nordling 2005 [9]	Low	Unclear	Low	Low	Low	Yes	Yes	Low	Unclear
Chapple et al. 2011 [10]	Low	Low	Low	Low	Low	Yes	Yes	Low	Unclear
Narayan et al. 1998 [11]	Low	Unclear	Low	Low	Low	Yes	Yes	Low	Unclear
Oelke et al. 2012 [12]	Low	Low	Low	Low	Low	Yes	Yes	Low	Unclear
Lepor 1998 [13]	Low	Unclear	Low	Low	Low	Yes	Yes	Low	Unclear
Kawabe et al. 2006 [14]	Low	Unclear	Low	Low	Low	Yes	Yes	Low	Unclear
Yokoyama et al. 2013 [15]	Low	Low	Low	Low	Low	Yes	Yes	Low	Unclear
Kim 2016[a]	Low	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear	High

IPSS, International Prostate Symptoms Score.
[a] American Urological Association 2016 abstract, a randomised, double-blind, phase 3 trial in Korean men.

the studies described randomization, blinding, ITT analysis, and had no selective reporting bias except for the study by Kim et al. [5] using RCT, double-blind method in Korean men is one abstract of American Urological Association 2016.

Outcome Findings

Indirect treatment comparison

A total of 7 trials included 2,767 subjects (placebo, 1,234; Tam 0.2, 344; Tam 0.4, 1,189) in indirect comparison analysis [2,10-15]. Fig. 2 showed all outcomes indirect comparison analysis results between Tam 0.2 and Tam 0.4. The adjusted indirect

comparison analysis effect size and heterogeneity statistic P-value of IPSS, QoL, PVR, and Qmax were 0.02 (95% confidence interval [CI], -0.25 to 0.29) and P=0.880, 0.07 (95% CI: -0.23, 0.37) and P=0.663, 0.07 (95% CI, -0.24 to 0.39) and P=0.641, and -0.06 (95% CI, -0.72 to 0.60) and P=0.868, respectively. There were not statistical differences between 2 treatments and there were no evidence of heterogeneity in all outcomes.

Mixed treatment comparison

A total of 8 trials included 3,238 subjects (placebo, 1,394; Tam 0.2, 503; Tam 0.4, 1,341) in MTC analysis for IPSS [5,9-15]. Fig. 3
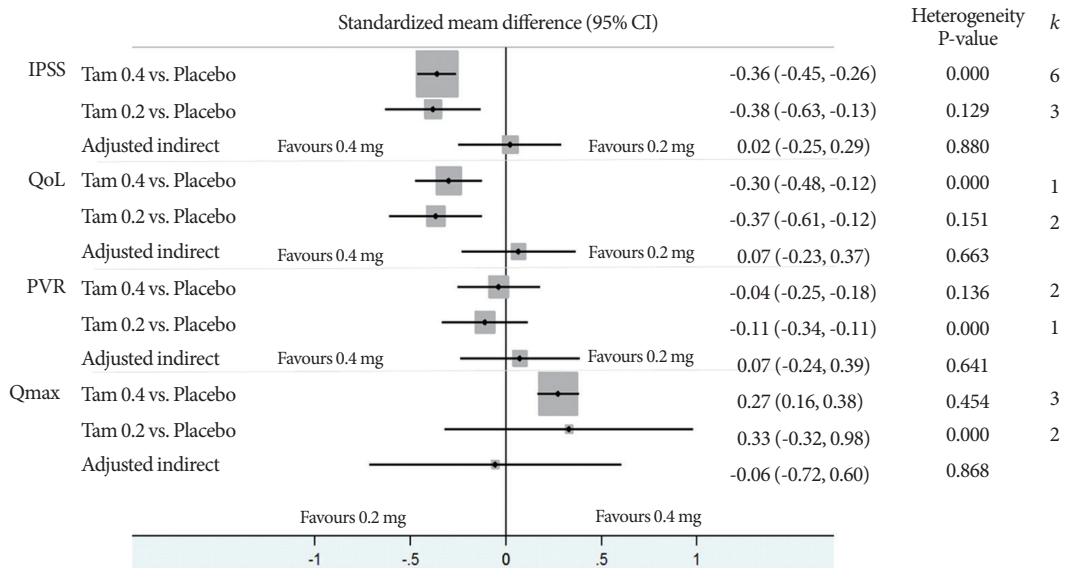
Fig. 2. Standardized mean difference of adjusted indirect comparisions. k, number of effect sizes; CI, confidence interval; IPSS, International Prostate Symptoms Score; QoL, quality of life; PVR, postvoid residual; Qmax, maximal flow rate; Tam 0.2, tamsulosin 0.2 mg; Tam 0.4, tamsulosin 0.4 mg.
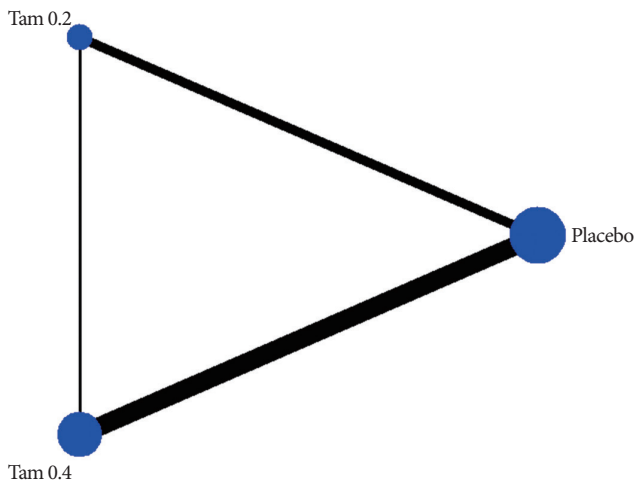

Fig. 3. The network plot of pairwise comparisons from the included trials. The lines indicate available direct comparisons from included randomized controlled trials. The width of the lines is proportional to the number of studies for the comparisons; Tam 0.2, tamsulosin 0.2 mg; Tam 0.4, tamsulosin 0.4 mg.

shows the network plot of pairwise comparisons from the included trials (dTam 0.2-placebo [5,14,15], dTam 0.4-placebo [5,9-13], and dTam 0.4-Tam 0.2 [5]). Fig. 4 presented the contribution plot for each direct comparison in columns. The entire influences of direct comparison were 39.8%, 35.2%, and 25.0% for dTam 0.2-placebo, dTam 0.4-Tam 0.2, and dTam
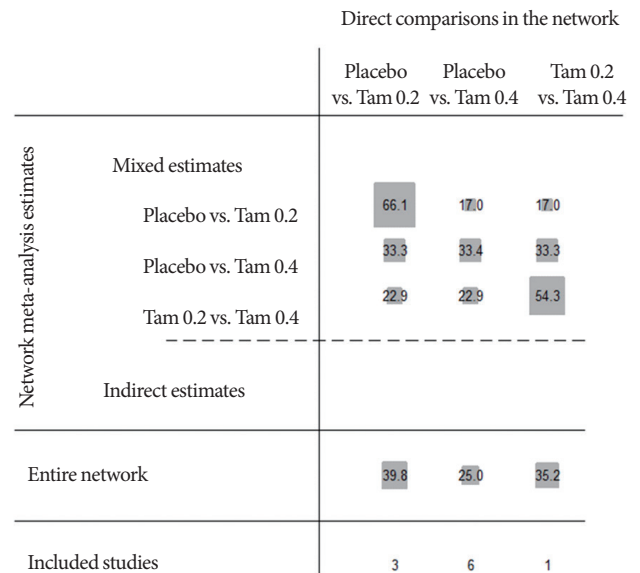

Fig. 4. Contribution plot for mixed treatment comparison network. The size of each square is proportional to the weight attached to each direct summary effect (horizontal axis) for the estimation of each network summary effects (vertical axis). The numbers re-express the weights as percentages; Tam 0.2, tamsulosin 0.2 mg; Tam 0.4, tamsulosin 0.4 mg.

0.4-placebo, respectively.

The inconsistency test gives a P-value of <0.001, thus we can use only direct comparison analysis effect sizes of Tam 0.2 vs.
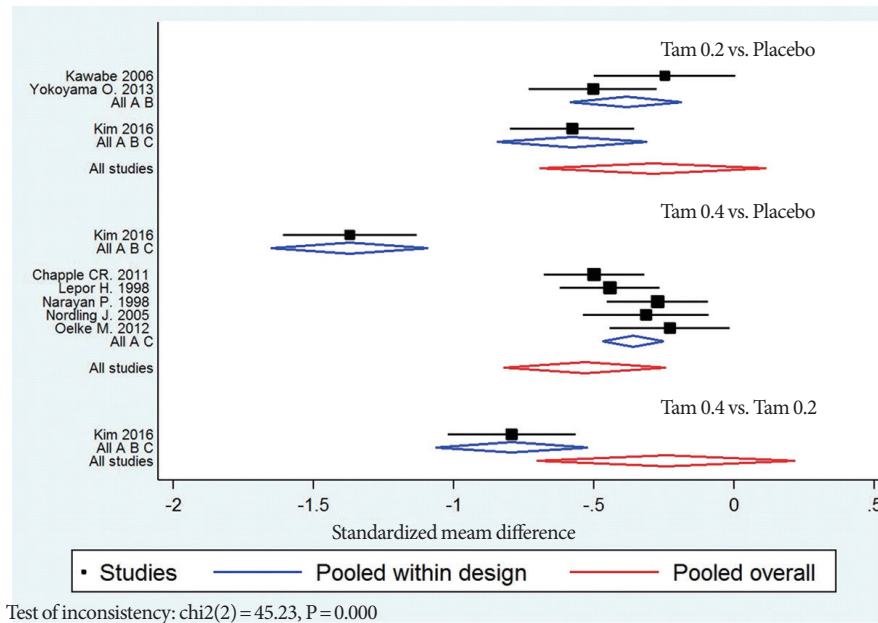
Fig. 5. Standardized mean difference of mixed treatment comparisions including direct comparison; Tam 0.2, tamsulosin 0.2 mg; Tam 0.4, tamsulosin 0.4 mg.
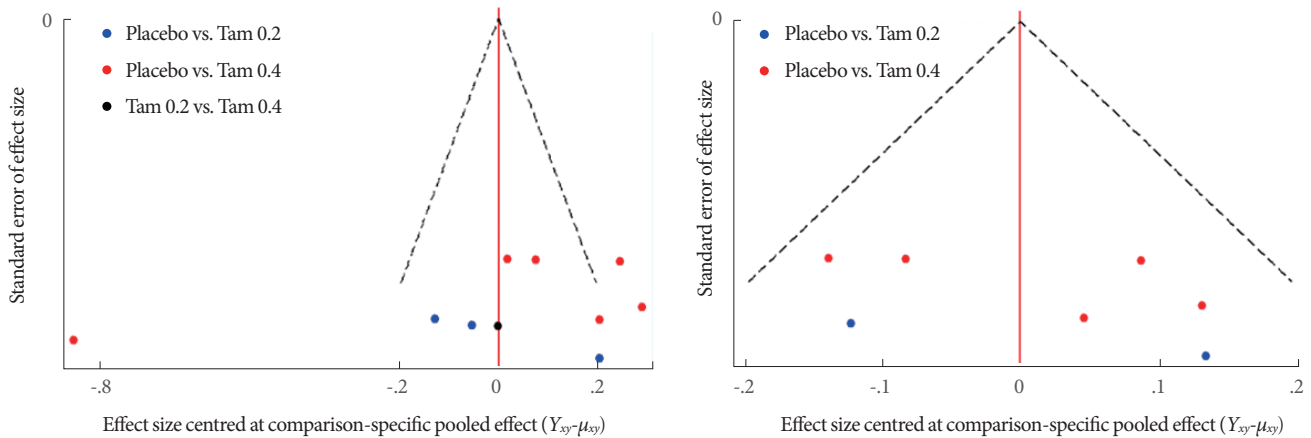

Fig. 6. Comparison-adjusted funnel plot of the included studies; Tam 0.2, tamsulosin 0.2 mg; Tam 0.4, tamsulosin 0.4 mg.

placebo and Tam 0.4 vs. placebo. However, the standardized mean difference (SMD) within design was -0.79 (95% CI, -1.02 to -0.56) in Tam 0.4 vs. Tam 0.2 that was from only study by Kim et al. [5]. The primary outcome of MTC was that the pooled overall SMD was -0.24 (95% CI, -0.71 to 0.22) in Tam 0.4 vs. Tam 0.2. This mixed comparison analysis result demonstrated that there were no significantly statistical differences between Tam 0.4 and Tam 0.2 even though we input the direct comparison of Tam 0.4 and Tam 0.2 (Fig. 5).

Fig. 6 illustrates the comparison adjusted funnel plot. Left side

funnel plot was using all trials that appeared asymmetric. When excluding the direct comparison trial of Tam 0.4 vs. Tam 0.2 by Kim et al. [5], the right side funnel plot appeared more symmetric that implied the absence of small study effects in the network.

Publicaton bias

Fig. 6 illustrates the comparison adjusted funnel plot. Left side funnel plot was using all trials that appeared asymmetric. When excluding the direct comparison trial of Tam 0.4 vs. Tam 0.2 by Kim et al. [5], the right side funnel plot appeared more sym-

metric that implied the absence of small study effects in the network.

DISCUSSION

We performed network meta-analysis including indirect and MTCs because of the lack of head-to-head studies comparing the efficacy between Tam 0.2 and Tam 0.4 in Asian BPH patients. No significant differences were noted in subjective and objective parameters treated with Tam 0.2 and Tam 0.4 after 12 to 13 weeks by ITC. These results demonstrate that Tam 0.4 did not show a better treatment effect than Tam 0.2 as the initial treatment dose. In a MTC, there was also no significant difference in the outcomes of those treated with Tam 0.2 vs. Tam 0.4. Based on these results of indirect and MTCs, we conclude that Tam 0.4 did not have better efficacy compared with the standard Tam 0.2 in Asian BPH patients.

The standard therapeutic dose of tamsulsoin is different between Asian and Western men due to the lower body mass index (BMI) of Asian men compared with Western men. Therefore, studies to determine the optimal dose of tamsulosin were done at 0.1, 0.2, and, 0.4 mg/day for Japanese patients and 0.4 and 0.8 mg/day for Western patients in Europe and the United States [2]. Tam 0.2 was adopted as a standard dose for Asian as well as Japanese patients based on a study by Kawabe et al. [16]. According to their study comparing with efficacy of tamsulosin at 0.1–0.4 mg in Japan, obstructive symptoms such as hesitancy, intermittency, and Qmax were significantly improved at the dose of Tam 0.2 mg. Similar to this result, administration with Tam 0.2 improved LUTS in other studies of Asian countries [17-19]. Moreover, Korean BPH patients treated with Tam 0.2 showed improvement of IPSS scores and Qmax comparable to the patients treated with terazosin as the dose was increased from 1 to 5 mg. However, the adverse events associated with treatment were significantly lower in patients administered with Tam 0.2 [2].

Previous studies to evaluate the efficacy and safety of Tam 0.2 as an initial treatment dose demonstrated 23.5%–50.5% of improvement in IPSS scores and approximately 20% of improvement of Qmax after treatment in an Asian population [4]. According to studies in Western men, IPSS scores were improved by 30%–45% and Qmax was increased by 15%–30% compared with the baseline after treatment with Tam 0.4 as an initial dose [20]. These results observed in Western men are similar to the degree of IPSS scores and Qmax in Asians. Therefore, Tam 0.2

as an initial dose in Asian BPH patients with lower BMI seems to be appropriate in light of these previous studies. Likewise, the network meta-analysis indicated that IPSS scores, Qmax, and PVR of the patients treated with Tam 0.2 were not significantly different compared with the patients treated with Tam 0.4 in the present study. Thus, Tam 0.2 as an initial dose is considered to be sufficient to improve BPH associated LUTS in Asian men. A study to analyze the prescription pattern of alpha-blockers in Korea observed that Tam 0.2 was the most frequently recommended medicine among various alpha-blockers. This prescription characteristic in real life might indirectly reflect the efficacy and safety of Tam 0.2 as an initial dose [21]. Without a doubt, Tam 0.2 in Asian men with BPH is the standard therapeutic dose based on the above findings. Only one recent study by Kim et al. [5] reported that patients treated with Tam 0.4 as an initial dose showed better effects compared with men treated with Tam 0.2.

Although the general recommendation for the initial dose of tamsulosin for Asian men is 0.2 mg and efficacy has been demonstrated, there are patients whose LUTS is not improved after treatment with Tam 0.2. A cross-sectional study in Korea demonstrated that 35.5% of BPH patients were not satisfied after treatment with Tam 0.2 [22]. The reason for dissatisfaction was low efficacy and side effects. They found that age and IPSS severity at baseline contributed to the decreases in patient satisfaction. Therefore, there were attempts to investigate the role of dose escalation in BPH patients whose treatment was unsuccessful with the usual dose of Tam 0.2. Kim et al. [23] increased their tamsulosin dose to 0.4 mg, and improvement of IPSS voiding symptom scores and Qmax were observed. They also noted that the patients with older age, severe daytime frequency, and lower Qmax at baseline were more likely to require dose escalation compared with patients who were satisfied with Tam 0.2. This study suggests that dose escalation of tamsulosin could in some cases be applicable to Asian men with BPH, although dose titration is not usually recommended. Moreover, these results also mean that Tam 0.4 was inappropriate as a standard initial dose in Asian men because only patients with older age and more severe symptoms were unsatisfied with Tam 0.2. There was one more study to suggest tamsulosin dose escalation for patients dissatisfied with initial treatment. It was a randomized placebo controlled trial, and the authors compared effects and adverse events after increasing the tamsulosin dose to 0.4 mg in Korean patients who were unsatisfied with the initial treatment of Tam 0.2 [24]. After a 12-week treatment with Tam

0.4, Qmax was significantly improved compared with the placebo, although IPSS scores were not significantly different. In addition, adverse events such as cardiovascular disease and abnormal ejaculation were not different between the dose escalation group and the placebo. This study suggests that the dose escalation to Tam 0.4 could be considered for Asian men who do not show improvement of LUTS after standard treatment with Tam 0.2. Therefore, dose escalation to Tam 0.4 might be worth considering in cases where patients do not respond fully to Tam 0.2.

However, reassessment of the results by Kim et al. [5] observed that better efficacy of Tam 0.4 over Tam 0.2 as an initial dose is necessary before we adopt their findings for initial treatment of BPH in Asian men. Subanalysis of the data showed that initial treatment with Tam 0.4 led to a more significant decrease of IPSS scores especially in patients who complained of more severe LUTS as reported by IPSS scores of more than 20 at baseline. In other words, these results mean that only the patients with severe symptoms who did not respond to the standard therapeutic dose of Tam 0.2 showed a more significant improvement of IPSS. This was similar to the previous study where the patients with severe LUTS at baseline required a dose escalation to Tam 0.4 [23]. As a result, only the patients with severe LUTS in the recent study by Kim et al. [5] could show more significant improvement of IPSS after treatment with Tam 0.4, excluding patients with mild- to moderate-LUTS who could be generally treated with Tam 0.2. Moreover, the report by Kim et al. [5] in 2016 was not an article but an abstract, and therefore, we could obtain from the study very restricted data. For example, only the results after 12 weeks of treatment were provided, even though the authors evaluated IPSS scores, Qmax, and PVR at 4, 8, and 12 weeks. Furthermore, subanalysis data of the baseline symptoms, including mild- to moderate- as well as severe LUTS, seems to be necessary to compare the actual efficacy. Therefore, the study by Kim et al. [5] did not provide sufficient evidence to show that Tam 0.4 had better effects in Asian men compared with Tam 0.2.

A recent report about the better effects of Tam 0.4 as compared with the standard dose of Tam 0.2 was contrary to the clinical recommendation of tamsulosin dosage in the Asian BPH population; therefore, reassessment is needed. Network meta-analysis of indirect and direct studies suggested that the efficacy of Tam 0.2 was not significantly different compared with Tam 0.4 as an initial therapeutic dose, and inconsistency was observed between the recent study in 2016 and others.

Based on these results, evidence is lacking to support that Tam 0.4 has better therapeutic effects compared with Tam 0.2 as an initial dose for all Asian BPH men. Therefore, initial dose of tamsulosin for Asian BPH patient should be 0.2 mg.

REFERENCES

1. Dunn CJ, Matheson A, Faulds DM. Tamsulosin: a review of its pharmacology and therapeutic efficacy in the management of lower urinary tract symptoms. Drugs Aging 2002;19:135-61.

2. Wilde MI, McTavish D. Tamsulosin. A review of its pharmacological properties and therapeutic potential in the management of symptomatic benign prostatic hyperplasia. Drugs 1996;52:883-98.

3. Shim SR, Kim JH, Chang IH, Shin IS, Hwang SD, Kim KH, et al. Is Tamsulosin 0.2 mg effective and safe as a first-line treatment compared with other alpha blockers?: a meta-analysis and a moderator focused study. Yonsei Med J 2016;57:407-18.

4. Shim SR, Kim JH, Choi H, Lee WJ, Kim HJ, Bae MY, et al. General effect of low-dose tamsulosin (0.2 mg) as a first-line treatment for lower urinary tract symptoms associated with benign prostatic hyperplasia: a systematic review and meta-analysis. Curr Med Res Opin 2015;31:353-65.

5. Kim KS, Kim JH, Lee SH, Ha US, Han DH, Chang IH, et al. Efficacy of dose escalation of tamsulosin for the treatment in symptomatic benign prostatic hyperplasia of lower urinary tract symptoms: a randomised, double-blind, phase 3 trial in Korean men. J Urol 2016;195(4 Suppl):e466.

6. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.

7. Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in metaanalysis. In: Altman DG, Egger M, Smith GD, editors. Systematic reviews in health care: meta-analysis in context. London: BMJ Publishing Group; 2001. p. 285-312.

8. Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. BMJ 2003;326:472.

9. Nordling J. Efficacy and safety of two doses (10 and 15 mg) of alfuzosin or tamsulosin (0.4 mg) once daily for treating symptomatic benign prostatic hyperplasia. BJU Int 2005;95:1006-12.

10. Chapple CR, Montorsi F, Tammela TL, Wirth M, Koldewijn E, Fernández Fernández E, et al. Silodosin therapy for lower urinary tract symptoms in men with suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo-

and active-controlled clinical trial performed in Europe. Eur Urol 2011;59:342-52.

11. Narayan P, Tewari A. A second phase III multicenter placebo controlled study of 2 dosages of modified release tamsulosin in patients with symptoms of benign prostatic hyperplasia. United States 93-01 Study Group. J Urol 1998;160:1701-6.

12. Oelke M, Giuliano F, Mirone V, Xu L, Cox D, Viktrup L. Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomised, parallel, placebo-controlled clinical trial. Eur Urol 2012;61:917-25.

13. Lepor H. Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. Tamsulosin Investigator Group. Urology 1998;51:892-900.

14. Kawabe K, Yoshida M, Homma Y; Silodosin Clinical Study Group. Silodosin, a new alpha1A-adrenoceptor-selective antagonist for treating benign prostatic hyperplasia: results of a phase III randomized, placebo-controlled, double-blind study in Japanese men. BJU Int 2006;98:1019-24.

15. Yokoyama O, Yoshida M, Kim SC, Wang CJ, Imaoka T, Morisaki Y, et al. Tadalafil once daily for lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a randomized placebo- and tamsulosin-controlled 12-week study in Asian men. Int J Urol 2013;20:193-201.

16. Kawabe K, Ueno A, Takimoto Y, Aso Y, Kato H. Use of an alpha 1-blocker, YM617, in the treatment of benign prostatic hypertrophy. YM617 Clinical Study Group. J Urol 1990;144:908-11.

17. Lee E, Lee C. Clinical comparison of selective and non-selective alpha 1A-adrenoreceptor antagonists in benign prostatic hyperplasia:

studies on tamsulosin in a fixed dose and terazosin in increasing doses. Br J Urol 1997;80:606-11.

18. Li NC, Chen S, Yang XH, Du LD, Wang JY, Na YQ, et al. Efficacy of low-dose tamsulosin in chinese patients with symptomatic benign prostatic hyperplasia. Clin Drug Investig 2003;23:781-7.

19. Park CH, Chang HS, Oh BR, Kim HJ, Sul CK, Chung SK, et al. Efficacy of low-dose tamsulosin on lower urinary tract symptoms suggestive of benign prostatic hyperplasia : a nonblind multicentre korean study. Clin Drug Investig 2004;24:41-7.

20. Djavan B, Marberger M. A meta-analysis on the efficacy and tolerability of alpha1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. Eur Urol 1999;36:1-13.

21. Kang DH, Lee JY, Chung JH, Cho HJ, Cho JM, Moon HS, et al. Analysis of prescriptions of alpha-blockers and phosphodiesterase 5 inhibitors from the urology department and other departments. Int Neurourol J 2011;15:216-21.

22. Choi H, Sim JS, Park JY, Bae JH. Assessment of tamsulosin 0.2 mg for symptomatic bladder outlet obstruction secondary to benign prostatic enlargement: data from a Korean multicenter cross-sectional study. Urol Int 2015;95:50-5.

23. Kim JW, Oh MM, Yeo JK, Bae JH, Joo KJ, Choi JB, et al. Efficacy of dose escalation of tamsulosin for the treatment of lower urinary tract symptoms. Low Urin Tract Symptoms 2012;4:96-102.

24. Kim JJ, Han DH, Sung HH, Choo SH, Lee SW. Efficacy and tolerability of tamsulosin 0.4 mg in Asian patients with lower urinary tract symptoms secondary to benign prostatic hyperplasia refractory to tamsulosin 0.2 mg: a randomized placebo controlled trial. Int J Urol 2014;21:677-82.