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The Efficacy of Adjunctive Tamsulosin and Analgesic Combination Compared to Analgesic Only in extracorporeal shock wave lithotripsy (ESWL) for renal stones

A Systematic Review and Meta-Analysis

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Objective: This systematic review aimed to evaluate the efficacy of tamsulosin and analgesic combination compared to analgesics only for renal stone patients following an ESWL therapy.

Method: The independent variables in this study were the administration of tamsulosin and analgesic combination; and analgesic only consisting of Non-steroidal anti-inflammatory drugs (NSAID), corticosteroids, or opioids. Stone-free rate (SFR) and renal colic incidence. A systematic search was performed in the PUBMED and Science-Direct databases for relevant randomized controlled trials (RCT)s. The risk of bias of the included studies was evaluated using the Cochrane risk of bias (RoB) tool 2.

Result: Five studies with 821 patients were included based on the primary and secondary screening. In general, these five studies had low risks of bias, except for one study due to a deviation from the initial intervention. SFR analysis of the five RCTs was performed using a fixed-effects model due to the homogeneity of the studies (I^2=13%). The combination group had a higher SFR compared to the analgesic only group (OR = 2,34 95% CI 1,67-3,28, p<0,00001). Combination group had a lower renal colic incidence compared to the analgesic only group (OR = 0,20 95% CI 0,11-0,37, p < 0,00001). The analysis was performed using a random-effects model due to the heterogeneity between studies (I^2=62%).

Conclusion: Tamsulosin and analgesics combination can be recommended for renal stone patients following ESWL as it has a higher SFR, and lower renal colic occurrence compared to analgesic only.

Keywords: *tamsulosin, analgesics, ESWL, renal stone, kidney stone*

I. INTRODUCTION

Since the introduction of extracorporeal shock wave lithotripsy (ESWL) in the early 1980s, the procedure has been recommended as the first line therapy for kidney and ureteral stones less than 20 mm in size (1). It is different than other more invasive procedures, such as percutaneous nephrolithotomy (PCNL) and ureteroscopy (URS) as it can be performed in an outpatient setting (2). The success rate of ESWL ranges from 33 to 91% depending on the stone characteristics, lithotriptor effectiveness, patient's characteristics, and operator experience (3). Tamsulosin is an alpha adrenoreceptor antagonist specific for α-1A and α-1D, which are mostly found in the distal ureter.

Tamsulosin could inhibit the peristaltic activity and contraction of the ureter, thus accommodating stone passage and expulsion (4). Patients undergoing ESWL also require analgesics. Aside from causing morbidity, pain could affect the procedure's success due to excessive movements. Pain may also limit the energy that could be given to the patient (5). Pain management is thus necessary during the procedure to ensure its effectiveness (6). As of the conduction of this review, there hasn't been any systematic reviews which compare the efficacy of tamsulosin and analgesics combination with analgesics only in patients with kidney stone after ESWL, especially in terms of stone-free rate and renal colic. Therefore, we aimed to evaluate the efficacy of tamsulosin and analgesics combination compared to analgesics only in patients with kidney stone after undergoing an ESWL treatment.

II. RESEARCH METHODS

We performed a systematic review following the Cochrane Handbook and PRISMA guideline with registered review protocol (PROSPERO: CRD42020209813) (7,8). We searched studies through PubMed and ScienceDirect using our pre-defined eligibility criteria until February 2021. We used the MeSH terms related to urinary stones, tamsulosin, and analgesic to find the relevant studies. The full strategies used for database searching were available in the supplementary material. All records were screened for eligibility by two independent authors and any disputes between the two reviewers were resolved by discussion with a third author. The study selection process was demonstrated in figure 1 (9).

Eligibility criteria

We included randomized controlled trials (RCTs) that compared the combination of tamsulosin and analgesic versus analgesic alone in patients with renal stones less than 25 mm undergoing ESWL and reporting the following outcome: stone-free rate (SFR) and colic pain. We excluded in-vitro studies, case series, reviews, abstracts, trials with different treatment comparisons, and studies with no-full text in English.

Data extraction and risk of bias assessment

We extracted the baseline data using pre-defined data extraction forms, which include author & year of publication, study design, age of the participant, number of participants, and the treatment protocol. We assessed the bias in the included trials using the Cochrane Risk of bias that evaluating the randomization process, deviations from intended intervention, missing data, outcome measurements, and selection bias (10).

Data analysis

The primary outcomes analyzed in this study were SFR and colic pain measured with odds ratio (OR) with 95% confidence interval (95% CI). The heterogeneity for the included trials was assessed using the I2 index and chi-square test. Low heterogeneity was defined as I2 index <50% and heterogeneity P-value> 0.05. If the heterogeneity was considered to be low, we used the fixed-effects model. Otherwise, we use the DerSimonian random-effects model (11,12). A p-value less than 0.05 was considered statistically significant. All analyses were performed using the statistical software RevMan version 5.4.

III. RESULTS

Of 515 published articles, 430 records were removed during the manual duplication removal process and 61 records were screened for title and abstracts, as shown in figure 1. Finally, five studies fulfilled the inclusion criteria and were included in the meta-analysis. A total of 821 patients with urinary stones were further analyzed with the average age of participants ranged from 38-53 years. The baseline characteristics of the included trials were described in Table 1 and the summary for risk of bias evaluation was presented in figure 2. Almost all of the included trials reported a low risk of bias. However, a trial by Hussein et al. showed high risk in terms of deviation of intervention and unclear bias for the missing outcome data. Furthermore, a trial by Gravina et al. had an unclear risk for deviation from the intervention.

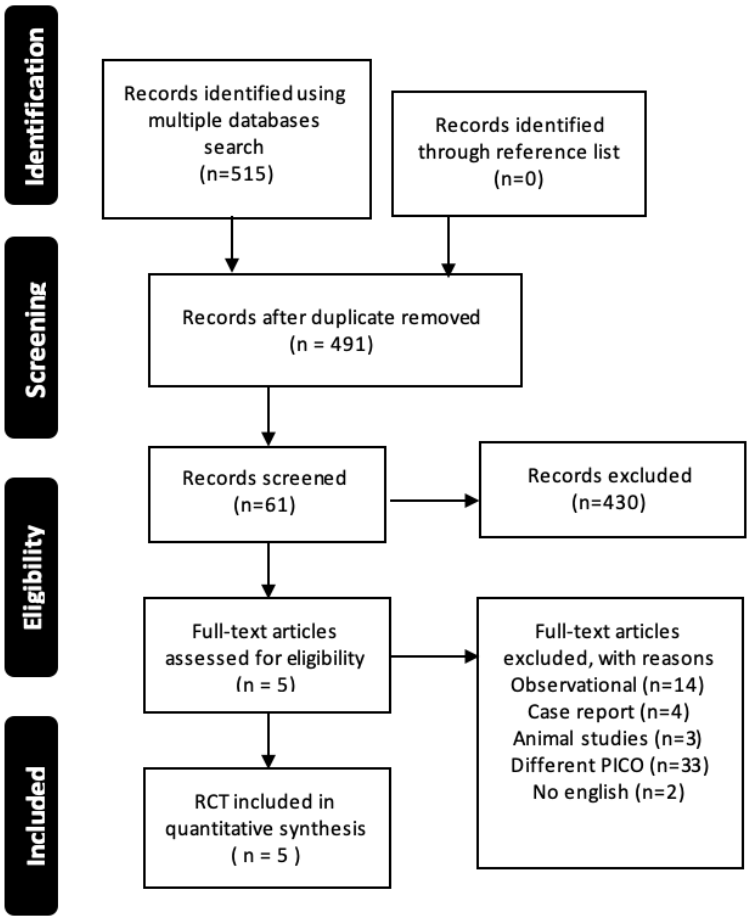

Figure 1. PRISMA flow diagram of meta-analysis

Table 1. Baseline characteristics of the included trials

First Author	Design	Age (years)	Intervention/ control (n)	Intervention group Treatment Protocol	Control group Treatment Protocol
Gravina 2005 [13]	RCT	48.2	65/65	Tamsulosin 0,4 mg + Natrium Diclofenac 75 mg I.M. / day + 16 mg methylprednisolone 2x/ day	Natrium Dikcofenac 75 mg I.M. / day + 16 mg methylprednisolone 2x/ day
Hussein 2010 [14]	RCT	42	67/69	Tamsulosin 0,4 mg + Natrium Diclofenac 75 mg I.M. / day	Natrium Diclofenac 75 mg I.M. / day
Georgiev 2011 [15]	RCT	53	99/87	Tamsulosin 0,4 mg + Natrium Diclofenac 100 mg / day + Prednisolone 20mg/ day for 100 days	Natrium Diclofenac 100 mg / day + Prednisolone 20mg/ day for 10 days
Syed 2014 [16]	RCT	40	60/60	Tamsulosin 0,4 mg + Natrium Diclofenac 50 mg tablet 2x/ day + Pethidine I.V.	Natrium Diclofenac 50 mg tablet 2x/ day + Pethidine I.V.
Abul 2016 [17]	RCT	38.2	123/126	Tamsulosin 0,4 mg + Natrium Diclofenac 50 mg tablet 2x/ day for two days	Natrium Diclofenac 50 mg tablet 2x/ day for two days

Figure 2. Risk of bias evaluation results

Stone free rate

Five studies assessed the SFR, which included 444 participants allocated to tamsulosin + analgesic group (n=444) and analgesic only group (n=407) (13–17). The analysis for heterogeneity for the included trials (I^2=13%; heterogeneity p-value=0.33). Therefore we selected the fixed-effects model to determine the result of the analysis. From the pooled analysis, the treatment group reported a significantly higher SFR compared to control group (OR 2.34, 95%CI = 1.67-3.28, p-value<0.05). The summary of the polled analysis was presented as a forest plot (Figure 3).

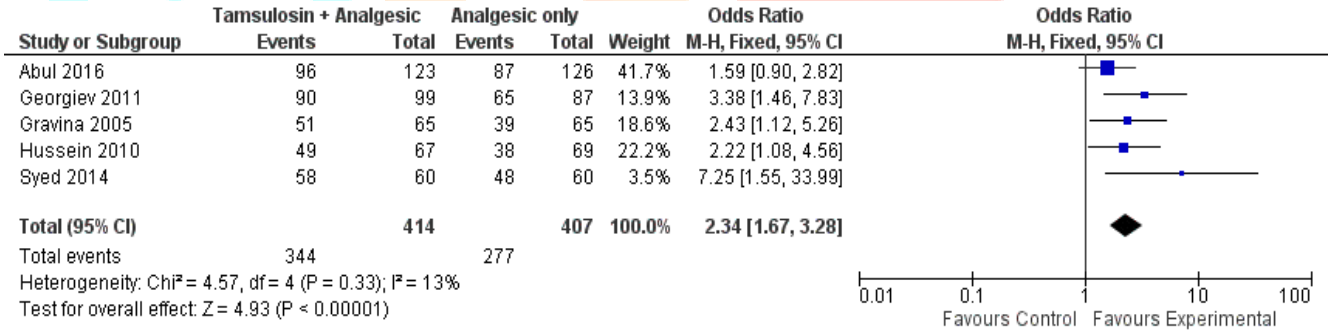

Figure 3. Forest plot comparing tamsulosin + analgesic versus analgesic only on SFR

Renal Colic

Four trials reported renal colic outcomes from 701 participants, which were allocated to the combination group (n=354) and analgesic alone group (n=347) in figure 4. The pooled analysis showed significant heterogeneity among the trials (I2=62%, heterogeneity p-value = 0.05) and thus a DerSimonian random-effects model was selected. After weighting the trials according to the number of included participants, the pooled analysis showed that the treatment group had a significantly lower incidence of colic pain (OR 0.20 , 95%CI = 0.11-0.37, p value<0.05).

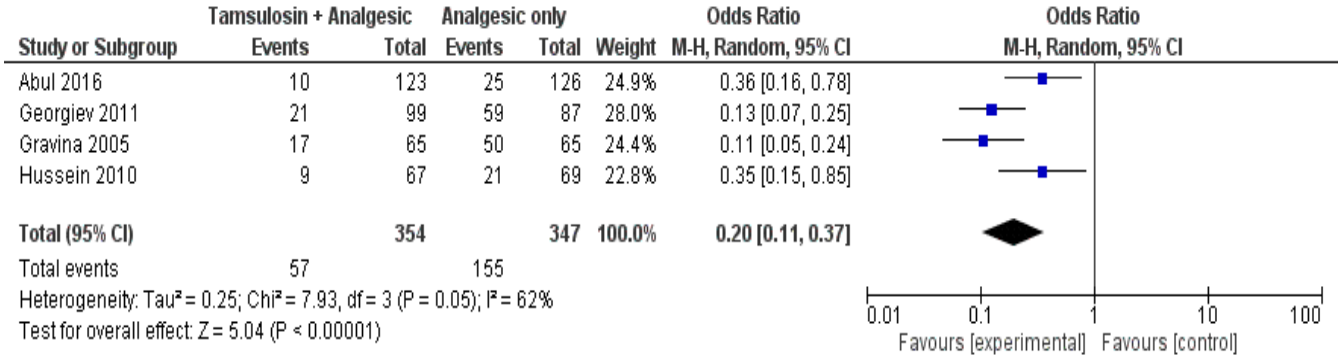

Figure 4. Forest plot comparing tamsulosin + analgesic versus analgesic only on colic pain

IV Discussion

Even though ESWL has been established as a minimally invasive method for stone management, several patients still require additional sessions to sufficiently eliminate the stones (18). As an adjunct to this treatment, pharmacological treatments are sometimes used. Tamsulosin has an important role in spontaneous stone expulsion without pain for ureterovesical stones less than 8 mm in size (19). Tamsulosin also affects c-fibers, thus blocking pain conduction (20). This review aimed to evaluate the SFR and renal colic of patients of both treatment groups. All five RCTs included in this study evaluated stones less than 25 mm in size and 0.4 mg of tamsulosin. All studies used natrium diclofenac as the oral analgesic, however two studies added steroids (prednisolone and methylprednisolone), and one study added opioid (pethidine) (13,15).

Previous RCTs and meta-analyses reported that post-ESWL tamsulosin administration could accommodate stone expulsion, increase SFR, and reduce analgesic use (21). Chen et al reported that tamsulosin combined with ESWL showed favorable results for renal and proximal as well as distal ureter (22). There is a significant SFR difference of the combination group compared to analgesic only (OR = 2,34; CI 95% = 1,67-3,28, $p<0.05$). Stone size influences the success of tamsulosin administration. Medical expulsive therapy (MET) using tamsulosin is effective for patients with stones more than 10 mm in size after undergoing ESWL. Other RCTs showed that MET is useful in spontaneously expulsing stones more than 5 mm in size (4).

This review also showed that the combination of tamsulosin and analgesic can significantly reduce acute renal colic compared to the analgesics only group (OR 0.20, 95%CI = 0.11-0.37, $p<0.05$). The reduction of pain is achieved by tamsulosin due to its afinity to the α-1D receptor in the ureter (13–15,17). The addition of corticosteroid in two of the included RCTs was due to the belief that it could reduce mucosal edema due to stone obstruction (13,23).

This review was limited due to the addition of corticosteroid and opioid in a few included RCTs. The duration of drug administration was also varied between the studies.

V Conclusion

Our meta-analysis study showed that tamsulosin and analgesics combination can be recommended for renal stone patients following ESWL as it has a higher SFR, and lower renal colic occurrence compared to analgesic only.

REFERENCES

[1] Türk C, Neisius A, Petrik A, Seitz C, Skolarikos A, Thomas K, et al. EAU Guidelines on Urolithiasis. Eur Assoc Urol. 2020;

[2] Shoukry RA, Al-Ansary AM. Transcutaneous Electric Nerve Stimulation (TENS) for pain relief during Extracorporeal Shock-Wave Lithotripsy (ESWL). Egypt J Anaesth [Internet]. 2019 Oct 2;35(1):71–6. Available from: https://doi.org/10.1080/11101849.2019.1655202

[3] Bovelander E, Weltings S, Rad M, van Kampen P, Pelger RCM, Roshani H. The influence of pain on the outcome of extracorporeal shockwave lithotripsy. Curr Urol. 2018;12(2):81–7.

[4] Ye Z, Zeng G, Yang H, Tang K, Zhang X, Li H, et al. Efficacy and safety of tamsulosin in medical expulsive therapy for distal ureteral stones with renal colic: a multicenter, randomized, double-blind, placebo-controlled trial. Eur Urol. 2018;73(3):385–91.

[5] Vergnolles M, Wallerand H, Gadrat F, Maurice-Tison S, Deti E, Ballanger P, et al. Predictive risk factors for pain during extracorporeal shockwave lithotripsy. J Endourol. 2009;23(12):2021–7.

[6] Hashem A, Ghobrial FK, Elbaset MA, Atwa AM, Fadallah M, Laymon M, et al. Efficacy of pethidine, ketorolac, and lidocaine gel as analgesics for pain control in shockwave lithotripsy: A single-blinded randomized controlled trial. Investig Clin Urol. 2019;60(4):251–257.

[7] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.

[8] Book Series C, Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions THE COCHRANE COLLABORATION ®.

[9] Moher D, Liberati A, Tetzlaff J AD. PRISMA 2009 Flow Diagram. Vol. 6, The PRISMA statement. 2009. p. 1000097.

[10] Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(7829):1–9.

[11] Thompson SG, Sharp SJ. Explaining heterogeneity in meta-analysis: a comparison of methods. Stat Med. 1999 Oct;18(20):2693–708.

[12] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88.

[13] Gravina GL, Costa AM, Ronchi P, Galatioto GP, Angelucci A, Castellani D, et al. Tamsulosin treatment increases clinical success rate of single extracorporeal shock wave lithotripsy of renal stones. Urology. 2005 Jul;66(1):24–8.

[14] Hussein MM. Does tamsulosin increase stone clearance after shockwave lithotripsy of renal stones? A prospective, randomized controlled study. Scand J Urol Nephrol. 2010;44(1):27–31.

[15] Georgiev MI, Ormanov DI, Vassilev VD, Dimitrov PD, Mladenov VD, Popov EP, et al. Efficacy of tamsulosin oral controlled absorption system after extracorporeal shock wave lithotripsy to treat urolithiasis. Urology. 2011 Nov;78(5):1023–6.

[16] Syed S, Eng TY, Thomas CR, Thompson IM, Weiss GR. Current issues in the management of advanced squamous cell carcinoma of the penis. Urol Oncol Semin Orig Investig. 2003;21(6):431–8.

[17] Ahmed A, Shalaby E, El-feky M, Kotb A, Elsotohi E, El-kholy Jr. M, et al. Role of Tamsulosin Therapy after Extracorporeal Shockwave Lithotripsy for Renal Stones: Randomized Controlled Trial. Urol Int. 2016 Oct;97(3):266–72.

[18] Küpeli B, Irkilata L, Gürocak S, Tunç L, Kiraç M, Karaoğlan Ü, et al. Does tamsulosin enhance lower ureteral stone clearance with or without shock wave lithotripsy? Urology. 2004;64(6):1111–5.

[19] Pricop C, Novac C, Negru D, Iiie C, Pricop A, Tanase A. Can selective alpha blockers help the spontaneous passage of the stones located in the uretero bladder junction. Rev Med ChirSoc Med Nat. 2004;108:128–33.

[20] Kinnman E, Nygårds E-B, Hansson P. Peripheral α-adrenoreceptors are involved in the development of capsaicin induced ongoing and stimulus evoked pain in humans. Pain. 1997;69(1–2):79–85.

[21] De Nunzio C, Brassetti A, Bellangino M, Trucchi A, Petta S, Presicce F, et al. Tamsulosin or silodosin adjuvant treatment is ineffective in improving shockwave lithotripsy outcome: a short-term follow-up randomized, placebo-controlled study. J Endourol. 2016;30(7):817–21.

[22] Chen K, Mi H, Xu G, Liu L, Sun X, Wang S, et al. The efficacy and safety of tamsulosin combined with extracorporeal shockwave lithotripsy for urolithiasis: a systematic review and meta-analysis of randomized controlled trials. J Endourol. 2015;29(10):1166–76.

[23] Yang T-X, Liao B-H, Chen Y-T, Li H, He Q, Liu Q-Y, et al. A network meta-analysis on the beneficial effect of medical expulsive therapy after extracorporeal shock wave lithotripsy. Sci Rep. 2017;7(1):1–10.