Efficacy of Pregabalin, Solifenacin, or Combination therapy for Ureteral Stent Related Symptoms: A Systematic Review and Meta-Analysis

Nicholas Andrian Singgih, M.D.*, Jacinda Risha Oktaviani, M.D.*, William Adipurnama, M.D.*, Cecilia Noviyanti Salim, M.D.*, Kevin Tandarto, M.D. , Athaya Febriantyo Purnomo, M.D.***,****, Egi Edward Manuputty, M.D.***

**Department of Urology, Primaya Hospital PGI Cikini, Jakarta, Indonesia, **Department of Internal Medicine, University of Diponegoro, Semarang, Indonesia, ***Department of Urology, Faculty of Medicine, Universitas Brawijaya, Saiful Anwar General Hospital, Malang, Indonesia, ****Department of Oncology, University of Oxford, Oxford, United Kingdom.*

ABSTRACT

Objective: The Double-J (DJ) ureteral stent is essential in urology but can lead to Ureteral Stent-Related Symptoms (USRS), prompting research into various therapies to enhance patient comfort. The purpose of this study is to assess the efficacy of pregabalin, solifenacin, or combined therapy on ureteral stent-related symptoms.

Materials and Methods: We conducted thorough searches in four databases, which included PubMed, Cochrane, EBSCO, and ProQuest. PRISMA Guideline 2020 was applied in this study. The risk of bias was assessed using Newcastle-Ottawa Scale and Cochrane Risk of Bias 2.0.

Results: Ten studies consisting of 1477 participants were included in this study. Solifenacin monotherapy could significantly decrease total USSQ (mean difference (MD) -16.62; p=0.001), urinary symptoms (MD -9.16; p=0.002), and sexual matters (MD -0.81; p=0.002). Pregabalin monotherapy could significantly decrease pain (MD -7.29; p<0.00001). Compared to solifenacin monotherapy, combination therapy of pregabalin and solifenacin could significantly decrease total USSQ (MD -12.40; p <0.0001), urinary symptoms (MD -1.88; p=0.007), pain (MD -6.82; p<0.00001), sexual matters (MD -0.77; p <0.00001), and additional problems (MD -1.51; p=0.0007).

Conclusion: Combination therapy of pregabalin and solifenacin had the best advantages in lowering USRS, especially urinary symptoms, pain, sexual matters, and some other additional problems.

Keywords: Double-J ureteral stent; lower urinary tract symptoms; pregabalin, solifenacin; ureteral Stent related symptoms (Siriraj Med J 2023; 75: 909-923)

INTRODUCTION

Ureteral stents are utilized in more than 1.5 million people globally each year.[1,2] They are commonly employed in urological procedures and play a pivotal role in maintaining urinary flow while facilitating postoperative recovery.[3] They are implanted for a short period of time to ease ureteral obstruction, avoid ureteral strictures, encourage healing, and manage urine leakage.[4] However, they frequently introduce a range of discomforting symptoms, collectively referred to as Ureteral Stent-Related Symptoms (USRS). These symptoms, which encompass pain, urinary frequency, urgency, and hematuria, can significantly diminish patients' quality of life and impede their postoperative rehabilitation.[5]

While pregabalin is primarily recognized by the FDA as a gamma-aminobutyric acid (GABA) medication for diabetic neuropathy, central pain, and headaches, emerging research suggests it may also be effective in alleviating

Corresponding author: Nicholas Andrian Singgih
E-mail: nicholasandrian1606@gmail.com
Received 29 September 2023 Revised 12 October 2023 Accepted 28 October 2023
ORCID ID:http://orcid.org/0000-0002-7331-3070
https://doi.org/10.33192/smj.v75i12.265648

lower urinary tract symptoms (LUTS).[6] Solifenacin, an antimuscarinic medication, is licensed for the treatment of overactive bladder. Recent studies have indicated that USRS has improved and that it can be used to relieve symptoms after ureteroscopy and lithotripsy.[7]

This systematic review and meta-analysis aim to synthesize existing evidence, critically assess the strengths and limitations of individual studies, and provide a comprehensive overview of the current state of knowledge regarding these interventions.

MATERIALS AND METHODS

Protocol registration and literature search

This systematic review and meta-analysis have been registered in PROSPERO under the registration number CRD42023451928, and the study will strictly follow the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020.[8] A comprehensive literature search will be conducted in electronic databases such as PubMed, EBSCO, ProQuest, and the Cochrane Library, until agust 2023. The search strategy will involve a combination of medical subject headings (MeSH terms) and relevant keywords, including "ureteral stent", "stent-related symptoms", "Pregabalin","Solifenacin", "combination therapy", and "randomized controlled trial". The search will be limited to articles published in English.

Eligibility criteria

The inclusion criteria for this study were patients diagnosed with USRS, which involved pregabalin/solifenacin monotherapy or combination, randomized controlled trials, observational, cohort, and case control studies, and published in the English language. The exclusion criteria were insufficient data reporting or unavailable full-text articles, case reports, letters to the editor, and proceeding abstract conferences.

Data extraction

The data extraction process was independently conducted by 3 reviewers. The data extraction included the author's name, year of publication, the mean age of respondents, country of origin, provided intervention, number of respondents, outcomes (Ureteral Stent Symptom Questionnaire - USSQ), duration of follow-up, and conclusion. USSQ is a valid reliable multidimensional questionnaire to assess ureteral stent symptoms and their impact on quality of life.[3]

Quality assessment

Five reviewers were involved in assessing the biased quality of the studies. For cohort and case-control studies, we utilized the Newcastle-Ottawa Scale (NOS), a widely used tool for evaluating the quality of non-randomized studies. On the other hand, for randomized studies, we employed the Cochrane Risk of Bias Tool 2.0. This tool evaluates five domains, which include the randomization process, bias arising from deviations in the intervention, bias due to incomplete outcome data, bias from the methods of outcome measurement, and bias related to outcome selection and reporting.

Meta analysis

Quantitative data will be collected using the Cochrane Collaboration application called Review Manager 5.4. For the analysis of the primary outcome using continuous data, we included the mean difference (MD) and a 95% confidence interval (CI). A p-value below 0.05 was considered statistically significant. In this meta-analysis, heterogeneity among studies will be assessed using I^2 (I^2; Inconsistency). The heterogeneity will be considered high if I^2 >50%, moderate if I^2 26-50%, and low if <26%. A P-value of < 0.05 is considered statistically significant.

RESULTS

Literature search

Fig 1 provides a comprehensive flow diagram that outlines the study selection process, including subsequent exclusions made during the review. In four databases, the search keyword turned up a total of 101 studies. After deleting the duplicate records, 80 records were screened and 15 were evaluated for eligibility. In total, we included 10 full-text English studies from eight different countries (Saudi Arabia, Greece, Taiwan, Iran, Egypt, Korea, China, and India) in the systematic review, and of these studies, six were included in the meta analysis.

Data extraction

The design of the studies included one non randomized prospective study and nine randomized controlled trials (RCTs). This study consisted of 1477 participants. The mean age of participants in groups ranged from 29.5 to 53.8. Intervention groups were solifenacin, pregabalin, solifenacin and pregabalin, and control or placebo. Dosage of pregabalin was 75 mg twice a day. Dosage of solifenacin varied between 5 mg a day or 10 mg a day. The literature described no significant difference in dosage 5 mg and 10 mg for ureteral stent symptoms, thus we included both dosages in meta analysis.[9] Duration of intervention was within two to four weeks.

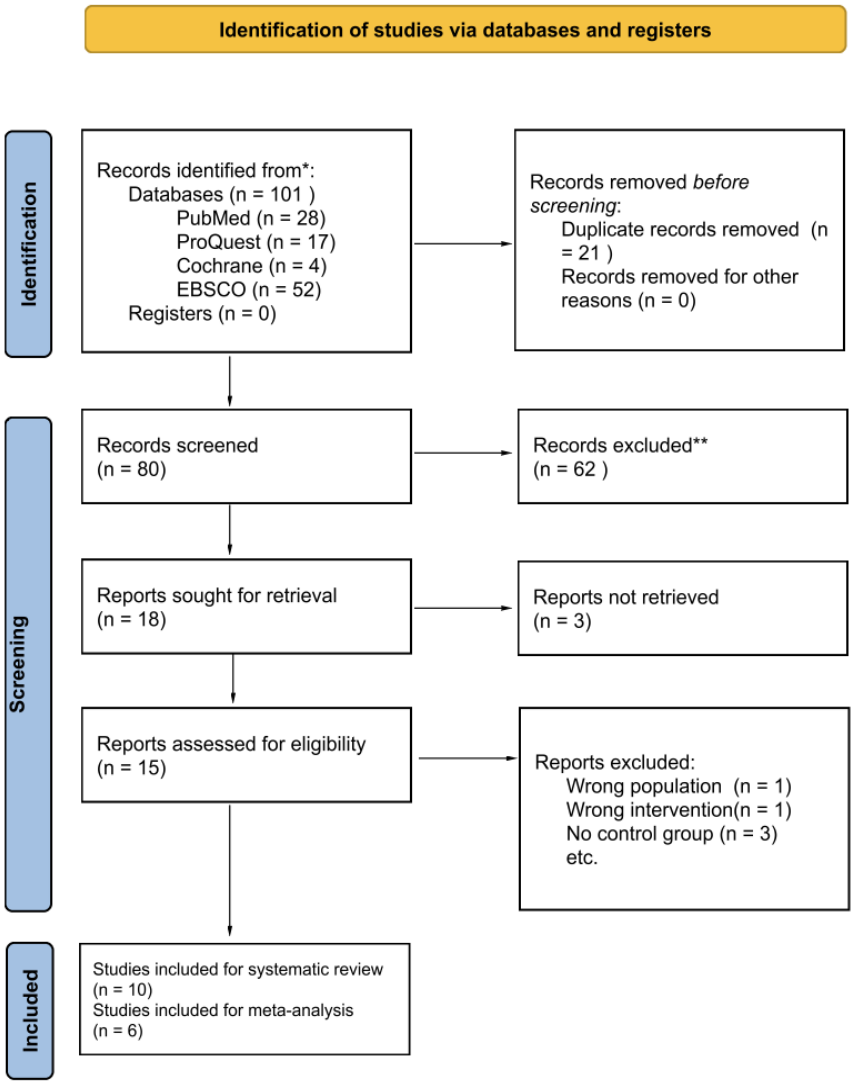

Fig 1. PRISMA flowchart 2020 of the included studies.

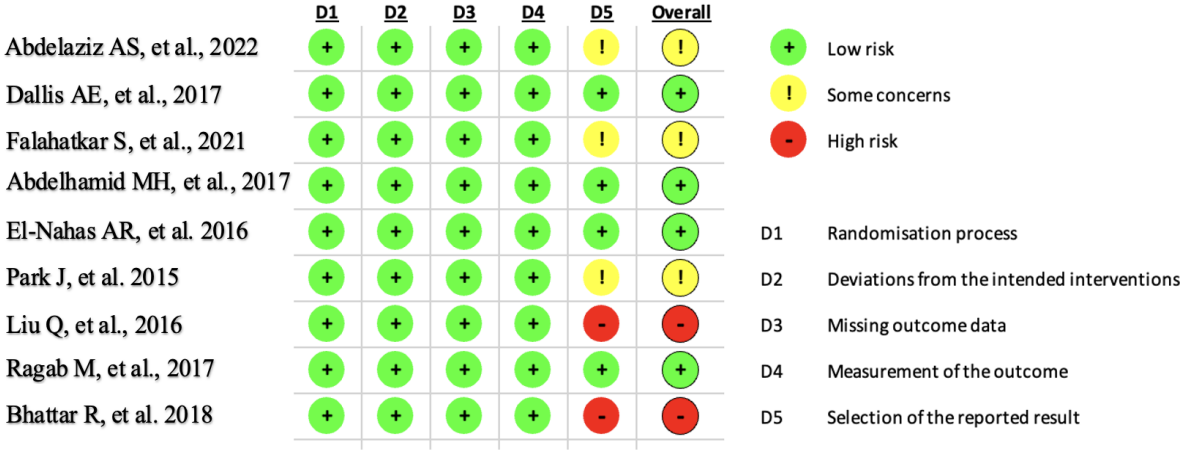

Fig 2. Cochrane risk of bias 2.0 for randomized controlled trial

Risk of bias assessment

The risk of bias assessment for randomized controlled trials (RCTs) is presented in Fig 2. Four studies indicated a low risk of bias, and 2 studies indicated a high risk of bias. The risk of bias assessment for non-RCT studies is presented in Table 2. According to the assessment using the Newcastle Ottawa Scale (NOS), it showed a low risk of bias.

TABLE 1. Baseline characteristic of included studies.

Author, year	Country	Design of Study	Drugs	Age (mean)	Total of Respon-dents	Diameter/Length of ureteral stent	Indication of the Ureteral Stent	Duration of Inter vention	Outcome	Side effect
Abdelaziz AS, et al., 2022.[10]	Saudi Arabia	RCT	Solife nacin 5 mg Well hydration	36.6 38.1	63	Diameter: 6 Fr, length: 24-28 cm (polyurethane DJ-stent)	Rigid URS, RIRS	2 weeks	USSQ	Consti pation, dry mouth
Dallis AE, et al., 2017.[11]	Greece	RCT	Solife nacin 5 mg Placebo	49.8 47.8	120	Diameter: 6F, length: 24-26 cm (Percuflex plus, Boston Scientific, Natick, MA)	ESWL, uretero scopy treatment, hydrone phrosis	4 weeks	USSQ	NA
Lee YJ, et al., 2013.[12]	Taiwan	Prospec tive non ran domized Control	Solife nacin 10 mg 53.4	53.8	140	Diameter: 6-7 Fr, length: 22-26 cm (Polyurethane by Cook Ireland Ltd)	URS lithotripsy	2 weeks	USSQ	Urinary retention, dry mouth, constipa tion, headache
Falahat kar S, et al., 2021.[13]	Iran	RCT	Prega balin 75 mg BID Solife nacin 5 mg Combi nation of pre gabalin and solife nacin Control	43.5	256	NA	URS	4 weeks	USSQ	Flushing, dry mouth, drowsi ness, dizziness, body pain, headache Dry mouth, drowsi ness, dizziness, body pain Flushing, dry mouth, drowsi ness, dizziness, headache
Abdelha mid MH, et al., 2017.[14]	Egypt	RCT	Solife nacin 10 mg Placebo	38 39.7	140	Diameter: 5-8 Fr, length 24-28 cm (polyurethane double-loop ureteral stent, Coloplast, Germany)	URS lithotripsy	2 weeks	USSQ	constipa tion, dry mouth, headache

TABLE 1. Baseline characteristic of included studies. (Continue)

Author, year	Country	Design of Study	Drugs	Age (mean)	Total of Respon-dents	Diameter/Length of ureteral stent	Indication of the Ureteral Stent	Duration of Inter vention	Outcome	Side effect
El-Nahas AR, et al., 2016.[15]	Egypt	RCT	Solifenacin 5 mg Placebo	39.6 40.8	87	Diameter: 6 F, length: 24-26 cm. (PercuflexÂ®, Boston Scientific, Marl-borough, MA, USA)	Calcular obstruction, post uretero scopy	2 weeks	USSQ	NA
Park J, et al., 2015.[16]	Korea	RCT	Solifenacin 5 mg Control	51.2 48.7	43	Diameter: 6F, length: 20-28 cm. (Percuflex®, Boston Scientific)	Post-uretero scopy	2 weeks	USSQ	NA
Liu Q, et al., 2016.[17]	China	RCT	Solifenacin 5 mg Control	41.6 40	54	Diameter: 4.7 Fr, length: 26 cm. (NLAY®, Bard Inc)	Before and after flexible uretero scopy	2 weeks	USSQ	Dry mouth
Ragab M, et al., 2017.[3]	Egypt	RCT	Solifenacin 5 mg Pregabalin 75 mg BID Combination of pregabalin and solifenacin Control	38.7 40.3 39.2 39.6	489	Diameter: 6 F, length: (Percuflex®, Boston Scientific)	Post URS	2 weeks	USSQ	Dry mouth, flushing, somnolence, headache Somnolence, headache, drowsiness dry mouth, flushing, somnolence, headache, drowsiness, body pain
Bhattar R, et al., 2018.[18]	India	RCT	Solifenacin 10 mg Placebo	29.9 29.5	85	Diameter: 6 F, length: not mentioned. (Polyurethane)	Patient underwent PCNL and URS	2 weeks lithotripsy	USSQ	NA

TABLE 2. Newcastle Ottawa Scale for Cohort (NOS).

No	Author, year	Selection				Comparability	Outcome			Total Score
		Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstrain that outcome of interest was not present at start of study	Comparability of cohort on the basis of the design or analysis	Assessment of outcome	Was follow up long enough for outcome to occur	Adequacy of follow up cohort	
1	Lee YJ, et al. (2013)	1	1	1	1	1	1	1	1	8

Meta analysis

Solifenacin monotherapy

Six studies are included in the meta analysis of solifenacin vs control. Total USSQ was significantly lower in the solifenacin group (MD -16.62; 95% CI, -26.59 to -6.66; p=0.001). Among all USSQ subgroup analyses, solifenacin could significantly decrease urinary symptoms (MD -9.16; 95% CI, -14.83 to - 3.49; p=0.002) and sexual matters (MD -0.81; 95% CI, -1.33 to -0.30; p=0.002). The heterogeneity was high in all subgroup studies. Detailed meta analysis of solifenacin vs control is presented in Fig 3. Solifenacin monotherapy funnel plots of bias are presented in Fig 4.

Pregabalin Monotherapy

Two studies are included in the meta analysis of pregabalin vs control. Total USSQ was lower in the pregabalin group but not significant (MD -10.78; 95% CI, -22.23 to 0.68; p=0.07). Among all USSQ subgroup analyses, pregabalin could significantly decrease pain (MD -7.29; 95% CI, -9.05 to -5.53; p<0.00001). The heterogeneity was high in subgroup studies of urinary symptoms, pain, general health, sexual matters, and additional problems. A detailed meta analysis of pregabalin vs control is presented in Fig 5. Pregabalin monotherapy funnel plots of bias are presented in Fig 6.

Combination therapy versus solifenacin monotherapy

Two studies are included in the meta analysis of pregabalin and solifenacin vs solifenacin monotherapy. Total USSQ was significantly lower in the combination group (MD -12.40; 95% CI, -18.58 to -6.23; p<0.0001). Among all USSQ subgroup analyses, combination therapy could significantly decrease urinary symptoms (MD -1.88; 95% CI, -3.25 to -0.52; p=0.007), pain (MD -6.82; 95% CI, -7.30 to -6.35; p<0.00001), sexual matters (MD -0.77; 95% CI, -0.99 to -0.55; p<0.00001), and additional problems (MD -1.51; 95% CI, -2.39 to -0.64; p=0.0007). The heterogeneity was high in subgroup studies of urinary symptoms, general health, work performances, and additional problems. A Detailed meta analysis of pregabalin and solifenacin vs solifenacin is presented in Fig 7. Combination therapy and solifenacin monotherapy funnel plots of bias are presented in Fig 8.

DISCUSSION

Numerous physio-pathological disorders or illnesses may block the upper urinary tract. The cause of blockage might be extramural, such as severe urological or non-urological neoplasia, or intraluminal, such as renal or ureteral stones, ureteral strictures, or papillary urothelial neoplasms.[1] An observational study described stenting and post-operative care could resolve post operative problems. Ureteral stent was introduced in the 1960s to bypass this blockage temporarily. It is a long tube device with a J-shaped (or known as a pigtail) on both sides to anchor in the kidney and bladder.[1]

The precise cause of USRS remains uncertain, but the prevailing understanding attributes it primarily to the stent's mechanical irritation of the ureter and bladder's trigonal area. This irritation leads to disturbances in ureteral peristalsis, detrusor spasms, inflammation of the bladder mucosa, and urine reflux into the kidney.[19,20] More than 80 percent of patients with USRS, including discomfort and storage symptoms can reduce their quality of life (QoL), despite the fact that most ureteral stents help patients improve drainage.[21]

In this meta analysis, solifenacin significantly reduces

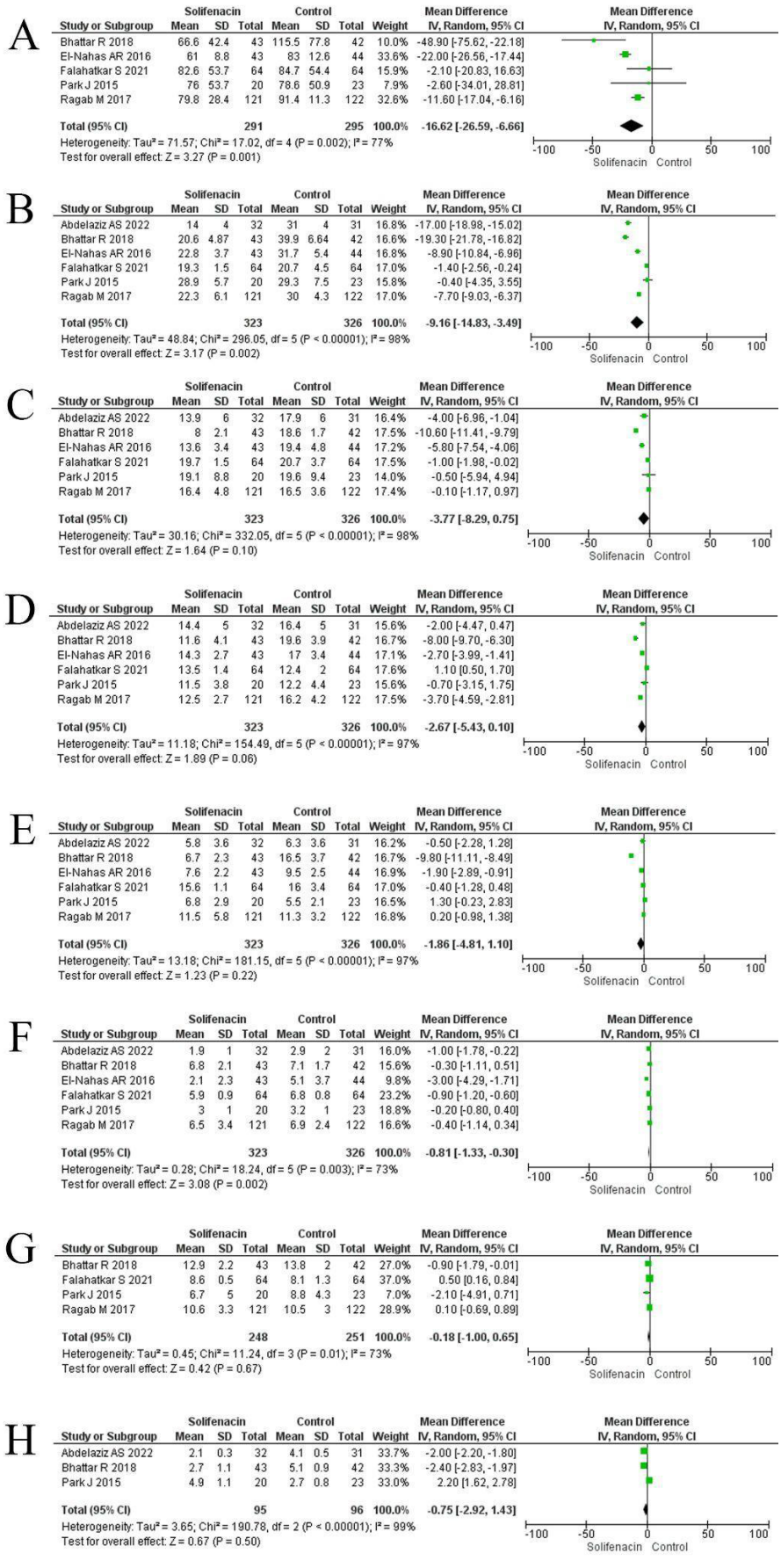

Fig 3. Forrest Plot Solifenacin vs Control. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

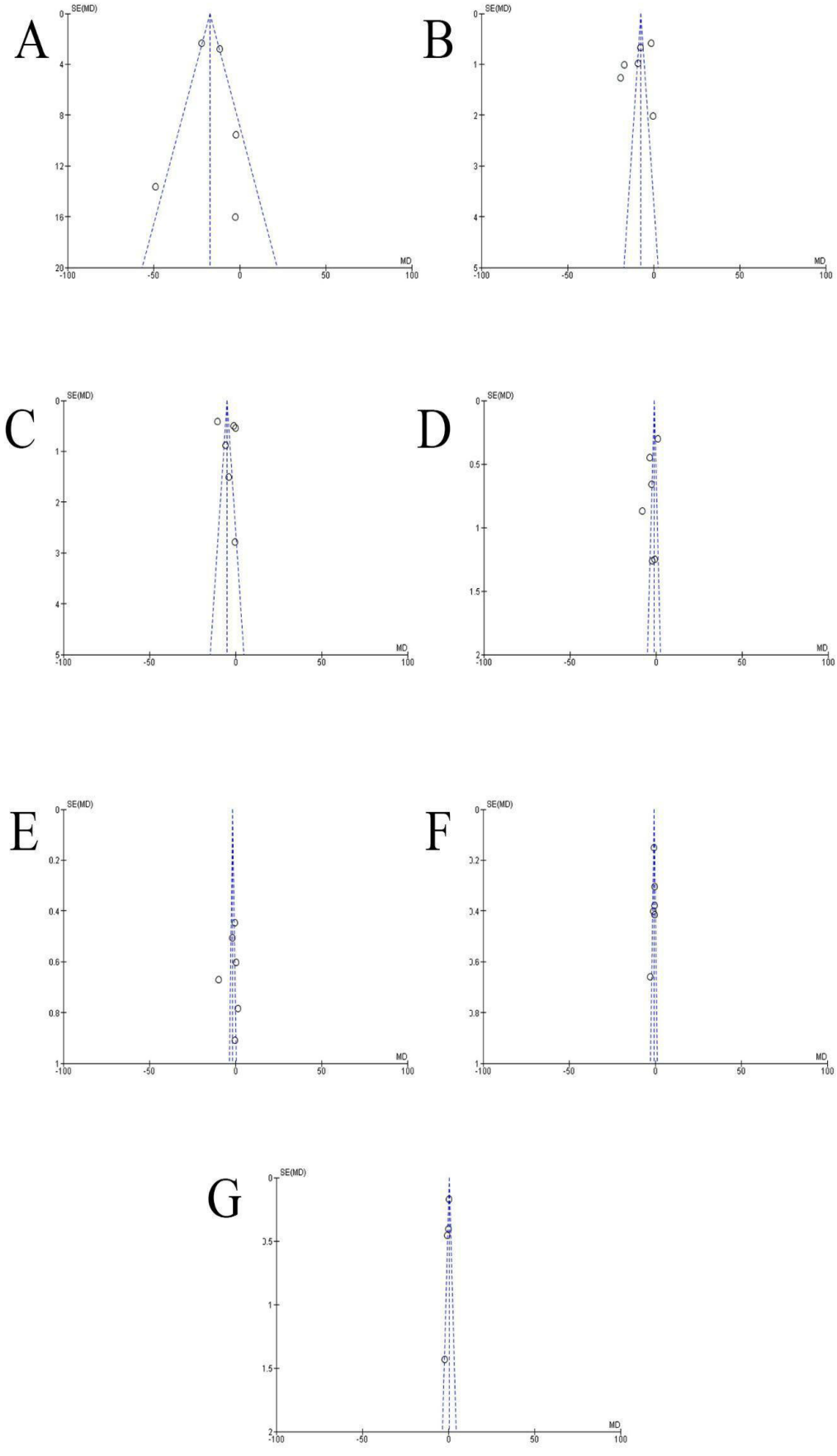

Fig 4. Funnel Plot Solifenacin vs Control. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

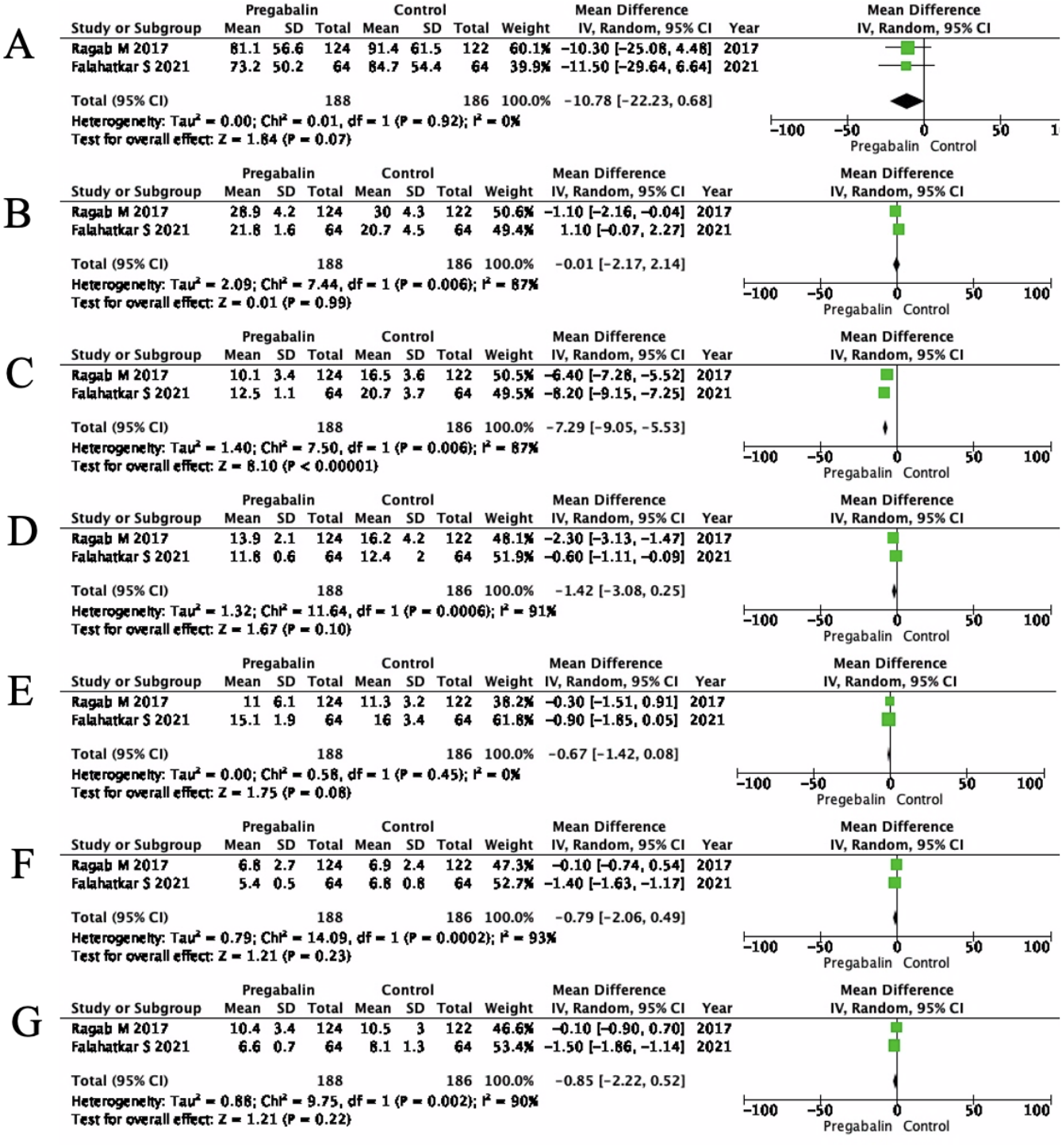

Fig 5. Forrest Plot Pregabalin vs Control. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

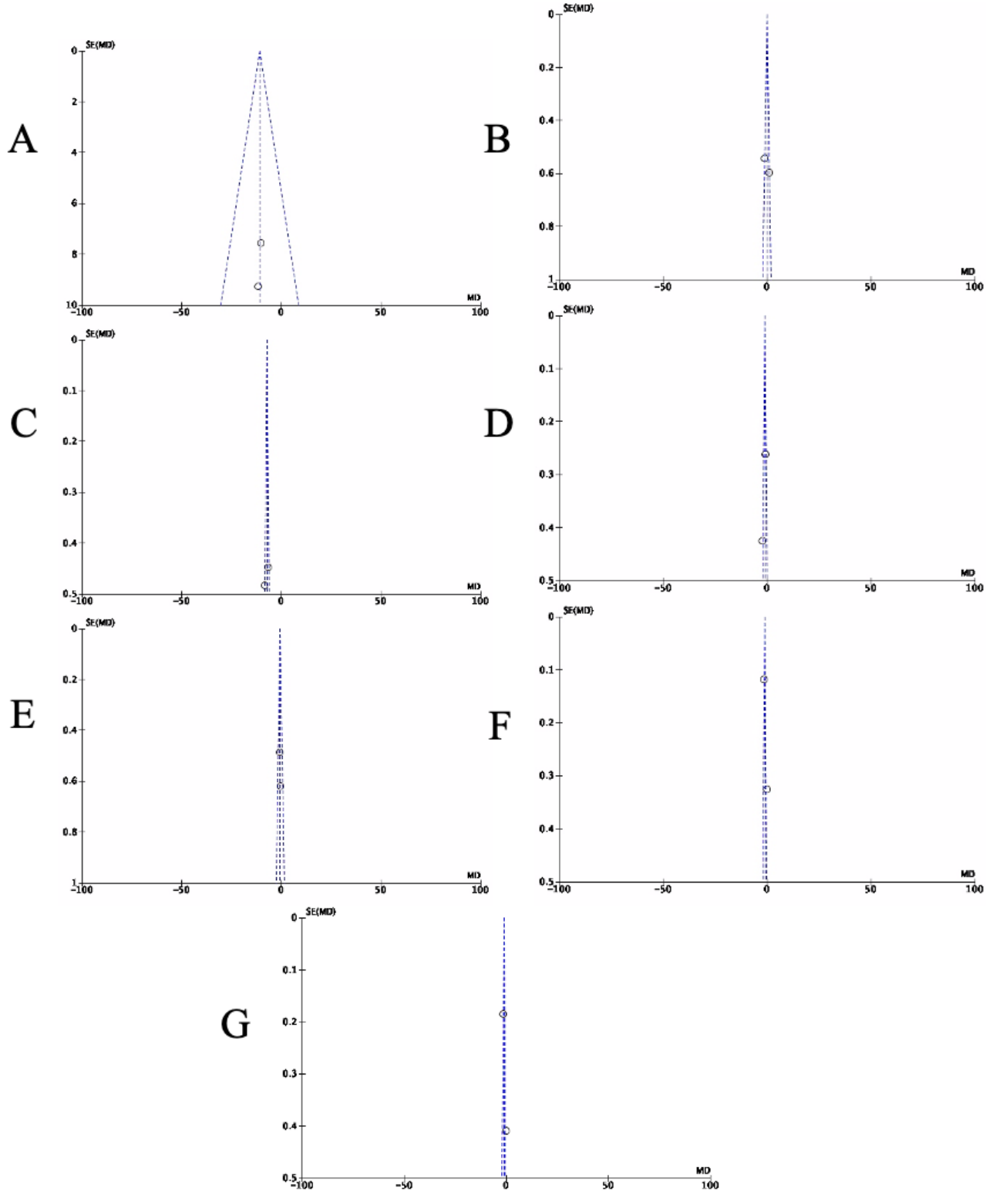

Fig 6. Funnel Plot Pregabalin vs Control. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

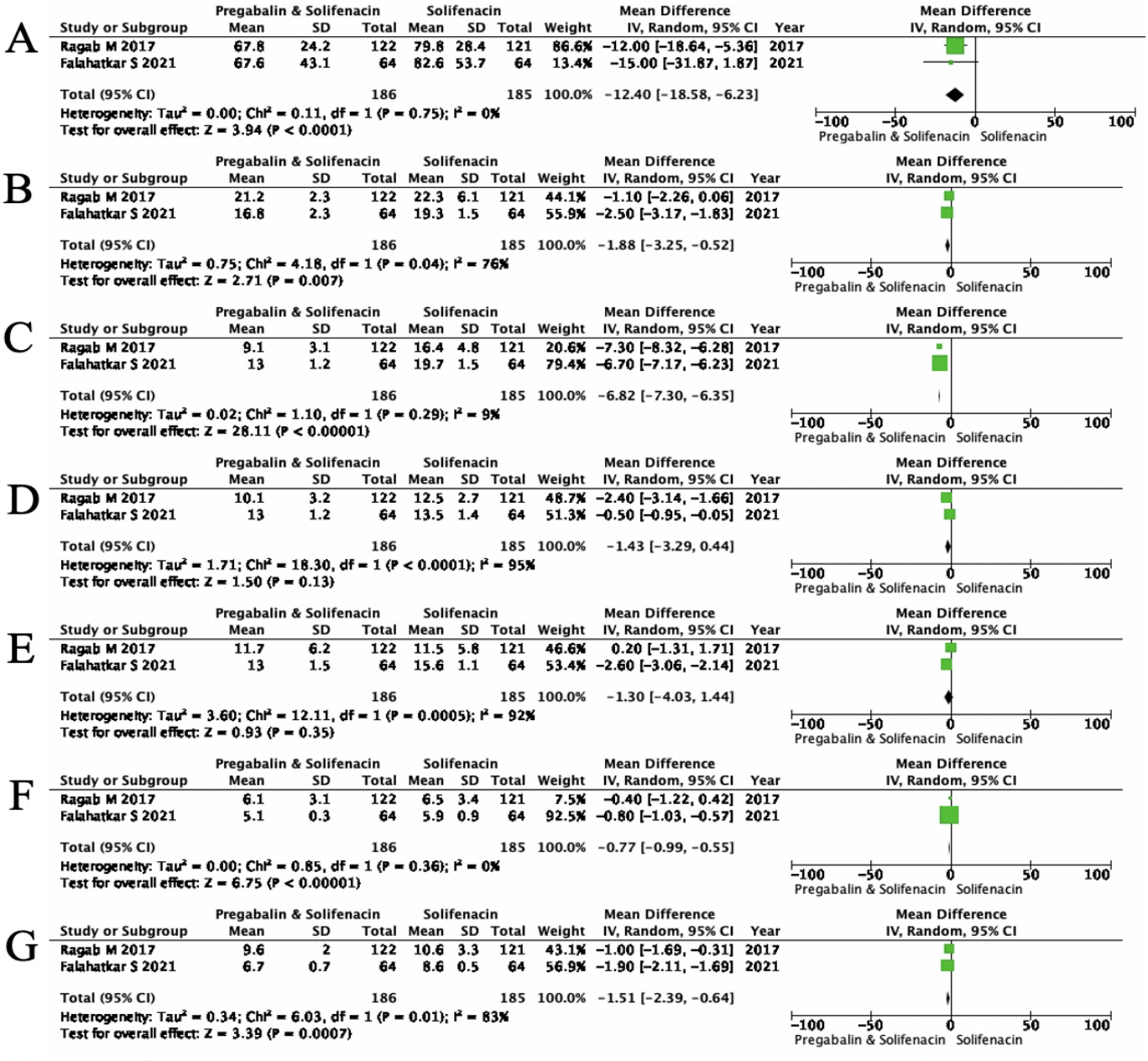

Fig 7. Forrest Plot Combination of pregabalin and solifenacin vs Solifenacin. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

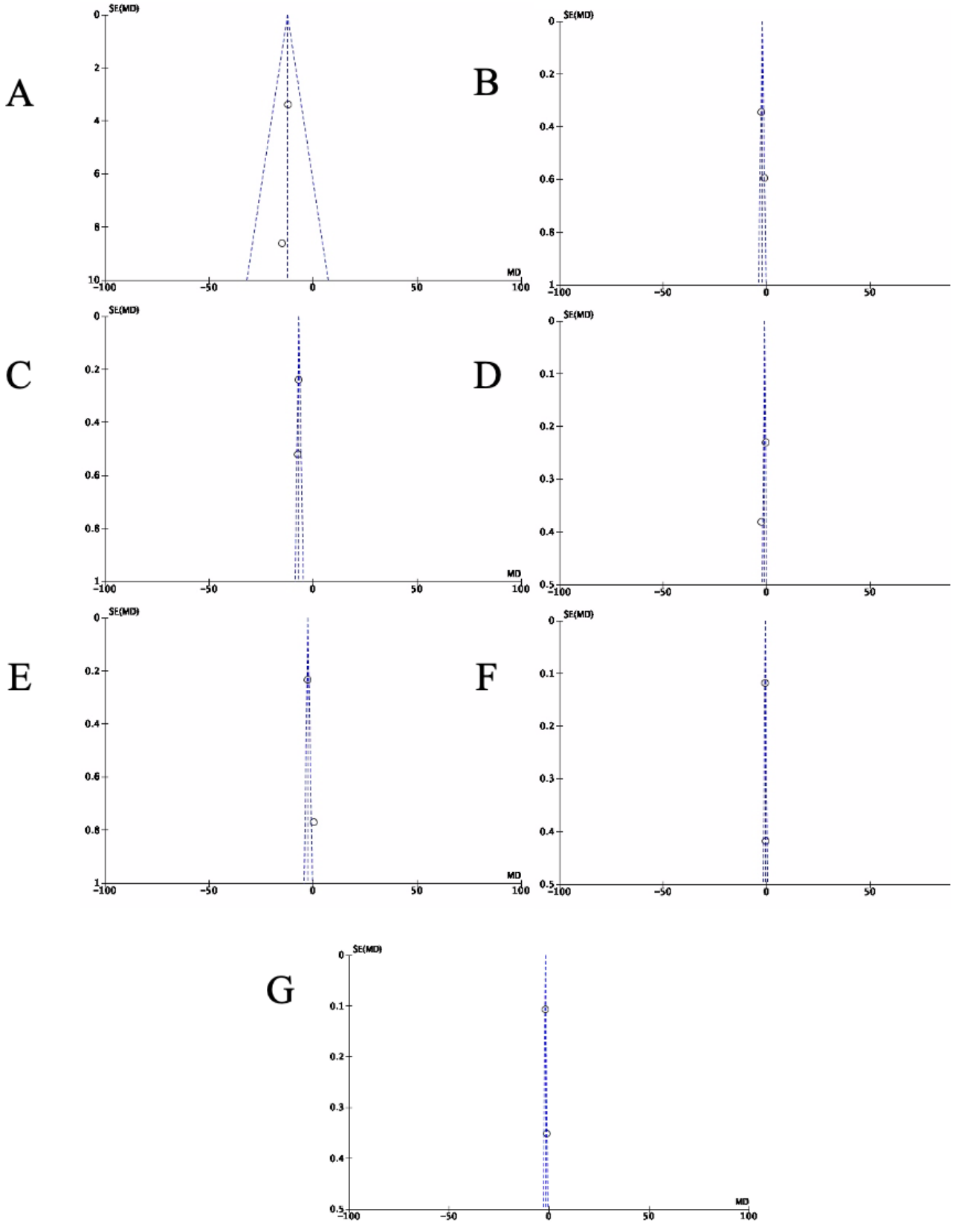

Fig 8. Funnel Plot Combination of pregabalin and solifenacin vs Solifenacin. A: Total USSQ. B: Urinary Symptoms. C: Pain. D: General Health. E: Work Performance. F: Sexual Matters. G: Additional Problems.

total USSQ. Specifically, it significantly reduces urinary symptoms and sexual matters compared to control. During urological surgery, bladder irritation causes the detrusor to contract involuntarily through the activation of muscarinic receptors (M2 and M3).[22] Being presented with favorable outcomes, solifenacin as an antimuscarinic drug, has been applied to treat symptoms brought on by the urinary bladder stent's distal end, which causes the bladder to contract involuntarily.[10,23]

Evrüke and Taş in their study showed that solifenacin therapy has demonstrated a favorable influence on the sexual functioning of premenopausal and postmenopausal women experiencing LUTS. As a result of solifenacin therapy leading to reduced urgency and urge incontinence (especially during intercourse), women might experience increased confidence and a greater willingness to engage in sexual activities with their partners, potentially elucidating the enhanced sexual functioning.[24,25] On the other hand, Kosilov K, et al. in their study showed that sexual satisfaction of BPH patients significantly increased with the administration of dutasteride and an increased dose of solifenacin (20mg/day). Their hypothesis posits that a higher dose of solifenacin may alleviate smooth muscle spasms in the detrusor and nearby pelvic organs, potentially improving microcirculation and enhancing tissue oxygenation. This effect could partially counteract the decrease in erectile function and stimulate afferent nerve structures, leading to improved orgasms. They also suggested that alleviated hyperactivity symptoms (urgency and nocturia) can give patients psychological comfort.[26]

A study by Lee YJ, et al. described solifenacin could lower USRS primarily urgency, urgent incontinence, bodily discomfort from stents, and hematuria in people of both sexes.[11] Several other combinations of medicines have been researched to reduce USRS, such as mirabegron and solifenacin, tamsulosin and solifenacin, silodosin and tadalafil, silodosin and solifenacin, solifenacin and tadalafil.[11,18,27] In comparison to solifenacin monotherapy, solifenacin with mirabegron significantly reduced OAB symptoms related to double-J stents and provided a superior quality of life without worsening undesirable side effects.[27] Combination of tamsulosin and solifenacin has a significant impact on urinary index score compared to each one of them and placebo.[11] In a study with 120 participants, mirabegron monotherapy had lower scores on the IPSS and OAB questionnaires compared to tamsulosin and solifenacin combination.[28] Silodosin and solifenacin were more effective in lowering USRS compared to either monotherapy or other combinations for silodosin, solifenacin, and tadalafil.[18]

In our research, pregabalin only significantly reduces the pain component of USSQ. Pregabalin, characterized by its chemical name (S)-3-(aminomethyl)-5-methylhexanoic acid, is recognized for its pharmacological effectiveness as the S-enantiomer of a racemic 3-isobutyl gamma amino butyric acid analogue, serving as a well-established anticonvulsant and analgesic agent.[29] It can inhibit the release of numerous neurotransmitters at synapses, which may explain why it decreases neuronal excitability and inhibits the inflammatory reactions elicited by afferent C nerve fiber. In addition, it benefits from central regulation of the dorsal horn neuron sensitization, which reduces postoperative pain associated with inflammation.[3,30] A randomized controlled study by Choppa S, et al. found that administering a single dose of 150 mg pregabalin 1 hour before percutaneous nephrolithotomy (PCNL) experienced less incidence and intensity of IID than those who received a placebo without experiencing any major side effects.[22] PCNL is the first-line management for stones larger than 20 mm.[31] A randomized controlled study by Rosen G, et al. found that preoperative pregabalin did not reduce pain after ureteroscopy compared to a placebo. Further study of pregabalin efficacy for post operative ureteroscopy is needed.[32] In our study, 75 mg of pregabalin was administered twice daily postoperatively with the aim of reducing USSQ (Ureteroscopy Stone Specific Questionnaire) scores.[3,13]

In our meta-analysis, the combination therapy of solifenacin and pregabalin versus solifenacin monotherapy has been statistically shown to reduce the total USSQ score, urinary symptoms, pain, sexual problems, and additional issues. These findings suggest that combination therapy has a more positive effect compared to monotherapy. This is in accordance with a study conducted by Falahatkar S, et al. that used a combination therapy of solifenacin and pregabalin for 4 weeks. The combination therapy successfully improved the scores of urinary symptoms, pain, sexual activity, overall condition, and work performance in the patient.[13] Solifenacin monotherapy alone does not reduce pain levels, but when combined with pregabalin, it can effectively reduce pain levels.[33]

Solifenacin is a medication that effectively and safely treats overactive bladder and has few adverse effects. In a prospective study comparing the dose of solifenacin, 5 mg solifenacin didn't show a significant number of side effects compared to placebo. On the other hand, 10 mg solifenacin showed a higher number of minor and self-limited side effects such as headache, constipation, and dry mouth.[9] In this review, most of the studies described headache, constipation, and dry mouth as side effects. Moreover, some studies also described urinary retention,

drowsiness, dizziness, and body pain. Pregabalin and gabapentin are two of the gabapentinoids that demonstrate opioid-sparing effects, are reasonably safe for individuals with renal or cardiac risk factors, do not prevent fusion during spinal surgery, and lessen the side effects of intravenous patient-controlled analgesia. Adverse effects, such as sedation, dizziness, and peripheral edema, are important considerations in the use of gabapentinoids, and they tend to become more pronounced with higher doses.[34] A systematic review and meta analysis studying the safety and efficacy of gabapentinoids for neuropathic pain described dizziness, somnolence, euphoria, constipation, dry mouth, peripheral oedema, and increased weight were several significant adverse effects of gabapentinoids use.[35] Two studies using pregabalin twice a day reported some side effects such as flushing, dry mouth, drowsiness, somnolence, dizziness, body pain, and headache.

Besides medicines, several stent characteristics have been studied to reduce USRS. The choice of stent material is something that can be considered to reduce USRS. A study by Gadzhiev N, et al. described silicone material for ureteral stents could lower body pain compared to polyurethane.[21] Silicone also has a lower potential for encrustation.[36] New stent shapes that might lessen tissue irritancy and urine reflux have lately received a lot of attention in the development of innovative stent designs.[1] "Pigtail suture stent" at the distal end can reduce USRS more than a J-shaped stent.[36] According to a meta analysis, urinary symptoms and pain are worse as the stent diameter gets bigger. As a result, smaller diameter stents ought to be chosen.[37] Materials used in the included studies were material of polyurethane, proprietary copolymer (Percuflex®), and proprietary polymer (InLay®), with a diameter of 4.7 to 8 Fr which has been adjusted to the patient's condition. Furthermore, a systematic review and meta analysis by Bao X, et al. reported that patients who had stents crossing the midline experienced more uncomfortable symptoms across subcategories such as urine symptoms, work performance, additional problems, overall health, storage symptoms, and quality of life. Urologists must make sure the ureteral stent is positioned correctly before implanting it.[38]

Postoperative follow up plays an important role in reducing USRS. According to statistics gathered from patients admitted to Thammasat University Hospital in the year 2020, 16 out of a total of 134 patients (8.9%) failed to show up on the scheduled day to have their stents changed or removed. Between the months of January and June of 2021, another 24 out of 121 patients (20%) neglected to show up for their appointments. Urinary tract infections, DJ stent mispositioning risk, ureteric stone development around the stents, and acute renal failure are all increased by indwelling ureteral stents. Some of these problems can lead to worsening USRS.[4]

In the systematic review and meta-analysis, several limitations were identified. First, the sample size for the combination of solifenacin and pregabalin in the population was still relatively small. Second, there was variability in the duration of follow-up among studies, which can potentially introduce bias. Third, there was variation in the dosages of solifenacin used in different studies. Fourth, this study still lacks a wide range of outcome measures. For future research, it is recommended to increase the sample size specifically for the combination of solifenacin and pregabalin, standardize the duration of follow-up across studies, and use consistent dosages of the medications. Additionally, it is advisable to include the size of ureteral stents and document any potential side effects associated with each drug.

CONCLUSION

Solifenacin monotherapy could decrease USRS especially urinary symptoms and sexual matters. Pregabalin monotherapy could only decrease pain related to USRS. Compared to solifenacin monotherapy, a combination therapy of pregabalin and solifenacin could significantly reduce the total USSQ score, especially in terms of decreasing urinary symptoms, pain, sexual matters, and additional problems.

REFERENCES

1. De Grazia A, Somani BK, Soria F, Carugo D, Mosayyebi A. Latest advancements in ureteral stent technology. Transl Androl Urol. 2019;8(S4):S436-41.
2. Yavuz A, Kilinc MF, Aydin M, Ofluoglu Y, Bayar G. Does tamsulosin or mirabegron improve ureteral stent-related symptoms? A prospective placebo-controlled study. Low Urin Tract Symptoms. 2021;13(1):17-21.
3. Ragab M, Soliman MG, Tawfik A, Abdel Raheem A, El-Tatawy H, Abo Farha M, et al. The role of pregabalin in relieving ureteral stent-related symptoms: a randomized controlled clinical trial. Int Urol Nephrol. 2017;49(6):961-6.
4. Pansaksiri T, Noppakulsatid P. Efficacy evaluation of smartphone-based Stent tracking application in follow-up patients with ureteral stents: A prospective study. Siriraj Med J. 2023;75(6): 466-72.
5. Joshi HB, Newns N, Stainthorpe A, MacDONAGH RP, Keeley FX, Timoney AG. Ureteral Stent symptom questionnaire: Development and validation of a multidimensional quality of life measure. J Urol. 2003;169(3):1060-4.
6. Ansari MS, Bharti A, Kumar R, Ranjan P, Srivastava A, Kapoor R. Gabapentin: A novel drug as add-on therapy in cases of refractory overactive bladder in children. J Pediatr Urol. 2013; 9(1):17-22.
7. Ho C-H, Chang T-C, Lin H-H, Liu S-P, Huang K-H, Yu H-J. Solifenacin and tolterodine are equally effective in the treatment of overactive bladder symptoms. J Formos Med Assoc. 2010; 109(10):702-8.

8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906.
9. Adil Mohammed A, Goerge Ghazala S, Al-Ibraheem NP. Effect of two different doses of solifenacin succinate therapy (5 mg, 10 mg) for the treatment of ureteral stent (Double J) related symptoms in comparison to placebo. Tren Med. 2018;18(6).
10. Abdelaziz AS, Salama NM, Ghoneem AM. Mirabegron vs. solifenacin in control of endoscopically inserted ureteral stent-related symptoms. World J Urol. 2022;40(8):2113-9.
11. Dellis AE, Papatsoris AG, Keeley FX Jr, Bamias A, Deliveliotis C, Skolarikos AA. Tamsulosin, solifenacin, and their combination for the treatment of Stent-related symptoms: A randomized controlled study. J Endourol. 2017;31(1):100-9.
12. Lee Y-J, Huang K-H, Yang H-J, Chang H-C, Chen J, Yang T-K. Solifenacin improves double-J stent-related symptoms in both genders following uncomplicated ureteroscopic lithotripsy. Urolithiasis. 2013;41(3):247-52.
13. Falahatkar S, Beigzadeh M, Mokhtari G, Esmaeili S, Kazemnezhad E, Amin A, et al. The effects of pregabalin, solifenacin and their combination therapy on ureteral double-J stent-related symptoms: A randomized controlled clinical trial. Int Braz J Urol. 2021;47(3):596-609.
14. Abdelhamid MH, Zayed AS, Ghoneima WE, Elmarakbi AA, El Sheemy MS, Aref A, et al. Randomized, double-blind, placebo-controlled trial to compare solifenacin versus trospium chloride in the relief of double-J stent-related symptoms. World J Urol. 2017;35(8):1261-8.
15. EL-Nahas AR, Tharwat M, Elsaadany M, Mosbah A, Gaballah MA. A randomized controlled trial comparing alpha blocker (tamsulosin) and anticholinergic (solifenacin) in treatment of ureteral stent-related symptoms. World J Urol. 2016;34(7):963-8.
16. Park J, Yoo C, Han DH, Shin DW. A critical assessment of the effects of tamsulosin and solifenacin as monotherapies and as a combination therapy for the treatment of ureteral stent-related symptoms: a 2 × 2 factorial randomized trial. World J Urol. 2015;33(11):1833-40.
17. Liu Q, Liao B, Zhang R, Jin T, Zhou L, Luo D, et al. Combination therapy only shows short-term superiority over monotherapy on ureteral stent-related symptoms – outcome from a randomized controlled trial. BMC Urol. 2016;16(1):66.
18. Bhattar R, Tomar V, Yadav SS, Dhakad DS. Comparison of safety and efficacy of silodosin, solifenacin, tadalafil and their combinations in the treatment of double-J stent- related lower urinary system symptoms: A prospective randomized trial. Turk J Urol. 2018;44(3):228-38.
19. Wang J, Zhang X, Zhang T, Mu J, Bai B, Lei Y. The role of solifenacin, as monotherapy or combination with tamsulosin in ureteral stent-related symptoms: a systematic review and meta-analysis. World J Urol. 2017;35(11):1669-80.
20. Koprowski C, Kim C, Modi PK, Elsamra SE. Ureteral Stent-associated pain: A review. J Endourol. 2016;30(7):744-53.
21. Gadzhiev N, Gorelov D, Malkhasyan V, Akopyan G, Harchelava R, Mazurenko D, et al. Comparison of silicone versus polyurethane ureteral stents: a prospective controlled study. BMC Urol. 2020;20(1):10.
22. Jayaram K, Choppa S, Gurajala I, Kar P, Durga P, Devraj R, et al. Effect of pregabalin on postoperative pain and instrumentation-induced dysuria in patients undergoing percutaneous nephrolithotomy: A prospective randomized, double-blinded placebo-controlled study. J Anaesthesiol Clin Pharmacol. 2022;38(4):566.
23. Wang J, Zhou Z, Cui Y, Li Y, Yuan H, Gao Z, et al. Meta-analysis of the efficacy and safety of mirabegron and solifenacin monotherapy for overactive bladder. Neurourol Urodyn. 2019;38(1):22-30.
24. Fischer KM, Louie M, Mucksavage P. Ureteral stent discomfort and its management. Curr Urol Rep. 2018;19(8):64.
25. Evrüke İM, Taş İS. The effect of solifenacin treatment for urge urinary incontinence on sexual function in premenopausal and postmenopausal women: a prospective observational study. Cukurova Med J. 2023;48(1):200-7.
26. Kosilov K, Kuzina I, Kuznetsov V, Gainullina Y, Kosilova L, Karashchuk E, et al. The risk of sexual dysfunction and effectiveness of treatment of benign prostatic hyperplasia with severe lower urinary tract dysfunction with combination of dutasteride and solifenacin. J Sex Med. 2018;15(11):1579-90.
27. Tang Q-L, Zhou S, Liu Y-Q, Wu J, Tao R-Z. Efficacy and safety of combination of mirabegron and solifenacin in patients with double-J stent related overactive bladder: a prospective study. Sci Rep. 2022;12(1):18844.
28. Sahin A, Yildirim C, Yuksel OH, Ürkmez A. Treatment of ureteral catheter related symptoms; mirabegron versus tamsulosin/solifenacin combination: A randomized controlled trial. Arch Esp Urol. 2020;73(1):54-9.
29. Verma V, Singh N, Singh Jaggi A. Pregabalin in Neuropathic Pain: Evidences and Possible Mechanisms. Curr Neuropharmacol. 2014;12(1):44-56.
30. Chaisewikul R, Saejong R, Tongsai S, Thamlikitkul V. Comparative effectiveness and safety of original gabapentin and generic gabapentin in treating patients with neuropathic pain at Siriraj hospital, Bangkok, Thailand. Siriraj Med J. 2012;64(6):172-77
31. Chotikawanich E, Leewansangtong S, Liangkobkit K, Nualyong C, Srinualnad S, Chaiyaprasithi B, et al. The feasibility and outcomes of retrograde intrarenal surgery to treat staghorn renal calculi. Siriraj Med J. 2023;75(5):362-8.
32. Rosen G, Hargis P, Lough C, Kahveci A, Moss A, Golzy M, et al. Mp10-20 single dose preoperative pregabalin in ureteroscopy – results of a randomized controlled trial. J Urol. 2023;209(Suppl 4):e122.
33. Agarwal MM, Elsi Sy M. Gabapentenoids in pain management in urological chronic pelvic pain syndrome: Gabapentin or pregabalin? Neurourol Urodyn. 2017;36(8):2028-33.
34. Park K-H, Chung N-S, Chung H-W, Kim TY, Lee H-D. Pregabalin as an effective treatment for acute postoperative pain following spinal surgery without major side effects: protocol for a prospective, randomized controlled, double-blinded trial. Trials. 2023;24(1):422.
35. Meaadi J, Obara I, Eldabe S, Nazar H. The safety and efficacy of gabapentinoids in the management of neuropathic pain: a systematic review with meta-analysis of randomised controlled trials. Int J Clin Pharm. 2023;45(3):556-65.
36. Mathias S, Wiseman O. Silicone vs. Polyurethane Stent: The final countdown. J Clin Med. 2022;11(10):2746.
37. Ehsanullah SA, Bruce A, Juman C, Krishan A, Krishan A, Higginbottom J, et al. Stent diameter and stent-related symptoms, does size matter? A systematic review and meta-analysis. Urol Ann. 2022;14(4):295-302.
38. Bao X, Sun F, Yao H, Wang D, Liu H, Tang G, et al. Distal end of Double-J ureteral stent position on ureteral stent-related symptoms: A systematic review and meta-analysis. Front Surg. 2022;9:990049.