The following is an abridged republication of a published Cochrane Review, reprinted with permission.

Medical and surgical interventions for the treatment of urinary stones in children: A Cochrane Review

Lenka Barreto; Jae Hung Jung; Ameera Abdelrahim; Munir Ahmed; Guy P. C. Dawkins; Marcin Kazmierski

Acknowledgement: *This article is based on a Cochrane Review published in the Cochrane Database of Systematic Reviews (CDSR) 2018, Issue 6. Art. No.: CD010784. DOI:10.1002/14651858.CD010784.pub2.*

Cite as: *Can Urol Assoc J* 2019 April 26; Epub ahead of print. http://dx.doi.org/10.5489/cuaj.5787

Published online April 26, 2019

***

Abstract

Introduction: We performed systematic review to assess the effects of different medical and surgical management of urinary stones in children.
Methods: We performed a comprehensive search using multiple databases (MEDLINE, EMBASE, Cochrane Register of Controlled Trials), trials registries (World Health Organization International Clinical Trials Registry Platform Search Portal and *ClinicalTrials.gov*), and abstract proceedings of major urological and paediatric urology meetings, with no restrictions on the language of publication or publication status, up until December 2017. We included all randomized controlled trials (RCTs) and quasi-RCTs. Two review authors independently assessed the eligibility of studies for inclusion, extracted data, and assessed risk of bias in accordance with the Cochrane 'Risk of bias' tool. We performed statistical analyses using a random-effects model and assessed the quality of the evidence according to GRADE.
Results: We included 14 studies with a total of 978 randomized participants in our review, informing seven comparisons with shock wave lithotripsy, percutaneous nephrolithotripsy, ureterorenoscopy (regardless of the type of lithotripsy), open stone surgery, and medical expulsive therapy. There was very low quality of evidence in the most comparisons with regards to the effectiveness and adverse events for the treatment of paediatric upper renal tract stone disease.

Conclusions: Based on mostly very low-quality evidence for most comparisons and outcomes, we are uncertain about the effect of nearly all medical and surgical interventions to treat stone disease in children. There is a critical need for better quality trials assessing patient-important outcomes in children with stone disease to inform future guidelines on the management of this condition.

Introduction

The prevalence rate of urinary tract stones in children in low- to middle-income countries such as Pakistan and Turkey is 5% to 15%, compared with 1% to 5% in high-income countries [1, 2]. The manifestation and clinical presentation of urinary stones in children differs from the adult population and can vary with age. Fifty percent of children will present with abdominal pain, 33% with haematuria and 11% with infection. Children under the age of five years most commonly present with blood in the urine, while pain is a more common finding in older children [3].

The most appropriate management strategy in children depends on the size, location and composition of the stone. Shock wave lithotripsy (SWL) is a commonly used for smaller upper urinary tract stones as long as there is adequate drainage of the urinary system below the level of the stone. In children with larger and more complex stone disease percutaneous nephrolithotripsy (PCNL) is widely used. This technique is considered in children with large upper tract stones (1.5 cm or larger). Children with stone size from 4 mm within the ureter or collecting system may be treated by ureterorenoscopy with different contact lithotripsy techniques such as laser, ultrasound, and pneumatic lithotripsy. Open stone surgery may be used in very young children with large stones or in children with a large stone which would require multiple endoscopic procedures and in children with a stone in the presence of congenital anomalies of the urinary system or orthopaedic anomalies. Laparascopic and robotic surgery are becoming more popular in the treatment of various urological conditions requiring a surgical approach but is not yet commonly used in the treatment of paediatric stones [4]. Medical expulsion therapy involves the administration of medications to accelerate and facilitate the spontaneous passage of ureteric stones. Corticosteroids, hormones, nonsteroidal anti-inflammatory agents, calcium-channel blockers and alpha-adrenergic blockers have been used in the conservative management of stone disease. While there are existing systematic reviews that assess the effects of medical expulsive therapy and ureteroscopy, the reviews are less rigorous and include non-randomised controlled trials regardless of study design [5, 6, 7, 8, 9]. Furthermore, none apply the GRADE approach or use the same methodology as Cochrane reviews.

Therefore, we performed the systematic reviews to assess the effects of different medical and surgical interventions in the treatment of urinary tract stones of the kidney or ureter in children.

Methods

Please see the protocol and review published in Cochrane Library for further details on the methods.

Search strategy and selection criteria

The search strategy was developed with the Cochrane Renal Group's Trials Search Co-ordinator. The latest search was conducted on 31st December 2017 of the Cochrane Central Register of Controlled trials, MEDLINE and Embase. No language limitations were applied. We also searched the references of full articles retrieved for our review to identify any additional studies. To identify unpublished trials or trials in progress, we searched the following sources: ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform Search Portal (apps.who.int/trialsearch/) and the International Standard Randomised Controlled Trial Number registry (controlled-trials.com). We conducted a search of abstract proceedings of major urological and paediatric urology meetings, covering the years 2012 to 2017. We contacted the authors of studies identified as potentially eligible to obtain clarification on missing data.

Two review authors (LB and AA) independently screened all potentially relevant records and classified studies in accordance with the criteria for each provided in the Cochrane Handbook for Systematic Reviews of Interventions [10]. The conflict resolution was performed by a third author (MK) independently. We reviewed randomised controlled trials (RCTs), including pseudo-RCTs.

Types of participants

We included children (aged 0 to 18 years) with upper tract urinary stones confirmed by imaging, who required medical or surgical intervention.

Types of interventions

We have examined and compared shock wave lithotripsy, percutaneous nephrolithotripsy, ureterorenoscopy (regardless of the type of lithotripsy), open stone surgery and medical expulsive therapy.

Types of outcomes measured

Primary outcomes measured were stone-free rate, serious adverse events or complications of treatment and secondary procedures for residual fragments. Secondary outcomes measured were hospital stay and pain.

Assessment of risk of bias in included studies

Two review authors (LB, AA) independently assessed the risk of bias of each included study on a per outcome basis. We resolved all disagreements by discussion and consensus. We assessed risk of bias using the Cochrane 'Risk of bias' assessment tool. We judged risk of bias domains as 'low risk', 'high risk', or 'unclear risk' and evaluated individual bias items as described in the Cochrane Handbook for Systematic Reviews of Interventions [10].

Data collection and synthesis

Data extraction was carried out independently by two authors (LB and MK) using data extraction forms created in Microsoft Excel. We resolved any disagreements by discussion or, if required, by consultation with a third review author (AA). We combined data from individual studies for meta-analysis where interventions were similar enough.

We expressed dichotomous outcome results (SFR, adverse events and complications after treatment, number of second procedures for residual fragments measuring 4 mm or more as RRs with 95% confidence intervals (CIs). We used the MD where continuous scales of measurement are used to assess the effects of treatment (mean hospital stay, pain scale, pain medication).We summarised data using a random-effects model. We interpreted random-effects meta-analyses with due consideration of the whole distribution of effects.

Heterogeneity was analyzed using a Chi^2 test on N-1 degrees of freedom with an alpha of 0.05 used for statistical significance and with the I^2 test [11]. I^2 values of 25%, 50% and 75% generally correspond to low, medium and high levels of heterogeneity. When we encountered heterogeneity, we attempted to determine possible reasons for it by examining individual study and subgroup characteristics. In the event of excessive heterogeneity unexplained by subgroup analyses, we planned not to report outcome results as the pooled effect estimate in a meta-analysis but to provide a narrative description of the results of each study.

Subgroup and sensitivity analyses

We expected the following characteristics to introduce clinical heterogeneity, and we planned to carry out subgroup analyses with investigation of interactions.

- Size of the kidney stone (less than 10 mm versus 10 mm or more).
- Location of the stone (renal pelvis versus ureter).

Summary of findings tables (SoF)

We presented the overall quality of the evidence (QoE) for each outcome according to the GRADE approach, which takes into account five criteria not only related to internal validity (risk of bias, inconsistency, imprecision, publication bias), but also to external validity, such as directness of results [12].

Results

Search results

We identified a total of 700 references from all searches. After removal of duplicates, we screened the titles and abstracts of 617 records and excluded 597. We screened 20 full-text articles and excluded 5 articles. A total of 14 studies (15 articles) were included in the final review. The flow of studies identified to be included in the review is summarised in a flow chart (Figure 1). Detailed characteristics of included studies are summarised in Table 1.

Participants

The mean age of trial participants ranged from 20.3 months to 11.1 years (with an age range of 0.5 to 17 years). Ethnic groups were not described; however, two studies were conducted in Turkey [22, 24], seven studies in Egypt [17, 19, 21, 23, 25, 27, 28], two studies in Iran [14, 15], one in India [18], one in China [20], and one in Italy [16]. Major exclusion criteria were renal abnormalities and coagulopathy. Inclusion criteria related to stone size and age. In the surgical group, stone size range was 5 mm to 45 mm [14- 20]. In the medical therapy group, stone size ranged from 2 mm to 12 mm [22- 25, 27], and less than 1 cm [21]. In the medical and surgical intervention group the median stone size was 12 mm (10 mm to 16 mm) [28].

Effects of interventions

<u>Shock wave lithotripsy versus dissolution therapy for intrarenal stones</u>

We found a single study with 87 participants (39 randomised to SWL and 48 to oral citrate) [28]. The follow-up period was three months.

1. Stone-free rate
   We are uncertain about the effects of SWL on SFR (RR 1.13, 95% CI 0.90 to 1.41; very low QoE).
2. Serious adverse events or complications of treatment
   We are uncertain about the effects of SWL on serious adverse events (RR 1.23, 95% CI 0.08 to 19.05; very low QoE).
3. Secondary procedures for residual fragments
   We are uncertain about the effects of SWL on secondary procedures for residual fragments (RR 0.66, 95% CI 0.29 to 1.50; very low QoE).
   There were no data for Hospital stay and Pain.

<u>Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones.</u>

We found a single study with 60 participants (30 randomised to slow SWL and 30 randomised to rapid SWL) [19]. The follow-up period was a minimum of one month.

1. Stone-free rate
   We are uncertain about the effects of slow SWL on SFR (RR 2.25, 95%CI 1.16 to 4.36; very low QoE).
2. Serious adverse events or complications of treatment
   We could not estimate the risk of serious adverse events or complications of treatment due to there being no reported events.
3. Secondary procedures for residual fragments
   We are uncertain about the effects of slow SWL on secondary procedures for residual fragments (RR 0.38, 95%CI 0.11 to 1.28; very low QoE).
   There were no data for Hospital stay and Pain.

<u>Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and distal ureteric stones.</u>

We found three studies with 153 participants (75 randomised to SWL and 78 randomised to ureteroscopy) [15-17]. All studies were included in the analyses, except for the outcome 'hospital stay', which included data from 2 studies [15, 17]. While two studies reported the follow-up period two weeks to eight months [15, 16], one [17] did not report the period.

1. Stone-free rate

We are uncertain about the effects of SWL on SFR (RR 0.62, 95% CI 0.43 to 0.88; very low QoE).
2. Serious adverse events or complications of treatment
   We are uncertain about the effects of SWL on severe adverse events (RR 0.56, 95% CI 0.12 to 2.58; very low QoE).
3. Secondary procedures for residual fragments
   We are uncertain about the effects of SWL on secondary procedures (RR 3.47, 95%CI 1.32 to 9.15; very low QoE).
4. Hospital stay (hours)
   We are uncertain about the effects of SWL on hospital stay (MD -10.71, 95% CI -34.09 to 12.67; very low QoE).
5. Pain
   We did not find any data related to pain.

<u>Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones</u>
We found a single study with 221 participants (110 randomised to SWL and 111 randomised to mini-PCNL) [18]. The follow-up period was three months.
1. Stone-free rate
   SWL likely has lower SFR (RR 0.88, 95% CI 0.80 to 0.97; moderate QoE).
2. Serious adverse events or complications of treatment
   SWL may reduce severe adverse events (RR 0.13, 95% CI 0.02 to 0.98; low QoE).
3. Secondary procedures for residual fragments
   SWL may increase the need of secondary procedures (RR 2.50, 95% CI 1.01 to 6.20; low QoE).
4. Hospital stay (days)
   SWL likely reduces hospital stay (MD -3.40, 95% CI -5.43 to - 1.37; moderate QoE).
5. Pain
   We did not find any data related to pain.

<u>Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones</u>
We found a single study with 23 participants (10 randomised to PCNL and 13 randomised to tubeless PCNL) [14]. The follow-up period was one month.
1. Stone-free rate
   We are uncertain about the effect of PCNL in SFR (RR 1.16, 95% CI 0.88 to 1.53; very low QoE).
2. Serious adverse events or complications of treatment
   We are uncertain about the effect of PCNL on serious adverse events (RR 0.42, 95%CI 0.02 to 9.43; very low QoE).
3. Secondary procedures for residual fragments
   We are uncertain about the effect of PCNL on secondary procedures (RR 0.42, 95%CI 0.02 to 9.43; very low QoE).
4. Hospital stay (hours)

PCNL may increase hospital stay (MD 19.16, 95% CI 10.24 to 28.08; low QoE).
5. Pain (dose of morphine: mg/kg)
PCNL likely requires larger doses of morphine (MD 0.08, 95% CI 0.05 to 0.11; moderate QoE).

Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

We found a single study with 78 participants (38 randomised to PCNL and 40 randomised to tubeless mini-PCNL) [20]. The follow-up period was 12 months.

1. Stone-free rate
PCNL likely results in no difference in SFR (RR 1.03, 95% CI 0.93 to 1.14; moderate QoE).
2. Serious adverse events or complications of treatment
We did not find any data related to serious adverse events.
3. Secondary procedures for residual fragments
There were no reported events.
4. Hospital stay (days)
PCNL likely increases hospital stay (MD 3.14, 95% CI 2.78 to 3.50; moderate QoE).
5. Pain
We did not find any data related to pain.

Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

We found six studies with a different number of participants in each analysis [21, 22, 23-25, 27]. The follow-up period ranged from three to four weeks.

1. Stone-free rate
We included six studies with 335 participants (alpha-blocker 185, placebo with/without analgesics 150) in the analysis for SFR [21, 22, 23-25, 27]. Alpha-blockers may increase SFR (RR 1.34, 95% CI 1.16 to 1.54; low QoE).
2. Serious adverse events or complications of treatment
There were no serious adverse events or complications in either group.
3. Secondary procedures for residual fragments
We included one study with 39 participants (alpha-blocker 19, placebo with/without analgesics 20) [22]. We are uncertain about the effect of alpha-blockers on secondary procedures (RR 0.53, 95% CI 0.15 to 1.81; very low QoE).
4. Hospital stay
We did not find any data related to hospital stay.
5. Pain
We included two studies with 98 participants (alpha-blocker 51, placebo with/without analgesics 47) [23, 27]. We are uncertain about the effect of alpha-blockers on pain episodes (MD -1.49, 95%CI -3.04 to 0.06; very low QoE).

Subgroup analysis and sensitivity analysis

We were able to perform subgroup analysis only in the comparison of shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy. There was a difference in hospital stay with an MD of 0.00 (95% CI −1.07 to 1.07) in the participants with renal stones [18] versus an MD of −24.00 (95% CI -39.45 to -8.55) in the participants with distal ureteral stones (P = 0.002, I^2 = 89.2%). However, no differences were found in SFR (P = 0.57, I2 = 0%), Serious adverse events or complications of treatment (P = 0.70, I^2 = 0%) and Secondary procedures for residual fragments (P = 0.66, I^2 = 0%).

We could not conduct any sensitivity analyses.

Risk of bias in included studies

Further details on the assessment of Risk of Bias were stated in the review published in Cochrane Library. Assessments of risk of bias are summarised in Figure 2.

Summary of findings tables

We summarised the results in summary of findings tables in accordance with GRADE methodology (Table S3-9).

Discussion

To date, we have not identified any non-Cochrane review that used similar rigorous methodology including a published protocol. However, there were a few reviews for this topic. We identified two systematic reviews assessing ureteroscopy [6, 7] and three systematic reviews assessing medical expulsive therapy [5, 8, 19].

Ishii et al. looked at the effects of ureteroscopic approach. They concluded that the use of ureteroscopy as the first-line surgical management is a safe and highly effective intervention, with a small proportion of the study population having minor complications. Also, Saad et al. compared PCNL to ureterorenoscopy in 38 randomized patients [29]. While they reported no difference in SFR, serious adverse events or complications of treatment and secondary procedures, they reported 43 renal units instead of randomized participants which causes unit of analysis error.

Tian et al. analyzed effects of alpha-blockers (tamsulosin and doxazosin) on stone expulsion rate, stone expulsion time, and treatment-emergent adverse events with four RCTs and one cohort study. The results of the review regarding the stone expulsion rate suggested that adrenergic alpha-antagonists significantly improved the stone expulsion rate compared to the placebo. There was no significant difference between the adrenergic alpha-antagonists and the placebo groups in terms of adverse events. In addition, Glina et al analyzed alpha-1 adrenergic blockers as medical expulsive treatment in children with distal ureterolithiasis with three RCTs in the meta-analysis and concluded that use of an alpha-1 adrenergic blocker is related to a greater incidence of expulsion of ureteral calculi and fewer episodes of pain when compared to ibuprofen.

Although all interventions assessed in this review are used to treat stone disease, the patient populations they apply to vary greatly by stone size and age. This limits any assessments across randomised comparisons. In addition, the definition of the SFR varied across the studies. In some studies, the SFR was accepted if the fragments post-treatment were less than or equal to 4 mm [14, 19, 20], whereas other studies classified SFR as no remaining fragments in the renal tract. The length of follow-up varied between the studies and was generally limited to short-term follow-up of three months or less. There is a need for long-term follow-up data. Regarding the predefined primary and secondary outcomes in this review, half of the studies reported on all primary outcomes (SFR, complications and rate of secondary procedures) [14-18, 19, 20, 28]. Only three studies reported pain [14, 23, 27] as an outcome and five studies reported on hospital stay [14, 15, 17, 18, 20]. We were unable to conduct any of the predefined subgroup analyses except one comparison of SWL versus ureteroscopy. Questions around differential effectiveness and safety of these interventions therefore remain unanswered. A majority of the studies are recent. This is potentially due to the increasing incidence of the nephrolithiasis in children 18 years old and younger [30] and increased recognition of the importance of trials in paediatric urology. The majority of comparisons assessed in this review relate to surgical innovation. With regards to ureterorenoscopes and nephroscopes, there have been recent advancements in terms of miniaturisation, increased functionality (improved scope flexibility) and visualization (introduction of digital scopes0 [31]. These recent advances are not captured in this review, given the paucity of trials and limiting applicability. Factors which could have significant impact on the treatment outcomes - such as contributing metabolic abnormalities, stone composition and preoperative renal function - have not been considered in most of the studies. This could have an impact on the choice of treatment modality and treatment outcomes. The applicability of the findings to high-income countries needs consideration as the majority of included studies were conducted in middle- and low-income countries with possible variation in risk factors for stone formation, availability of certain interventions and access to paediatric care.

Although we attempted to conduct a comprehensive search irrespective of language and publication status, it is possible that we missed non-English studies in non-indexed journals. In addition, the reporting quality of most included studies was poor, prompting us to contact the authors for further information. Due to the time-intense nature of this effort, we limited this to one attempt only. Increased efforts may have yielded a better response rate. The focus of this systematic review was direct evidence from randomised trials in paediatric patient populations. Given that the QoE was very low, it is possible that indirect evidence from adult populations or observational studies may have yielded higher quality evidence for at least some comparisons.

References

1. Shah AM, Kalmunkar S, Punekar SV, et al. Spectrum of pediatric urolithiasis in Western India. *Indian Journal of Pediatrics* 1991;58(4):543–9.
2. Elsobky E, Sheir KZ, Madbouly K, et al. Extracorporeal shock wave lithotripsy in children: experience using two second-generation lithotripters. *BJU International* 2000;86(7):851–6.
3. Santos-Victoriano M, Brouhard BH, Cunningham RJ 3rd. Renal stone disease in children. *Clinical Pediatrics* 1998;37(10):583–99.
4. Dahm P, Sedrakyan A, McCulloch P. Application of the IDEAL Framework to Robotic Urologic Surgery. *European Urology* 2014;65(5):849–51.
5. Glina FP, Castro PM, Monteiro GG, et al. The use of alpha-1 adrenergic blockers in children with distal ureterolithiasis: a systematic review and meta-analysis. *International Brazilian Journal of Urology* 2015;41(6):1049–57.
6. Ishii H, Griffin S, Somani BK. Flexible ureteroscopy and lasertripsy (FURSL) for paediatric renal calculi: results from a systematic review. *Journal of Pediatric Urology* 2014;10(6):1020–5.
7. Ishii H, Griffin S, Somani BK. Ureteroscopy for stone disease in the paediatric population: a systematic review. *BJU International* 2015;115(6):867–73.
8. Tian D, Li N, Huang W, et al. The efficacy and safety of adrenergic alpha-antagonists in treatment of distal ureteral stones in pediatric patients: A systematic
6. review and meta-analysis. *Journal of Pediatric Surgery* 2017;52(2):360–5.
9. Velazquez N, Zapata D, Wang HH, et al. Medical expulsive therapy for pediatric urolithiasis: Systematic review and meta-analysis. *Journal of Pediatric Urology* 2015;11(6):321–7.
10. Higgins JP, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. *The Cochrane Collaboration*, 2011.
7. Available from www.cochrane-handbook.org.
11. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327(7414):557–60.
12. Guyatt GH, Oxman AD, Vist GE et al. GRADE: what is “quality of evidence” and why is it important to clinicians? *BMJ* (Clinical Research Ed) 2008;336:995–8
13. Barreto L, Jung JH, AbdelrahimA, et al. Medical and surgical interventions for the treatment of urinary stones in children. *Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD010784.
14. Aghamir SM, Salavati A, Aloosh M, et al. Feasibility of totally tubeless percutaneous nephrolithotomy under the age of 14 years: a randomized clinical trial. *Journal of Endourology* 2012;26(6):621–4.
15. Basiri A, Zare S, Tabibi A, et al. A multicenter, randomized, controlled trial of transureteral and shock wave lithotripsy which is the best minimally invasive modality to treat distal ureteral calculi in children?. *Journal of Urology* 2010;184(3):1106–9.
16. De Dominicis M, Matarazzo E, Capozza N, et al. Retrograde ureteroscopy for distal ureteric stone removal in children. *BJU International* 2005;95(7):1049–52.
17. Gamal W, Mmdouh A, Sogah. FURS vs shockwave lithotripsy for treatment of (1-2) cm renal stones in children with a solitary kidney: A prospective randomized study. *The Journal of Urology*. 2017;197:578.
18. Kumar A, Kumar N, Vasudeva P, et al. A single center experience comparing miniperc and shockwave lithotripsy for treatment of radiopaque 1-2 cm lower caliceal

renal calculi in children: a prospective randomized study. *Journal of Endourology / Endourological Society* 2015;29(7):805.
19. Salem HK, Fathy H, Elfayoumy H, et al. Slow versus rapid delivery rate shock wave lithotripsy for pediatric renal urolithiasis: a prospective randomized study. *The Journal of Urology* 2014;191(5):1370.
20. Song G, Guo X, Niu G, et al. Advantages of tubeless mini-percutaneous nephrolithotomy in the treatment of preschool children under 3 years old. *Journal of Pediatric Surgery* 2015;50(4):655.
21. Aldaqadossi HA, Shaker H, SaifelnasrM, et al. Efficacy and safety of tamsulosin as a medical expulsive therapy for stones in children. *Arab Journal of Urology* 2015;13:107–11.
22. Aydogdu O, Burgu B, Gucuk A, et al. Effectiveness of doxazosin in treatment of distal ureteral stones in children. *Journal of Urology* 2009;182(6):2880–4.
23. Elgalaly H, Eliwa A, Seleem M, et al. Silodosin in the treatment of distal ureteric stones in children: A prospective, randomised, placebo-controlled
8. study. *Arab Journal of Urology* 2017;15:194–8.
24. Erturhan S, Bayrak O, Sarica K, et al. Efficacy of medical expulsive treatment with doxazosin in pediatric patients. *Urology* 2013;81(3):640–3.
25. Fahmy A, Rhasad H, Kamal A, et al. Silodosin for medical expulsive therapy in children with distal ureteral stone: a prospective randomized, placebo-controlled, single blind study. *The Journal of Urology*. 2017; Vol. 197:1217.
26. Mokhless I, Youssif M, Zahran A. Tamsulosin for the management of distal ureteral stones in children: a prospective randomized study [abstract no: S2-2]. *22nd Annual Congress of the European Society for PediatricUrology (ESPU)*; 2011 Apr 27-30; Copenhagen, Denmark. 2011.
27. Mokhless I, Zahran AR, Youssif M, et al. Tamsulosin for the management of distal ureteral stones in children: a prospective randomized study. *Journal of Pediatric Urology* 2012;8(5):544–8.
28. Elderwy A, Kurkar A, Hussein A-M, et al. Dissolution therapy versus shock wave lithotripsy for radiolucent renal stones in children: a prospective study. *The Journal of Urology* 2014;191(5):1491.
29. Saad KSM, Youssif ME, Hamdy S, et al. Percutaneous nephrolithotomy vs retrograde intrarenal surgery for large renal stones in pediatric patients: A randomized controlled trial. *Source Journal of Urology* Dec 2015;194(6):1716-20.
30. Sas DJ, Hulsey TC, Shatat IF, et al. Incidence of kidney stones in children evaluated in the ER is increasing. *The Journal of Pediatrics* 2010;157(1):132–7.
31. Borofsky MS, Shah O. Advances in ureteroscopy. *Urologic Clinics of North America* 2013;40(1):67–78.

Figures and Tables

Fig. 1. Flow chart.

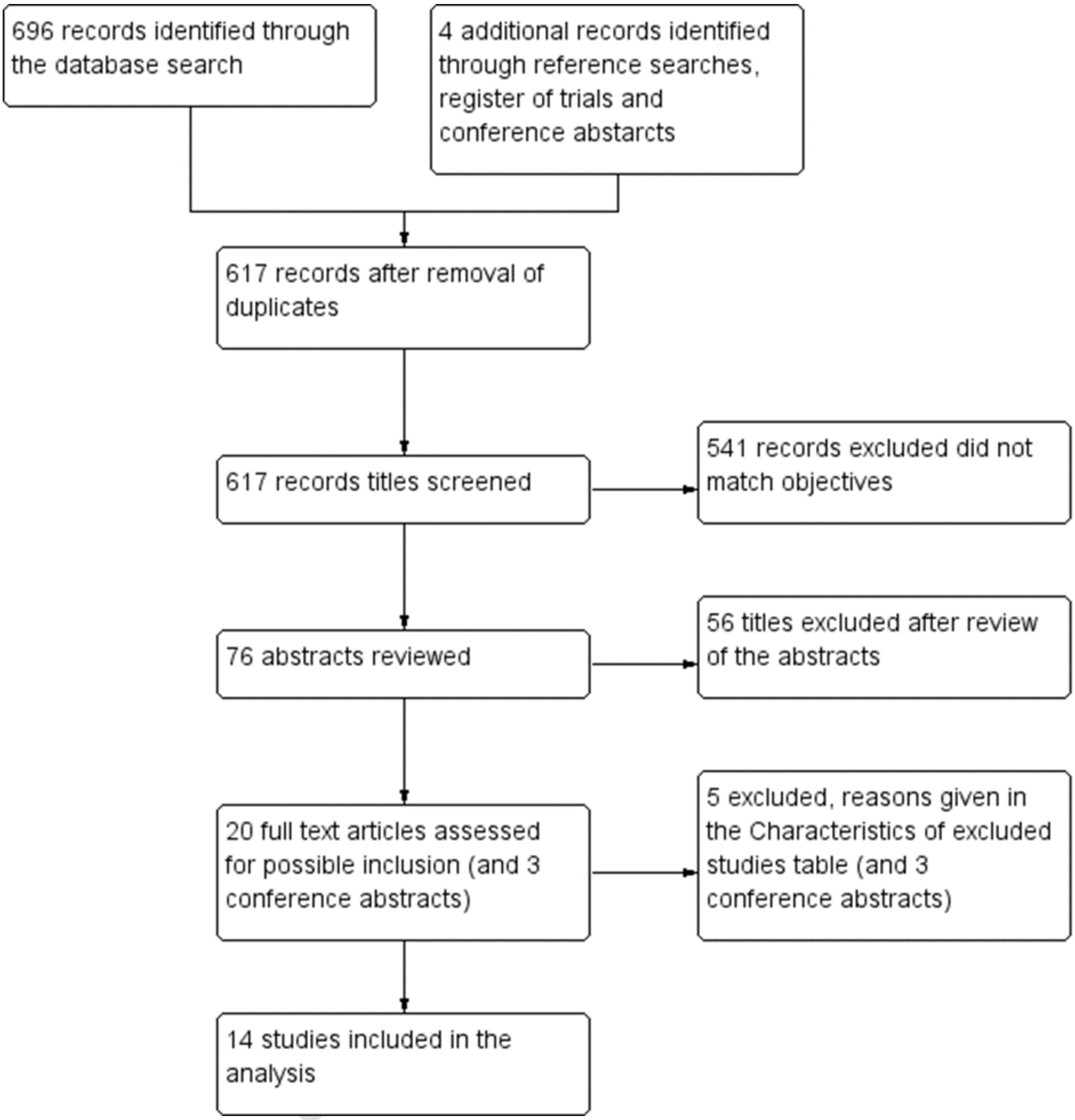

Fig. 2. Summary of risk of bias assessment.

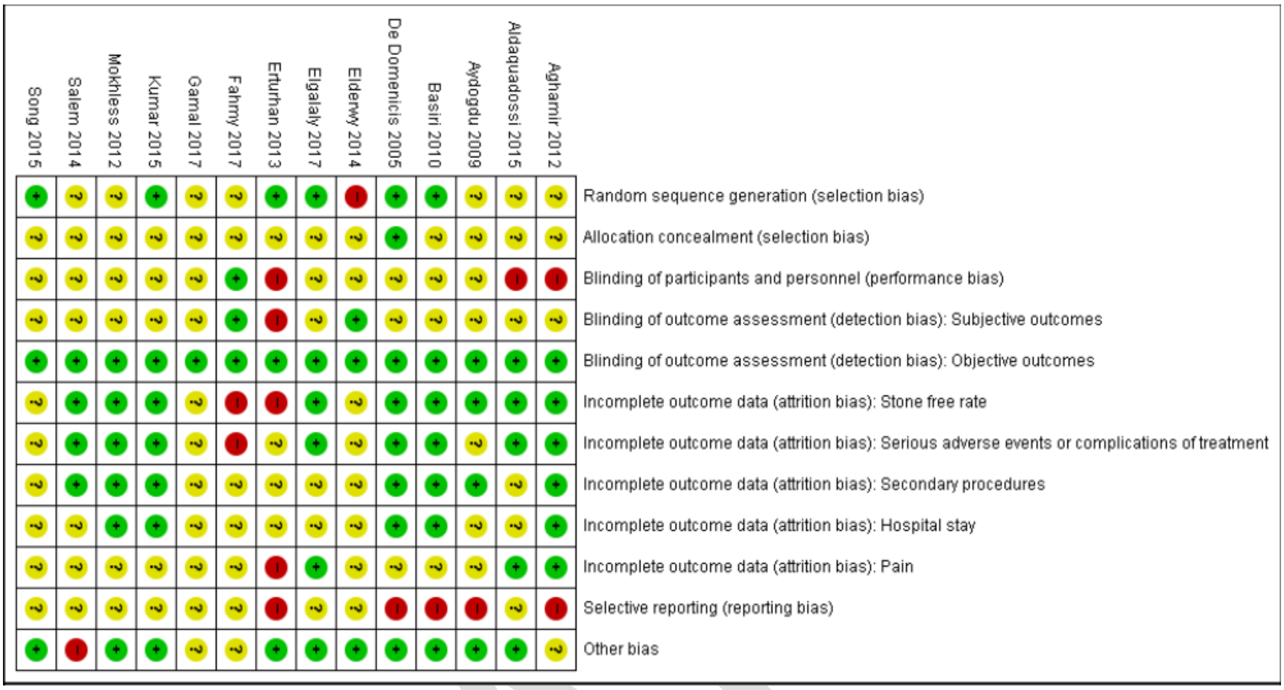

Table 1. Characteristics of included studies

Study	**Population**	**Intervention**	**Comparison**	**Outcome measured**	**Followup**	**Funding sources**	**COI**
Aghamir 2012	<14 years old, renal stone >2.5 cm or renal stone with lesser diameter, and extracorporeal shockwave lithotripsy failure	Tubeless percutaneous nephrolithotomy	Standard percutaneous nephrolithotomy	1. Stone clearance 2. Complications	24-48 hours after surgery, one week and one month after surgery	Not stated	Not stated
Aldaquadossi 2015	Group 1: 33 children - mean age 7.7 years; group 2: 34 children - mean age 7.25 years, distal ureteric stone of <1 cm, and below the common iliac vessels	Alpha-1 blocker (tamsulosin) therapy in addition to ibuprofen	Ibuprofen only	1. Stone clearance 2. Analgesic requirement	Weekly for 4 weeks	None	None
Aydogdu 2009	2–14 years old, radiopaque lower ureteral stone 2–10 mm	Ibuprofen	Doxazosin and ibuprofen	1. Stone clearance 2. Secondary procedures	19 days (mean)	Not stated	Not stated
Basiri 2010	1–13 years old, distal ureteral calculi 15-56 mm^2	Transureteral lithotripsy	Shock wave lithotripsy	1. Stone clearance 2. Complications 3. Secondary procedures 4. Hospital stay	2 weeks postoperatively with ultrasound, another at 3 months with excretory urography (more frequent if persistent stone present)	Not stated	Not stated

De Domenici 2005	2–17 years old, radioopaque calculi in distal ureter	Ureteroscopy plus intracorporeal lithotripsy	Extracorporeal shock wave lithotripsy	1. Stone clearance 2. Complications 3. Secondary procedures	6–8 months	Not stated	Not stated
Elderwy 2014	0.5–13 years old, renal calculi 7–24 mm <500 HU	Dissolution therapy	Standard shock wave lithotripsy	1. Stone clearance 2. Complications 3. Secondary procedures	Every 3–4 weeks and every 3–4 months thereafter length of treatment: 3 months	Not stated	Not stated
Elgalaly 2017	<18 years old, single unilateral radiopaque DUS, and largest stone diameter of ≤10 mm	Silodosin	Placebo	1. Stone clearance	For 3 weeks with weekly examinations length of treatment: 3 weeks	None	None
Erturhan 2013	3–15 years old, lower ureteral stones	Ibuprofen only	Alpha-1 blocker (doxazosin) therapy in addition to ibuprofen	1. Stone clearance	3 weeks with weekly examinations	Authors declare no relevant financial interests	Not stated
Fahmy 2017	<18 years old, unilateral, single, radio-opaque distal ureteral stones <10 mm in size	Silodosin	Tamsuosin or placebo	1. Stone clearance 2. Complications	Stone-free rate assessed after 4 weeks. Further details of followup not supplied.	None	Not declared

Gamal 2017	<15years old, with a renal stones (1–2 cm) in a solitary kidney	Flexible ureteroscopy plus lasertripsy	Shockwave lithotripsy	1. Stone clearance 2. Complications 3. Secondary procedures	Followup: stone-free rate assessed after 1 month. Further details of followup not supplied	None	Not declared
Kumar 2015	<15 years old, single lower caliceal stone 1–2 cm	Mini percutaneous nephrolithotomy	Shockwave lithotripsy	1. Stone clearance 2. Complications 3. Secondary procedures	3 weeks	Not stated	No competing financial interests exist
Mokhless 2012	2–15 years old, distal ureteric calculi <12 mm	Tamsulosin and standard analgesia	Placebo and standard analgesia	1. Stone clearance	4 weeks	None	No conflict of interest
Salem 2014	3–14 years old, renal calculi 10–20 mm	Slow delivery rate shock wave lithotripsy	Rapid delivery rate shock wave lithotripsy	1. Stone clearance 2. Secondary procedures	2 and 4 weeks	Not stated	Not stated
Song 2015	7–36 months old, renal stones with cumulative diameter <4.5 cm	Tubeless mini percutaneos nephrolithotomy	Standard percutaneous nephrolithotomy	1. Stone clearance 2. Complications 3. Secondary procedures	1, 3, 6, 12 months postoperatively	Not stated	Not stated