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REVIEW ARTICLE

Sterile water injections for management of renal colic pain: a systematic review

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ABSTRACT

Background: Since the 1950s a small number of centres have used sterile water injections (SWI) to treat renal colic pain. We undertook this review to determine the efficacy of SWI to manage the pain of renal colic.

Methods: We searched the electronic databases PubMed, Cochrane Central Register, CINAHL, and Scopus from database inception to 7 November 2021 for randomized controlled trials that met the inclusion criteria.

Results: Six trials were included in the review ($n = 894$ patients). Two placebo controlled trials were included in the meta-analysis. Other trials compared SWI to Diclofenac, Morphine, or oral Paracetamol. The overall quality of the trial was low. Compared to a placebo SWI demonstrated a significant reduction in self-reported pain at 30 min (Mean difference [MD] = −4.68, 95% Confidence Interval [CI] = −5.21, −4.15. $p < 0.001$, $I^2 = 0\%$) and at or beyond 60 min post-injection (MD = −5.34 95% CI = −5.85, −4.82, $p \leq 0.001$, $I^2 = 0\%$). Pain relief provided by SWI was significantly better than oral paracetamol and equivalent to Diclofenac and Morphine. No significant side-effects were attributed to SWI use in any trials.

Discussion/conclusion: SWI could be a suitable alternative for management of renal colic pain where alternatives such as non-steroidal anti-inflammatory and opioid drugs are either unavailable or contraindicated. However, further research is required to establish the role of SWI in renal colic pain management.

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Introduction

Nephrolithiasis is the most common cause of acute renal colic pain occurring in up to 12% of the population [1,2]. The typical presentation is severe flank to groin pain caused by ureteric obstruction, stretching, and compression of the renal capsule of the pelvis [3]. Migration of the stone causes inflammatory cascade activation resulting in prostaglandin release and ureteric spasm with stimulation of A□ and C fibres. Referred pain results from somatovisceral convergence in the spinal cord. Other symptoms such as tachycardia, nausea and vomiting are also common [3]. As up to 90% of stones will pass spontaneously, initial management focuses on providing analgesia. Both non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are frequently used to manage acute nephrolithiasis pain [4]. NSAIDs directly address the prostaglandin mediated origins of the pain, are widely available and easy to administer. Recent reviews have suggested that NSAIDs provide superior analgesia to opioids [5]. However, they are contraindicated in patients with a history of renal failure or gastrointestinal bleeding [6]. Furthermore, in pregnant women, NSAIDs may have adverse foetal effects such as premature closure of the ductus arteriosus depending on gestation at administration [7]. Whilst opioids can also provide pain relief with the advantage of titration to degree of pain, they are associated with an increase in nausea and vomiting [5].

A limited number of randomised controlled trials have explored the use of injections of small volumes of sterile water into the skin to manage renal colic pain. This method has been cited in the literature as early as 1949 [8]. Techniques vary from four injections surrounding the area of pain [9] to a single injection at the most painful trigger point [10]. The procedure is increasingly used in childbirth to manage labour related back pain, which shares similar visceral and referred pain mechanisms to nephrolithiasis. A large randomised controlled trial of the use of sterile water injections (SWI) for labour back pain reported significant analgesia for up to 90 min compared with a saline placebo with no side effects other than the injection discomfort [11]. Given the broad availability of sterile water and the lack of contraindications to use, the procedure may offer a useful alternative or adjunct to current pain therapies. We conducted a systematic review of randomised controlled trials of SWI compared to placebo, NSAIDs and opioids to assess the evidence for the use of SWI for renal colic pain.

Methods

A prospective protocol was prepared according to the preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines [12] and registered with the PROSPERO register of systematic reviews (CRD42021284882)

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although, due to COVID-19, this registration was not checked for eligibility by the PROSPERO team.

Search strategy

A systematic search and retrieval of the literature was undertaken on 7 November 2021 using the PubMed, Cochrane Central Register of Controlled Trials, CINAHL and Scopus databases to identify relevant studies. The terms for the search were 'renal', 'lithiasis', 'urolithiasis', 'nephrolithiasis', 'calculi', 'colic', 'stone', uteric, 'pain', 'analgesia', 'analgesic', 'water', 'injection', 'inject', 'administer' and variations of these terms (e.g. lithiasis*). Additional studies were identified by screening reference lists and citations of articles of interest. Papers originally published in a language other than English were included where an English translation version was available. Each database was searched independently and results uploaded into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia. www.covidence.org) and duplicates removed.

Inclusion and exclusion criteria

Studies were eligible for inclusion in the review if they were randomised controlled trials (RCTs) that assessed the use of SWI compared to a control group receiving either a placebo or other pain relief medication for the management of renal colic pain. Non-randomised studies, case reports, trial protocols, conference abstracts, editorials and reviews were excluded. Study selection was undertaken independently by two reviewers (NL and LBM) and difference resolved through discussion.

Data extraction and quality assessment

The full text of eligible studies were retrieved to extract available data. Extracted data included author, year, country, sample size, inclusion and exclusion criteria, intervention and control, outcome measures and results (age range, gender stone size, mean visual analogue pain scores pre- and post-treatment and rescue analgesia). We approached study authors for clarification and/or additional data as necessary. The Cochrane Risk of Bias Tool included within Covidence was applied to evaluate the methodological quality of included studies. Assessment was based solely on information published in the article. The Quality assessment was undertaken independently by two reviewers with differences resolved by consensus.

Data analysis

The outcomes for this review were reduction in self-reported pain using a visual analogue scale (VAS) taken prior to treatment and at 30 and $\geq$60 min post-treatment, and the number of participants requiring rescue analgesia. The VAS is an ungraded line anchored at either end by the phrases such as 'no pain' and 'worst pain imaginable'. The VAS can be either 10 cm (score 0–10) or 100 mm (score 0–100). All studies were included in the narrative review based on the relevant control or comparison group. Where extracted data was suitable for meta-analysis this was conducted under an intention-to-treat protocol, with outcomes evaluated based on the treatment allocation following the original randomisation process. RevMan analytical software (Ver 5.3, The Nordic Cochrane Centre, 13 June 2014) was used for statistical analysis. Summarised mean difference (MD) was used to compare continuous VAS data and risk ratio (RR) with 95% confidence interval were used for dichotomous variables. A two-sided $p < .05$ was considered to be statistically significant. The I^2 test was used to assess for heterogeneity due to the limited number of studies available with a random effects model used if significant ($I^2 > 50\%$). Conversely, a fixed-effects model was adopted if there was no evidence of significant heterogeneity.

Results

Included studies

Six RCTs from four countries and involving 894 patients met the inclusion criteria and were included in this review [9,10,13–16] (Figure 1). The trials took place between 1981 and 2021. Four studies were published in English [10,13–15] and one in Danish [9]. Five trials used SWI to treat acute episodes of renal colic pain [9,10,13–15] and one for ongoing renal colic pain relief immediately prior to and during shockwave lithotripsy [16]. Two trials compared SWI to a normal saline placebo [9,10], one trial compared SWI to both a normal saline placebo and Diclofenac (75 mg intramuscular injection) [13], one compared SWI to Diclofenac only [16], one compared SWI administered with Morphine to Morphine only (0.1 mg/per kg intravenously) [14] and one trial compared SWI to Paracetamol (1 gram orally) [15]. Five studies recruited males and females [9,10,13,14], Inclusion in one study was limited to pregnant women, though gestation was not specified [15]. Confirmation of renal stone by radiological imaging or ultrasound was an inclusion for all studies. Stone size was reported in four studies, three as mean ± SD)

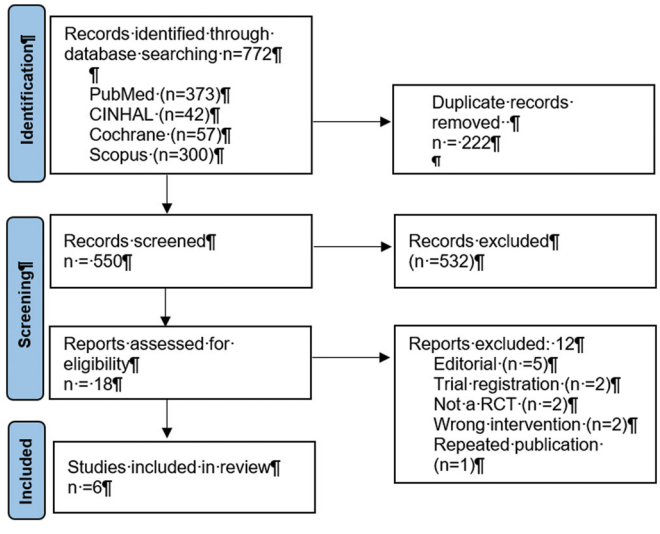

Figure 1. PRISMA flow diagram.

[10,15,16] and one as a range (<5 mm, 5–10 mm and <10 mm) [13]. In these studies there was no difference in stone size between comparison groups (Table 1).

Risk of bias assessment

The overall quality of the six studies assessed was low, only one study was rated as low risk of bias in all seven categories [13]. The randomisation process and blinding of participants, clinicians and outcome assessors was not fully described in most studies. Two studies were described in the text as double blind, though no process for how this was achieved was detailed [10,14]. In one study blinding was not possible due to the difference in medication administration (parenteral versus oral) [15] (Figure 2).

SWI compared to placebo

Three studies compared SWI to a normal saline 0.9% placebo [9,10,13]. Two trials consisted of two arms (SWI versus placebo) [9,10] and one study used three arms (SWI or Diclofenac versus placebo) [13]. From the latter study we extracted the SWI and saline placebo data for meta-analysis. Both trials used a single injection of 0.5 mLs intracutaneously [10,13]. In these two studies the single injection was given at the most painful point, however it is not clear if this was a point indicated by the patient or a palpated trigger point. One trial used four intracutaneous injections of 0.1 mL in a rhombus bound by the L2, posterior superior iliac spines and the iliac crest and 12th costal margin [9]. Two studies reported pre- and post-treatment VAS pain scores [10,13]. The study by Bengtsson et al. [9] used a dichotomous scale of Positive (participants reporting full or good effect for at least 10 min) and Negative (partial or no effect).

In the study by Ahmadnia and Youseni the pre-treatment VAS scores were not significantly different (Mean ± SD; SWI = 9.86 ± 0.4 versus placebo = 9.96 ± 0.19, $p = 0.12$) [10]. However, in the trial by Moussa et al. [17] the authors reported that the pre-treatment VAS scores for the three groups were not statistically different although the cited data (SWI = 9.6 ± 0.61, Diclofenac = 9.72 ± 0.64, Placebo = 9.20 ± 0.89, $p = .006$) suggests a statistical difference between the control and both intervention groups. However, previous studies have suggested that differences in VAS scores of less than 1 cm may not be clinically relevant [18].

Post-injection VAS scores or two studies for SWI and placebo groups at 30 min and ≥60 min were included in the meta-analysis [10,13]. The difference between SWI and placebo was significant at both 30 min (–4.68 [–5.21 to −4.15], $p < .0001$) and ≥60 min (–5.34 [–5.85 to −4.82], $p < .0001$) (Figure 3). In the study by Bengtsson et al. [9], 16 of the 18 patients in the SWI group (89%) reported a positive effect compared to five of 14 in the control group (36%).

Two studies were included in the meta-analysis of rescue analgesia [10,13]. Participants in the SWI group were significantly less likely to use rescue analgesia compared to the placebo group (RR = 0.11, 95% CI = 0.05 − 0.23, $p < 0.0001$) (Figure 4). The study by Bengtsson et al. [9] did not report on rescue analgesia.

SWI compared to diclofenac

Two studies compared SWI to Diclofenac. In the three arm RCT conducted by Moussa et al. [13] participants ($n = 50$) received 75 mg of Diclofenac intramuscularly compared to the SWI group who were given a single 0.5 mL injection intracutaneously at the most painful point. The VAS in the Diclofenac group reduced from 9.20 (±0.89) pretreatment to 1.88 (±1.19) 30 min post-injection compared to the SWI group of 9.6 (±0.61) to 1.98 (±1.41) pre- and post-treatment, respectively. The difference between the two groups at 30 min post-treatment was not statistically significant ($p = .702$). At 60 min the post-treatment VAS for Diclofenac was 1.88 (±1.58) and for SWI it was 1.58 (±1.05), again the difference between groups at this time point was not significant ($p = .266$). Four participants in the SWI group (8%) and seven in the Diclofenac group (14%) required rescue analgesia (RR = 0.57; 95% CI = 0.17–1.83; $p = 0.346$).

The trial by Gul and Gul [16] compared a SWI of 2–3 mL intracutaneously ($n = 216$) to 75 mg of Diclofenac intramuscularly ($n = 308$) for renal colic pain experienced prior to shock-wave lithotripsy (SWL). No reason for the difference in group sizes was provided in the manuscript though there was no significant difference between groups in the baseline variables. The VAS prior to injection was 6.4 (±2.9) in the SWI group and 6.6 (±3.2) with Diclofenac. At 30 min post-injection and prior to SWL treatment the VAS were 1.8 (±1.1) SWI and 1.69 (±1.2) Diclofenac, the difference between groups was not significant ($p = 0.397$) [16]. We did not review the differences in pain reported during the SWL as the origins and quality of this pain may relate more to the treatment itself. Three participants in the SWI group and four in the Diclofenac group required rescue analgesia ($p = 0.272$) though the timing of this in relation to the injections was not reported [16].

SWI compared to morphine

Mozafari et al. [14] compared a single water injection of 0.5 mL intracutaneously administered at the most painful point ($n = 49$) with both 0.1 mg/kg Morphine diluted with 0.5 mL of sterile water administered intravenously and a single SWI of 0.5 mL intracutaneously ($n = 49$). No rationale for the morphine/SWI combination was provided in the manuscript. We were unable to contact the authors via email. The VAS prior to treatment was 8.1 (±1.26) for the SWI and 9.46 (±1.0) for the morphine/SWI group. At 30 min post-injection the VAS scores were 2.97 (±1.51) SWI and 2.34 (±1.89) morphine/SWI ($p = 0.035$). At 60 min post-injection the differences were 1.89 (±1.7) SWI and 0.52 (±0.79) morphine/SWI ($p < 0.001$). Rescue analgesia was not reported [14]. Side-effects such as itching and nausea were more common in the SWI group. It was not reported if the itching was localized to the injection site or generalized. Nausea is commonly

Table 1. Characteristics of included studies.

Author, Year, Country	Sample size	Inclusion criteria	Exclusion criteria	Intervention	Control/comparative intervention	Outcome measures	Baseline demographic and clinical results
Ahmadnia and Younesi Rostami [10] 2004 Iran	100/50/50 Treatment group $n = 50$ Control group $n = 50$	Age 21–55 Confirmation of renal calculi by ultrasound (U/S) or intravenous pyelogram (IVP)	No imaging evidence of renal calculi by U/S or IVP	Single injection of 0.5 mL sterile water (SWI) intracutaneously at most painful point	Single 0.5 mL normal saline (N/S) injected intracutaneously at most painful point	VAS (0–10 mm) of pain prior to injections and at 30 and 90 min post-treatment	Male $n = 72$, Female $n = 28$ Mean (SD) age: SWI 35.26 years (±9.16) Placebo 33.90 years (±9.96) Mean (SD) stone size SWI 7.14 mm (±1.76) Placebo 7.20 mm (±1.85) $p = 0.878$
Bengtsson et al. [9] 1981 Denmark	32/18/14 Treatment group = 18 Control group = 14	All patient over 18 years admitted to hospital (1 May 1979–1 October 1980) with clinical renal colic, haematuria, radiologically verifying stone in upper urinary tract or signs of recently departed stone	Not defined	Four injections of 0.1 mL sterile water intracutaneously in a rhomboid bound by the L2, posterior superior iliac spines and the iliac crest and 12th costal margin	Four injections of 0.1 mL isotonic saline intracutaneously rhomboid bound by the L2, posterior superior iliac spines and the iliac crest and 12th costal margin	The latency period until possible pain relief was recorded on a scale (1) pain relief, (2) good effect, (3) certain effect, (4) no effect	Males $n = 31$, Female $n = 9$ (pre-treatment exclusions $n = 8$) Mean age 46 years (range 24 − 72) Stone size not reported
Gul and Gul [16] 2020 Turkey	524/216/308 SWI $n = 216$ Diclofenac Sodium $n = 308$	Age > 18 Confirmation of renal calculi > 2 cm by ultrasound (U/S), Kidney/ Ureter/Bladder. Radiography or intravenous pyelogram (IVP). No previous shock wave lithotripsy (SWL) or surgery	Distal obstructions, pregnancy, active urinary tract infection, frequent analgesic use, allergy to Diclofenac, contraindications to NSAIDs use	Single injection of 2–3 mL of sterile water intracutaneously into a palpated trigger point between the 12th costal margin and iliac crest 30 min prior to SWL	Diclofenac Sodium 75 mg intramuscular injection 30 min prior to SWL	VAS (0–10 mm) of pain prior to analgesic intervention, just prior to SWL administration and 14 − 24 kV in 2 kV increments	Male $n = 289$, Female $n = 221$ Mean (SD) age: SWI 41.2 years (±9.4) Morphine 39.9 years (±10.1) Mean stone size SWI 15.6 ± 2.3 mm Morphine 14.8 ± 2.8 mm, $p = 0.517$.
Moussa et al. [13] 2021 Lebanon	150 / 50/50/50 SWI $n = 50$ Diclofenac $n = 50$ Control group $n = 50$	Age 18–60 years. Confirmation of uretal or kidney stones by non-contrast enhanced computed tomography	Analgesia prior to randomisation. Infection at injection site	Intervention 1: 0.5 mL intracutaneously at the most painful point Intervention 2: Diclofenac 75 mg intramuscularly	Single 0.5 mL normal saline (N/S) injected intracutaneously at most painful point	VAS (0–10 mm) of pain prior to injections and at 30, 45 and 60 min post-treatment	Gender not reported Mean age 38 years (range 28–40) Stone size SWI *n* (%): <5 mm 15 (30) 5–10 mm 27 (54) >10 mm 8 (16) Diclofenac: <5 mm 13 (26) 5–10 mm 31 (62) >10 mm 6 (12) Placebo: <5 mm 17 (34) 5–10 mm 27 (54) >10 mm 6 (12)
Mozafari et al. [14] 2020 Iran	98 /49/49 SWI $n = 49$	Age 18–55 years Kidney stones confirmed	Contraindication to morphine use, pregnancy,	Single injection of 0.5 mL sterile water (SWI) intracutaneously at most	0.1 mg/kg morphine diluted with 0.5 mL of sterile	VAS (0–10 mm) of pain prior to injections and	Males $n = 87$ Female $n = 7$ Mean (SD) age

(*continued*)

Table 1. Continued.

Author, Year, Country	Sample size	Inclusion criteria	Exclusion criteria	Intervention	Control/comparative intervention	Outcome measures	Baseline demographic and clinical results
	SWI and morphine $n = 49$	with imaging Pain score ≥ 5 (VAS 0–10)	breastfeeding, neuropathic pain in back or below chest, history of cardiac arrhythmia, peritonitis, pyelonephritis, Glasgow Coma Score < 15, weight < 100 kg, analgesic use $<$ 6 h prior to presentation at hospital, drug dependency, methadone use	painful point	water administered intravenously into the cubital vein over 2 minutes and a single injection of 0.5 mL sterile water (SWI) intracutaneously at most painful point	at 15, 30, 45, and 60 min post-treatment	SWI 33.36 (±7.22) Morphine 35.95 (±8.87) Stone size not reported
Xue et al. [15] 2013 China	45 / 21/24 SWI $n = 21$ Paracetamol $n = 24$	Pregnant women Confirmation of uretal stone on duplex Doppler U/S and transvaginal U/S	Previous treatment for renal colic	Single injection of 0.5 mL sterile water (SWI) intracutaneously at most painful point	Paracetamol 1 g orally	VAS (0–100 mm) of pain prior to injections and at 15, 30 and 60 min post-treatment	Gender: Females only Mean (SD) age: SWI 27.62 years (±2.16) Paracetamol 27.25 years (±2.44) Mean (SD) stone size SWI 5.67 (±1.68) Paracetamol 5.96 (±1.40)

Figure 2. Risk of bias assessment.

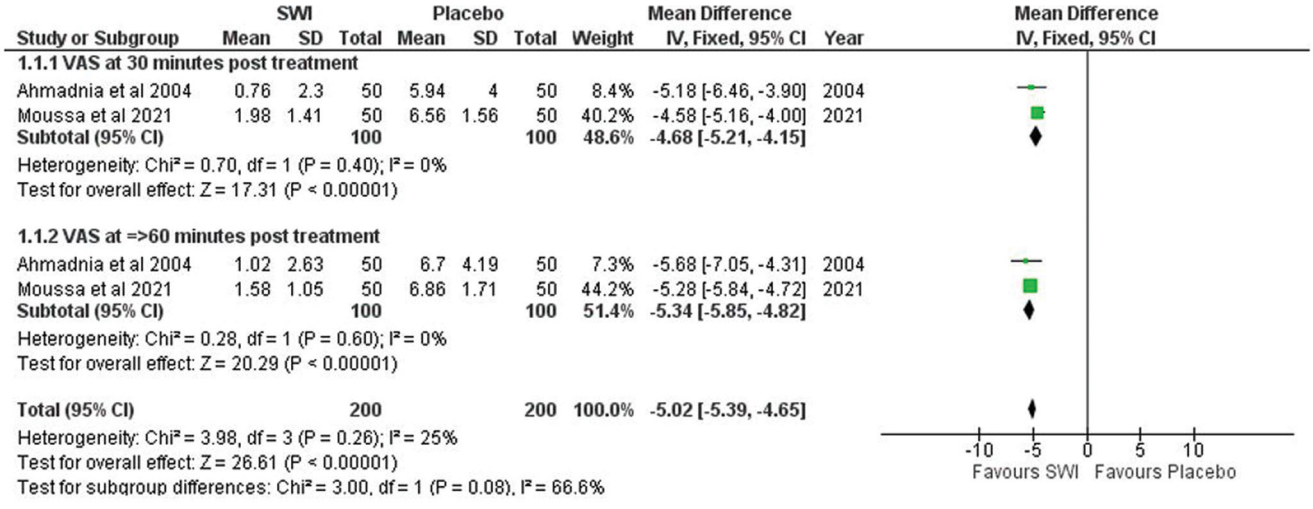

Figure 3. Comparison of SWI versus placebo, VAS scores at 30 and $\geq$ 60 min after treatment.

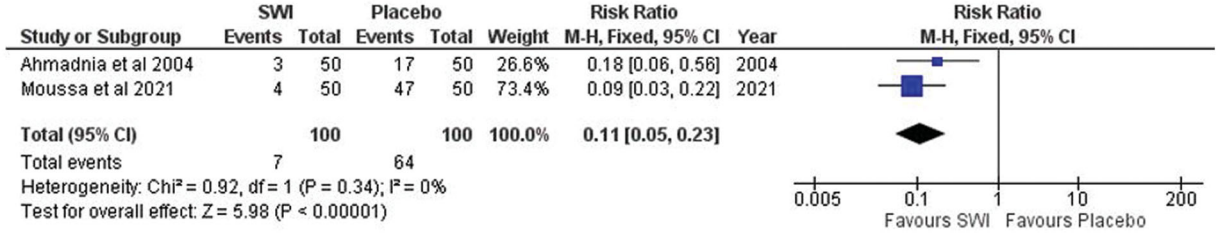

Figure 4. Comparison of SWI versus placebo, rescue analgesia administered after treatment.

reported with renal colic so it would not be certain that this was specifically a reaction to the SWI.

SWI compared to paracetamol

A single SWI of 0.5 mL administered at the most painful point was compared to 1 g paracetamol orally in the RCT by Xue et al. [15]. The study population consisted of pregnant women ($n = 21$ SWI, $n = 24$ paracetamol). The VAS prior to injection in the SWI group was 90.48 (±11.17) and 85.42 (±10.62) in the paracetamol group. Post-injection scores at 30 min were 14.76 (±11.23) SWI and 45.42 (±12.5) paracetamol ($p < 0.000$) and 10.48 (±8.65) SWI, 32.08 (±14.44) paracetamol at 60 min ($p < 0.000$). One participant in the SWI group (5%) and eight in the paracetamol group required rescue analgesia (RR = 0.14; 95% CI = 0.019 − 1.05, $p = 0.55$).

Discussion/conclusion

The main finding of the systematic review and meta-analysis is that SWI as an analgesic for renal colic pain was superior to a normal saline placebo and oral paracetamol for over 60 min after treatment. The pain relief experienced following SWI was comparable to Diclofenac injection (75 mg). Compared to placebo and diclofenac, fewer participants in the SWI required rescue analgesia. The evaluation of SWI to morphine is less certain as the comparison group included both SWI and morphine given in conjunction. A systematic review and meta-analysis concluded that non-steroidal anti-inflammatory drugs (NSAIDs) (predominantly diclofenac) were equivalent to opioids and intravenous paracetamol in analgesic effect with fewer side-effects such as vomiting and less need for rescue analgesia [5]. While the volume of evidence presented in our review is limited, it does suggest that SWI can play a role in pain management in renal colic.

The analgesic effect of SWI is thought to be based on the mechanisms of counter-irritation [19,20], the noxious stimulation, tissue distension and increased osmotic pressure of SWI triggers pain gate-control cells within the dorsal horn and the stimulation of endorphins suppressing the transmission from pain receptor neurons within the spinal cord [21,22]. This has led to it being described as using 'referred stimulation' to relieve referred pain [23]. The effect of SWI suggests a strong referred component of renal colic pain. A number of theories have suggested for the phenomenon of referred pain largely based on the concept of nociceptive dorsal horn neurons receiving convergent inputs from various tissues though many of these theories do not explain particular features of referred pain such as the time delay between the original stimulus and the perceived pain [24]. The quantum tunneling of potassium ions and the time taken for the frequency of action potentials referred to neurons to increase to the point where pain is experienced has been theorised to contribute to the time delay characteristic of referred pain [25]. Interestingly, Di Maio [8] reported that injections of 'twice distilled water' given at painful trigger points provided almost complete relief from renal colic pain; however, when this was given for pain associated with congenital hydronephrosis or chronic pyelonephritis the pain relief lasted only a few minutes, suggesting a different pain pathway in these conditions.

Most of the studies cited in this review used a single sterile water injection ranging from 0.5 mL [10,13–15] to 2–3 mL [16]. Only Bengtsson et al. [9] describe using four injections. None of the studies provide a specific rationale for choice of number of injections. Gul and Gul [26] state they used the single injection technique described in a previous study. All the studies exploring the best techniques for delivering SWI consider low back pain experienced during childbirth. These studies have compared both numbers of injections, location in relation to area of pain and depth of injections (intracutaneous versus subcutaneous). The four injections are usually positioned at points bordering the area of pain or specified anatomical landmarks, whereas single injections are situated over the most painful point, or trigger point, indicated by the patient [27], as was the case in the trials in this review that used a single injection. A trial comparing a single to a four injection technique reported a significantly greater analgesic effect from four injections with a longer duration, up to 2 h, though the perceived injection pain was also greater with four injections [28]. The number of injections appears to have a greater influence over the degree of analgesia rather than specific sites or volume of water administered [27].

While all of the studies in this review employed an intracutaneous injection, the anatomical depth of the injection, i.e., intracutaneous or subcutaneous, is a technique consideration in mitigating the injection pain, a known deterrent to repeated use [27]. Trials comparing intracutaneous to subcutaenous suggest no difference in resulting pain relief. A reduction in perceived pain with subcutaneous injection was noted in non-clinical participants [29], however this could not be confirmed in clinical practice [30]. This may have been due to the competing labour pain or the concurrent use of other analgesics such as nitrous oxide inhalation at the time the injections were given. A recent study reported reduced water injection pain following prior application of topical anesthetic cream [31], however the use of such agents has not been tested in clinical practice trials. Similarly, it is not known if reducing the degree of noxious stimulus will impact on the resulting analgesia. The current weight of evidence suggests that four injections, either intracutaneously or subcutaneously, provided by two clinicians simultaneously, is the technique most likely to produce an effective and sustained period of analgesia [27].

The broad availability of sterile water, lack of side-effects other than the injection pain, and the simplicity of administration would offer some distinct advantages in certain clinical scenarios. NSAIDs may be contraindicated in pregnant women and patients with a history of chronic renal disease. Rural and remote areas of Australia often have poor access to kidney disease management services and a potentially higher rate of nephrolithiasis due to the drier climate [32,33]. Remote Australian Indigenous populations have a higher incidence of chronic renal disease and failure [32]. Renal colic pain is also one of the most common urological medical events on commercial airlines, with Paracetamol often the

only available analgesic [34]. A review of the management of renal colic in low resource conditions advises that onsite conservative surveillance is reasonable in the presence of safe and effective pain relief [35]. Intracutaneous or subcutaneous injections of sterile water require a low level of training and skill with no risk of overdosage or adverse systemic reaction, making it an ideal first line procedure where alternatives are either unavailable or contraindicated.

This review has a number of limitations. Overall, the number of available trials was small and the majority had a high or unclear risk of bias particularly in relation to blinding of participants and clinicians. This could contribute to a treatment bias and inaccurate reporting. Varying techniques contribute to the overall heterogeneity of the included studies. Therefore, the results of the review should be viewed with some caution.

Conclusions

This review suggests that SWI provides better analgesia than no treatment (placebo) and comparable pain relief to Diclofenac and morphine with a considerably lower potential for contraindications and side-effects. However, the current supporting evidence is small with a number of methodological inconsistences. Further trials are needed to explore the analgesic potential of SWI across populations and clinical settings. The use of topical agents to mitigate the injection pain and subsequent effect of quality of pain relief are also areas for future research.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Gandhi DA, Hashemzehi DT, Batura MD. The management of acute renal colic. Br J Hosp Med. 2019;80(1):C2–C6.
[2] Fisang C, Anding R, Müller SC, et al. Urolithiasis–an interdisciplinary diagnostic, therapeutic and secondary preventive challenge. Dtsch Arztebl Int. 2015;112(6):83–91.
[3] Travaglini F, Bartoletti R, Gacci M, et al. Pathophysiology of Reno-Ureteral Colic. Urol Int. 2004;72(1):20–23.
[4] Holdgate A, Pollock T. Systematic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic. BMJ. 2004;328(7453):1401.
[5] Pathan SA, Mitra B, Cameron PA. A systematic review and meta-analysis comparing the efficacy of nonsteroidal anti-inflammatory drugs, opioids, and paracetamol in the treatment of acute renal colic. Eur Urol. 2018;73(4):583–595.
[6] Welk BK, Teichman JMH. Pharmacological management of renal colic in the older patient. Drugs Aging. 2007;24(11):891–900.
[7] Valovska M-TI, Pais VM. Contemporary best practice urolithiasis in pregnancy. Ther Adv Urol. 2018;10(4):127–138.
[8] Di Maio G. Interception of renal colic by intradermal injection of twice-distilled water at the pain points. Minerva Med. 1949; 40(43 Pt 2):265–268.
[9] Bengtsson J, Worning AM, Gertz J. Pain due to urolithiasis treated by intracutaneous injection of sterile water. A clinically controlled double-blind investigation. Ugeskr Laeg. 1981;143(51):3463–3465.
[10] Ahmadnia H, Younesi Rostami M. Treatment of renal colic using intracutaneous injection of sterile water. Urol J. 2004;1(3): 200–203.
[11] Lee N, Gao Y, Collins SL, et al. Caesarean delivery rates and analgesia effectiveness following injections of sterile water for back pain in labour: a multicentre, randomised placebo controlled trial. EClinicalMedicine. 2020;25:100447.
[12] Moher D, Shamseer L, Clarke M, PRISMA-P Group, et al. Preferred reporting items for systematic review and Meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.
[13] Moussa M, Papatsoris AG, Chakra MA. Intradermal sterile water injection versus diclofenac sodium in acute renal colic pain: a randomized controlled trial. Am J Emerg Med. 2021;44:395–400.
[14] Mozafari J, Verki MM, Tirandaz F, et al. Comparing intradermal sterile water with intravenous morphine in reducing pain in patients with renal colic: a double-blind randomized clinical trial. Rev Recent Clin Trials. 2020;15(1):76–82.
[15] Xue P, Tu C, Wang K, et al. Intracutaneous sterile water injection versus oral paracetamol for renal colic during pregnancy: a randomized controlled trial. Int Urol Nephrol. 2013;45(2):321–325.
[16] Gul A, Gul M. Intracutaneous sterile water injection for pain relief during extracorporeal shock wave lithotripsy: comparison with diclofenac sodium. Urolithiasis. 2020;48(2):103–108.
[17] Moussa M, Papatsoris AG, Chakra MA. Reply to correspondence: intradermal sterile water injection (ISWI) versus diclofenac sodium in acute renal colic pain: a randomized controlled trial. MS 23153. Am J Emerg Med. 2020;44:395–400.
[18] Kelly A. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. Emerg Med J. 2001;18(3):205–207.
[19] Wand-Tetley JI. Historical methods of counter-irritation. Ann Phys Med. 1956;3(3):90–99.
[20] Gammon GD, Starr I. Studies on the relief of pain by counterirritation. J Clin Invest. 1941;20(1):13–20.
[21] Melzack R, Wall PD. A new theory. A gate control system modulates sensory input from the skin before it evokes pain perception and response. Science. 1965;150(3699):971–979.
[22] Le Bars D, Dickenson AH, Besson J-m. Diffuse noxious inhibitory controls (DNIC). II. Lack of effect on non-convergent neurones, supraspinal involvement and theoretical implications. Pain. 1979; 6(3):305–327.
[23] Derry S, Straube S, Moore RA, et al. Intracutaneous or subcutaneous sterile water injection compared with blinded controls for pain management in labour. Cochrane Database Syst Rev. 2012;1: CD009107.
[24] Arendt-Nielsen L, Svensson P. Referred muscle pain: basic and clinical findings. Clin J Pain. 2001;17(1):11–19.
[25] Qaswal AB. A theoretical study to explain the referred pain phenomenon and its characteristics via quantum tunneling of potassium Ions through the channels of neuronal membrane. NeuroQuantology. 2019;17(3):43.
[26] Iguchi M, Katoh Y, Koike H, et al. Randomized trial of trigger point injection for renal colic. Int J Urol. 2002;9(9):475–479.
[27] Mårtensson LB, Hutton EK, Lee N, et al. Sterile water injections for childbirth pain: an evidenced based guide to practice. Women Birth. 2018;31(5):380–385.
[28] Lee N, Webster J, Beckmann M, et al. Comparison of a single vs. a four intradermal sterile water injection for relief of lower back

pain for women in labour: a randomised controlled trial. Midwifery. 2013;29(6):585–591.
[29] Mårtensson L, Nyberg K, Wallin G. Subcutaneous versus intracutaneous injections of sterile water for labour analgesia: a comparison of perceived pain during administration. Int J O&G. 2000; 107(10):1248–1251.
[30] Mårtensson L, Wallin G. Labour pain treated with cutaneous injections of sterile water: a randomised controlled trial. Br J Obstet Gynaecol. 1999;106(7):633–637.
[31] Mårtensson LB, Gunnarsson B-M, Karlsson S, et al. Effect of topical local anaesthesia on injection pain associated with administration of sterile water injections-a randomized controlled trial. BMC Anesthesiol. 2022;22(1):1–10.
[32] Gardiner FW, Bishop L, Gale L, et al. Poor access to kidney disease management services in susceptible patient populations in rural Australia is associated with increased aeromedical retrievals for acute renal care. Intern Med J. 2020;50(8):951–959.
[33] Pathan SA, Mitra B, Bhutta ZA, et al. A comparative, epidemiological study of acute renal colic presentations to emergency departments in Doha, Qatar, and Melbourne, Australia. Int J Emerg Med. 2018;11(1):1–6.
[34] Hancock J, Sui W, Alves P, et al. Urological in-flight medical events on commercial airlines. J Urol. 2020;203(5):991–995.
[35] Moynihan MJ, Manganiello MD. A review of urologic conditions in remote and austere environments: presentation, evaluation, and management. Wilderness Environ Med. 2020;31(3):358–366.