A Prospective, Randomized Study of the Clinical Effects of Shock Wave Delivery for Unilateral Kidney Stones: 60 Versus 120 Shocks per Minute

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Purpose: We assessed the effects of different shock wave delivery rates in patients treated with shock wave lithotripsy for renal stones, particularly treatment success, degree of renal injury and pain experienced, and analgesic demand.

Materials and Methods: A total of 206 patients with renal stones were prospectively randomized to receive shock waves delivered at 60 (group 1) or 120 (group 2) shocks per minute using a Sonolith® Vision at a single institution in October 2008 and August 2010. The primary outcome was successful treatment 12 weeks after 1 lithotripsy session. Secondary outcome measures included the degree of renal injury, as reflected by changes in urinary markers of renal injury, as well as patient pain scores and analgesia consumed during treatment.

Results: Mean stone size in groups 1 and 2 was 8.95 and 9.28 mm, respectively ($p = 0.525$). The overall treatment success rate was 43.2%. It was significantly better in group 1 than in group 2 (50.5% vs 35.9%, $p = 0.035$). There was no between group difference in the success rate for stones 10 mm or less but the success rate was statistically better for group 1 patients with stones greater than 10 mm ($p = 0.002$). Immediately after shock wave lithotripsy there was a statistically significant greater increase in urinary NAG ($p = 0.003$) and interleukin-18 ($p = 0.022$) in group 1. There was no between group difference in pain scores, analgesic consumption during shock wave lithotripsy or unplanned hospital visits.

Conclusions: Slower shock wave delivery yielded better treatment outcomes, particularly for stones greater than 10 mm, without increasing patient pain or analgesic demand. However, slower shock wave delivery also appeared to cause a statistically significant increase in acute renal injury markers, although the clinical implication was uncertain.

Key Words: kidney, kidney calculi, lithotripsy, iatrogenic disease, pain

Abbreviations and Acronyms

CT = computerized tomography

IL-18 = interleukin-18

MSD = mean stone density

NAG = N-acetyl-β-D-glucosaminidase

NCCT = noncontrast computerized tomography

NGAL = neutrophil gelatinase-associated lipocalin

SWL = shock wave lithotripsy

Submitted for publication January 26, 2012.

Study received institutional review board approval.

Supported by Hong Kong Research Grant Council General Research Fund 471508.

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For another article on a related topic see page 996.

EXTRACORPOREAL SWL remains a recommended first line treatment for renal stones. There have been continuous modifications in its applications meant to further improve treatment outcomes. A recently investigated treatment variable is the shock wave delivery rate. Increasing evidence suggests that a slower delivery rate improves stone clearance.[1] However, we believe that treatment assessment should also include the risk of renal injury and patient tolerance. Animal studies suggest that a slower shock wave delivery rate may produce less renal injury[2] but to our knowledge this has not been ver-

0022-5347/12/1883-0837/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2012.05.009
Vol. 188, 837-842, September 2012
Printed in U.S.A.

ified in clinical studies. Thus, we assessed the effects of different shock wave delivery rates on stone clearance, renal injury and patient perception of pain.

MATERIALS AND METHODS

This was a single center, prospective, randomized study. The study was approved by the institutional ethics review board and done in accordance with good clinical practice guidelines and the Declaration of Helsinki (trial registration ChiCTR-TRC-09000627). All patients provided written informed consent before enrolment.

Patients

Patients 18 years old or older with a solitary 5 to 20 mm renal stone were recruited for study. Patients with multiple stones in the same calyx or a stone associated with any anatomical renal or ureteral abnormality and patients with a ureteral stent/nephrostomy tube were excluded from analysis, as were those with cystinuria or a history of allergy due to alfentanil.

Study Procedures

After background information was obtained NCCT was done with a multidetector row CT scanner to confirm stone presence and size, and measure various stone parameters. A spot urine sample (50 cc) was collected to measure urine markers.

Patients were randomized to SWL at 60 (group 1) or 120 (group 2) shocks per minute. We chose 60 shocks per minute based on an in vitro study showing that this was the most effective shock wave delivery rate.[3] At our center 120 shocks per minute has been used routinely, as commonly used elsewhere.[4–9] All patients were treated with the Sonolith Vision, an electroconductive lithotripter with an aperture of 219 mm, focal distance of 130 mm, maximal focal zone of 25 $\times$ 3.6 mm and peak pressure at a focal point of 92 to 106 MPa.

Patient controlled analgesia was used during treatment. The preset intravenous bolus dose of alfentanil was 40 μg and the lockout period was 1 minute. All treatments were aimed to deliver 1,000 J energy at 14.4 kV, which was the manufacturer recommended maximum energy per treatment session, unless stone localization failed or the patient could not tolerate the procedure.

Upon completion of treatment patients were asked to rate the level of pain verbally on a scale of 0 to 10. Another spot urine sample was collected for marker measurement immediately after treatment.

Followups were performed on days 2 and 7, and weeks 4 and 12. At each followup a spot urine sample was collected and plain x-ray was done for outcome assessment. If patients were considered stone free on x-ray at week 12, NCCT was performed to confirm stone clearance. Further treatment was based on clinical information, residual stone size and patient choice. All re-treatment was done after week 12 unless earlier treatment was indicated.

Urinary Marker Measurement

Spot urine was collected to monitor renal injury markers. The urinary markers assessed included NAG, NGAL and IL-18. NAG was measured with a commercial colorimetric assay kit. NGAL and IL-18 were measured with enzyme-linked immunosorbent assay kits. All marker levels are shown as the ratio with regard to urinary creatinine, which was measured by an automated analyzer. All measurements were made in duplicate and the mean was used for analysis.

Main Outcome Measures

The primary outcome measure was successful treatment, defined as stone-free status or residual fragments less than 4 mm 12 weeks after SWL. Secondary outcome measures included the degree of renal injury, as reflected by changes in urinary marker levels, and patient pain scores, analgesic consumption and complication rates.

Sample Size

The study protocol called for the recruitment of 220 patients. Sample size was calculated based on previous studies by assuming a success rate of 65% for group 1 and 45% for group 2. With these assumptions an estimated 214 patients were needed to provide 80% power with significance at 5% and a 10% dropout rate.

Randomization and Allocation Concealment

All eligible patients were randomly assigned to the 2 groups at a 1:1 ratio. Preset, sequentially numbered envelopes containing paper with group allocations were prepared by a research assistant according to the randomization scheme generated by a website (http://www.randomization.com) with a block size of 2 or 4 and without stratification. Randomization was achieved by the duty urologist drawing an envelope before SWL. Investigators and radiologists who assessed clinical outcomes and the research staff that measured urine markers were blinded to patient treatment information.

Statistical Analysis

Differences between the 2 groups were analyzed statistically. Demographic data were analyzed by the Student t and Mann-Whitney U tests. Categorical variables were analyzed by the chi-square or Fisher exact test. Two-tailed $p < 0.05$ was considered statistically significant.

Outcome analysis was done on an intent to treat basis. Logistic regression was also used to assess the individual effects of various potential predictive factors, including the shock wave delivery rate, on treatment outcome.

Differences in urinary marker levels were analyzed by the Student t test. The mean posttreatment maximum change in urinary markers and the difference in urinary markers after treatment were assessed by the paired t test for normally distributed data and otherwise by the Wilcoxon signed rank test.

Pain scores and analgesic consumption of the 2 groups were compared by the Mann-Whitney U test. Complications were compared by stratified chi-square analysis or the Fisher exact test, when appropriate. Data were analyzed using PASW® Statistics 18.0.

RESULTS

A total of 220 patients fulfilled recruitment criteria and provided consent for the trial in October 2008 and August 2010. Of the patients 14 were excluded from study after consent, including 7 with no renal