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# Adjuvant Therapy After Surgical Stone Management

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**The aim of this article was to review the most widely researched adjuvant medical therapies for the surgical management of urolithiasis. Articles were identified and reviewed from PubMed and Medline databases with MeSH headings focusing on the various surgical treatments of urolithiasis and adjuvant therapy. Additional articles were retrieved from references and conference proceedings. Surgical treatments reviewed included shockwave lithotripsy, ureteroscopy, and percutaneous nephrolithotomy. Adjuvant therapy was considered medical or complementary therapy as an adjunct to these surgical interventions. Adjuvant therapy for the surgical management of urolithiasis has been documented to increase stone-free rates, reduce stone remission rates, prevent renal damage, and decrease postoperative morbidity. A variety of agents have been studied, ranging from antioxidants to alpha-blockers and to alkalinizing agents. Additionally, there is increasing interest in complementary adjuvant therapy (ie, acupuncture). Adjuvant therapy is a fertile area for research in the surgical management of urolithiasis. The optimal agents have yet to be determined and therefore further investigation is warranted and necessary.**

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**Index Words:** *Calculi; Nephrolithiasis; Kidney; Percutaneous nephrolithotomy; Ureteroscopy; Medical expulsive therapy; Shockwave lithotripsy*

The prevalence of nephrolithiasis in the modern era is rising with an estimated prevalence of 5.2% in the United States.<sup>1</sup> The majority of symptomatic stones ( $\approx 90\%$ ) will pass either spontaneously or with the aid of medical expulsive therapy (MET). The remainder of patients requires surgical intervention to assist in calculus removal, including shockwave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PNL). In the adjuvant setting, medical and complementary approaches, which minimize side effects and increase surgical efficacy, are an important area of investigation. The aim of this article was to identify the most widely documented and applicable adjuvant therapies to surgical stone management.

## Materials and Methods

A search of MEDLINE (1950-January 2008) and PubMed (1950-January 2008) was conducted to identify articles pertaining to the surgical management of nephrolithiasis and adjuvant medical therapy. MeSH headings included but were not limited to SWL, URS, PNL, and adjuvant and expulsive therapy. Article references were searched to identify additional studies to review. Conference proceedings were also reviewed to identify areas of new investigation yet to be published. All relevant articles and abstracts were evaluated by the authors. Articles were chosen for incorporation into the current text based on study design or the novel use of medical agents to facilitate surgical stone management. Additionally, because of the limited number of prospective, randomized, controlled trials identified, retrospective studies and abstracts were also reviewed and reported when more robust evidence was lacking.

## Results

### Adjuvant Medical Therapy

Medical therapy has been used to improve stone-free status, to decrease stone remission rates, decrease renal damage such as during SWL, and to reduce postoperative patient discomfort. The effects of adjuvant medications

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are reported for the following common surgical treatments of symptomatic urinary calculi: SWL, URS, and PNL. Previous studies have suggested that residual fragments after SWL or PNL may lead to high rates of symptomatic episodes as well as high rates of repeated intervention.<sup>2,3</sup> After SWL, 43.1% of patients with residual stone fragments 4 mm or less developed symptomatic episodes or required intervention.<sup>2</sup> Patients with residual fragments (>2 mm) post-PNL experienced a significantly greater number of stone-related events (71% *v* 24%,  $P = .03$ ) and required significantly more secondary interventions (53% *v* 8%,  $P = .005$ ).<sup>3</sup> Therefore, adjuvant therapies that reduce the incidence of residual stone fragments should limit the need for repeat stone-removal procedures.

### Shock-Wave Lithotripsy

The majority of data on adjuvant medical therapy is found in SWL studies. A number of trials of varying design evaluating stone-free rates (SFRs), stone recurrence, and renal protective measures are reported. Perhaps because of the need to actively pass fragments after SWL, adjuvant therapy remains an active area of urologic research.

### Stone-Free Rates

Investigators have documented improvement in stone-clearance rates with alkalinizing agents, alpha-blockers, and calcium-channel blockers after SWL. Although not studied in patients after SWL, diuretics, steroids, narcotics, and nonsteroidal anti-inflammatory drugs have been evaluated for medical expulsive therapy without surgical intervention. These agents are potential areas of future research.

Alkalization has been shown to significantly improve the clearance of residual fragments after SWL. Cicerello et al<sup>4</sup> documented the efficacy of alkalization with the use of sodium citrate. A randomized prospective trial of 70 patients, 40 calcium stone patients, and 30 infection stone patients was performed in patients treated with sodium-potassium-citrate (6-8 g/d in 3 divided doses). Patients treated with adjuvant therapy had improvement in SFRs at 12 months, from 32% to 75% and 40% to 86% for calcium and infection stones, respec-

tively. This effect was improved on by the administration of potassium citrate, which increased SFRs from 65% and 75% to 67% and 81% at 6 and 12 months, respectively.<sup>5</sup>

Additional confirmation of the positive effects of potassium citrate was provided by Soygur et al.<sup>6</sup> After controlling for age, sex, and urinary values of calcium, citrate, and uric acid, participants were randomized to potassium citrate 60 mg/d or no medical therapy. The SFR of the treatment group was 100% at 1 year compared with 71% in the untreated group. The mechanism of action for the promotion of stone clearance by alkali therapy, in particular its effect on infection stones, remains unknown.

Diuretics have been used to increase SFRs after SWL. The potential mechanisms of action are increased urinary flow rates and alterations in urinary chemistry. Hydrochlorothiazide administration increased SFRs (72% *v* 36%,  $P = .001$ ) during a 36-month longitudinal analysis of patients receiving adjuvant therapy.<sup>7</sup> Additionally, a significant difference was noted for those patients on adjuvant therapy who were found to be hypercalciuric (86% *v* 12%,  $P = .001$ ).

MET improved the spontaneous clearance of ureteral calculi.<sup>8</sup> The most commonly used agents were calcium-channel blockers and alpha-blockers. Both classes of medication provided beneficial properties when used in the adjuvant setting combined with SWL. One investigation evaluated the use of either combination nifedipine and deflazacort or no MET after SWL in a randomized, prospective manner.<sup>9</sup> Complete fragment expulsion was documented at 45 days and was reported as 75% in the MET group compared with 50% of the untreated group ( $P = .02$ ). Sarcia et al<sup>10</sup> evaluated the impact of verapamil (250 mg 3 times a day) versus forced diuresis or no intervention on spontaneous stone passage after SWL. In this small, nonblinded study of 70 patients, they reported that stone clearance was similar whether verapamil (46%) or forced diuresis (46%) was initiated; both approaches were superior to no intervention (18%).<sup>10</sup> A larger number of investigators reported their experiences with alpha-blockers. Significant improvement of SFR after SWL was observed with tamsulosin, ranging from 71% to 97%

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