# Critical Review Form
## Therapy

Alfuzosin Stone Expulsion Therapy for Distal Ureteral Calculi: A Double-Blind, Placebo Controlled Study
*J Urology* 2008; 179: 2244-2247

**Objective:** **To evaluate "the efficacy of the selective $\alpha_{1a}$-blocker alfuzosin as medical expulsive therapy for distal ureteral stone passage". (p. 2244).**

**Methods:** **Between Jan 2005 and June 2007 "consecutive" patients seeking medical attention for distal ureteral calculi at one hospital were recruited excluding those with stones > 8mm (by CT), Creatinine > 1.8mg/dL, solitary kidney, concurrent UTI, current α-blocker use, pregnancy, or known urethral strictures.**

**In the pharmacy, a computer random number generator was used to allocate consenting subjects to receive alfuzosin (dose not provided) or placebo in a one-to-one ratio. Patients and investigators were blinded to allocation arms, but no clear statement of physician blinding or outcome assessor blinding is provided.**

**Patients recorded their comfort level in a pain diary via daily visual analog scale and narcotic diary. They also recorded the date and time of stone passage. Treatment failures were labeled as uncontrollable pain, fever, severe hydronephrosis, or failure of stone passage at 4-weeks. Follow-up occurred weekly until stone passage and included abdominal x-ray (or CT if the stone was radiolucent). Adverse drug effects, comfort level, BP, and stone position were assessed at weekly visits.**

**The study had 80% power with Type I error 0.05 and estimated effect size 27% if there were 35 patients in each arm.**

| Guide | | Comments |
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| **I.** | **Are the results valid?** | |
| **A.** | **Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?** | |
| 1. | Were patients randomized? | Yes, via a random number generator in pharmacy. |
| 2. | Was randomization concealed (blinded)? | Yes, to investigators and patients. |
| 3. | Were patients analyzed in the groups to which they were randomized? | No clear statement of intention-to-treat and 7 were excluded after randomization. |

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| 4. | Were patients in the treatment and control groups similar with respect to known prognostic factors? | No difference in age, gender, BP, hydronephrosis, or stone size, but the alfuzosin-group started with a higher pain score (8.94 vs. 7.59, p = 0.01). |
| **B.** | **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?** | |
| 1. | Were patients aware of group allocation? | No |
| 2. | Were clinicians aware of group allocation? | Yes, unless investigators and treating clinicians were one and the same. |
| 3. | Were outcome assessors aware of group allocation? | No |
| 4. | Was follow-up complete? | Among randomized subjects, no loss to follow-up is reported. |
| **II.** | **What are the results (answer the questions posed below)?** | |
| 1. | How large was the treatment effect? | • Mean stone size in 2 groups 3.96 and 3.67 mm.<br>• Overall spontaneous stone passage rate 75% with no difference between placebo (77%) and alfuzosin (73%) groups and no effect of stone size.<br>• Stones passed more quickly in alfuzosin group than in placebo arm (5.2 vs. 8.5 days).<br>• The alfuzosin group experienced a greater decrease in pain scores after initial ER visit (4.8 cm vs. 3.6 cm on VAS, p = 0.0005). Based upon May 2007 JC, this is not clinically significant.<br>• Alfuzosin did not significantly reduce operative interventions or narcotic use. |

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| | | • While no subjects in placebo arm experienced adverse events, 12% of alfuzosin had minor side effects including dizziness and orthostatic hypotension. |
| 2. | How precise was the estimate of the treatment effect? | No CI were provided. |

| III. | **How can I apply the results to patient care (answer the questions posed below)?** | |
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| 1. | Were the study patients similar to my patient? | Yes – ED patients with generally small symptomatic kidney stones. |
| 2. | Were all clinically important outcomes considered? | No assessment of quality of life, missed work days, overall patient satisfaction, ED recidivism, or medication compliance. |
| 3. | Are the likely treatment benefits worth the potential harm and costs? | Probably not with alfuzosin although referenced cost-effectiveness analysis suggests $1,132 per patient with MET. |

**Limitations**

1) **No analysis of NNT or 95% CI.**

2) **Alfuzosin dosing regimen not reported.**

3) **No assessment or reporting of ancillary interventions which could have impacted stone passage rates or pain scores (steroids, antibiotics, NSAID's, fluid maintenance).**

4) **No assessment of QOL or workdays lost.**

5) **No blinding of treating physicians – possible *co-intervention bias*.**

6) **No discussion of clinically relevant change in pain scores.**

7) **Possible *selection bias* since "consecutive" enrollment recruited only 76 patients in 18 months. In contrast, Italians (PGY-II paper) recruited 480 subjects in one-year. Were EM physicians really notifying Urology investigators when every renal colic patient presented?**

8) **Kidney stones very small (> 4mm). Perhaps no MET needed for smaller kidney stones?**

9) **The T-test used to determine p-values was inappropriate for skewed variables. Instead, a survival model should have been developed, although this cannot be accomplished with Excel.**

10) **Once the 7 subjects were lost to follow-up, the study became underpowered and may have suffered from a Type II error.**

**Bottom Line**

**Alfuzosin should not be first-line α-antagonist used in MET for small (<4mm) distal ureteral kidney stones since this agent does not improve expulsion rates or clinically significant pain scores.**