Ureteral Stent Pain: Is It Preventable?

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Old School

Modern Era
Battle of Saratoga (August 1777)
Welcome to Our Meeting!
Saratoga Race Track
Ureteral Stent Pain and Its Management

- Very common procedure and probably overused
- Bothersome symptoms and pain in 80% of patients
  - Urinary Frequency
  - Urinary Urgency
  - Dysuria
  - Incomplete emptying
  - Flank pain
  - Suprapubic pain
  - Incontinence
History of the “Double-J Stent”

- Many modifications
- 1978-Finney described indwelling stent with proximal curl in the renal pelvis and distal curl in the bladder
- Ideal properties of a stent
  - Hold position (memory)
  - Stay in place over time (durometry)
  - Easy manipulation of shape (elasticity)
  - Excellent tensile strength and elongation capacity
  - Biocompatibility and durability
  - Visualized on fluoroscopy
Ureteral stent
USSQ (Ureteral stent systems questionnaire)

- Validated questionnaire for research
- 38 items (6 sections)
  - Pain
  - Voiding symptoms
  - Work performance
  - Sexual matters
  - Overall general health
  - Additional problems
- Cumbersome to use and many patients won’t fill out
USSQ Results

- 76% of patients voiding symptoms
- 70% of patients had enough pain to reduce activity level by 50% or more
- Impact on post-op course and return to normal function
- Not translated in to many languages
- Standardized research tool
Adult Patients with Ureteral Stones

- Uncomplicated <10 mm and distal stones can have observation
  - MET is now more controversial
- Re-image prior to surgery if changes management (passed stone, change in location)
- 4-6 weeks for trial of passage, then decide about intervention (shared decision making)
- SWL least morbid and lowest complication, but URS greater stone-free rate in single procedure
- Mid and distal ureteral stone-URS is first line therapy, but may offer SWL
Proposed Mechanisms of Stent Pain

- Large amount of research, still don’t know the answer
- Reflux of urine through the stent while voiding
- High pressure transmitted to renal pelvis
- Movement of stent curl in bladder
- Stent excursion >2.5 cm during daily activities and movement; less pain at night or while at rest
- Irritation of bladder mucosa
Biofilms and morbidity with short-term stents
Biofilms

- May aggravate some lower urinary tract symptoms
- Not main trigger for stent-associated morbidity in the short-term
Proper Stent Position is Key

- Length of stent
- Size not really important (4.8, 6, 7 Fr)
  - Multiple studies do not show less symptoms with smaller diameter stents-2019 study with some benefit with 4.7 Fr stent compared to larger size (n=181 patients)
- Position in renal pelvis
  - Proximal curls in a calyx cause more irritation
  - Position in bladder
  - Distal curl should not cross the midline

Should you take more time to worry about stent position?

- Disruption of GAG layer
Prevention Strategies

- Review indications for stenting
  - Do you really need a stent?
  - Not generally needed pre-procedure unless sepsis or complicated infection
  - No ureteral injury
  - No stricture or anatomic abnormality
  - Normal contralateral kidney and renal function
  - Don’t anticipate other staged procedures
  - Stent type (dual durometer with softer bladder curls for longer term indwelling stents)
Medications in the OR/Immediate Post-op

- Ketorolac or oxybutynin-immediately helps for 1-2 hours
- Lidocaine instilled-no difference in pain
- Peri-ureteral Botox-showed some effect
- Tricolsan-no benefit
- Ketorolac-eluting stent-young, male patients showed promise, but no difference in physician phone calls, pain scores, early stent removal, or requests for pain medication
- B+O suppositories (if available)-occasional benefit especially if poorly controlled pain or unable to tolerate oral medications
Alpha-Blockers as adjunctive therapy

- Tamsulosin and Alfuzosin
  - Moderate clinical benefit-multiple studies
  - Work at bladder neck and prostatic smooth muscle in men to decrease outlet resistance and voiding pressures
  - Also effective in females
  - Tamsulosin slightly more selective
<table>
<thead>
<tr>
<th>Drug</th>
<th>30-day supply</th>
<th>Cash price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamsulosin</td>
<td></td>
<td>$11-$120</td>
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<tr>
<td>Silodosin</td>
<td></td>
<td>$298</td>
</tr>
<tr>
<td>Alfuzosin</td>
<td></td>
<td>$12-$58</td>
</tr>
<tr>
<td>Doxazosin 4mg</td>
<td></td>
<td>$15</td>
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</tbody>
</table>
Anticholinergic Medications

- Decrease frequency and urgency through direct effects on muscarinic receptors in bladder
- Multiple studies with Solifencin/Vesicare™
- Usual side effects of dry mouth and constipation
- Combination therapy is probably best
  - Zhou meta-analysis of 13 randomized controlled trials
    - Lower IPSS, pain scores, and improved quality of life
Other options

Phenazopyridine (Pyridium)  
Pregabalin (Lyrica)
Mechanism of Action/other options

- Pyridium - urinary tract specific analgesic
  - Rare abuse potential - patient with repeated suicide attempts using this drug for overdose
  - Limit course to < 3 days

- NSAIDs - COX inhibitors to reduce ureteral contractility and inflammation
  - Reduce renal prostaglandin synthesis with decrease in renal blood flow and lower renal and ureteral pressures

- Pregabalin/Lyrica®
  - GABA analogue for chronic pain, but shown to counteract hyperplasia and firing of unmyelinated C fibers that are activated by mechanical irritation and inflammation from stent placement
Narcotics?
No Routine Rx for Post-op Narcotics!
References


How much?
Grades of Evidence

- **Grade A** - well designed randomized-controlled trials (RCT), highly-generalizable results; can also be exceptional observational studies with consistent findings
  - Only one statement had Grade A evidence!
- **Grade B** - RCT with weakness, some observational studies
- **Grade C** - studies with small sample size, only observational studies
- **Expert Opinion or consensus statements**
Distal Ureteral Stones—Still a valid treatment
Controversy of Medical Expulsive Therapy
Do You Believe in Miracles?
What Happened?

- 3 better designed randomized clinical trials
  - UK-SUSPEND (Lancet, 2015)-1167 patients
  - Australia (Annals of Emergency Medicine, January 2016)-403 patients
  - STONE (JAMA Internal Medicine, June 2018)-512 patients

- Results- No difference in stone passage rates between alpha blocker and placebo
- Still some suggestion for efficacy for larger stones in the distal ureter
- Chinese study (much larger numbers) also suggests this conclusion (3450 patients)
Comparable age, gender, stone size, and laterality
3296 patients available for analysis
RR 1.10 for stone passage
NNT 13
6.1 day reduction in time to passage for larger >5 mm stones
Weekly non-contrast CT scans until passage (would never get approval from US IRB!)
Side effects of retrograde/anejaculation in men, dizziness, and headache
No serious adverse events
Side Effects and Off-Label Use

- Patient Counseling
  - Generally well tolerated
  - No specific label indication
  - Use in special populations-pediatrics, pregnant patients should be limited
  - Rare cross-reaction/allergy for patients with Sulfa allergy for Tamsulosin
Medically Expulsive Therapy in Urolithiasis: A Review of the Quality of the Current Evidence
Skolarikos A, Ghani KR, Seitz C, Van Asseldonk B, and Bultitude MF
European Urology Focus 3 (2017) 27-45

- Looked at accuracy of studies published to promote spontaneous passage of stones from the ureter.
- Although the majority of the studies were not designed properly, there is still some evidence to support medical expulsive therapy.
- Prior meta-analyses showed the likelihood of stone passage increased 44-65%.
- Needed to treat (NNT) 3-4 patients for one patient to benefit from the drug intervention.
- Reduced time to stone expulsion by 3-4 days.
- Reduced colic by 40%.
- Reduced need for auxiliary procedures by 60%.
- Low risk intervention, pooling of studies may exaggerate treatment effect.
Effect of Tamsulosin on Stone Passage of Symptomatic Ureteral Stones
A Randomized Clinical Trial (STONE)
JAMA Internal Medicine, published online June 18, 2018

- 2 phase double blind study done initially at single ER site, then expanded
- 1387 patients excluded from analysis
- 512 randomized
- 75% of the stones were smaller than 4 mm
- No difference in time to passage
- Need to revise current guidelines for ureteral stone management
Weak recommendations based on weak evidence
Still recommend offering alpha-blockers in addition to standard care for 4 weeks
Net benefit was small
Considerable uncertainty about patient preferences
Many may choose treatment, but some will not
Recommendation applies to documented ureteral stones on imaging vs. diagnosis on clinical symptoms alone
## Current Guidelines for Patients with Ureteral Stones

<table>
<thead>
<tr>
<th>Name</th>
<th>Target population</th>
<th>Guidance</th>
</tr>
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<tbody>
<tr>
<td>EAU Guidelines (2018)</td>
<td>Urologists</td>
<td>Offer alpha blockers as MET as one of the treatment options for (distal) ureteral stones &gt; 5mm (strong)</td>
</tr>
<tr>
<td>AUA Guidelines (2016)</td>
<td>Urologists</td>
<td>Uncomplicated ureteral stones should be offered MET with alpha blockers (strong)</td>
</tr>
<tr>
<td>EBM Guidelines (2017)</td>
<td>Primary care physicians</td>
<td>Alpha blockers may be prescribed to facilitate passage of small &lt;5 mm ureteral stones</td>
</tr>
<tr>
<td>Up to Date, 2016</td>
<td>Primary care physicians and urologists</td>
<td>We initiate treatment with Tamsulosin for 4 weeks to facilitate spontaneous stone passage in patients with stones &lt; 10mm in diameter</td>
</tr>
<tr>
<td>NHG 2016</td>
<td>General practitioners</td>
<td>Tamsulosin is not recommended</td>
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New Technology and Techniques
The Impact of Preoperative α-Adrenergic Antagonists on Ureteral Access Sheath Insertion Force and the Upper Limit of Force Required to Avoid Ureteral Mucosal Injury: A Randomized Controlled Study
J. Urology 199, 1622-1630, June 2018

- Randomized trial
- Use of alpha-blockers decreased force required to place working access sheath
- Similar to force needed in pre-stented patients
- Less evidence of ureteral mucosal injury
- May help if patient needs surgical intervention for more proximal ureteral/UPJ calculi
SHOULD WE OFFER ALPHA BLOCKERS FOR STONE MANAGEMENT?

- Confusing data and clinical trials
- Recent AUA Guidelines still suggest effectiveness
- Much debate, but little guidance
- Look more carefully at the evidence
- Clinical judgment
- Patient expectations
- Safety
- Cost