Prevention of CKD from Renal Calculi

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Content

• Renal stone: clinical aspects
• Urinary crystals: from crystals to stones
• Absolute treatment
• Clinical applications on prevention
Renal calculi: 
Cause of CKD in > 5%

Obstructive uropathy
Chronic tubulo-interstitial disease
End stage renal disease
Renal Stone: Composition

- Calcium Oxalate  70-75%
- Calcium Phosphate  <5 %
- Uric acid  10 %
- Infectious (Struvite)  15 %
- Cystine  1 %

Calcium stone: 10% lifetime prevalence in men
### Renal calculi: crystalline substances

#### Oxalate
- **Whewellite**: Calcium oxalate monohydrate, $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$
- **Weddelite**: Calcium oxalate dihydrate, $\text{CaC}_2\text{O}_4 \cdot (2+x)\text{H}_2\text{O}$

#### Phosphate
- **Hydroxyapatite**: Basic calcium hydrogen phosphate, $\text{Ca}_5 (\text{PO}_4)_3 (\text{HO})$
- **Brushite**: Calcium hydrogen phosphate, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$
- **Whitlockite**: $\beta$-tricalcium phosphate, $\beta-\text{Ca}_3 (\text{PO}_4)_2$
- **Struvite**: Mg ammonium phosphate hexahydrate, $\text{Mg(NH}_4)(\text{PO}_4).6\text{H}_2\text{O}$
  
  Octacalcium phosphate

#### Uric acid
- **Uric acid (dihydrate)**: $\text{C}_5\text{H}_4 \text{N}_4\text{O}_3 (.2\text{H}_2\text{O})$
- **Monosodium urate monohydrate**: $\text{Na C}_5\text{H}_4 \text{N}_4\text{O}_3 \cdot \text{H}_2\text{O}$

#### Others
- **$\lambda$-cystine**: $\text{S}_2 \text{C}_6\text{H}_{12} \text{N}_2\text{O}_4$
Crystal structure: Uric acid $\text{C}_5\text{H}_4\text{N}_4\text{O}_3$

Legend: Carbon atom (gray sphere), Nitrogen atom (black sphere), Oxygen (white sphere)
Clinical Presentation of Renal Stone Disease

- Passed stone
- Positive X-ray film
- Obstructive nephropathy
  - Back pain, Flank pain
  - Painful & painless hematuria
- Acute & chronic pyelonephritis
- Chronic Kidney Disease: tubulo-interstitial disease
Acute Stone Episode Suspected

History, P.E., CBC, UA

KUB + U/S or CT/IVP confirmed

obstruction? pain?

yes

urine infected?

no

stone treatment

yes

percutaneous nephrostomy

no

antibiotics

no

urine infected?
Management of Acute Pain (Renal colic) I

Bed rest + IV fluid/ KVO

Non-narcotic analgesic

• Ibuprofen* (400mg PO)
• Ketorac (30 mg IV, 90 mg PO)
• Ketoprofen, Diclofenac IV
• Aspirin (Gr X)
• Paracetamol* (1000 mg)
Management of Acute Pain (Renal colic) II

**Narcotics**
- Morphine* (0.1 mg/Kg IM): beware of respiratory suppression + spasmogenic effects
- Meperidine (1 mg/Kg IM)

**Adjuvant agents (to Narcotics)**
- Amitriptyline* (25-75 mg PO) anti-depressant + analgesic
- Hydroxyzine* (25 mg IM) anti-histamine + analgesic + anti-emetic
Renal stones are crystals bound together with “glues” in the proper conditions.
Pathogenesis & Pathophysiology

- Ion excretion
- Nidus
- Crystal formation
  - crystal nucleation: Saturation-supersaturation, Homogeneous & Heterogeneous (Epitaxis)
  - crystal growth (Inhibitors/Promotors)
  - crystal aggregation (Promotors)
- Stone formation
  - Free particle theory: Slow urine flow
  - Fixed particle theory: (Tubular) Cell-crystal reaction
    Tissue damage/Scars/Post-op
### Promoters & Inhibitors of stone disease

<table>
<thead>
<tr>
<th>Promoters</th>
<th>Inhibitors</th>
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<tbody>
<tr>
<td>Uric acid</td>
<td><strong>Citrate</strong></td>
</tr>
<tr>
<td>Polymerized THP</td>
<td>Magnesium</td>
</tr>
<tr>
<td></td>
<td>Pyrophosphate</td>
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<tr>
<td></td>
<td>Glycosaminoglycans</td>
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<td></td>
<td>Nephrocalcin</td>
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<td>Uropontin</td>
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<td>Non-polymerized THP</td>
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</table>
Stone formation

Diagram showing the formation of stones in the urinary system, with labels indicating different stages and locations such as Calcium phosphate, Calcium oxalate, Proximal tubule, Loop of Henle, Distal tubule, and Collecting duct.
Timing for Stone Formation

3 o’clock in the morning
Urine flow: 20-30 ml/hour
Urine flow rate: 0.00002 ml/hr/nephron
Renal Stone: Characteristics

- CaOx.H₂O: hard, dark brown, dull grey coat
- CaOx.2H₂O: small, spherical, tan cluster of platelets
- CaP: small, white, fine granule surface
- Uric acid: small, smooth, yellow-orange, radiolucent
- Struvite: large, light brown, dendritic/rough surface
- Cystine: very small yellow, dendritic, partial dense
Absolute treatment of Stone

• Get rid all of stones
  – Surgical/ Open: No residual stone
  – Non-surgical: some stones left

• Preventive measures
Clinical Application on stone prevention
Possible Prevention Guideline

- Decrease causative ion(s) in urine
- High urine flow: All day?
- Adjust urinary chem./ biochem./ physic.
- Increase citrate in urine
- Exercise?
Critical urine pH for crystal formation

Urine pH

- < 5.5 for Uric acid
- 6.0 - 6.5 for CaOx (<6.25)
- > 6.5 for CaP
- > 7.5 for Struvite
### Preventive Modalities: Drugs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>Hypocitraturia:</td>
<td>K citrate</td>
</tr>
<tr>
<td>Idiopathic:</td>
<td>K citrate/Thiazide/Allopurinol</td>
</tr>
<tr>
<td>Hyperuricosuria:</td>
<td>Allopurinol ± K citrate</td>
</tr>
<tr>
<td>RTA:</td>
<td>K citrate</td>
</tr>
<tr>
<td>Struvite stone</td>
<td>Get rid of UTI, residual stone</td>
</tr>
</tbody>
</table>

- K citrate
- Thiazide
- Allopurinol
- D-Penicillamine
- Orthophosphate
- Na cellulose
- PK citrate
- Mg
Uric acid stone is Preventable

- Uric acid: small, smooth, yellow-orange, radiolucent
- Stone former: urine uric acid
  > 800 mg/d (male),
  > 750 mg/d (female)
- Possibly induces calcium stone (as nidus)
Uric acid stone is Preventable

- Urine flow > 2000 ml./day
- Purine moderation
- Urinary alkalination (UpH 7): Sodamint, Potassium citrate
- Allopurinol
Take Home Messages

- Low causative ion in urine
- Reduce the promotor
- Increase the inhibitor
- Proper pH adjustment
- Correct UTI
- Early stone removal
- Regular follow-up
Appreciate Your Attention