Interstitial Cystitis

Dr. Gerard Testa
What Causes IC

- Auto Immune Disease
- Infection
- Glycosaminoglycan layer deficiency
- Reflex Sympathetic Dystrophy
- ? Hereditary
Classification of Interstitial Cystitis

• Ulcerative

• Non Ulcerative

• Bladder Capacity under anaesthesia

• Presence or absence of Mast cells

• Treatment success or failure
Glomerulations or Hunner's ulcer on cystoscopic examination, and

Pain associated with the bladder or urinary urgency
1. Bladder capacity >350 mL on awake cystometry using either gas or liquid as filling medium

2. Absence of intense urge to void with bladder filled to 100 mL of gas or 150 mL of water during cystometry, using a fill rate of 30-100 mL/min

3. Demonstration of phasic involuntary bladder contractions during cystometry using fill rate described above

4. Duration of symptoms less than 9 months and age <18

5. Absence of nocturia

6. Symptoms relieved by antimicrobials, urinary antiseptics, anticholinergics, or antispasmodics (muscle relaxants)

7. Frequency of urination while awake <8 times per day
8. Diagnosis of bacterial cystitis or prostatitis within 3 month period
9. Bladder or lower ureteral calculi
10. Active genital herpes
11. Uterine, cervical, vaginal, or urethral cancer
12. Urethral diverticulum
13. Cyclophosphamide or any type of chemical cystitis
14. Tuberculous cystitis
Hunner's Ulcer
Histamine

Proteoglycans

Leukotrienes

MAST CELL

ESTROGEN

Histamine

Proteoglycans

Leukotrienes

IG E
URINARY MARKERS

- HISTAMINE

- CYTOKINES
  - Interleukin 1b
  - Interleukin 6

- KALLEKRINE
  - Correlates with bladder pain, frequency and successful hydrodistension
Special Concerns

- Cancer
- Pregnancy
- Coping
Current Management of Interstitial Cystitis

- Therapy exists in many forms
- Treatment largely empiric – only a few regimes evaluated as placebo controlled trials
- Multimodal therapy commonly used - no single treatment universally effective
Current Management of Interstitial Cystitis

- **Conservative therapy**
  - **Diet**
    - 53-63% can identify acidic fluids or foods incite flair
      - Mechanisms for this poorly understood not due to decreased urinary Ph from ingestion (Fisher et al.)
    - Foods high in arylalkylamines
      - Mechanism tryptophan metabolites → Disruption of GAG layer (Kaufman et al.)
    - Special diet remains a reasonable first line therapy for patients with irritative voiding symptoms
    - Tolerable food for IC patients include:
      - Rice, pasta, potatoes, vegetables, chicken, meat, watermelons and grapefruit
Current Management of Interstitial Cystitis

- **Conservative therapy**
- **Behavioural therapy**
  - 50 – 75% reduction of symptoms in 50% of patients
  - Bladder training with deferment techniques → increase inter-void intervals
- **Treatment of Pelvic Floor Dysfunction**
  - Lilius reported 81% of his IC Patients to have spasm & tenderness of the levator ani musculature
  - Use of trans-rectal Thiele massage, biofeedback & electro-galvanic stimulation
Current Management of Interstitial Cystitis

• Oral Therapy
  – Pentosan Polysulphate (Elmiron)
    • Hwang et al in 1997 performed a meta-analysis evaluating 488 patients and determined that Elmiron was more efficacious than placebo in the treatment of frequency, urgency & pain in patients with interstitial cystitis
    • Dose 100 mg TDS 1 hr before or 2 hours after meals
      – Side effects 1-4 %
        ✫ Alopecia, diarrhoea, nausea, headache, rash, dyspepsia, abdominal discomfort, liver function abnormalities & dizziness
    • Should be taken for at least 3 months as symptom improvement may not be immediate
    • Dose Escalation has recently been evaluated to 300 mg TDS decreased time to improvement with no serious adverse events but increase in minor side effects
Current Management of Interstitial Cystitis

- **Oral Therapy**
  - **Hydroxyzine**
    - Antagonist of Substance P induced mast cell activation
    - Clinical benefit described by Theoharides
    - Average reduction of symptom score of 40% over 3 months
      - In IC patients with allergic problems mean reduction of symptom score of 55%
    - Also has anticholinergic, sedative and analgesic properties
    - Start at 10 mg Nocte with increases to 25, 50 & 75 mg on a weekly basis
    - Sedation may limit dose but there is a tachyphylaxis (sedation will abate after a few days)
Current Management of Interstitial Cystitis

- **Oral Therapy**
  - **Amitriptyline**
    - Central & peripheral anticholinergic properties
    - Central or antihistaminic sedation
    - Inhibition of serotonin and noradrenalin reuptake
    - Initial dose 10 mg Nocte. Increase to 25, 50 and 75 mg at 2-3 week intervals
    - Dry mouth and sedation typically the most common side effects
Current Management of Interstitial Cystitis

- Oral Therapy
  - Gabapentin (Neurontin)
    - Anticonvulsant with proven effectiveness in neuropathic pain syndrome
    - Mode of action uncertain
    - At doses of 1200mg daily (range 300 – 2100mg daily) 48% IC patients reported improvement in pain
    - Dosing begins 100 mg Nocte with increments of 100 mg every 3 to 7 days added next in the morning then at midday
Current Management of Interstitial Cystitis

• Oral Therapy
  – Narcotics – both long and short acting are used
  – Opioids may be used in conjunction with other oral IC agents with hydroxyzine and amitriptyline exhibiting the ability to potentiate narcotic pain relief
  – Opioids can be tapered as other IC treatments begin to take effect
Current Management of Interstitial Cystitis

• Intravesical Therapies

  Hydrodistension

  Mechanisms of action:
  (1) Mechanical damage or ischaemia to the submucoal bladder plexus
  (2) Widespread mast-cell degranulation with exhaustion of nociceptive and inflammatory mediators
Current Management of Interstitial Cystitis

• Intravesical Therapies

Dimethyl sulfoxide (DMSO)

Modes of possible action:

(1) antiinflammatory effect
(2) desensitisation or blockade of afferent nociceptive pathways
Current Management of Interstitial Cystitis

• Intravesical Therapies

  Bacillus Calmette-Guerin
  • Attenuated Strain of Mycobacterium bovis
  • Found by serendipity IC misdiagnosed as CIS
  • BCG response rate 60% vs 27% placebo - persistence of response 89% of responders
  • A large multi-centre phase 3 clinical trial evaluating the efficacy of BCG in patients with IC is currently underway
Current Management of Interstitial Cystitis

- Intravesical Therapies
  - Hyaluronic acid
    - component of the GAG layer
    - predominant concentration in the subepithelial connective tissue
    - patients refractory to previous medical therapy
    - Morales et al
    - Response was reported in 71% at 12 weeks
Current Management of Interstitial Cystitis

- Intravesical Therapies
  - Resiniferatoxin
    - Ultrapotent vanilliod receptor agonist
    - Functions through desensitization of bladder afferents
Current Management of Interstitial Cystitis

Surgical Therapy

Sacral Neuromodulation
Current Management of Interstitial Cystitis

10% of disease severe enough for major surgical intervention

Surgical procedures include:

- Subtrigonal or supratrigonal cystectomy and substitution cystoplasty
- Cystectomy with urinary diversion (either ileal conduit, continent diversion or neobladder)
**Conservative Therapy**

- Diet
- Behavioural therapy
- Treatment Pelvic Floor Dysfunction

**Oral Therapy**

- Pentosan Polysulfate
- Hydroxyzine
- Amitriptyline

- Gabapentin
- Narcotics

**Intravesical Therapy**

- Hydrodistention
- DMSO
- Multiagent Therapy

- BCG
- Hyaluronic Acid
- Resiniferatoxin

**Surgical Therapy**

- Sacral Neuromodulation

- Cystectomy with Substitution Cystoplasty
- Urinary Diversion with or without Cystectomy

**Conservative Therapy**

- Diet
- Behavioural therapy
- Treatment Pelvic Floor Dysfunction

**Oral Therapy**

- Pentosan Polysulfate
- Hydroxyzine
- Amitriptyline

- Gabapentin
- Narcotics

**Intravesical Therapy**

- Hydrodistention
- DMSO
- Multiagent Therapy

- BCG
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**Surgical Therapy**

- Sacral Neuromodulation

- Cystectomy with Substitution Cystoplasty
- Urinary Diversion with or without Cystectomy
Bibliography

- Parsons CL. Interstitial cystitis: successful management by increasing urinary voiding intervals. Urology 1991;37:207-212
- Parsons CL, Mullholland SG. Successful therapy of Interstitial cystitis with pentosan polysulphate. J Urol 1987;138:513-6
- Kirkemo AK, Miles BJ, Peters JM. Use of amytryptyline in interstitial cystitis (abstract) J Urol 1990;143:279A
Bibliography

• Hanno PM, Wein AJ. Conservative therapy of interstitial cystitis. Semin Urol 1991;9:143-7
• Sant GR. Intravesical 50% dimethyl sulfoxide in the treatment of interstitial cystitis. 1987;29(Suppl):17-21
Bibliography