Neuropathic Pain & Complex Regional Pain Syndrome in Children

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Neuropathic Pain

**Definition**

- Pain initiated or caused by a primary lesion or dysfunction in the nervous system
Neuropathic Pain
Symptoms

- Allodynia
  - Pain in response to normally non-painful stimuli
- Hyperalgesia
  - Increased response to noxious stimuli
- Spontaneous pain
  - Shooting, electric shock
- Dysaesthesias
  - Paradoxical or odd sensations
  - Pins & needles, burning
- Sensory deficits
  - Numbness, sensory loss
Neuropathic Pain
Aetiology

**Post surgery**
- Thoracotomy
- Multilevel surgery for CP

**Trauma**
- Phantom limb pain
- Spinal cord injury

**Neurological disease**
- Guillain-Barre - 79% neuropathic pain, severe in half
  - HMSN

**Hereditary**
- Erythomelalgia – mutation affecting Na 1.7 channel

**Metabolic disorders**
- Fabry’s disease – lysosomal storage disease
  - Neuropathic pain most frequent initial complaint

**Treatment related**
- 50-90% post cisplatin
- 50% post vincristine

**Tumour involvement – peripheral / CNS**

**CRPS**
Incidence of neuropathic pain

- Adults – 0.6 – 1.4%
  - Diabetic neuropathy
  - PHN
- Children – unknown
  - Lower
  - ? Under reporting
- Laboratory & clinical evidence that age at the time of injury has a role
Laboratory models for neuropathic pain

- **Spinal nerve injury**
  - Adult rats – marked allodynia
  - P3, P10 & P21 – did not display allodynia
  - Differences specific to neuropathic pain – mechanical allodynia displayed by very young animals exposed to inflammatory pain

- **Alterations in neuro-immune response to nerve injury in the young**
  - Reduced microglial response in spinal cord
  - Reduced T cell infiltration
  - Reduced activation of macrophages in DRG

Howard Pain 2005
Variation in the incidence of neuropathic pain with age at time of injury

Obstetric brachial plexus avulsion
- Surgical repair and testing 3-23 years later
- Excellent restoration of sensory function
- No chronic pain behaviours

Phantom pain post amputation
- Amputation < 6 yrs – 20% incidence of phantom pain
- Amputation > 6 yrs – 86% phantom pain

Peripheral nerve injury upper limb
- <5 years – no neuropathic pain or allodynia
- 5-12 years – allodynia elicited on QST but no spontaneous pain
- >12 years – spontaneous pain
Variation in the incidence of neuropathic pain with age at time of injury

- Spinal cord injury
  - < 20 years 26% incidence in neuropathic pain vs 58% older group
- Post thoracotomy
  - 0-6 yrs 3.2% - prolonged pain
  - 7-12 yrs 19.4% - prolonged pain
  - 13 -25 yrs 28.5% - prolonged pain
  - 3 patients who had pain still present: surgery > 10 years

- Incidence of neuralgia in UK (per 100 000)

<table>
<thead>
<tr>
<th>Neuralgia</th>
<th>Post-herpetic</th>
<th>Trigeminal</th>
<th>Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14 yrs</td>
<td>1</td>
<td>0.4</td>
<td>-</td>
</tr>
<tr>
<td>15-29 yrs</td>
<td>4</td>
<td>11</td>
<td>1.2</td>
</tr>
<tr>
<td>30 -44 yrs</td>
<td>11</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>45-59 yrs</td>
<td>47</td>
<td>65</td>
<td>21</td>
</tr>
<tr>
<td>60 – 74 yrs</td>
<td>143</td>
<td>70</td>
<td>51</td>
</tr>
<tr>
<td>&gt; 75 yrs</td>
<td>327</td>
<td>88</td>
<td>61</td>
</tr>
</tbody>
</table>
Management of neuropthic pain

- Physiotherapy/Psychology
- Treatment extrapolated from adult data
  - No high level evidence
- Anticonvulsants
  - **Gabapentin** – case reports only no RCTs in children
    - 5-10mg/kg/dose tds
    - Insufficient evidence for practice recommendations
  - FDA warning – increased incidence of suicidal ideation and completed suicides
- **Pregabalin**
  - Open label study, 30 children (10 -17 years), post chemo peripheral neuropathy
  - 150 -300mg/kg daily
  - Significant pain relief in 86%, mean decrease in VAS 59%
- **Lidocaine patch**
  - Case series
Management of Neuropathic Pain

- **Antidepressants**
  - Amitriptyline
    - Evening dose – 0.5-1mg/kg
    - Case reports only
  - Duloxetine (SSRI)
    - Case report – 2 adolescents diffuse pain & major depressive disorder
    - Increase risk of suicide in < 25 yrs

- **TENS**
  - Case reports/series

- **Regional techniques**
  - Neuraxial/peripheral nerve blocks
Complex Regional Pain Syndrome

Terminology & Diagnostic Criteria – Stanton & Hicks

- Precipitated by noxious event (not always identifiable)
- Spontaneous pain or allodynia which is disproportionate in duration, severity and distribution to the expected clinical course of the inciting event
- Evidence at some time of autonomic dysfunction
- Other differential diagnoses have been excluded

CRPS type 2 – associated with known peripheral nerve injury
Clinical features of CRPS in children

- Peak incidence in early adolescence
- Median 12 years (6-16)
- Lower limb affected 60 -85%
- 71 – 95% female
  - Typical high achieving
- Precipitating factor
  - Minor trauma 50 -60%
  - Major trauma or surgery 20 30%

Clinical Features of CRPS in children

- **Autonomic dysfunction**
  - Colour change 67-92%
  - Temperature change 60-85%
  - Swelling 33-85%
  - Sweating 23-43%

- **Dystrophic changes**
  - Nail/hair/skin changes
  - Disuse
  - Limited ROM – functional/structural

- **Motor symptoms**
  - Dystonia, tremor, myoclonus
    - Mild shaking to movement of whole limb
  - Associated with prolonged symptoms & worse outcome

- **Delay in diagnosis**
  - 2 days – 2 years
  - Periods of non weight bearing or immobilization
  - Multiple specialists
    - Orthopaedic surgeons, rheumatologists, neurologists, A&E physicians
Management of CRPS

Explanation & Education
- “CRPS is a disorder of pain neurophysiology, rather than being due to ongoing tissue damage”
- Encourage mobilisation

Physiotherapy

Psychology
- Prospective – 6 weeks CBT & Education & Physio (intensive vs less)
- All improved

Lee J Pediatr 2002

Drug therapy
- Analgesics – limited variable efficacy
  - NSAIDs, paracetamol, tramadol, strong opioids
- Gabapentin
  - Evidence of efficacy in adults
  - Case reports only in children
- Tricyclic antidepressants
  - Case reports only
Management of CRPS – Role of interventional techniques

Wide range in practice & beliefs
- Pain management programmes comprising purely physiotherapy & psychological techniques
- Centres that advocate early & repeated blocks

UK practice
- Children who are failing conservative treatment
- Aim achieve a pain free window
- Must be part of a multi-modal technique

Practical aspects
- GA
- US fluoroscopy guidance
- Catheter technique preferable to single shot
Regional techniques

- Sympathetic blocks
  - Lumbar
  - Stellate
- Epidural
- IV Regional sympathetic blocks
- Peripheral nerve blocks
- Spinal cord stimulation
- Intrathecal LA infusions (n=1)

No high level evidence – small case series
  - Cochrane review

Cepeda MS: Cochrane database 2005
# Interventions in CRPS - literature

<table>
<thead>
<tr>
<th></th>
<th>Number of patients/ episodes</th>
<th>Affected limb</th>
<th>Regional technique</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meier 2009</strong></td>
<td>23</td>
<td>23 - leg</td>
<td>Double blind crossover Lumbar sympathetic block vs IV lidocaine</td>
<td>Reduction pain scores &amp; allodynia with LSB</td>
</tr>
<tr>
<td><strong>Krane 2009</strong></td>
<td>25/35</td>
<td>27 - leg</td>
<td>8 - Epidural 16 - Sciatic nerve block 19 Lumbar sympathetic block 8 - Stellate ganglion block All blocks continuous</td>
<td>20 Complete resolution 8 Improvement 7 Poor response</td>
</tr>
<tr>
<td><strong>Cebrian 2009</strong></td>
<td>6</td>
<td>6 - arm</td>
<td>2 peripheral nerve block</td>
<td>5 complete resolution 1 Poor response</td>
</tr>
<tr>
<td><strong>Kachko 2008</strong></td>
<td>14</td>
<td>8 - leg 6 - arm</td>
<td>1 - Epidural 1- Stellate ganglion block (x12) 2 - Ankle block</td>
<td>13 full/partial recovery</td>
</tr>
<tr>
<td><strong>Dadure 2005</strong></td>
<td>13</td>
<td>12 - leg 1 - arm</td>
<td>Continuous PNB 12 - Popliteal 1 - Axillary All - Biers block</td>
<td>Complete response at 2 months</td>
</tr>
<tr>
<td><strong>Currie (personal comm)</strong></td>
<td>49</td>
<td>44 - leg 5 - arm</td>
<td>92 - lumbar sympathetic blocks 6 - Stellate ganglion blocks</td>
<td></td>
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</table>
Lumbar sympathetic plexus - anatomy

- Anterolateral border of vertebral body
- Separated from sensory & motor nerves by psoas muscle
- Needle advanced towards side of vertebra & then redirected past the anterolateral border of vertebral body
- L2 – L4
- Confirm position with X ray
Stellate ganglion block - anatomy

- Fusion of 1st thoracic and inferior cervical ganglion
- Anterior to C7
- Conveys sympathetic messages to head, neck & arm, T1 – T6
- Needle inserted between trachea & carotid artery
- Directed towards TP of C6
Spinal Cord Stimulation – for CRPS in adolescents

- Low intensity electrical impulses to trigger the dorsal columns – area of intense pain replaced with paraesthesia
- Reversible
- Expensive & invasive

- 7 girls aged 11-14 years
- Severe therapy resistant CRPS
- Trial stimulation for 1-2 weeks before implantation of generator
- Analgesia developed over 2-6 weeks – sustained at follow up 1-8 years
- Complete 5/7
- Useful reduction 2/7

Olsson GL; EJP 2008
Which block to use

- No high level evidence
- First do no harm
- Least invasive – peripheral nerve blocks
  - US guided
  - Catheter technique
  - Volumetric pumps
  - Sparing of muscle power in contralateral leg
- Operator familiarity
- Indications for sympathetic block
  - Decreasing evidence for role of sympathetic nervous system in CRPS
  - Compared with epidural less weakness with sympathetic block – more able to undertake physical therapy
Adverse effects of regional techniques

- Infection
- Haematoma
- Nerve damage
- LA toxicity
- Allergic reactions

Encourage or reinforce a passive rather than an active role for the patient in their recovery

Patient may become dependent on regional blocks

Berde C Anesthesiology 2005
Placebo Effect

- The greater the invasiveness of the procedure the greater the placebo effect.
- The greater the expectation for pain relief the greater will be the placebo effect.
- The placebo tends to be of less duration.
- Tends to be less reproducible with each successive treatment.
CRPS – Residual/Recurrent Symptoms

Residual symptoms - incidence varies in different case series
- 12% symptoms at 2 years
- 54% residual pain or dysfunction
- 33% relapse, 52% ongoing pain – median follow up 12 years (2-22)

Recurrence
- 25-35%
- Majority within first 6 months after treatment

Sherry 1999 Clin J Pain
Tan Injury 2009
CRPS - Summary

- Awareness & early diagnosis
  - Avoidance of immobilisation
- Intensive physiotherapy with CBT – most important treatment modalities
  - Adequate resources required
- Many children have disease severity that precludes their ability to tolerate PT & CBT alone
  - First do no harm
  - Least invasive techniques
- Ultimate aim of treatment is restoration of function