Innovations in the pharmacological treatment of pain
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Contents

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• Distress vs pain
• Specific drugs
• Drug routes
• Evidence base
Principles

• Keep it simple
• Don’t try to be too clever
• Innovation doesn’t not mean using obscure drugs.

• Learn how to use existing medication correctly
• Children are not small adults
• Neonates are not small children
  ➢ Drug absorption
  ➢ Drug distribution
  ➢ Drug metabolism
  ➢ Drug excretion

`APPM formulary has neonatal doses.`
Consider distress rather than pain

- Pain Syndrome –
  - Central pain (TCA)
  - Visceral hyperalgesia (gabapentin)
  - Dysautonomia (clonidine)
Consider distress rather than pain

• Dystonia – standard baclofen
  ➢ Trihexyphenidyl (past)
  ➢ Gabapentin (present)
  ➢ Risperidone (future)
Gabapentin vs Pregabalin

- *Gabapentin my first choice*
- **Pregabalin** (unlicensed in <18yrs)
  - Binding affinity 6 times greater cf gabapentin
  - Oral bioavailability >90%
  - Doesn’t bind to plasma proteins
  - Ok in hepatic impairment
  - Caution in renal disease
Clonidine

- Dystonia
- Dysautonomia
- Synergistic analgesia with opioids
- Effects abolished by TCA /antipsychotic
- Patches available
Patch

- Lidocaine
- Fentanyl
- Buprenorphine
- Clonidine
Old drugs to reconsider

- Ketamine
- Methadone.
New routes
Transmucosal

Drug absorption generally efficient:
- No stratum corneum (unlike skin)
- Rich blood supply to move drug to circulation
- Avoids first pass metabolism (liver)
- Avoids degradation in the GI tract
Transmucosal

- Drugs can pass through the cells (transcellular) if they are lipophilic.
- They can go between cells if they are hydrophilic and small enough.
- The pH of the drug and how ionised it is also affect how well it is absorbed.
- Buccal enhancers have also been developed by drug companies to increase muco-adhesiveness or speed of absorption.
What makes the ideal drug?

Oral transmucosal drug delivery for pediatric use

Jenny K.W. Lam *, Yingying Xu, Alan Worsley, Ian C.K. Wong

The summary of ideal physicochemical properties of drug candidates for buccal or sublingual formulation development.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Ideal properties</th>
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<tbody>
<tr>
<td>High potency</td>
<td>Single dose &lt;10 mg</td>
</tr>
<tr>
<td>High lipophilicity</td>
<td>Log $P$ (octanol/water) &gt;2.0</td>
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<tr>
<td>Fairly good water solubility</td>
<td>Select drug salts with good solubility if necessary</td>
</tr>
<tr>
<td>Acid/base properties</td>
<td>Unionized form at mucosal</td>
</tr>
<tr>
<td>Small molecular size</td>
<td>Smaller the better, less than 800 Da</td>
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Transmucosal

- Midazolam (seizures, agitation, anxiety)
- Fentanyl (breakthrough pain)
- Diamorphine (breakthrough pain)
- Ketamine (breakthrough neuropathic pain)
- Levomepromazine (nausea / vomiting)
- Buscopan (colicky pain bowel / urinary tract)

Patient and family empowerment.
Evidence

• In the good old days
  – maxi dose of midazolam in syringe driver

• The reality of evidence based medicine
  - Morphine given buccally
Morphine given buccally – the question

• Delphi study (Lynda Brookes) – 50% units used morphine, 50% diamorphine. Very few fentanyl why.
• Our review of evidence – 50:50 split as to whether it works.
Use of buccal morphine in the management of pain in children with life-limiting conditions: Results of a Laboratory study

Renée McCulloch¹³, Mohammed Sattar², Ellen M Henderson³, Majella E Lane⁴, Myra BluebondLangner³⁵


• Not absorbed
Where to get help

• APPM drug formulary
  http://www.appm.org.uk/10.html
Thank you for coming and listening