Innovations in the pharmacological treatment of pain 2018

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Principles

- Keep it simple
- Don’t try to be too clever

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- 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

<u>APPM formulary has neonatal doses.</u>

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

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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?

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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.

Parameters	Ideal properties
High potency	Single dose <10 mg
High lipophilicity	Log *P* (octanol/water) >2.0
Fairly good water solubility	Select drug salts with good solubility if necessary
Acid/base properties	Unionized form at mucosal
Small molecular size	Smaller the better, less than 800 Da

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.

Morphine given buccally – the answer

Use of buccal morphine in the management of pain in children with life-limiting conditions: Results of a Laboratory study

Renée McCulloch[13], **Mohammed Sattar**[2], **Ellen M Henderson**[3], **Majella E Lane**[4], **Myra BluebondLangner**[35]

Palliative Medicine, vol. 32, 2: pp. 554-558. , First Published June 20, 2017.

- **Not absorbed**

Where to get help

- APPM drug formulary http://www.appm.org.uk/10.html

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Thank you for coming and listening