

# Transmucosal

Dr Ross Smith, Consultant in Paediatric Palliative Medicine

Stolen from - Dr Naomi Taylor, ST8 Paediatric Palliative Medicine

# What is the problem?

- Historically - Diamorphine - rapid acting buccal administration
  - Suitable if enteral route is lost or rapid onset of action required
  - Needle free - Administered by parents in the home
- Shortage of Diamorphine
- Need to find another alternative
- Focus - look at options for buccal administration
- Transmucosal routes = buccal, sublingual, orodispersible, nasal & rectal

# Warning

- Severe lack of evidence
- But use combination of sources to come to sensible and safe solutions

# Orodispersible and transmucosal alternative medications for symptom control in adults

BMJ Supportive &  
Palliative Care  
Dec 2020

Note: Adults

Anna Elizabeth Sutherland <sup>1</sup>, Melinda Presland,<sup>1</sup> Emily Harrop,<sup>2,3</sup>  
Matthew Carey,<sup>1</sup> Mary Miller <sup>3,4</sup> Ian Chi Kei CK Wong <sup>5,6</sup>

## ABSTRACT

**Background** Paediatric palliative care makes frequent use of orodispersible and transmucosal drug delivery routes. The limited published experience of this practice suggests that it enables the delivery of needle-free symptom relief, with the potential to train family carers to administer anticipatory medications without reliance on trained health professionals.

**Aims** To identify orodispersible and potential transmucosal alternatives that may be used in adults in the event of a patient having no oral or intravenous route and no access to subcutaneous injections.

## AIM

Our aim in writing this guide is to provide a resource from which healthcare professionals can select medications to control symptoms when patients do not have an oral route and when injectable medications are not available. This will enable high-quality needle-free palliative care, particularly in the community. We aim to summarise the evidence available regarding the transmucosal route, how transmucosal medications are administered, why they are effective and how transmucosal medications might be integrated into clinical practice.

Sutherland et al  
2020  
“orodispersible  
and transmucosal  
alternative  
medications for  
symptom control  
in adults”  
(available from  
<https://spcare.bmj.com/content/early/2020/11/30/bmjspcare-2020-002784>).

# Sciencey bit

- Mucosal membranes absorb lipophilic drugs
    - Minimise first pass metabolism
    - => Quick onset
  - Often very helpful
  - Often useful when unable to absorb enterally too
- 
- Lipophilic means to dissolve in fats, oils, lipids

Sutherland et al 2020 "orodispersible and transmucosal alternative medications for symptom control in adults" (available from <https://spcare.bmj.com/content/early/2020/11/30/bmjspcare-2020-002784>).

# Morphine

- Some reports of anecdotal benefit to buccal morphine
- Evidence - Morphine **does not adequately pass the buccal mucosa**<sup>1</sup>.
  - NOT Liphophilic
  - Effect from buccal may be swallowing and enteral absorption.
  - For this reason **not usually recommended for buccal** use
- Where no alternatives available
  - not unreasonable to trial buccal (or sublingually<sup>2</sup>) given anecdotal experience of benefit.
  - but likely lower bioavailability than oral
- **Can be administered rectally**<sup>2</sup>

1. (McCulloch R et al. 2018 Use of buccal morphine in the management of pain in children with life-limiting conditions: Results of a laboratory study, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5788078/>)

2. Sutherland et al 2020 "orodispersible and transmucosal alternative medications for symptom control in adults" (available from <https://spcare.bmj.com/content/early/2020/11/30/bmjspcare-2020-002784>).

# Oxycodone

- Also not lipophilic (Similar to Morphine)
- + lowest concentration for IV is 10mg/ml
- Sutherland et al - Can be given sublingually or buccally
- Anecdotal evidence buccal can work (similar to Morphine)

# Buprenorphine

- Sublingual administration is possible with buprenorphine melts.
- Lowest dose available is 200 micrograms - can be halved (ie to administer 100 micrograms).
  - These are relatively high doses for many paediatric patients.
- For comparison Buprenorphine '5' patch
  - administers 5 micrograms buprenorphine/hour = 120micrograms (so half a melt almost equivalent to total daily dose from a '5' patch (= 12mg oral morphine equivalent/24 hours).
- Whilst APPM does state can use 100mcg every 6-8hrs for 16-25kg this is very large amount
  - Morphine: Buprenorphine conversion 100:1 (PCF7)
  - Thus, this dose is equivalent to 10mg morphine
  - (625mcg/kg of morphine equiv if 16kg seems v large!)
- **Transdermal patches v useful**
- **but be very cautious with sublingual – probably better alternatives**



# Fentanyl

- Administered via a number of routes – nasal, sublingual and buccal.
  - nasal spray – Supply issue + smallest is 50micrograms/spray) – relatively high dose
  - Oromusocal lozenges available but smallest is 200 micrograms – high dose
- **Buccal** not documented in APPM formulary but is in Sutherland et al 2020
  - Uses dose equivalence between nasal/buccal and sublingual routes
- But beware APPM formulary - use different start doses
  - oromusocal (15micrograms/kg)
  - **intranasal (1-2 micrograms/kg)**
  - Discussed with Dr Harrop – one of authors of paper - recommend **use a 1microgram/kg starting dose.**
  - Conversion of oral morphine: fentanyl is usually 100:1 but 150:1 is sometimes used (source PCF7 p910)
  - Given usual starting doses of Morphine and this conversion feels like 1 mcg/kg reasonable.
- Fentanyl comes -50 microgram/ml IV solution can be given via any routes.
  - relatively small doses can be given (5 micrograms = 0.1ml and can be diluted down)
- Mucositis is risk with buccal and sublingual administration and filter needles needed for IV soln
- **Use starting dose 1 microgram /kg buccal Fentanyl (use IV Solution)**
  - **Anecdotal evidence + abstract (with Cardiff) – Use in pain (1mcg/kg) and dyspnoea (0.5mcg/kg)**

# Results from Sutherland et al

- Alfentanil  
(*buccal, SL, nasal*)
- Atropine (*SL*)
- Buprenorphine (*SL*)
- Carbamazepine (*rectal*)
- Cyclizine  
(*SL, rectal*)
- Diazepam (*rectal*)
- Diamorphine  
(*intranasal, SL*)
- Diclofenac (*rectal*)
- Docusate (*rectal*)
- Domperidone  
(*orodispersible*)
- Fentanyl  
(*nasal, buccal, SL*)
- Glycopyrronium (*SL*)
- Haloperidol  
(*buccal, SL*)
- Hyoscine hydrobromide  
(*chewable*)
- Ibuprofen  
(*orodispersible, chewable*)
- Ipratropium (*nasal*)
- Levomepromazine  
(*buccal, SL*)
- Loperamide  
(*orodispersible*)
- Lorazepam (*SL*)
- Miconazole (*buccal*)
- Morphine (*rectal, SL*)
- Olanzapine (*orodispersible*)
- Ondansatran  
(*orodispersible, rectal*)
- Oxycodone (*SL*)
- Paracetamol  
(*orodispersible, rectal*)
- Prochlorperazine  
(*buccal*)
- Risperidone  
(*orodispersible*)

# Levomepromazine

- Buccal or Sublingual
- Conversion 1:1:1:1 (Enteral: Buccal: SC: IV)
  - Adult PCF (pg 199 – ‘Although PO bioavailability of levo suggests when converting PO to SC a reduction may be required, most use same dose regardless of route’)
  - Adult PCF - Anti-emetic start dose adult 6.25mg PO/SC
  - Sutherland (adult) - 3-25mg buccal/sublingual (or 6.25-12.5mg PRN max TDS)
  - APPM - 12-17yr 3mg-25mg PO Once or twice day, SC 5-25mg/24hrs
- **We have used buccal successfully in several of our patients (1:1:1:1)**
  - **Use IV solution (although paper says can use oral tablet crushed with water)**
  - Particularly helpful if vomiting enteral meds

# Haloperidol

- **Buccal or Sublingual**
- Conversion 1:1:1 (Enteral: Buccal: SC)
  - Adult PCF (pg 196 – ‘PO bioavailability suggests may need reduction of up to 50% from PO to SC. **Although unlikely to be problematic when titrating to effect and a 1:1 ratio is convenient.**’)
  - Adult PCF - Anti-emetic start dose adult 0.5-1.5mg/24h CSCI or PO/SC at bedtime
  - Sutherland (adult) - 0.5-1.5mg 6-8hrly buccal / sublingual
  - APPM - 12-17yr oral 1.5mg OD to 5mg BD, SC 1.5-5mg /24 hours SC
- **We have used buccal successfully in one of our patients**
  - **Started on quite low doses but 1:1 i.e. used oral doses in APPM**
  - Particularly helpful if vomiting enteral meds

# Summary – Most useful

- Fentanyl
  - Buccal / Nasal / Sublingual
  - Use 1mcg/kg IV Solution
- Levomepromazine
  - Buccal / Sublingual
  - Used oral doses in APPM (generally titrate up from lower starting dose)
- Haloperidol
  - Buccal / Sublingual
  - Used oral doses in APPM (generally titrate up from lower starting dose)

# Appendix

# Example Fentanyl Dose Calculation (1)

- 5yr old girl, approaching end of life
- At home, need for fast acting opioid
  - Diamorphine not available
- Background opioid = 2 x 'butrans 5' patches (due to dose escalation)  
= 24mg oral morphine equivalent = 24000 micrograms
- 1/10<sup>th</sup> background = 2.4mg oral morphine equivalent (2400 micrograms)
- Fentanyl conversion 100:1
- 25 micrograms buccal fentanyl used for PRN breakthrough dose

# Example Fentanyl Dose Calculation (2)

- 17yr old boy
- End stage respiratory and renal failure
- On ward on NIV – approaching end of life
- Rapidly escalating doses of oxycodone for pain and breathlessness  
? Enteral absorption reliable.
- Using 2mg oxycodone PRN for pain
- 2mg oxycodone = 3-4mg oral morphine equivalent  
higher dose assumed as escalating symptoms  
= 4000 micrograms oral morphine  
= 40 micrograms buccal fentanyl  
BUT weight = approx 60 kg and no concerns renal excretion fentanyl so  
rounded up to  
50 micrograms buccal fentanyl used as starting dose (=1ml IV solution)



## Example Fentanyl Dose Calculation (3)

- 6 week old baby, undiagnosed rapidly progressive neuromuscular disorder
- On CSCI 1mg morphine/24 hours
- Required 6 x PRNs of buccal fentanyl 3.5 micrograms (1microgam/kg)  
= 21micrograms/24 hours
- Conversion Oral Morphine: Fentanyl 100:1  
OME in 24 hours =  $21 \times 100 = 2100$  micrograms = 2.1mg  
= 1.05mg SC/IV Morphine
- CSCI increased to 2mg/24 hours
- Breakthrough fentanyl dose for CSCI of 2mg/24 hours  
= 2000 micrograms/24 hours SC  
= OME 4000 micrograms/24 hours  
 $1/10^{\text{th}} = 400$  micrograms = 4 micrograms fentanyl PRN