

Poll Questions:

1. On a yearly basis, approximately how many cases do you prescribe a pre-med sedative for?
1-5 6-10 >10
2. In your experience, what route of administration is most commonly used?
PO Buccal Intra-nasal IM IV
3. What would your drug of choice be (type, dose in mg/Kg and route of administration) in the following clinical scenarios?
 - Mild/ moderate anxiety (e.g.: needle phobia)
 - Extreme anxiety & agitation/ absolute refusal (e.g.: not wanting to come to theatre/ fighting with parents or carer)
 - Learning difficulties (e.g.: Asperger's/ Autism)

Editorial:

Many procedures are too demanding and distressing for children and the use of techniques such as play therapy, hypnosis and relaxation can be limited in gaining assent to perform a procedure on a child. This situation is frequently encountered in paediatric anaesthesia, in the immediate peri-operative period. Sedation is an effective way of calming a paediatric patient but requires a certain degree of cooperation and assent in itself when it comes to administration of the sedative (especially if administered via the oral or intravenous route). [1]

The decision of when to use a pre-med sedative rests with the anaesthetist and is one made on the balance of smoother induction, calmer patient and less distressed parent versus over-sedation and paradoxical reactions. The type of pre-med used is often influenced by:

Patient factors – learning difficulties, allergies or other medications being taken

Surgical Factors – type of surgery/ procedure and the indication or importance of it

Previous experience – both of the patient, parents and the anaesthetist. [6]

Main Classes of Pre-Med Sedatives Used:

- Benzodiazepines e.g. Midazolam, Temazepam
Act as agonists at GABA_A receptors within the central nervous system. Produce a somnolent state at correct doses with reduced anxiety and postoperative nausea and vomiting. Overdose can induce a comatose state with respiratory depression.
- α_2 -Adrenoceptor agonists e.g. Clonidine
Clonidine acts at central pre-synaptic α_2 adrenoceptors to reduce the influx of intracellular calcium and therefore reduce the release of noradrenaline. This induces

sedation and also a reduction in sympathetic tone with a resulting decrease in blood pressure.

- Opiates e.g. Oral Morphine
Morphine works at μ -opioid receptors throughout the spinal cord and central nervous system to alleviate pain and also induces sedation and respiratory depression. In overdose it will cause coma and apnoea.

Dosage Information:

<i>Drug</i>	<i>Age group</i>	<i>Dose</i>	<i>Onset</i>	<i>Duration</i>
Temazepam	12 – 18 years	10-20mg	1 hour	2 – 4 hours
Oral Midazolam	1 month – 18 years	0.5mgkg ⁻¹ Max 20mg	30-45 minutes	45 – 60 minutes
Buccal Midazolam	6 months – 18 years	0.2mgkg ⁻¹ Max 10mg	10-20 minutes	30 – 45 minutes
Clonidine	6 months – 18 years	4mcgkg ⁻¹	45-60 minutes	45 – 90 minutes
Oral Morphine	6 months – 18 years	0.2mgkg ⁻¹ Max 10mg	20-30 minutes	1 – 2 hours

[6]

Current Trends:

Recent polls suggest that Midazolam, in the oral route of administration, is the overall preferred method of pre-med sedation. NICE CG 112 recommends the use of Midazolam for conscious sedation (minimal or moderate) in children and young people and it is usually a preferred sedative for use as a pre-medication in diagnostic procedures and elective surgery as it is an effective anxiolytic and has a good safety profile. [2]

However, even with a switch to the newer oral preparation (instead of the intravenous form being given orally) this can be an unreliable form of pre-med, as its' bitter taste makes it less favourable to ingest and thus its pharmacodynamic properties can be unreliable due to the marked variability in absorption.

There has consequently been a move to use the newer preparation of buccal Midazolam as it is tasteless and rapidly absorbed from the oral mucosa, thus requiring little cooperation from the child.

Comparison of the Pharmacokinetic properties of the different preparations of Midazolam:

Route of Administration	Bioavailability	Peak Plasma Concentration	Dose	Adverse features
Buccal	74.5%	10 minutes	0.2-0.3mg/ kg	-----
Intra-nasal	78%	10 minutes	0.2mg/ kg	Unpleasant & painful
Oral	35-41%	60 minutes	0.5mg/ Kg	Bitter, poor intake

Currently, buccal Midazolam is only licenced for use in status epilepsy. Published clinical studies have shown that when used to treat status epilepsy, buccal Midazolam had no severe events. As such, parents are instructed to administer it at home prior to the arrival of paramedics. Common side effects include sedation, somnolence, depressed level of consciousness, respiratory depression and nausea & vomiting. Relative contra-indications to its use are chronic respiratory insufficiency, chronic renal failure and impaired cardiac function. [3]

As set out above one can see that the onset of action (OOA), bioavailability and ease of ingestion of buccal Midazolam are superior to that of the other preparations. [4], [5]

Ease of ingestion is especially important as the exact timing of dose administration can be difficult to predict. This also bears an impact on fasting times as general anaesthesia cannot be undertaken less than 2 hours after semi-clear fluids have been ingested. Thus, if having to wait 60 minutes before OOA of oral preparations but 2 hours before general anaesthesia can take place; it is very likely that the effects of oral midazolam will have worn off...

When administered via the buccal route fasting is not affected. In addition, a rapid OOA (10 minutes) would mean that the drug could be administered just prior to leaving the ward, allowing enough time for OOA whilst en route to theatre...

Summary:

Pre-medication in itself is an ever-changing practice that varies widely. As such, each Trust will have a specific guideline set to guide those less familiar with its use.

It is important to be aware of newer preparations of sedatives that may be beneficial due to improved pharmacodynamic and pharmacokinetic profiles. In an era of emphasis being placed on the efficient running of theatres, pre-med agents with a faster OOA & safer side-effect profile can make a big difference to the overall running of a high-turnover list with challenging patients.

A summary of suggested uses of the most common Pre-meds used is listed below:

Oral Midazolam: consider where time permits and oral medicines well tolerated.

Buccal Midazolam: consider where short onset time is of benefit or where oral medicines are poorly tolerated. Rapid onset allows administration with minimal delay to list order or with improved tolerance by patient.

Oral Temazepam: consider in patients >40kg. Commonly used in adult practice with well-recognised effect profile in larger patients.

Oral Morphine: Consider combining with oral midazolam in patients with a history of failed pre-medication and severe anxiety. Sometimes used in isolation for cardiac patients, due to the combined benefits of its sedative and analgesic properties.

Oral Clonidine: Consider in patients who have had previous adverse experience to benzodiazepines. May offer improved side effect profile for some patients.

We welcome feedback and will be interested to hear of any alternative practice or differing opinions.

Dr Bianca Tingle
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Resources:

1. Michael R. J. Sury. *Paediatric Sedation*. Continuing Education in Anaesthesia, Critical Care & Pain | Volume 4 Number 4 2004.
2. Sedation in children and young people. NICE clinical guidelines 112. December 2010.
3. Summary of Product Characteristics; Buccolam 5mg Oromucosal solution. Last updated on eMC 18/02/2014.
4. R. Schwagmeier, S. Alincic & H. W. Striebel. Midazolam pharmacokinetics following intravenous and buccal administration Br J Clin Pharmacol 1998; 46:62, Issue 5, pages 535-536, May 2007.
5. De Boer AG, de Leede LGJ & Breimer DD. Drug absorption by sublingual and rectal routes. Br J Anaesthes 1984; 56:69-82.
6. Jonathan Mathers, Caroline Wilson and Helen Hume-Smith: Pre-medication in children for General Anaesthesia, GOS Guideline 11th March 2014.

