PAEDIATRIC HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 22: ANAESTHETICS
NEMLC 31 MARCH 2022 – REPORT

MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/NOT ADDED
22.3.2.1 General Anaesthesia - Preparation	Clonidine, oral	Added
	Clonidine, IV	Not added
	Dexmedetomidine	Not added
	Ketamine, intranasal	Added
	Midazolam, intranasal	Added
22.3.2.2 General Anaesthesia – Induction of Anaesthesia	Etomidate	Added
22.3.2.3 General Anaesthesia – Maintenance of Anaesthesia, Analgesia	Paracetamol IV	Added
22.3.3 Post-operative care	Paracetamol IV	Added
	Tilidine	Retained

22.3.2.1 General Anaesthesia - Preparation

Clonidine oral: added
Clonidine IV: not added
Dexmedetomidine: not added
Midazolam intranasal: added
Ketamine intranasal: added

Clonidine oral
See clonidine oral medicine review.

Clonidine IV: not added
Dexmedetomidine: not added
An external comment was received recommending the addition of IV clonidine and dexmedetomidine. Clonidine IV is not registered in this country and only accessible through section 21 application, thus cannot be added to the essential medicines list. Dexmedetomidine has historically not been included due to its large cost, however it is on the Tertiary prioritization list for review consideration.

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Midazolam intranasal: added

Ketamine intranasal: added

The intranasal routes for administration of midazolam and ketamine were added. These routes provide for an alternative, effective, non-invasive administration route of these agents. This route is safe and fast acting, and a practical route for administration to children. [1,2] The text was updated to indicate the this route is off-label but sometimes utilised in practice.

The text was amended as follows:

Agent	Route	Dose	Time to peak effect (minutes)
Midazolam	Oral	0.25 - 0.5mg/kg (max 15mg)	10-30
	Intranasal**	0.3 mg/kg	10-15
	Intravenous	0.025-0.1 mg/kg*	3-5
Clonidine	Oral	3 - 5 mcg/kg	60-90
Ketamine	Oral	6 - 10 mg/kg	30
	Intranasal**	1 - 5 mg/kg	20
	Intramuscular	2 - 4 mg/kg	20

*Titrate to effect. Repeat dose at 5 minute intervals until desired level of sedation is achieve.

** Off-label route is sometimes employed in practice.

Midazolam:

- This is a commonly used premedication agent that is generally well tolerated.
- It can be safely used in most children, but caution is advised in children with:
  - Risk factors for paradoxical excitation - e.g. children under 3 years, Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD).
  - Avoid in patients with obstructive sleep apnoea (OSA), as can cause respiratory depression.

OR

Clonidine:

- Preferred agent in children with:
  - Behavioural disorders such as ADHD, and children with ASD.
  - Obstructive sleep apnoea.
- Does not cause respiratory depression.
- Can cause bradycardia, which is clinically insignificant.
- Provides analgesia in addition to anxiolysis and sedation.
- Is tasteless and well tolerated. Even smaller children will swallow the tablets, but they can also be crushed and added to juice or water.

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Alternative in certain circumstance:

Ketamine:

- Is cardio stable and does not cause respiratory depression.
- Provides analgesia in addition to anxiolysis and sedation.
- In exceptional circumstances, can be used IM, e.g. when dealing with a combative child who is unable to understand what is needed and will not accept other routes of administration.

Intranasal administration of medicines can be administered with the patient reclining (or held) at 45 degrees, preferably using a mucosal atomiser device. The syringe is held horizontally and applied to the nare, and the contents expelled in one

[1] Pansini V, Curatola A, Gatto A, Lazzareschi I, Ruggiero A, Chiaretti A. Intranasal drug administration for analgesia and sedation in children admitted to pediatric emergency department. A narrative review. Annals of Translational Medicine. 2021. 9(2):189.

[2] South African Society of Anaesthesiologists (SASA). SASA Paediatric Guidelines for the safe use of procedural sedation and analgesia for diagnostic and therapeutic procedures in children: 2021-2026. https://doi.org/10.36303/SAJAA.2021.27.4.S2.2635

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rapid dose. Use undiluted medicines to minimise the volume of drug. Doses of 1mL or more should be divided between two nares.

22.3.2.2 General Anaesthesia – Induction of Anaesthesia

Etomidate: added

Etomidate was added as an additional intravenous agent for induction of anaesthesia. This is in line with the Adult Hospital Level Standard Treatment Guidelines and Essential Medicines List, 2019, recommendations. This provides a more 'cardio-stable', and can be used for patients at risk of cardiovascular collapse

Endotracheal intubation

An external commentator proposed the addition of formulas to estimate endotracheal intubation tube sizes. The Committee agreed with this recommendation and the following was added:

To estimate the correct ETT size, the table below can be used as a guide. Alternatively, formulas can be used:
ETT size (ID (mm): Age (years) /4 + 3.5 (cuffed ETT)
Age (years)/4 + 4 (uncuffed ETT)
ETT depth: age (years)/2 + 12. Confirm clinically with auscultation that air entry is heard bilaterally and observe airway pressures.

22.3.2.3 Maintenance of Anaesthesia

Analgesia

Paracetamol IV: added

See paracetamol IV review.

22.3.3 Post Operative Care

Paracetamol IV: added

See paracetamol IV review.

Tilidine: Retained

Tilidine has been removed from the market in South Africa, however there are still hospitals with stock. It was proposed that tilidine be retained while stock is still available.

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PAEDIATRIC HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 22: ANAESTHETICS
NEMLC 25 MARCH 2021 – REPORT UPDATE

MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/NOT ADDED
22.3.1 Local and Regional Anaesthesia	Bupivacaine	Table added
	Lidocaine	Table added
22.3.2.1 General Anaesthesia - Preparation	Clonidine	Addition under consideration
22.3.2.2 General Anaesthesia – Induction of Anaesthesia	Thiopental sodium	Removed
22.3.2.3 General Anaesthesia – Maintenance of Anaesthesia Intravenous anaesthetics	Ketamine	Added
	Propofol	Added
Analgesia	Paracetamol IV	Addition under consideration
Muscle Relaxants	Cisatracurium	Added
Prophylaxis of post-operative nausea and vomiting	Dexamethasone	Added
	Ondansetron	Added
22.3.4 Management of Anaesthetic and Post-anaesthetic Complications	Propofol	Added
	Lidocaine	Added
Laryngospasm	Suxamethonium	Intralingual route added
Bronchospasm	Treatment from 'acute asthma attack section'	Added
Local Anaesthetic Systemic Toxicity (LAST)	Lipid emulsion 20%	Added

General

This Chapter was previously a combined Anaesthesia and Intensive Care combined chapter. For this review cycle it has been recommended that this be split as the Intensive Care Chapter is being expanded.

22.3.1 Local and Regional anaesthesia

Lidocaine: table added
Bupivacaine: table added

Information around local anaesthetic onset of action, duration of action, and maximum doses was captured in table format for ease of reference, as below:

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Table 1: Local anaesthetic agents

Local anaesthetic	Onset of action	Duration of action	Maximum dose (with adrenaline (epinephrine)	Maximum dose (without adrenaline (epinephrine)
Lidocaine	2-5 mins	1-2 hours	7 mg/kg (0.3ml/kg of 2% solution)	3 mg/kg (0.15ml/kg of 2% solution)
Bupivacaine	10-40 mins	4-6 hours	2-3 mg/kg (0.4-0.6 ml/kg of 0.5% solution)	2-3 mg/kg

**Lignocaine amended to lidocaine – the approved international nonproprietary name (INN).*

22.3.2.1 General Anaesthesia - Preparation

Clonidine: Addition under consideration.

Oral clonidine is under consideration for addition as premedication for anaesthesia. This would be an additional agent to oral midazolam and oral ketamine, for use particularly in children with behavioural disorders, autism spectrum disorder and obstructive sleep apnoea.

22.3.2.2 General Anaesthesia – Induction of Anaesthesia

Thiopental Sodium: Removed

Thiopental sodium was removed as an intravenous induction agent option. This agent has had stock availability challenges, and thus it was recommended that it be removed. Both propofol and ketamine as listed as alternatives.

Capnography added

Capnography has been listed as a mandatory monitor to ensure safe anaesthesia. The 4th National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society Report finding[3] indicate that capnography and monitoring should be universally used in anaesthesia cases. Capnography has shown to lead to earlier identification of airway obstruction.

NEMLC requested addition of evidence to support inclusion of capnography. The following was evaluated and presented:

- Capnography has been included by the World Health Organisation (WHO) and the World Federation of Societies of Anaesthesiologist (WFSA) as an essential safety monitoring device.[4]
- A retrospective case series on malpractice claims for delayed detection of oesophageal intubation from the anaesthesia a closed claims project database showed that 96% of the cases of oesophageal intubation with delayed detection resulted in patient death or severe brain damage. Of these 49% occurred in the operating theatre of anaesthesia location.[5]

[3] Cook T, Woodall N, Frerk C. Major Complications of Airway Management in the United Kingdom. NAP4 Report ant Findings. March 2011.

[4] Wollner E, Nourian MM, Booth W, et.al. Impact of capnography on patient safety in high- and low-income settings: a scoping review. British Journal of Anaesthesia. 2020, 125 (1): e88-e103.

[5] Honardar MR, Posner KL, Domino KB. Delayed detection of esophageal intubation in anesthesia malpractice claims: brief report of a case series. Anesth Analg. 2017; 125: 1948-1951.

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- A systematic review and meta-analysis evaluated the effect of capnography on sedation-related adverse events during procedural sedation and analgesia for ambulatory surgery.[6] This analysis included 13 studies. The findings showed that the addition of capnography to visual assessment and pulse oximetry was associated with a significant reduction in mild (RR 0.77, 95% CI 0.67 to 0.89) and severe (RR 0.59, 95% CI 0.43 to 0.81) desaturation, as well as the use of assisted ventilation (OR 0.47, 95% CI 0.23 to 0.95). No difference was seen in endpoints for apnoea, aspiration, bradycardia, hypotension, premature procedure termination, respiratory failure and death.
- A Cochrane review evaluated whether capnography in addition to standard monitoring is more effective than standard monitoring along to prevent cardiorespiratory adverse events in emergency department patients undergoing procedural sedation and analgesia.[7] Of the three trials that were included (n=1272), there was no difference seen in the rates of oxygen desaturation between the capnography and standard monitoring group (RR 0.89, 95% CI 0.48 to 1.63, moderate quality evidence). There was also no difference in rate of airway interventions performed (RR 1.26, 95% CI 0.94 to 1.69). In a paediatric sub-group analysis, there was no significant difference between the intervention and control group (RR 0.97, 95% CI 0.71 to 1.34), moderate quality evidence due to the variance in the definition of airway interventions.

Capnography is considered by the WHO and WFSA as an essential monitoring device. The data is variable, with some showing no additional benefit, and others showing significant benefit compared to standard monitoring. Data is additionally complicated by heterogeneity in terms of levels of sedation, definitions of outcomes, patients included, settings etc. It is however the opinion of the Paediatric Committee that this safety monitor would be a useful safety addition in the paediatric theatre setting.

22.3.2.3 Maintenance of Anaesthesia

Inhalational (volatile) anaesthesia

- Age related minimum alveolar concentration (MAC) values added.

Table 2: Age-related MAC values

Age (months)	Isoflurane	Sevoflurane
1	1.6	3.2-3.3
2	1.9	3.2-3.3
14	1.8	2.5
44	1.6	2.5
480	1.2	2.5

Intravenous anaesthetic agents

Propofol: Added

Ketamine: added

[6] Saunders Rhodri, Struys MMRF, Pollock RF, Mestek M Lightdale JR. Patient safety during procedural sedation using capnography monitoring: a systematic review and meta-analysis. BMJ Open. 2017, 7:e013402.

[7] Wall BF, Magee K, Campbell SG, Zed PJ. Capnography versus standard monitoring for emergency department procedural sedation and analgesia. Cochrane Database of Systematic Reviews. 2017, issue 3, CD010698.

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Intravenous anaesthetic agents were previously not included in the maintenance section, however these options are required in cases where volatile agents are contraindicated. Propofol and ketamine were included as for induction of anaesthesia.

Analgesia

Multimodal analgesia section added

Text around multimodal analgesia (use of multiple pharmacological agents in combination) was added. This approach promotes optimal pain management through synergy of agents, as well as minimizing opiate requirements.[8]

Paracetamol IV: Addition under consideration

It is proposed that IV paracetamol be considered for addition for the management of post-operative pain. Technical review and economic evaluation is planned with assistance from external resources.

Muscle relaxant during maintenance phase

Cisatracurium: Added for patients with renal impairment

This recommendation is in line with the Adult STGs and EML recommendation.

Prophylaxis for post-operative nausea and vomiting added (PONV)

Dexamethasone IV: added

Ondansetron IV: Added

No previous recommendations were made for the prophylaxis of PONV. The use of dexamethasone and ondansetron in this indication is in line with current recommendations and guidelines. [9, 10]

The NEMLC proposed that the 5-HT3 receptor antagonists be considered as a class if there was sufficient data for other class members. The Paediatric ERC reviewed this recommendation. The majority of the data lies with ondansetron, particularly regarding appropriate dosing. The Paediatric ERC thus recommended that for this indication, the 5-HT3 receptor antagonists not be considered a class, and ondansetron be retained as the recommended option.

22.3.4 Management of Anaesthetic and Post-anaesthetic Complications

Laryngospasm

Propofol: Added

Lidocaine: Added

Suxamethonium: Intralingual route added (with diagram)

[8] Kumar K, Kirksey MA, Duong S, Wu CL. A Review of Opioid-Sparing Modalities in perioperative pain management: methods to decrease opioid use postoperatively. International Anesthesia Research Society. 2017, 125 (5): 1749-1760.

[9] Urits I, Orhurhu V, Jones MR, et.al. Postoperative Nausea and Vomiting in Paediatric Anaesthesia. Turkish Journal of Anaesthesiology and Reamination. 2020, 48(2): 88-95.

[10] Gan TJ, Belani KG, Bergese S, et. al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesthesia-analgesia. 2020

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Laryngospasm is one of the most common complications and thus it was felt there needed to be more guidance with explicit information on what to do in the various situations. Propofol and lidocaine were added in cases where laryngospasm is complete, and patient starts to desaturate.[11] The intralingual route of suxamethonium was added for case where there is no intravenous access.[12]

Bronchospasm

This section previously referred to the Respiratory System Chapter section on acute asthma attacks. For the updated chapter the therapy steps have been moved to this section for ease of management.

Magnesium sulphate: added

Ketamine: added

Adrenaline: added

Hydrocortisone: added

Malignant Hyperthermia

Link to the comprehensive management guidelines for the Association of Great Britain and Ireland were added as a link.

Local Anaesthetic Systemic Toxicity (LAST)

Section added.

Lipid emulsion 20%: Added

This recommendation is in line with the Adult STGs and EML recommendation.

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[11] Collins S, Schedler P, Veasey B, et. al. Prevention and Treatment of laryngospasm in the pediatric patient: A Literature Review. AANA. 2019, 87(2): 145 - 151

[12] Al-alami AA, Zestos MM, Baraka AS. Pediatric laryngospasm: prevention and treatment. Current Opinion in anesthesiology. 2009, 22:388-395.