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### An Update on the Perioperative Management of Children with Upper Respiratory Tract Infections

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#### Abstract

#### **Purpose of review**

This review summarises the current evidence for the management for children with recent upper respiratory tract infections. Furthermore, the review includes management guidelines for children with upper respiratory tract infections.

#### **Recent findings**

Good history and clinical examination is sufficient in most children presenting with URTI. Testing for immune markers or preoperative NO measurement does not add any additional value. Preoperative bronchodilator administration, iv induction with propofol and non-invasive airway management all reduce the occurrence of respiratory adverse events.

#### Summary

Most children can be safely anaesthetised even in the presence of an upper respiratory tract infection if the perioperative anaesthesia management is optimised. In this review article we have included a management algorithm for children with URTI presenting for elective surgery.

#### Keywords

Pediatric anesthesia, upper respiratory tract infections, respiratory adverse events, anesthesia management.

#### Introduction

The common cold or upper respiratory tract infections (URTI) are frequently present in children. Although URTI is commonly mild and self-limiting in nature, it does place a burden on society due to the increased use of health care resources and absences form work or school (1).

Performing anaesthesia in children with URTI increases the risk of perioperative respiratory adverse events (PRAE, e.g. laryngospasm, bronchospasm, desaturations, breath holding) (2–7).

The purpose of this review is to summarize current evidence regarding perioperative anaesthetic management of children with an URTI.

#### **Definition of URTI**

Most studies define URTI as two of the following symptoms: rhinorrhoea, sore or scratchy throat, sneezing, nasal congestion, malaise, cough, or fever >  $38^{\circ}(6, 7)$ .

#### Prevalence / Incidence of URTI

While a child under the age of 4 has on average up to 8 URTI per year (1), the incidence of URTI decreases with age with adults having on average 2 colds per year (1). URTI occurrence is seasonal with increased emergence during the colder months in the temperate and during the rainy season in the tropical regions (1).

Between 25 and 45% of children presenting for elective surgery will have a history of a recent URTI (7, 8); therefore, unsurprisingly, URTI is the most common cause of surgery cancellation in children (9).

Most children with URTI have symptoms for around one week but these can persist for up to three weeks (1).

While URTIs in children are most commonly caused by a viral infection (1), bacterial superinfections are regularly found (1). Rhinovirus is by far (up to 80%) the most frequent virus causing URTI in children (10). Other viruses include: parainfluenza, respiratory syncytial, influenza, entero-, and, adeno-, metapneumo-, and human boca virus (10). Testing for the infective agent is not routinely performed in children with URTI as such results do not change anaesthetic management. However, many experts acknowledge an RSV infection as a more severe respiratory infection, which requires particular attention and a careful risk benefit analysis before proceeding with anaesthesia and surgery especially in infants (11).

#### Prevalence / Incidence of PRAE

The risk of PRAE is significantly increased in children with URTI (2–7, 12). Children with a current and/or recent URTI experience between 24 and 30% PRAE as opposed to children without URTI (8 to 17% PRAE) (5, 7). This is even more pronounced in infants and those born prematurely (7).

#### Pathophysiology URTI

Symptoms depend on the anatomical location of the infected mucus membranes. For example, the rhinovirus most often inoculates the nasal mucosa and will cause a runny nose but can then spread to the throat and trachea whereas the influenza virus has a predilection to the tracheobronchial epithelia (1).

Viral infection of the mucus membranes causes airway inflammation. Similar to asthma, airway inflammation can lead to increased secretions, airway susceptibility and bronchial hypersensitivity with increased risk of PRAE predominantly laryngospasm and bronchospasm (13, 14).

In addition, some viruses can produce neuraminidase that inhibit M2 receptors thereby increasing the release of acetylcholine (13). Furthermore, viral induced liberation of tachykinin and neuropeptides have been described (13). Both pathways increase the likelihood of bronchospasm.

#### **Preoperative Assessment**

#### Does the child have an URTI?

Hallmark of a cold is nasal discharge, sneezing, sore throat and cough (1). The most frequent symptoms are rhinorrhoea (66%), followed by nasal congestion (37%), sneezing (29%), productive cough (26%), sore throat (8%) and fever (8%) (5). Bronchitis and tracheitis can cause dry cough and wheeze. Hoarse voice indicates laryngitis. Non-specific symptoms including irritability, loss of appetite, fatigue, muscle pain, headache. Fever is not uncommon in children (1).

#### Additional risk factors in children with URTI

#### Table 1

Several risk factors for the occurrence of PRAE in children with URTI have been identified (13). These can be divided into patient factors, surgical factors and anaesthetic management, see Table 1.

In children with URTI history of fever (RR 2.9), "green" instead of "clear runny nose" (RR 3.2 and 1.4 respectively) or "moist" instead of "dry cough" (RR 3.2 and

1.8 respectively) are associated with increased risk of bronchospasm and laryngospasm (7).

Lee et al have proposed a "COLDS" score to assess the risk of PRAE in children with URTI presenting for elective surgery (15). The following parameters: current symptoms, onset of symptoms, additional lung disease, planned airway type, and planned surgery score 1, 2 or 5 points. Whilst this "COLDS" score has not been validated the use of such a score might have some merit. The lowest overall score will be 5 emphasizing that no anaesthesia in children with current or recent URTI is without any risk. It is suggested that any category scoring the 5 should be regarded as a red flag alerting the perioperative team of the increased risk of PREA and allowing to team to modify the risk of the child where possible.

#### **Preoperative management**

#### Timing of procedure

There is much debate but no consensus regarding the optimal timing of elective surgery in children with recent URTI. The duration of airway susceptibility and bronchial hyper reactivity in children following a URTI remains unclear but is known to persist well beyond resolution of symptoms. Given the high frequency of URTI in children, this may make it difficult to find a time in which the child is truly well.

There are no randomised controlled trials regarding best timing of general anaesthesia in children with URTI (16).

Observational trials have the inherent selection bias with the sickest children having their surgery postponed.

Most studies show that a current/recent URTI bare similar risk of PRAE (5, 7, 17).

There are only few studies examining the effect of different time points after URTI on the occurrence of PRAE. One observational trial found that children with an URTI < 2 weeks and 2 to 4 weeks had an increased risk of PRAE (OR 5.2 and 3.8 respectively) as opposed to children with an URTI 4 to 6 weeks prior surgery (OR 0.2) (17). However, the sample size was small and inhomogeneous.

In the largest observational study to date, von Ungern-Sternberg et al found in 9297 children presenting for elective surgery that children with current and recent URTI (<2 weeks) had more PRAE (25 and 29% respectively) than did children without URTI or with URTI between 2 and 4 weeks (12 and 8% respectively) (7).

Some authors suggest that children with a mild URTI can be safely anesthetised as the problems encountered are generally easily treated without long term sequelae (9).

Whether a surgery should be cancelled should be a decision balancing risk and benefit for each individual child including: patient and surgical risk factors of developing PRAE, waste of public health care resources, previous surgery cancellation, operation wait time, distance to travel for parents and difficulties for parents to organise time off work.

Figure 1 depicts an algorithm to guide preoperative management in children with URTI scheduled for elective surgery (9, 13).

In general, cancellation of children with URTI is only rarely necessary. While some suggest more caution and to reschedule children with URTI, delaying surgery by 4-6 weeks following each of the 6-8 URTI/year, severely restricts the ideal surgical time frame and may lead to recurrent cancellations which again impact negatively on the patient, his/her family as well as the health care system. Furthermore, even when the URTI may be gone and airway hyperreactivity reduced, the risk of PRAE is still present due to inherent conditions such as wheezing or exposure to smoking. Therefore it is not surprising that the majority of pediatric anaesthetists will still proceed with anesthesia even in the presence of URTI (13, 18, 19). The right balance needs to be found between clinical judgement of fitness for surgery and risk of PRAE linked to the presence of other risk factors. When processing with anaesthesia and surgery, it is critical to optimise the perioperative management to reduce the risk of PRAE.

#### Additional investigations

Good history and clinical examination is sufficient in most children presenting with URTI. Testing for immune markers or preoperative NO measurement does not additional value (20, 21). We do not routinely recommend any additional investigations in children presenting with URTI for surgery.

If suspicion arises of the presence of undiagnosed asthma or a bacterial infection (e.g. group A streptococcus tonsillitis) referral should be made to a specialist to initiate appropriate investigations and treatment (e.g. antibiotics, bronchodilators, steroid) (22). In children < 1 year of age, who are suspicious for RSV infection, a rapid test may be considered (11).

#### Perioperative management

Table 2

Premedication

We do not recommend the use of benzodiazepine for premedication in children with URTI as first line agents as this may be associated with increased PRAE (7, 17). Alpha-2 antagoinsts, e.g. clonidine, dexmedetomidin may be better suited if premedication is required (22).

#### Lignocaine

We do not recommend the use of topical lignocaine to reduce the occurrence of laryngospasm in children with URTI. An observational trial found topical lignocaine to increase desaturation without reducing laryngospasms in children with URTI (23).

In contrast, lignocaine gel placed on LMA reduced mainly postoperative coughing in a small RCT of children with URTI (24). Although only short lived, IV lignocaine has been shown to suppress the laryngospasm reflex in healthy children and therefore may be useful in children with URTI (25).

#### **Bronchodilators**

We recommend preoperative salbutamol in children with current and recent (<2 weeks) URTI. A large prospective observational trial (n=600) showed salbutamol inhaled 10 to 30 min prior induction (2.5 mg if weight <20 kg, 5 mg if weight >20 kg) to reduce overall PRAE mainly bronchospasm (6% vs 11%, P = 0.03) and severe coughing (6% vs 12%, P = 0.03) (18).

In contrast, IV glycopyrolate after induction of anaesthesia does not reduce PRAE in children with URTI (26).

#### Airway management

In children with URTI and an increased risk of PRAE we recommend the airway management to be performed by an experienced paediatric anaesthetist as multiple attempts and insertion by less experienced staff has been shown to affect the incidence of PRAE (7).

The majority of observational studies and RCT show that endotracheal tubes (ETT) are associated with the highest risk of PRAE compared with less invasive airways (e.g. laryngeal mask airway (LMA) or face mask). The face mask is associated with the smallest risk of PRAE in children with URTI (3, 5, 7, 8, 26, 27). We therefore recommend the use of face mask or LMA over ETT where possible.

Small children in general and particularly those with URTI are prone to experience PRAE (5, 7, 8, 28). A recent randomised controlled trial shows that infants < 1 year especially benefit most from LMA over ETT in terms of occurrence of PRAE (29). The rate of major PRAE (laryngospasm and bronchospasm) is five fold increased with ETT compared with LMA (RR 5·30, 95% CI 1·62–17·35, p=0·002) when used for children undergoing minor elective procedures (29). However, it has to be emphasised that using LMA in infants and children with current or recent URTI reduces but does not abolish the occurrence of PRAE (12). When using ETT in children with URTI we recommend the use of cuffed over uncuffed ETT to improve ventilation and minimise leakage around the tube (7).

In general, the risk of PRAE is higher on removal than on insertion of airway devices (7, 26). Observational data suggests that deep removal of LMA or ETT reduces the occurrence of PRAE (7). However, recent RCT reveal somewhat conflicting results. Von Ungern-Sternberg et al compared the effect of deep vs awake extubation of ETT in 100 children undergoing adeno-tonsillectomy (30). The overall incidence of PRAE was similar between the two groups. Awake extubation was associated with increased coughing (60 vs. 35%, P 0.03) whereas airway obstructions (relieved by simple airway manoeuvres) were increased following deep extubation (26 vs. 8%, P 0.03). In contrast, Baijal et al did not find a difference in PRAE comparing deep vs awake extubation of ETT in 905 children undergoing adeno-tonsillectomy (28).

Unpublished data suggests that in children with URTI LMA deep removal may be more beneficial than awake as deep removal as it is associated with reduced desaturations and coughing.

#### **Anaesthetic Agents**

Propofol has good airway reflex (laryngospasm and bronchospasm) blunting properties and is therefore the ideal agent to be used during the induction in children with increased risk of PRAE (22, 31). Propofol does have some bronchodilator effects but these are small in comparison to volatile anesthetic agents.

Observational data in children with URTI as well as a large randomised controlled trial in children at particular risk for PRAE (including those with URTI) suggest that an IV propofol induction is associated with a significant reduction of PRAE when compared with an inhalational induction with sevoflurane (8, 32). Volatile anesthetic agents have good bronchodilator properties but limited effects in suppressing airway reflexes (22). Volatile anaesthetic agents can be used to treat severe bronchospasm or severe asthma.

When using volatile anesthetic agents for either induction or for maintenance we recommend the use of sevoflurane (5, 7, 22). Sevoflurane has the best bronchodilatatory effect of all currently available volatile anaesthetic agents.

On the contrary, desflurane is associated with a significantly increased risk for PRAE due to its property to increase airway resistance and irritability and should not be used in children particularly not in those with URTI (7, 22, 33).

The literature on the use of neuromuscular blocking agents in children with URTI is scarce.

#### Intravenous vs inhalational induction

While a recent RCT comparing IV vs inhalational induction (32) demonstrated a significant reduction in PRAE in children at a particularly high risk for PRAE receiving an IV propofol induction, this included children with a variety of risk factors including (but not exclusively) children with current or recent URTIs. While Propofol is associated with a reduced occurrence of laryngospasm compared with sevoflurane, cough and breath holding is increased (31).

Additionally, a recent study examining the effect of two concentrations of sevoflurane for maintenance of anaesthesa (2.5%, MAC 1 vs 4.7%, MAC ED 95 Intubation) found that higher concentrations of sevoflurane did not protect against the occurrence of laryngospasm (34). Laryngeal reflexes could still be found at a BIS of 0 (34).

Overall we recommend an IV induction and maintenance with propofol over inhalational induction for children with URTI to reduce the incidence of PRAE.

#### Conclusions

Most children can be safely anaesthetised even in the presence of an upper respiratory tract infection if the perioperative anaesthesia management is optimised. The detailed algorithm can be used as an aide to guide clinicians in their everyday decision making.

#### Key points

- Children with current and recent (up to two weeks) URTI have an increased risk of a perioperative respiratory adverse event (e.g. laryngospasm, bronchospasm, desaturation, breath holding).
- In such children, the following risk factors further increase the risk for PRAE: age < 2 years, prematurity, passive smoking, respiratory comorbidities, airway surgery, and use of an ETT.
- In children with severe URTI (green runny nose, moist cough, wheezing, fever, lethargy), we recommend to postpone surgery if possible for at least two weeks.
- In order to reduce the risk of PRAE in children with current or recent URTI, anaesthetic management can be optimised as follows: experienced staff performing airway management, use of preoperative inhaled salbutamol, IV induction with propofol, avoidance of desflurane, use of TIVA or sevoflurane with a propofol or lignocaine bolus prior to any airway manipulations.

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Patient	<ul> <li>copious secretions / presence of sputum</li> </ul>
	<ul> <li>nasal congestion</li> </ul>
	<ul> <li>paternal smoking / passive smoking</li> </ul>
	<ul> <li>history of reactive airway disease,</li> </ul>
	- younger age
	<ul> <li>prematurity (&lt;37 weeks)</li> </ul>
	- parental belief, "the child has is sick/a cold"
Surgery	<ul> <li>surgery of the airways</li> </ul>
	<ul> <li>ear nose throat (ENT) surgery</li> </ul>
	- eye surgery
	<ul> <li>upper abdominal surgery</li> </ul>
	- cardiac surgery
Anaesthetic management	- invasive airway (endotracheal intubation)
	- anaesthetic agents (desflurane)
	<ul> <li>experience and compentence of the</li> </ul>
	anesthesiologist in pediatric anesthesia

## Table 1 - Risk factors for the occurrence of PRAE in children with URTI(4-8, 12, 13)

#### Table 2 - Evidence based perioperative management of children with URTI

#### Premedication

- Avoid use of benzodiazepine for premedication (7, 17)
- Use of clonidine if premedication is required (22)

#### Lignocaine

- Consider IV lignocaine to suppress laryngospasm in high risk patient / high risk procedure (25)
- Avoid topical lignocaine to vocal cords (23)
- Lignocaine gel on LMA may be beneficial to reduce postoperative coughing (24)

#### Bronchodilators

- We recommend preoperative salbutamol (inhaled 10 to 30 min prior induction, 2.5 mg if weight <20 kg, 5 mg if weight >20 kg) in children with current and recent (<2 weeks) URTI (18)

#### Airway management

- We recommend the least invasive airway device (face mask over LMA over ETT) (3, 5, 7, 8, 12, 26–28) (29).
- When using ETT we recommend where possible the use of uncuffed over cuffed ETT tubes (7)
- Deep removal of LMA and ETT might reduce laryngospasm and PRAE but is associated with increased airway obstructions (7, 28–30)
- We recommend airway control to be done by an experienced anaesthetist in children with URTI at increased risk of PRAE (7)

#### **Anaesthetic Agents**

- Propofol has good airway reflex (laryngospasm and bronchospasm) blunting properties but only mild bronchodilator effect (22, 31)
- Volatile anesthetic agents have good bronchodilator properties but limited effects in suppressing airway reflexes (22)
- We recommend the use of volatile anaesthetic agents to treat severe intraoperative bronchospasm
- We don't recommend the use of volatile anaesthetic agents to treat severe laryngospasm
- When using volatile anaesthetic agents sevoflurane is to be preferred over other volatile anaesthetic agents (5, 7, 22)
- Desflurane should be avoided (7, 22, 33)

#### Intravenous vs inhalational induction

- In high risk children we recommend IV induction with propofol over inhalational induction (8, 31, 32, 34)

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This single center randomized controlled trial in 300 children showed that intravenous propofol as opposed to inhalational sevoflurane reduced PRAE during induction (32 vs. 11%) and during the perioperative period (43 vs. 26%).

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In this prospective observational trial, 40 children scheduled for elective surgery received sevoflurane 2.5% (1 MAC) and 4.7% (ED95Intubation) in random order. In contrast to defensive airway reflexes including cough, expiration reflex, and spasmodic panting, the incidence of laryngospasm was only partially reduced, even under high concentrations of sevoflurane.

## Figure 1 Algorithm to guide perioperative management in children with URTI scheduled for elective surgery

Recommendations for the perioperative management of children with URTI scheduled for elective surgery. <u>Modified from (13)</u>.