Anaesthesia for tonsillectomy in HIV-infected children with pulmonary arterial hypertension

Tonsillectomy is a very common procedure, often performed as an outpatient procedure.

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Tonsillectomy is one of the most common procedures performed by general practitioners and ENT specialists annually. It is frequently performed as an outpatient procedure after insufficient pre-operative investigations. Indications for this procedure include severe recurrent tonsillitis, chronic tonsillitis, peritonsillar abscess, obstructive sleep apnoea (OSA) and biopsy for possible malignancy.

In the confirmed HIV-positive population, tonsillectomy may be complicated by not only concurrent antiretroviral therapy and its side-effects, but also frequently by undiagnosed pulmonary arterial hypertension (PAH).

Given the incidence of HIV infection in our country, it is highly likely that a large percentage of children presenting for this procedure are HIV positive, even if not yet confirmed by clinical HIV testing. Tonsil hyperplasia is a common finding in this population.

In the confirmed HIV-positive population, however, tonsillectomy may be complicated by not only concurrent antiretroviral therapy and its side-effects, but also frequently by undiagnosed pulmonary arterial hypertension (PAH). Undiagnosed or mismanaged PAH has the potential to cause a pulmonary hypertensive crisis, which is often irreversible and fatal. What was to be uncomplicated tonsillectomy may result in a descending spiral of complications and catastrophe. Apart from the routine concerns regarding tonsillectomy, including the high risk for postoperative nausea and vomiting (PONV) and risk for rebleeding, practitioners should be aware of other pertinent issues that play an important role in the pre-operative management of these patients. These patients should definitely not be regarded as normal healthy subjects undergoing a minor procedure. Some of the many controversies regarding the management of PAH include:

- Should these tonsillectomies be performed as day-case procedures?
- Should there be routine pre-operative screening for PAH and by whom?
- Should routine echocardiography be done pre-operatively?

PAH is defined as the presence of a mean pulmonary arterial pressure (PAP) that exceeds 25 mmHg at rest or 30 mmHg during exercise. Patients with PAH are generally considered to be at greater risk for the development of life-threatening peri-operative cardiovascular complications.[1] An acute increase in pulmonary vascular resistance will increase right ventricular afterload and can lead to right ventricular dysfunction. PAH crisis describes the situation where pulmonary pressure exceeds systemic blood pressure, causing acute right heart failure, decreased pulmonary blood flow, decreased cardiac output, and hypoxia and biventricular failure. In 1998 a clinical classification of PAH was proposed that incorporates pathophysiological mechanisms, clinical presentation and therapeutic options, and is now widely used in clinical practice (Table 1).[2,3]

PAH is reported to occur at an increased frequency in HIV-infected patients. The prevalence of HIV-associated pulmonary arterial hypertension (HAPAH) has remained at 0.5% before and after the introduction of antiretroviral (ARV) medication, and may be increasing because this medication prolongs survival of patients with HIV. In fact, the role of ARVs in the development and/or progression of HAPAH is controversial; some studies demonstrate a benefit while others show worsening of PAH.[4] The reason that ARV therapy does not favourably affect the prevalence of HAPAH is unclear. Clinical studies are equivocal; some show that ARV therapy impairs blood-vessel lining endothelial function,[5] whereas others have shown that HIV does not directly infect vascular endothelial cells or smooth-muscle cells, hence the association between HIV and PAH may not be related to viral load or immune status, partially explaining why ARV therapy does not prevent PAH.[4]

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Pathophysiology

PAH can develop as a consequence of individual factors, as well as a combination of interlinked factors, including chronic infection, tonsil hyperplasia, OSA, ARV

therapy, and HIV-associated pulmonary hypertension *per se* (Fig. 1).

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HIV infection may lead to chronic and recurring tonsillitis, which causes tonsil hyperplasia, leading to chronic airway obstruction, chronic hypoxaemia and subsequently PAH. HIV infection, as well as ARV therapy itself, can lead to the development of PAH. Chronic hypoxaemia due to airway obstruction from OSA coinciding with HIV-related tonsil hyperplasia may also cause PAH.

Management

Pre-operative

History and examination should be directed at revealing the indication for surgery. One should be alert to signs of PAH (dyspnoea on exercise, chronic cough, fatigue), complications or side-effects of ARV therapy, and symptoms and signs of OSA. A history of dyspnoea or severe snoring indicating OSA should alert the clinician to refer the patient for specialist management.[6] There are no distinct physical or imaging findings that distinguish HIV-related PAH from other causes of PAH (Table 2).

Medication for PAH includes: diuretics, anticoagulants, phosphodiesterase V inhibitors, calcium channel blockers, bosentan and sildenafil. The patient may be on any of these drugs. None of these drugs should be discontinued preoperatively, and should be restarted as soon as possible after surgery. If there is certainty about presence of PHT and the patient is on no therapy, it is advisable to administer sildenafil pre- and postoperatively (0.3 - 0.5 mg/kg 6-hourly).

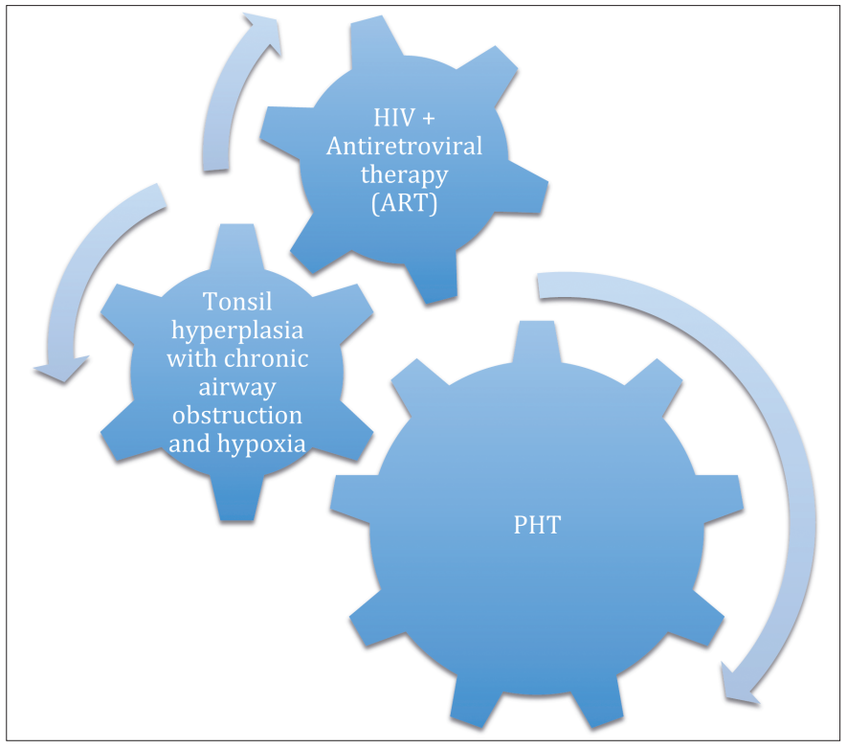

Fig. 1. The interlinking of factors leading to the development of pulmonary arterial hypertension (PHT – pulmonary hypertension).

It is vital to identify all medications that the patient is using, including the side-effect profile of each, especially ARVs, antihypertensives, steroids, antibiotics and warfarin.

Be on the lookout for the syndromic child (Down's) and congenital heart disease (CHD).

Careful examination of the airway is vital, as well as the breathing pattern. Airway management can be planned in advance avoiding the 'can't intubate, can't ventilate' situation, which will most surely result in the development of a pulmonary hypertensive crisis.

Special investigations to exclude or diagnose PAH include: chest X-ray (CXR), ECG and echocardiography.

A history of dyspnoea or severe snoring indicating obstructive sleep apnoea should alert the clinician to refer the patient for specialist management.

ECG findings include right ventricular hypertrophy, right axis deviation, and right atrial enlargement. Unfortunately the ECG in the normal paediatric population may mimic signs of right heart involvement, especially in younger patients. This makes the ECG an unreliable investigation in this situation. CXR may show cardiomegaly and pulmonary arterial enlargement. If in doubt an echocardiogram should be obtained. Look for right ventricular dilatation, right atrial dilatation and tricuspid regurgitation. Pulmonary artery catheterisation may be required to confirm the presence of PAH and its severity.[7] Careful planning with meticulous attention to detail will be needed to avoid the dreadful complications associated with these illnesses. The aim is to prevent the PAH crisis by avoiding all stress situations, i.e. hypoxia, hypercarbia, acidosis,

Table 1. The Dana Point Classification of pulmonary hypertension[2,3]

1. Pulmonary arterial hypertension
   - 1.1 Idiopathic PAH
   - 1.2 Heritable
     - 1.2.1 BMPR2
     - 1.2.2 ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)
     - 1.2.3 Unknown
   - 1.3 Drug and toxin induced
   - 1.4 Associated with
     - 1.4.1 Connective tissue diseases
     - 1.4.2 HIV infection
     - 1.4.3 Portal hypertension
     - 1.4.4 Congenital heart disease
     - 1.4.5 Schistosomiasis
     - 1.4.6 Chronic haemolytic anaemia
   - 1.5 Persistent PHT of the newborn
   - 1.6 Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
2. PHT caused by left-heart disease
   - 2.1 Systolic dysfunction
   - 2.2 Diastolic dysfunction
   - 2.3 Valvular disease
3. PHT caused by lung diseases and/or hypoxia
   - 3.1 Chronic obstructive pulmonary disease
   - 3.2 Interstitial lung disease
   - 3.3 Other pulmonary diseases with mixed restrictive and obstructive patterns
   - 3.4 Sleep disordered breathing
   - 3.5 Alveolar hypoventilation disorders
   - 3.6 Chronic exposure to high altitude
   - 3.7 Developmental disorders
4. Chronic thromboembolic PHT
5. PHT with unclear multifactorial mechanisms
   - 5.1 Haematological disorders: myeloproliferative disorders, splenectomy
   - 5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis
   - 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   - 5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

PAH – pulmonary arterial hypertension; BMPR2 – bone morphogenetic protein receptor 2; ALK1 – activin receptor-like kinase-1; PHT – pulmonary hypertension.

hypothermia, and pain. By choosing a safe anti-anxiety drug like hydroxyzine for premedication while avoiding oversedation in an airway-compromised patient, the pre-operative period can be safely managed. Anecdotally, in the already hospitalised patient, premedication with morphine and supplemental oxygen by nasal prongs can also be helpful in the pre-operative situation.

Intra-operative

Careful airway management is essential. Avoid unnecessary airway instrumentation where possible. Maintain spontaneous breathing until it is verified that ventilation is appropriate, with smooth intubation and blunting of airway reflexes. Make use of short-acting opioids and airway topicalisation to accomplish this. Avoid unnecessary suction and bucking (coughing) on the endotracheal tube or tonsil plate. Ventilation strategy should avoid overinflation, using lowest tidal volumes possible, and high fractionated oxygen tension (FiO_2).[8]

Although a contentious issue, the current recommendation is a careful deep extubation performed with the child in the lateral decubitus position. Confirm homeostasis before attempting extubation, and ensure adequate prophylaxis for PONV. Continuous positive airway pressure (CPAP or BiPAP) rather than increased FiO_2 should be used postoperatively to improve oxygenation when signs of OSA are present.

It is vital to identify all medications that the patient is using, including the side-effect profile of each, especially antiretrovirals, antihypertensives, steroids, antibiotics and warfarin.

Effective analgesia is absolutely essential, but be alert to oversedation with possible resultant airway obstruction. Short-acting opioids like sufentanil or alfentanil can be of great benefit in this situation.

Anaesthetic drug choice will depend on the type of ARV that the patient is using, as differences in enzyme induction and side-effect profile are very common. In general, isoflurane and sevoflurane are associated with clinical pulmonary vasodilatation and are accepted components of a balanced

Table 2. Symptoms, signs and ECG findings in pulmonary arterial hypertension

Symptoms	Signs	ECG findings
Dyspnoea on exertion	Tachypnoea	Right atrial hypertrophy
Fatigue	Tachycardia	Right ventricular hypertrophy
Chest pain	Distended neck veins	R/S ratio >1 in V1
Syncope	Left parasternal lift	Deep S waves in precordial leads
Palpitations	Audible tricuspid regurgitation murmur	Right atrial enlargement shows peaked P waves in inferior leads
Lower extremity swelling	Ascites Lower extremity oedema	

anaesthetic technique in patients with PAH. Volatile agents may unfortunately lead to a dose-dependent depression of cardiac contractility and reduction in systemic vascular resistance (SVR), which may reduce systemic blood pressure and precipitate right ventricular ischaemia and failure.

Fentanyl has minimal pulmonary and systemic haemodynamic effects, attenuates the pulmonary response to noxious stimuli and serves as an important component of a balanced anaesthetic in children with PAH. Bradycardia and hypotension observed with the use of remifentanil may cause an undesired reduction in cardiac output.

Propofol should be avoided, as the decrease in SVR can cause significant biventricular failure, especially in patients with cardiac shunts or severe PAH where the decreased SVR will augment right-to-left shunt and worsen hypoxia. Ketamine remains controversial but current studies show that patients with severe PAH generally have the most significant adverse pulmonary vascular responses to ketamine. Avoid hypovolaemia and hypothermia as these can also elicit a hypertensive response.[9] Nitrous oxide increases pulmonary vascular resistance and should also be avoided.

Monitoring

Standard monitoring including pulse oximetry, ECG, blood pressure, capnography and temperature is essential. Invasive arterial blood pressure monitoring should only be reserved for surgery done in tertiary care institutions.

Ventilation strategies include high concentrations of oxygen, low tidal volumes (6 ml/kg of predicted body weight), a respiratory rate sufficient to achieve mild hypocarbia and optimum levels of positive end-expiratory pressure (5 - 15 cmH_2O). The practitioner must also look out for and avoid air bubbles in intravenous lines because of the potential for right-to-left embolisation through an open foramen ovale.

Post-operative

Patients with HAPAH should not be operated on as day cases. Surgery should be done in a facility where high care is available for confirmed PAH patients, with proper monitoring peri-operatively. Effective analgesia should be implemented and careful airway observation is mandatory. Pre-operative chronic medication should be restarted without delay. Postoperative pain control can be achieved with correct dosing of drugs like Valoron drops and oral paracetamol.

Management of a PAH crisis

Administer 100% oxygen and apply proper airway management, which may involve reintubation and hyperventilation. It is important to attenuate noxious stimuli and use pharmacological pulmonary vasodilators. The latter include nitroglycerine, aminophyline, and prostacycline. Inhaled nitrous oxide is also used in specialist centres. Right ventricular function should be supported by the use of inodilators, e.g. milrinone (not freely available in South Africa) or dobutamine.[10]

Management of *post-tonsillectomy bleed* in these patients needs special consideration. This is a very serious situation with all the necessary triggers for eliciting a pulmonary hypertensive crisis, including hypoxia, oedema, anxiety, anaemia, hypovolaemia and aspiration. These patients should be managed by an anaesthetist skilled in paediatric anaesthesia. The patient must be optimally resuscitated, with induction performed in the lateral decubitus position, thus avoiding direct suction of the tonsillar bed. The airway management should be done according to the anaesthetist's clinical judgement after evaluation for oedema, stridor, etc. Depending on the presence of an intravenous line, a rapid sequence induction can be attempted. When haemostasis is confirmed, the patient can be awakened.

References available at www.cmej.org.za

In a nutshell

- HIV infection, tonsil hyperplasia, and obstructive sleep apnoea are commonly found in combination, and any child known to have HIV infection and current respiratory symptoms should alert the practitioner to the possibility of PAH.
- Careful consideration should be given to utilising an anaesthetic technique that reduces noxious stimuli to the minimum.
- The anaesthetist should be familiar with the patient's pre-operative status, able to provide optimal peri-operative care and be skilled in the management of complications pertaining to PAH.
- These patients, once diagnosed, should not be done as day cases, but rather managed in an institution that can deliver optimal peri-operative care.
- Once pulmonary hypertension is clinically diagnosed, echocardiography is mandatory before attempting anaesthesia or surgery.
- The routine screening of HIV-infected children who present for tonsillectomy by paediatricians or anaesthesiologists would be ideal, but unfortunately in our environment, not possible.
- Careful pre-operative evaluation and appropriate referral to specialist centres will ensure that the disastrous consequences of PAH are minimised.