orphanaesthesia

Anesthesia recommendations for patients suffering from

Congenital Central Hypoventilation Syndrome

Disease name: Congenital Central Hypoventilation Syndrome

ICD 10: G47.3

Synonyms: Undine Syndrome, Ondine's Curse

Central hypoventilation syndrome (CHS) is a rare disorder, which can be both congenital and acquired. Congenital central hypoventilation syndrome (CCHS) is caused by chromosomal mutations in the PHOX2B gene on chromosome 4p12. The non-congenital or acquired form of CHS may be due to brain stem tumour, infarct, or edema. As the acquired form of this disease is quite rare the main focus of this article will be the congenital form of central hypoventilation syndrome.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Disease summary

The main characteristic of CCHS disease is small tidal volumes and monotonous respiratory rates while awake and asleep, with more profound alveolar hypoventilation during sleep. Due to hypoventilation these patients develop hypercapnia and hypoxemia but lack the normal ventilatory responses to overcome these conditions while asleep. However, while awake they do have the ability to consciously alter the rate and depth of breathing. While sleeping, these children will have shallow respirations interspersed with periods of apnoea most commonly during non-REM sleep.

CCHS is a lifelong condition and will require some form of ventilatory support throughout life either positive pressure ventilation via tracheostomy or nasal mask. Other forms of long-term management include negative pressure ventilation and diaphragmatic pacing. CCHS usually manifests itself in the new born period with episodes of cyanosis and apnea and most infants will require mechanical ventilation immediately after birth. CCHS can also present in later infancy, childhood and even adulthood is termed as Late Onset CCHS (LO-CCHS).

The diagnosis of LO-CCHS should be considered if there is hypoventilation, cyanosis or seizures after administration of CNS depressants or anaesthetics, pulmonary infection and treatment of obstructive sleep apnoea. LO-CCHS reflects the variable penetrance of the PHOX2B mutations. As the PHOX2B gene plays a role in neural crest cell migration this disease is also linked with other neurocristopathies such as Hirschsprung disease caused by an absence of segmental colonic ganglia. Presence of Hirschsprung disease occurs in 20% of patients with CCHS and has been termed as Haddad syndrome. In addition CCHS may also be associated with tumours of the neural crest and a number of symptoms due to autonomic nervous system dysfunction (ANSD). These include heart rate variability and transient abrupt asystoles, decreased pupillary light response, esophageal dysmotility, breath holding spells, reduced body temperature, sporadic profuse sweating and lack of physiological responses to the challenges of exercise and environmental stressors.

Typical surgery

Dental surgery, tracheotomy, insertion of diaphragmatic pacers, insertion of cardiac pacemakers, gastrostomy tube insertion, anti-reflux surgical procedures and patients with Hirschsprungs disease may require colostomy for distal intestinal obstruction. Due the presence of pulmonary hypertension some patients may have to undergo cardiac catheterization for right and left heart studies.

Type of anaesthesia

There is no definite recommendation of the use of general anaesthesia or regional anaesthesia.

In the opinion of the author regional anaesthesia should be used where it is appropriate as it avoids respiratory depression in order to avoid prolonged mechanical ventilation. Due to long standing hypoxia and apnoeic episodes, patients with CCHS have inevitably some degree of pulmonary hypertension and consequently right ventricular failure. This may not be the case in patients with LO-CCHS where the disease may have been present for a short time.

In patients with severe pulmonary hypertension and right ventricular failure spinal anaesthesia should be avoided as it may cause a profound sympathetic blockade, decrease in venous return and bradycardia that can lead to right heart failure. In these patients a carefully titrated lumbar epidural would seem to be the anesthetic of choice.

Peripheral nerve blockade for extremity surgery would have minimal effect on the patient's central respiratory drive and would also minimize the use of opioids for post-operative analgesia.

General anaesthesia can be challenging. If required it is important to use short acting agents e.g. remifentanil, propofol and desflurane. Inhalation anaesthetics may need to be avoided, as their clearance would depend on adequate postoperative ventilation, which may be deficient with patients suffering from CCHS. Short acting muscle relaxants such as succinylcholine can be used for tracheal intubation. However due to hypotonia it has been advised that succinylcholine should be avoided until more data is available concerning its use in this patient group. If muscle relaxation is to be used it is important to detect complete neuromuscular recovery prior to extubation of the trachea. Due to long standing disease and the need for mechanical ventilatory support most patients will have a definitive airway in place. In such cases a cuffed treacheostomy tube is required and if no definitive airway is present it is prudent to intubate the trachea, as these patients are at a higher risk of aspiration due to impaired gastric emptying secondary to autonomic dysfunction. Positive pressure ventilation is required as these patients will not breathe spontaneously when asleep.

Necessary additional diagnostic procedures (preoperative)

CCHS is a progressive respiratory disease characterised by hypoventilation. Due to this patients may present with cardiovascular symptoms secondary to pulmonary hypertension.

A chest x-ray should be obtained to rule out pulmonary infection and to determine heart size.

Lung function tests including lung volumes and arterial blood gas analysis should be performed to evaluate grade of pulmonary involvement.

Cardiac function test including electrocardiography and echocardiography should be performed for evaluating presence of cardiomyopathy. Invasive tests to determine degree of pulmonary hypertension would include right and left heart catheterization to determine pressures.

Seventy-two hour recordings of electrocardiography (Holter Monitoring) are required to rule out aberrant rhythms, sinus pauses and the frequency of shorter pauses (< 3 seconds).

Particular preparation for airway management

Due to autonomic dysfunction patients with CCHS have defective swallowing and decreased gastric emptying. This makes gastroesophageal reflux common in these patients. The laxity of the diaphragm also contributes to lower pressure in the oesophageal sphincter and this decreases the anti-reflux barrier. Therefore drugs are required to reduce gastric acid production and increase gastrointestinal motility.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. But the impaired mobility of advanced stage patients may suggest a higher risk of postoperative thrombosis.

Particular precautions for positioning, transport or mobilisation

Keep warm, oxygenated and CO_2 normal during transportation. Avoid hypothermia, hypoxia and hypercarbia as these factors can worsen pulmonary hypertension and cause right ventricular failure. Another reason to provide special care to temperature is that patients with CCHS can have problems with the central control of body temperature.

Probable interaction between anaesthetic agents and patient's long-term medication

If the patient has been receiving respiratory stimulants i.e. aminophylline or other sympathomimetics then the inhalation agent halothane should be avoided as it can increase the risk of cardiac arrhythmias.

Provide steroid substitution in patients who are on long standing oral steroid therapy or those who have discontinued within the last 6 months.

Anaesthesiologic procedure

Anaesthesia for patients with CCHS should be performed in centres equipped with an Intensive Care Unit.

There are no reported cases where succinylcholine has been used in patients with CCHS. It is advised that succinylcholine should be avoided in cases where hypotonia is present due to the risk of hyperkalemia and rhabdomyolysis.

Inhalation agents should be used with caution as they may cause cardiac and respiratory depressant effects. Their clearance depends on adequate postoperative ventilation and a need for postoperative mehanical ventilatory support.

In case of cardiomyopathy avoid nitrous oxide because of cardio-depressant effects.

Propofol should be used with caution and injected slowly with close observation of the patients electrocardiogram monitoring. This is based on one case report that describes complete atrio ventricular heart block in a child with CCHS who received a bolus of propofol for induction of anaesthesia.

Opiates and local anaesthetics have been used without any complication. However short acting opiates such as remifentanil or fentanyl should be used to avoid prolonged effects.

Non-depolarizing neuromuscular blocking agents can be used safely in these patients, there are reports of the use of rocuronium without adverse effects. Careful monitoring of neuromuscular function should occur to detect complete recovery. However due to a diminished respiratory drive most patients can tolerate tracheal intubation and ventilation without the need for muscle relaxants.

Antagonisation of neuromuscular blockade with pyridostigmine or neostigmine seems to be possible.

Patients must be fully awake to be able to resume spontaneous ventilation, while asleep they will not have a respiratory drive and will be unable to breath.

Due to the respiratory depressant effects of anaesthetic agents and opioids it is likely that these patients will require a period of postoperative ventilatory support.

Particular or additional monitoring

Monitoring of the neuromuscular blockade is strictly recommended if any neuromuscular blocking agent is used: it is useful to obtain baseline values before injection the non-depolarizing neuromuscular blocking agent.

Monitor body temperature, oxygen saturation and end tidal CO_2 to avoid hypothermia, hypoxia and hypercarbia. These factors can cause pulmonary vasoconstriction worsening pulmonary hypertension and may cause right ventricular failure.

Due to autonomic dysfunction and cor pulmonale arterial cannulation for invasive blood pressure measurement and central venous line placement is recommended. In case of cardiomyopathy, transesophageal echocardiography is very useful.

It is imperative that neuromuscular blockade is monitored carefully and its effects are completely reversed after surgery.

Possible complications

In the case where the patient suffers from a seizure disorder then the inhalation agent enflurane should be avoided as it has shown evidence of electroencephalographic spike and wave activity.

At present there has been no literature concerning the use of succinylcholine in patients with CCHS. In the case where hypotonia is present succinylcholine should be used with caution as it may cause hyperkalemia and cardiac arrest.

Patients with CCHS are at risk for hyperkalemic cardiac arrest (succinylcholine) and rhabdomyolysis (volatile anesthetics).

Induction with propofol has been shown to cause complete atrioventricular heart block.

Sedative drugs and opioids can cause somnolence, which reduces the ventilator drive in patients with CCHS requiring postoperative ventilation.

Muscle relaxants such as rocuronium can be used but adequate monitoring and reversal is required. Residual muscle relaxation can result in prolonged postoperative ventilation and awareness.

CCHS patients are at risk for respiratory and cardiac insufficiency.

Postoperative care

After anaesthesia patients must be provided with rate controlled ventilatory support with supplemental oxygen. Postoperative monitoring should include electrocardiography and continuous blood pressure. In addition close monitoring of oxygenation and end tidal CO_2 should commence in the postoperative period. Serial arterial blood gas analysis is required.

Most patients may have an insitu tracheostomy and home ventilation which, can be restarted after surgery.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

In cases where there is severe ANSD complete cardiovascular collapse may occur on the induction of anaesthesia. Cardiac dysrhythmias, asystole, convulsions and respiratory arrest may occur.

Ambulatory anaesthesia

Ambulatory anaesthesia can be performed on patients with early disease with mild ANSD and in those cases having minimal and minor surgery, only if home ventilation is present.

Obstetrical anaesthesia

There are no reported cases of obstetric anaesthesia in patients with CCHS. However the use of epidural anaesthesia has shown to be safe with patients with CCHS. Spinal anaesthesia may not be safe in patients with advanced CCHS and right ventricular failure in these cases the anaesthetic of choice would be a carefully titrated lumbar epidural.

Literature and internet-links

1. Healy F, Marcus CL. Congenital central hypoventilation syndrome in children. Paediatr Respir Rev. 2011 Dec;12(4):253-63
2. Weese-Mayer DE, Rand CM, Berry-Kravis E, Jennings LJ, Loghmanee DA, Patwari PP, Ceccherini I. Congenital central hypoventilation syndrome from past to future: model for translational and transitional autonomic medicine. Pediatr Pulmonol 2009;44:521–535
3. Weese-Mayer DE, Berry-Kravis EM, Ceccherini I, Keens TG, Loghmanee DA, Trang H; ATS Congenital Central Hypoventilation Syndrome Subcommittee. An official ATS clinical policy statement: Congenital central hypoventilation syndrome: genetic basis, diagnosis, and management. Am J Respir Crit Care Med. 2010 Mar 15;181(6):626-44
4. Javaheri S. Central sleep apnea. Clin Chest Med. 2010 Jun;31(2):235-48
5. Lawicka M, Sawicka J, Bakowska G. Haddad syndrome Anaesthesiology Intensive Therapy 2013, vol. 45, no 1, 30–32
6. Paton JY, Swaminathan S, Sargent CW, Keens TG Hypoxic and hypercapnic ventilatory responses in awake children with congenital central hypoventilation syndrome. Am Rev Respir Dis. 1989 Aug;140(2):368-72
7. Salehi A. Pulmonary Hypertension: A Review of Pathophysiology and Anesthetic Management. Am J Ther. 2012 Sep;19(5):377-83
8. Bonnin M, Mercier FJ, Sitbon O, et al. Severe pulmonary hypertension during pregnancy: mode of delivery and anesthetic management of 15 consecutive cases. Anesthesiology. 2005;102:1133–1137
9. Strauser LM, Helikson MA, Tobias JD. Anesthetic care for the child with congenital central alveolar hypoventilation syndrome (Ondine's curse). J Clin Anesth. 1999 Aug; 11(5): 431
10. Sochala C, Deenan D, Ville A, Govaerts MJ. Heart block following propofol in a child. Paedriatr Anaesth 1999;9(4):349-51
11. Niazi AU, Mocon A, Varadi RG, Chan VW, Okrainec A. Ondine's curse: anesthesia for laparoscopic implantation of a diaphragm pacing stimulation system. Can J Anaesth. 2011 Nov;58(11):1034-8.

Last date of modification: April 2014

These guidelines have been prepared by:

Author
Ahtsham Niazi, MBBS, FCARCSI, FRCPC, Assistant Professor of Anaesthesiology, Toronto Western Hospital, University Health Network, Toronto, Canada
Ahtsham.Niazi@uhn.ca

Peer revision 1
Alana Kirkwood, Department of Anaesthesia, Great Ormond Street Hospital, London, UK
alana.kirkwood@gosh.nhs.uk

Peer revision 2
Reshma Amin, MD, FRCPC, MSc, Assistant Professor of Paediatric Medicine, Division of Respiratory Medicine, Hospital for Sick Children, University of Toronto, Toronto, Canada,
reshma.amin@sickkids.ca