orphanaesthesia

Anaesthesia recommendations for

PURA Syndrome

Disease name: PURA Syndrome

ICD 10: Q93.5

Synonyms: PURA-related neurodevelopmental disorder, 5q31.3 deletion syndrome

Disease summary: Genetic mutations of the gene coding for purine rich element binding protein A (PURA, (5q31.2) lead to a developmental disorder, named PURA syndrome. PURA is thought to play a role in control of DNA replication and transcription, neuron proliferation, dendrite maturation, and mRNA transportation to translation sites during neuronal development. The gene is relevant in brain development and may be involved in automatic regulation of breathing by the brainstem. PURA defects affect the development of neurons and may also affect the formation of maturation of myelination, leading to developmental problems and seizures, though the exact mechanism is unclear. Early signs of this disorder include hypotonia, hypothermia, swallowing disorders, seizures, central and obstructive sleep apnea. Later manifestations include neurodevelopmental delay, speech delay or absence, delayed and impaired gross motor development, intellectual disability, and seizure disorder. Challenges for an anesthesiologist are multifold and the proposed approach is deduced from the above mentioned clinical problems and from the anaesthetic implications of other phenotypically similar neurodevelopmental disorders. Primary anesthetic concerns focus on the respiratory, cardiovascular, and neurologic functions of the child as these patients could show an increased sensitivity to sedative medications.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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

Typical surgery

Gastrostomy, Orthopaedic surgery, correction of scoliosis, ophthalmologic procedures.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia.

There are no specific concerns of association of PURA syndrome with malignant hyperthermia, which helps in determining the type of induction agent or maintenance anesthetic to use.

Necessary additional pre-operative testing (beside standard care)

Thorough assessment of the respiratory, cardiovascular, and neurologic function with the help of the patient's neurologist or paediatrician is necessary for proper perioperative care. Additional testing should be guided by results of such assessment. Lung function testing is probably not feasible and will likely not provide any additional predictive value for post-operative respiratory complications. The dosage and possible side-effects (haematologic, metabolic) of the patient´s antiepileptic drugs should be checked.

Particular preparation for airway management

Similar neurodevelopmental disorders, such as Rett Syndrome and Angelman Syndrome, have shown a higher propensity for difficult endotracheal intubation than the general population. However, facial dysmorphism studies of small patient samples do not show facial features that would indicate increased risk for difficult endotracheal intubation or mask ventilation.

Hypotonia of the oropharyngeal muscles may predisposes to swallowing difficulties and possibly increases the risk of aspiration during induction and awakening.

Particular preparation for transfusion or administration of blood products

There is evidence from similar neurodevelopmental disorders that there may be a higher requirement for blood products in highly invasive surgeries (e.g. scoliosis surgery).

Particular preparation for anticoagulation

No evidence supports the need for particular anticoagulation. Post-pubertal patients who are not able to move adequately during the postoperative period should be considered for thromboprophylaxis.

Particular precautions for positioning, transportation and mobilisation

With alterations in muscle tone and potential spasticity/contractures that may develop, positioning should emphasize appropriate padding and avoidance of pressure spots.

Interactions of chronic disease and anaesthesia medications

Not reported.

Anaesthetic procedure

In case of elective procedure, even if short fasting times for clear fluids are currently recommended for healthy children, it is probably safer to ensure a longer than usual fasting time in PURA patients because of their risk of aspiration. Regarding risk of seizures, the usual antiepileptic drugs should be administered on the day of the procedure and high concentrations of sevoflurane and hyperventilation should be avoided.

An increased risk for apnoea, upper airway obstruction and aspiration should be considered during both induction and recovery of anaesthesia.

Because of PURA's association with central and obstructive sleep apnea, patients are at increased risk of sedation-related respiratory adverse events. It is likely that patients with PURA syndrome will show delayed recovery from respiratory depressants and increased sensitivity to sedative medications. Minimizing the dose of medications that decrease respiratory drive, mainly opioids and benzodiazepines is recommended.

It seems reasonable to apply principles of anaesthetic management used for patients with severe obstructive sleep apnea, with reduction of doses of opioids (typically 50% of usual) accompanied by continuous monitoring, including pulse oximetry, and the use of a prophylactic nasopharyngeal airway during the awakening period.

Altered muscle tone, typically presenting with hypotonia and poor tone of pharyngeal muscles, leads to considerations regarding intraoperative use of a neuromuscular blocking agent: if a neuromuscular blocking agent is needed, its dosage should be titrated to effect (taking into account the reduced muscle tone and mass) using neuromuscular monitoring (train-of-four, TOF) to ensure their adequate effect and reversal. It is likely that there will be variability in the presentation of these patients, leading to alterations in drug dosing and metabolism.

Hypothermia should be actively prevented.

Particular or additional monitoring

No monitoring specific to PURA syndrome.

Possible complications

Sedative drugs, including opioids and benzodiazepines may cause respiratory insufficiency.

Muscle relaxants dosage should be titrated to effect (taking into account the reduced muscle tone and mass) using neuromuscular monitoring to ensure their adequate effect and reversal.

Post-operative care

Postoperative continuous monitoring with pulse oximetry and respiratory rate is recommended, especially if patient history reveals apnoeas after full term birth or after stress. Following general anaesthesia admission for 24 hour monitoring is wise to survey that there are no recurrent episodes of apnea, hypopnea or desaturation, and that aspiration and reactions are as required.

Multimodal analgesia with an emphasis on non-opioid agents is recommended, with reduction of doses of opioids, should additional analgesia be necessary. Pain should be evaluated using a special scoring system for individuals that are unable to communicate their pain (e.g., the adapted Face, Legs, Activity, Cry, Consolability scale or FLACC scale) and with the help of the child's usual carers (parents).

Patients often have epilepsy with intractable seizures. Antiepileptic medications should be continued on schedule throughout the perioperative time frame, and IV antiepileptic substitution should be foreseen if the patient needs to remain npo in the postoperative period. It is unlikely that general anaesthesia should be a postoperative seizure trigger in this patient population but hypoventilation, pain and stress could result in an increased risk of seizures.

Disease-related acute problems and effect on anaesthesia and recovery

Pituitary dysfunction may exist. Provide steroid substitution in cases of corticotherapy.

Disease triggered emergency situations are focused on status epilepticus.

Ambulatory anaesthesia

Ambulatory anaesthesia (according to common guidelines) is not recommended. Given the association of the syndrome with both central and obstructive sleep apnea, we recommend this patient population be admitted to the inpatient unit.

Obstetrical anaesthesia

Not reported.

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