orphanaesthesia

Anaesthesia recommendations for patients suffering from

Rett syndrome

Disease name: Rett syndrome (RS)

ICD 10: F84.2

Synonyms: Autistic disorder (F84.0)

Rett syndrome is a rare inherited neurodevelopmental disease originally described by Andreas Rett in 1966, which occurs mostly in girls [1] and causes developmental and nervous system problems. Genetically, Rett syndrome results from mutations in the genes encoding methyl-cytosine-guanosine (CpG) binding protein 2 (MECP2) located on the X chromosome. In less than 10% of RTT cases, mutations in the genes CDKL5 or FOXG1 have also been found to resemble it [2]. Affected individuals have clinical features that overlap with autism. Infants with Rett syndrome seem to grow and develop normally in the early months. However, between 6 and 18 months and 3 years of age development stagnates and they begin to lose previously attained skills.

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

Symptoms include

- loss of speech (partial or complete)
- loss of purposeful hand movements such as grasping (partial or complete)
- stereotypic hand movements such as hand wringing or hand-washing
- balance problems (ataxia/apraxia of gait)
- breathing problems (periodic breathing with hyperventilation and breath holding)
- behaviour problems (particularly anxiety, self-abusive or aggressive)
- intellectual disability

The clinical criteria for the diagnosis of classic Rett syndrome were developed initially in the 1980s and recently updated in 2010. These criteria include an apparently normal pre- or perinatal period and first 6 months of life. Over the following months, there is a loss of developmental skills, which progresses to severe mental retardation and characteristic hand-wringing movements [3,4]. Other features include autistic-like behaviours, oral-motor dysfunctions, gastrointestinal motility disorders (including abdominal bloating), scoliosis, autonomic dysfunction and somatic developmental impairment [5]. Various movement disorders are exhibited including dystonia, choreoathetosis and myoclonic jerks. [6,7]

Rett syndrome has no cure. We can treat some of the symptoms with medication, surgery, and physical, occupational and speech therapy. Most people with RS live into middle age and beyond. They will usually need care throughout their lives.

Typical surgery

Scoliosis is common in RS and increases in frequency with age through puberty [8]. Scoliosis in individuals with Rett Syndrome often does not respond to orthotics. Surgery should be considered in patients with Cobb angles more than 40-50° or curves that cause pain or loss of function, and is best performed with a multidisciplinary team providing specialist anaesthetic and pain management support, seizure control, with the aim of promoting early mobilization [9]. Surgeons usually try to wait until the child is at least 10 years of age before performing spinal fusion. They may often recommend bracing, physiotherapy and physical activity to delay surgery in order to allow for as much growth as possible. The aims of surgery are to achieve a balanced, fused spine so that in upright positions such as sitting or standing, the shoulders and hips are more level.

In addition to orthopaedic issues, surgery may be indicated like tonsillectomy and adenoidectomy for the treatment of obstructive sleep apnea (OSA), placement of a gastrostomy for feeding difficulties, hip subluxation, or possibly for tendon release due to significant contractures.

Dental procedures.

Type of anaesthesia

Altered muscle tone and thoracic deformity may complicate the administration of general anaesthesia [10]. Patients with Rett syndrome are at increased risk of sedation-related transient adverse events. Most adverse events are related to prolonged apnea and airway compromise. Patients with Rett syndrome should not be sedated without appropriate personnel available who are skilled to intervene and who recognize the risks involved with sedating this unique population [11]. In patients with a genuine aspiration risk, rapid sequence intubation (RSI) with cricoid pressure may be considered.

Because these patients are unable to cooperate and have continuous abnormal limb movements, spinal or epidural anaesthesia is difficult. In addition, scoliosis could make placement of an epidural catheter difficult.

Necessary additional diagnostic procedures (preoperative)

Preoperative evaluation of a patient with RS is very important. We should check:

- The breathing patterns
- Arterial blood gases and lactic acid levels preoperatively (although arterial blood gases may be affected, lactic acid levels are rarely increased)
- The presence of gastrointestinal reflux and autonomic disturbances
- EEG for the seizure activity (could be a concern in pre or postoperative periods)
- ECG for arrhythmias associated with prolonged QT syndrome and
- The musculoskeletal system.

Parents and caregivers should be consulted about any other relevant information about the patient.

Particular preparation for airway management

A primary concern for anaesthesia providers is the potential for difficult endotracheal intubation related to limited mouth opening, micrognathia, and limited neck movement. As such, the ability to accomplish adequate bag-valve mask ventilation should be demonstrated prior to the use of neuromuscular blocking agents. Additionally, appropriate equipment for dealing with the difficult airway should be readily available, including indirect laryngoscopy tools or a tracheostomy set to secure the airway in the event of severe difficulty when securing the airway.

Various options for airway management in patients with limited mouth opening like antegrade fiberoptic-guided orotracheal or nasotracheal intubation, retrograde guidewire-assisted fiberoptic intubation and blind nasal intubation can be considered.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transport or mobilisation

Not reported.

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

Not reported.

Anaesthesiologic procedure

- Inhalational and intravenous anaesthetic agents are generally considered to have potent anticonvulsant properties. Many of these agents, including the barbiturates, propofol, and the volatile agents, have been used successfully.
- As the residual effects of anaesthetic agents may impact on both upper airway control and postoperative respiratory function, whenever feasible, short-acting agents whose effects dissipate rapidly, such as remifentanil, should be considered.
- Use of thiopental and succinylcholine, prokinetics such as cisapride, antipsychotics such as thioridazine, tricyclic antidepressants such as imipramine, antiarrhythmics such as kinidin, amiodarone, sotalol as well as erythromycin and ketaconazole should be avoided because of the potential to provoke QT abnormalities and cardiac arrhythmias.
- These patients are excessively sensitive to sedative drugs, and delayed recovery from anaesthesia has been reported. Hence, the drugs should be titrated to maintain an optimal depth of anaesthesia and avoid overdose. Spontaneous ventilation rather than controlled ventilation is preferred, as this would require administration of less anaesthetic agents.
- Additionally, anatomical malposition of the vessels may occur in these patients. The use of ultrasound guidance may be invaluable to aid in gaining adequate vascular access for major surgical procedures [12].

Particular or additional monitoring

Anaesthetic considerations for patients with prolonged QTc interval include avoidance of potential factors that may further prolong the QT interval including an increase in sympathetic tone; hypothermia; electrolyte abnormalities including hypokalemia, hypomagnesemia, and hypocalcemia; as well as various medications which may be administered during the perioperative period, as mentioned above.

Possible complications

- Hypermetabolic states observed in patients with Rett Syndrome raise the possibility that anaesthesia and anaesthetic agents may increase the risk of malignant hyperthermia, although this has not been reported in patients.

- Use of succinylcholine is controversial because of possible hyperkalemia and prolongation of the QTc interval, which may predispose the patient to fatal arrhythmias.

Postoperative care

- Regardless of the agents used, given the airway and respiratory co-morbid conditions seen in Rett syndrome, postoperative monitoring of respiratory function is recommended. Although postoperative mechanical ventilation can be anticipated in these patients, consideration must be given to the antagonism of neuromuscular blockade and the reversal of anaesthesia when circumstances so dictate.

- Previous anecdotal reports of anaesthesia in children with Rett syndrome have noted postoperative respiratory problems, including atelectasis and respiratory infections, which may require postoperative mechanical ventilation or reintubation.

- Non-invasive respiratory support techniques such as BiPAP would facilitate postoperative tracheal extubation in these patients.

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

The risk of prolonged QT interval and T-wave changes increases with age. These ECG abnormalities are considered as potential causes of sudden death encountered in up to a third of patients with Rett syndrome. Aside from medications, other intraoperative events may lead to a further prolongation of the QT interval, including increased sympathetic tone, which has been demonstrated to occur during endotracheal intubation. To minimize the risk of this, an adequate depth of anaesthesia should be ensured during such procedures.

Ambulatory anaesthesia

Ambulatory anaesthesia is possible following the common accepted guidelines if the procedure itself does not require a longer phase of supervision. This applies especially for oral surgery.

Not reported.

Literature and internet links

1. Rett A. On a unusual brain atrophy syndrome in hyperammonemia in childhood. Wien Med Wochenschr 1966;116:723-26
2. Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi H. Rett syndrome is caused by mutations in X-linked *MECP2*, encoding methyl-CpG-binding protein 2. Nature Genet. 23:185-188,1999
3. Hagberg B, Hanefield F, Percy AK, Skjeldal: An update on clinically applicable diagnostic criteria in Rett syndrome. Eur J Paediatr Neurol 2002;6:293-297
4. Neul JL, Kaufmann WE, Glaze DG, Christodoulou J, Clarke AJ, Bahi-Buisson N, Leonard H, Bailey MES, Schanen NC, Zappella M, Renieri A, Huppke P, Percy A, for the RettSearch Consortium. Rett Syndrome: Revised Diagnostic Criteria and omenclature. Ann Neurol 68:946-951, 2010
5. Armstrog DD . Review of Rett syndrome. J Neuropathol Exp Neurol 1997 Aug; 56(8):843-9
6. Al-Mateen M, Philippart M, Shields WD. Rett syndrome: A commonly overlooked progressive encephalopathy in girls. Am J Dis Child 1986 Aug; 140(8):761-5
7. Hagberg B, Aicardi J, Dias K, Ramos O. A progressive syndrome of autism, dementia, ataxia and loss of purposeful hand use in girls: Rett's syndrome: report of 35 cases. Ann Neurol 1983 Oct;14(4):471-9
8. Percy AK, Lane JB, Childers J, Skinner S, Annese F, Barrish J, Caeg E, Glaze DG, MacLeod P. Rett syndrome: North American database. J Child Neurol.2007;22:1338–1341
9. Downs J, Bergman A, Carter P, Anderson A, Palmer GM, Roye D, van Bosse H, Bebbington A, Larsson EL, Smith BG, Baikie G, Fyfe S, Leonard H. Guidelines for management of scoliosis in Rett syndrome patients based on expert consensus and clinical evidence. Spine (Phila Pa 1976). 2009 Aug 1;34(17)
10. Lugaresi E, Girignotta F, Montagna P: Breathing in Rett syndrome. Brain Dev 1985;7:329-333
11. Tofil N, Buckmaster M, Callans B, Winkler M, Islam M, Percy A. Deep sedation with Propofol in patients with Rett syndrome. J Child Neurol 21:210-213, 2006
12. Doniger SJ, Ishimine P, Fox JC, Kanegaye JT. Randomized controlled trial of ultrasoundguided peripheral intravenous catheter placement versus traditional techniques in difficult access pediatric patients. Pediatr Emerg Care 2009; 25: 154-9.

Last date of modification: August 2015

These guidelines have been prepared by:

Author
Dr Namrata Maheshwari, Anaesthesiologist, Department of Critical Care, Fortis Hospital, Mohali, India
drnamratamaheshwari@gmail.com

Peer revision 1
John Christodoulou, Director, Western Sydney Genetics Program, Head Discipline of Genetic Medicine, Sydney Medical School, University of Sydney, Australia
johnc@chw.edu.au

Peer revision 2
Alan Percy, Department of Neurobiology, Civitan International Research Center, University of Alabama at Birmingham, USA
apercy@uab.edu

Please note that this guideline has not been reviewed by an anaesthesiologist but by two disease experts instead.