

## Anaesthesia recommendations for **Rubinstein-Taybi syndrome**

**Disease name:** Rubinstein-Taybi syndrome

**ICD 10:** Q87.2

**Synonyms:** Michail-Matsoukas-Theodorou-Rubinstein-Taybi syndrome, Broad thumb-hallux syndrome, Rubinstein syndrome

**Disease summary:** Rubinstein-Taybi Syndrome (RTS) has an estimated prevalence of 1 in 100,000 to 125,000. It is considered to have autosomal dominant patterns of inheritance but most cases result from de novo mutations. Mutations in the CREBBP gene on Chromosome 16 which acts as a regulator of other genes in cell growth and division is the commonest mutation. A small percentage have mutations of a similar gene (EP300) and tend to have milder skeletal abnormalities. A deletion of the genetic material on the short arm of chromosome 16 which includes the CREBBP(16p13.3) is associated with severe forms. However, in 50% of cases no genetic basis is found.

Major causes of deaths, particularly during the first year, are aspiration pneumonia and heart disease. There are no definite diagnostic features in RTS. However, the following are usually present:

- Short stature
- Moderate to severe intellectual disability
- Distinctive facial features (which become more prominent with age, include highly arched eyebrows, long eyelashes, down-slanting palpebral fissures, convex nasal ridge, highly arched narrow palate, abnormally large or "beak-shaped" nose, retrognathia and micrognathia). An unusual smile with almost complete closure of the eyes is present in most cases. These lead to an increase risk of dental problems and obstructive sleep apnoea (OSA). There is also an association with choanal atresia.
- Broad thumbs and 1st toes (often angulated in the varus/valgus position)

RTS is also frequently associated with the following:

- Eye abnormalities: Over 80% of children with RTS have some form of eye abnormality eg. lacrimal duct obstruction (43% are bilateral), ptosis and strabismus (55%). Congenital glaucoma or glaucoma which develops in early life has been described.
- Congenital heart abnormalities 35-40% have a single defect (eg. ASD, VSD or PDA).
- Renal and Urinary tract: Renal anomalies are present in 50% and for this reason all children should have renal ultrasound on diagnosis. Almost all boys will have incomplete or delayed descent of testes with hypospadias being present in 11%. As a result of these anomalies there is an increased risk of chronic kidney disease and urinary infections.
- Musculoskeletal: There is an increased risk of scoliosis, hyperkyphosis and spina bifida with general hypermobility.

- An increased risk of tumours (mainly leukaemia in childhood and meningioma in adulthood) has been observed. There is also an association with neuroendocrine tumours.
- An increased risk of keloid scarring.

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Perhaps the diagnostic is wrong

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**Find more information on the disease, its centres of reference and patient organisations on Orphanet: [www.orpha.net](http://www.orpha.net)**

## **Typical surgeries**

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ENT: Adeno-tonsillectomy

Orthopaedic surgery: Correction of scoliosis

Plastic surgery: Correction of thumb and hallux anomalies craniofacial/ orthodontic surgery

Ophthalmic: DCR, syringe and probe, squint surgery Cardiac: dependent on cardiac defect

Urological: Hypospadias repair/ Orchidopexy

## **Type of anaesthesia**

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There is no definite recommendation for either general or regional anaesthesia. There is no evidence to support the use of TIVA vs. inhalational agents.

Regional anaesthesia can be performed. There are reports of spinal, epidural and caudal anaesthesia without complications. However, given the high incidence of spinal deformities, a proper risk analysis should be undertaken prior to embarking on neuroaxial blockade.

In patients with OSA, caution with or avoidance of sedation should be considered.

## **Necessary additional pre-operative testing (beside standard care)**

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Cardiac function tests including electrocardiography and echocardiography should be performed to evaluate the possibility of cardiac disease. Patients will usually have been reviewed by a paediatric cardiologist at diagnosis due to the frequency of associated cardiac anomalies.

Baseline renal function blood tests and ultrasound of the kidneys should have been performed as part of their initial diagnostic work-up.

Formal sleep studies (if signs and symptoms of OSA are elicited)

MRI/ US of spine may have been performed and would be useful if considering caudal anaesthesia due to high incidence of tethered cord.

## **Particular preparation for airway management**

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Congenital tracheal stenosis and tracheomalacia has been well described and therefore it may be prudent to use a relatively smaller size of endotracheal tube.

Difficult intubation and ventilation should always be anticipated as craniofacial abnormalities may make laryngoscopy and intubation difficult, particularly in the presence of micrognathia or microsomia. Alternative methods of intubation such as nasal intubation and fibre-optic intubation have been described as well as the successful use of laryngeal mask airways including second generation and intubating laryngeal masks.

The association with OSA means that consideration should be given to awake vs. deep extubation.

There is a higher risk of aspiration due to the increased incidence of gastroesophageal reflux.

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### **Particular preparation for transfusion or administration of blood products**

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There is no published evidence to support an increased transfusion requirement in patients with RTS.

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### **Particular preparation for anticoagulation**

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There is no published evidence to support the need for particular anticoagulation. However, these patients are likely to have greater periods of post-operative immobility and this may lead to a higher risk of thrombosis.

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### **Particular precautions for positioning, transportation or mobilisation**

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Cervical hyperkyphosis can be seen in 62% of patients with RTS, while scoliosis can be seen in 38%. This can make it challenging to position patients during intubation and for the surgical procedure. Attention should be given to pressure area care intraoperatively.

Patients may be prone to fractures and therefore care should be taken on transferring and positioning.

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### **Interactions of chronic disease and anaesthesia medications**

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None reported.

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### **Anaesthesiologic procedure**

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Avoid long acting sedatives and cautious use of opioids (due to high incidence of OSA).

There are anecdotal reports of the occurrence of arrhythmias following the use of suxamethonium and it is generally accepted that this drug is best avoided. Although other muscle relaxants have been used without adverse event, however in the presence of hypotonia it may be prudent to avoid them if possible.

Both TIVA and inhalation anaesthesia have been used and there is no evidence to suggest that one is superior to the other in this group of patients.

Antibiotic prophylaxis, appropriate for the planned surgery, should be given to those with an underlying cardiac lesion.

In patients with cardiac disease, the use of anticholinesterase and anticholinergic drugs may increase the risk of arrhythmia. For this reason, drugs such as atropine and neostigmine

should be avoided if possible in this cohort of patients. When considering the use of muscle relaxants in patients with cardiac disease, the use of rocuronium and sugammadex in combination may be preferable.

Local anaesthetics have been used without complication.

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### **Particular or additional monitoring**

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Facial nerve monitoring of neuromuscular blocking agents (NMBs) may be more appropriate as thumb anomalies and difficulty assessing adductor muscle response to stimulations.

In cases of high risk surgery, with major fluid shifts, arterial cannulation and central venous cannulation for invasive pressure measurements may be useful.

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### **Possible complications**

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Sedative drugs and opioids may cause post-operative respiratory depression; therefore these should be carefully titrated to avoid this. The use of regional anaesthesia may be beneficial in this regard.

Airway obstruction.

Aspiration pneumonia.

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### **Post-operative care**

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The degree of postoperative monitoring depends on surgical procedure and preoperative condition of the patient. ICU is not mandatory.

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### **Disease-related acute problems and effect on anaesthesia and recovery**

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Preparation for the possible complications as outlined above.

There are no reports of idiosyncratic drug reactions in relation to anaesthesia.

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### **Ambulatory anaesthesia**

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Published data regarding ambulatory anaesthesia for RTS is limited.

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### **Obstetrical anaesthesia**

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Published data is limited. Females with RTS have normal fertility. Their management should be tailored to their individual needs. Previous spinal surgery or spinal anomalies may

preclude or limit neuroaxial blockade. Remifentanyl PCA may be an option for intrapartum pain relief.

Active planning for a potential difficult airway should be in place.

## References

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### **Peer revision 1**

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

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