CASE REPORT

Prolonged paralysis with atracurium use in a patient with Rubinstein-Taybi syndrome

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SUMMARY

Rubinstein-Taybi syndrome (RTS) is a rare autosomal dominant disorder that occurs due to a microdeletion of chromosome 16p13. The craniofacial abnormalities in these patients may pose a challenge for anaesthetist performing tracheal intubation. However, there are no known reported cases of drug interaction with non-depolarising muscle relaxant in patients with RTS. This young patient with RTS presented with an unexpected prolonged atracurium effect during the course of anaesthesia. After ruling out other possible causes, we have come to a conclusion that RTS itself could have played a role in the prolonged effect of atracurium. However, further studies will be needed to confirm this hypothesis. In the meantime, care should be used when using muscle relaxants in patients with RTS.

BACKGROUND

Rubinstein-Taybi syndrome (RTS) is a rare autosomal dominant disorder that occurs due to a microdeletion of chromosome 16p13.¹ The incidence of RTS is 1 in 100 000 to 125 000. It is characterised by broad thumbs and toes, mental retardation, congenital heart disease, recurrent respiratory infections, craniofacial anomalies, breathing and swallowing difficulties and malformations of the kidneys, urogenital and skeletal system.² These patients have difficulties during tracheal intubation due to the craniofacial abnormality, and complications of anaesthesia due to respiratory infection and arrhythmia.³ However, there are no known reported cases of drug interaction with non-depolarising muscle relaxant in patients with RTS. We describe the case of a 16-year-old boy with RTS who had an unexpectedly prolonged paralysis after atracurium.

CASE PRESENTATION

A 16-year-old boy who weighed 38 kg and was 135 cm tall, diagnosed with RTS, was scheduled for kyphoscoliosis corrective surgery. He had underlying bronchial asthma and allergic rhinitis, which were well controlled with medication. Physical examination was significant for the presence of microstomia, macroglossia, narrow palate and micrognathia. An airway examination and assessment of the patient's Mallampati score were not possible as the patient was not cooperative. The patient did not show any limitations in the flexion or extension of the neck. A difficult airway (mask and endotracheal intubation) was anticipated. Results of biochemical tests and a complete blood

count were within normal limits. A transthoracic echocardiogram was done, showing a normal heart.

The patient had a severe kyphoscoliosis (Cobb angle T1–T12 80°) with small lung fields. The surgeon requested intraoperative spinal cord monitoring, and therefore, total intravenous anaesthesia was planned. Transcranial electrical motor evoked potential (MEP) was used to assess the functional integrity of the whole descending motor pathways, and to detect spinal cord dysfunction during surgery.

All necessary equipment to manage a difficult airway were prepared. After obtaining consent for anaesthesia and surgery, the patient was taken to the operating room. His blood pressure was 110/60 mm Hg, heart rate 100 beats/min and oxygen saturation on room air was 97%. His ECG tracing on lead II showed a normal sinus rhythm. Bispectral index (BIS) and a nerve stimulator on his ulnar nerve were also used.

General anaesthesia was induced with 2% propofol and remifentanyl at a target concentration of 4 µg/mL (Marsh model) and 4 ng/mL (Minto model), respectively. Endotracheal intubation was successfully accomplished with video laryngoscopy (King Vision Video Laryngoscope) with a single dose of atracurium (0.4 mg/kg). Mechanical respiration with air and oxygen was administered. The patient received a tidal volume of 250 mL and respiratory rate of 12 breaths per minute to maintain an ET_{CO₂} of 35–45 mm Hg. A right radial arterial catheter was placed for blood pressure monitoring, and an oropharyngeal temperature probe was inserted postinduction.

After the patient was placed in the prone position, neurological monitoring was applied. However, 60 min after anaesthesia induction, MEP tracing was judged to be poor. Also of concern was the lack of any response to Train Of Four stimulation, even after 90 min of postinduction. At that time, patient was haemodynamically stable, and BIS ranged between 50 and 55. There was no evidence of hypothermia or acidosis. Subsequently, 1/4 twitches were noted at the 110th minute, and only at the 120th minute, 4/4 twitches were evidenced by TOF. After almost 2 hours postinduction, a satisfactory MEP tracing was produced.

During the surgery, the patient's vital signs was stable with blood pressure ranging from 90–110/60–80 mm Hg, heart rate 90–100 beats/min, oxygen saturation 98%–100%, body temperature 36.7°C–37.2°C and BIS 50–60. The surgery lasted almost 5 hours, with an estimated blood loss of

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500 mL. Postoperatively, the patient was sent to the intensive care unit. He was successfully extubated 1 day later.

INVESTIGATIONS

A TOF monitor was used intraoperatively.

DIFFERENTIAL DIAGNOSIS

Prolonged paralysis after neuromuscular blockade due to:

1. hypothermia/hyperthermia
2. acidosis
3. hypernatraemia
4. hypokalaemia
5. hypermagnesium.

TREATMENT

The patient was ventilated, and sedation was continued until the return of adequate motor strength.

OUTCOME AND FOLLOW-UP

The patient was discharged from the hospital 1 week later. A follow-up at the clinic 1 month later revealed no complications from either his anaesthesia or surgery.

DISCUSSION

Patients with RTS undergoing general anaesthesia may prove to be a challenge for anaesthetist. Micrognathia, retrognathia, broad nasal bridge, beak-shaped nose, hypoplastic maxilla and small mouth usually lead to potential difficulties with airway management for anaesthesia and surgery.⁴ The presence of cervical hyperkyphosis (incidence of 62%) and scoliosis (incidence of 36%) may also make it difficult to align the axes of the oral cavity, pharynx and trachea, in order provide an optimal position during tracheal intubation.⁴ In our case, intubation was successfully performed with the aid of a video laryngoscope.

It has been a protocol at our centre to consider succinylcholine, a short-acting depolarising muscle relaxant, for patients with a risk of difficulty airway. However, we were concerned with a published case report of a brief cardiac arrhythmia in a patient with RTS after the use of succinylcholine.⁵ Although there were limited literatures on the use of succinylcholine in RTS, we remained concerned with the use of this drug in our patient. We also did not have rocuronium and sugammadex in our centre at that moment. These were the reasons why we considered using a single dose of non-depolarising agent to ease the tracheal intubation process. Literature reviews suggested atracurium as the drug of choice.⁶

Atracurium is a benzyloisoquinolinium non-depolarising neuromuscular blocking agent (NMBA) that is inactivated by plasma hydrolysis and Hofmann elimination. Therefore, it does not accumulate in patients with hepatic and/or renal insufficiency, making atracurium useful in surgical patients with liver and kidney compromise.⁷ Atracurium has been associated with a decrease in mean arterial pressure of up to 30 mm Hg within 2 min of initiation, which could be due to histamine release.⁸ However, we did not think of this as a concern as we were only going to provide a single smaller dose of atracurium in our patient with his well-controlled asthma.

With atracurium, recovery of 25% is achieved approximately 35 to 45 min after injection, and recovery is usually 95% approximately 60 to 70 min after injection.⁹ The duration of action of this NMBA made it a good choice for this patient and for this surgery.

There are several known causes for a prolonged action of NMBA. These causes are grouped as due to drug interactions,

metabolic or genetic causes.¹⁰ In our setting, we were especially concerned with hypothermia and the use of isoflurane, as both of these may prolong the block.^{11 12} We took extra precautions to eliminate all possible causes. However, our patient still had an unexpected prolonged effect of atracurium.

After ruling out all possible causes, we have come to a conclusion that RTS itself could have played a role in the prolonged effect of atracurium. However, further studies will be needed to confirm this hypothesis. In the meantime, care should be used when using muscle relaxants in patients with RTS.

Learning points

- ▶ Rubinstein-Taybi syndrome (RTS) may be a rare disease; however, a sound knowledge of anaesthesia management is very important for the safety of the patient.
- ▶ The use of muscle relaxant during anaesthesia must always be accompanied with adequate knowledge of pharmacology and drug interaction.
- ▶ Further studies are needed to explore any possible interaction of atracurium in patients with RTS.
- ▶ Close monitoring of neuromuscular blocking agent (NMBA) is essential to ensure the safe use of it.
- ▶ When using NMBA, monitoring of the neuromuscular junction and the return of normal strength are essential.

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REFERENCES

- 1 Petrij F, Dauwerse HG, Blough RI, et al. Diagnostic analysis of the Rubinstein-Taybi syndrome: five cosimids should be used for microdeletion detection and low number of protein truncating mutations. *J Med Genet* 2000;37:168–76.
- 2 Agarwal S, Ahmad YH, Talpesh M, et al. Anesthetic management of children with Rubinstein-Taybi syndrome--case reports. *Middle East J Anaesthesiol* 2011;21:309–12.
- 3 Twigg SJ, Cook TM. Anaesthesia in an adult with Rubenstein-Taybi syndrome using the ProSeal laryngeal mask airway. *Br J Anaesth* 2002;89:786–7.
- 4 Karahan MA, Sert H, Ayhan Z, et al. Anaesthetic Management of Children with Rubinstein-Taybi Syndrome. *Turk J Anaesthesiol Reanim* 2016;44:152–4.
- 5 Stirt JA. Letter to the Editor: Succinylcholine in Rubinstein-Taybi syndrome. *Anesthesiology* 1982;57:429.
- 6 Bozkirli F, Günaydin B, Celebi H, et al. Anesthetic management of a child with Rubinstein-Taybi syndrome for cervical dermoid cyst excision. *J Anesth* 2000;14:214–5.
- 7 Neill EA, Chapple DJ, Thompson CW. Metabolism and kinetics of atracurium: an overview. *Br J Anaesth* 1983;55:235–5.
- 8 Basta SJ, Ali HH, Savarese JJ, et al. Clinical pharmacology of atracurium besylate (BW 33A): a new non-depolarizing muscle relaxant. *Anesth Analg* 1982;61:723–9.
- 9 DBL Atracurium besylate injection. Retrieved on 3rd Sep 2017. 2017. <http://www.medsafe.govt.nz/profs/Datasheet/a/Atracuriumbesylateinj.pdf>
- 10 Sinclair RCF, Faleiro RJ. Delayed recovery of consciousness after anaesthesia. *Continuing Education in Anaesthesia Critical Care & Pain* 2006;6:114–8.
- 11 Leslie K, Sessler DI, Bjorksten AR, et al. Mild hypothermia alters propofol pharmacokinetics and increases the duration of action of atracurium. *Anesth Analg* 1995;80:1007–14.
- 12 Appiah-Ankam J, Hunter JM. Pharmacology of neuromuscular blocking drugs. *Continuing Education in Anaesthesia, Critical Care & Pain* 2004;4:2–7.

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