

Anaesthesia for a patient with B-thalassaemia

I Giannakikou^a and A Karra^{b*}

^aDepartment of Anaesthesia, Ygeia Hospital of Athens, Athens, Greece

^bDepartment of Intensive Care Unit, Medical Center of Athens, Athens, Greece

*Corresponding author, email: alekakarra@yahoo.it

B-Thalassaemia is a rare hereditary disease caused by partial or complete deficiency of β -haemoglobin chain synthesis. There is a lot of literature regarding anaesthetic management in other haemoglobinopathies (i.e. sickle cell disease), especially in the paediatric population, but there is scarce information regarding β -thalassaemia major in adults. With current medical management, β -thalassaemia major patients survive to adulthood and may present for a variety of surgical procedures, even unrelated to their disease process. It is important for the anaesthetist to be familiar with the pathophysiology of β -thalassaemia major and how the disease itself and its treatment or complications (iron deposition from multiple transfusions) can affect anaesthesia. A case of a 51-year-old woman with severe β -thalassaemia undergoing laparoscopic cholecystectomy is presented. The anaesthetic management and systematic review of the perioperative concerns in severe β -thalassaemia are discussed.

Keywords: anaesthesia, B-thalassaemia, laparoscopic cholecystectomy, non-cardiac surgery, pathophysiology

Case report

A 51-year-old woman with β -thalassaemia, of American Society of Anesthesiologists (ASA) physical status IV, presented for laparoscopic cholecystectomy. Her past medical history was significant for severe anaemia requiring multiple red blood cell transfusions since early childhood (on average two units of washed red blood cells every two weeks for a haemoglobin of less than 8.5 g/dl). This led to severe iron deposition (haemosiderosis) with severe multiple organ insufficiency. She suffered from right-sided heart failure with lower extremities oedema and ascites. Over the last year, she had had recurrent episodes of paroxysmal atrial fibrillation and was on oral anticoagulation and digoxin. She was diagnosed with pulmonary hypertension and her exercise tolerance was less than 10 uphill steps. She had cirrhosis Child-Pugh class B. She had hypothyroidism, primary ovarian failure and osteoporosis. Her last transfusion was a few days prior to surgery. She had a splenectomy at the age of 11.

Her home medications included digoxin, spironolactone, furosemide 80 to 125 mg on alternate days, thyroxine, ursodeoxycholic acid, allopurinol, deferiprone (oral chelating agent), calcium and warfarin (changed to low molecular weight heparin (LMWH) perioperatively).

On physical examination the patient was thin (41 kg). Her airway assessment revealed a Mallampati score of II, 4 cm mouth opening, 5 cm thyromental distance, short neck and tonsillar enlargement. She had frontal and maxillary bossing but no significant mandibular enlargement. On auscultation she was in a regular rhythm with an S3 sound. Her lower extremities were oedematous and ascites was present. She had no secondary sexual characteristics (pubic/axillary hair, breasts).

Her pertinent laboratory values were (abnormal values are given in bold):

| Laboratory tests | Patient's values | Normal values (SI units) |
|-----------------------------------|------------------------------|----------------------------|
| White cell count (WCC) | 16.2 c/mm³ | 4.9–10.8 c/mm ³ |
| Haemoglobin (Hb) | 12.1 g/dl | 11.8–17.8 g/dl |
| Haematocrit (Hct) | 36.8% | 37.7–47.9% |
| Platelets (PLTs) | 415 c/mm³ | 150–350 c/mm ³ |
| Prothrombin time (PT) | 11.2 s | 11–13.5 s |
| Sodium (Na) | 130 mEq/L | 136–150 mEq/L |
| Potassium (K) | 4.9 mEq/l | 3.5–5.5 mEq/L |
| Blood urea nitrogen (BUN) | 51.05 mmol/L | 8.0–16.4 mmol/L |
| Creatinine (Cr) | 88.4 micromol/L | 50–110 micromol/L |
| Thyroid stimulating hormone (TSH) | 2.74 mU/L | 0.4–4 mU/L |
| Total bilirubin (T. Bil) | 1.8 mg/dl | 0.20–1.2 mg/dl |
| Direct bilirubin (B. Bil) | 0.8 mg/dl | 0.0–0.5 mg/dl |
| Transaminase (AST) | 37 IU/L | 0–45 IU/L |
| Transaminase (ALT) | 30 IU/L | 0–45 IU/L |
| Alkaline phosphatase | 79 IU/L | 40–150 IU/L |

The electrocardiogram (ECG) showed sinus tachycardia at 98 beats per minute (bpm). Echocardiography revealed a dilated right atrium and right ventricle, decreased right ventricular function, mild mitral regurgitation and pulmonary hypertension. The left ventricle was not dilated and had good function. A chest radiograph showed cardiomegaly and an increased cardiothoracic ratio.

On arrival in the operating theatre standard ASA monitors, with the addition of an awake arterial line, were placed. The patient's blood pressure was 80/55 mm Hg with sinus rhythm at 80 bpm, while arterial haemoglobin oxygen saturation (SpO₂) was 97% at room air. A smooth intravenous induction was performed with etomidate, lidocaine and fentanyl. Paralysis was achieved with

rocuronium. Despite the facial deformity, tracheal intubation was uneventful. Anaesthesia was maintained with sevoflurane, O₂ and intermittent fentanyl boluses. Peritoneal insufflation with CO₂ was performed slowly, with the pressure limit set at 12 mm Hg. Throughout the operation vital signs were stable and oxygenation was followed with serial arterial blood gases (ABGs). The operation lasted approximately 40 min. At the conclusion of surgery residual paralysis was reversed with sugammadex and the patient was extubated after regaining consciousness. A total of 200 ml 0.9% normal saline (NS) was administered during the procedure (0.9% NS was preferred to other crystalloid solutions for its low potassium content). Postoperative pain was controlled with intravenous paracetamol. No anaesthetic or surgical complications were noted. She was discharged from hospital the following day.

Discussion

B-thalassaemia is a congenital haemolytic disorder caused by partial or complete deficiency of β -globin chain synthesis. It primarily affects people of Mediterranean origin and to a lesser extent people of Chinese, Asian and African descent. It is usually described in its mild form, β -thalassaemia intermedia. These patients are anaemic but do not require frequent transfusions. They may have hepatosplenomegaly. B-thalassaemia major arises from the absence of synthesis of β -globin chains (β -0 thal). It is inherited on chromosome 11 and patients are homozygous for two mutant alleles.¹ Anaesthetic management of these patients is dictated by the disease itself, the complications of its treatment (iron overload from multiple transfusions) and the use of preventive measures (chelating agents).

Anaesthetic considerations

Airway

B-thalassaemia major produces maximum erythropoietin release and massive marrow hyperplasia.¹ Patients may present with frontal bossing and expansion of the maxillofacial area.² There is a possibility of difficult mask ventilation and intubation due to facial deformity.^{3,4} Extramedullary haematopoiesis may also occur in the vertebral canal, compressing the spinal cord and causing several neurologic symptoms, necessitating caution during neck manipulation at laryngoscopy. Abnormal dentition increases the intubation difficulty and the possibility of tooth damage during intubation attempts.

Cardiovascular

Cardiac insufficiency, secondary to haemosiderosis from chronic transfusions, ranging from dyspnoea and peripheral oedema to congestive cardiomyopathy and cardiac failure may be present.⁵ Major β -thalassaemia patients may present with pulmonary hypertension and vascular damage (vasculopathy), secondary to disturbed nitric oxide physiology.¹ Angina, conduction defects, pericarditis, arrhythmias and sudden death are all more likely in patients with thalassaemia and iron overload (> 2500 μ g/L serum ferritin). A hyper-dynamic circulation with a high cardiac output, a compensatory mechanism to chronic anaemia, and decreased blood oxygen carrying capacity may also be present.

Liver

Chronic anaemia induces ineffective erythropoiesis in extramedullary erythropoietic tissue. Hepatomegaly may be present. Haemochromatosis, due to chronic transfusion therapy, can lead to liver fibrosis, cirrhosis, hepatic failure and hepatocellular carcinoma.⁵ Liver failure decreases the synthesis of plasma-binding proteins and causes hypoalbuminaemia.

Haematological

Chronic haemolysis leads to chronic anaemia and hyperbiliru-

binemia.² B-thalassaemia patients have splenomegaly and usually undergo splenectomy at a young age, so the long term post-splenectomy infectious and thromboembolic risks must be considered.⁶ Blood smear shows haemolytic anaemia and hypochromia with microcytosis. Regular blood transfusions result in a high incidence of RBC alloimmunisation, making available compatible blood a potential problem.⁷ Prior to blood transfusion care must be taken to reduce the risk of alloimmunisation, by matching donors of the same ethnic origin and using leukocyte-depleted and/or washed red blood cells. Intraoperative blood loss can be managed with cell salvage, thus avoiding alloimmunisation and further iron overload.^{1,8} For patients with a human leukocyte antigen (HLA) identical sibling, bone marrow transplantation is a therapeutic option for young patients.

Endocrine

Chronic iron overload affects most endocrine organs.⁹ It affects the pancreas, causing pancreatic dysfunction and diabetes mellitus; the parathyroids, presenting as hypoparathyroidism and hypocalcaemia; and the pituitary, manifesting as hypopituitarism, growth failure, hypogonadism and infertility.^{5,10}

Coagulopathy

Haemosiderosis-induced liver failure is associated with coagulopathy, thrombocytopenia and bleeding.⁵

Infectious

There is high incidence of blood-borne infections (hepatitis B, C and HIV), especially in older patients from underdeveloped countries. They also have a lifetime risk of aplastic crisis from infection with parvovirus B infection.

Pharmacokinetics

B-thalassaemia patients may have increased plasma volume due to shunting through expanded bone marrow. Hypoalbuminaemia and decreased plasma-binding proteins impair drug binding and metabolism and affect drug half-lives. Chelating agents (i.e. deferasirox) affect drug-metabolising enzymes (CYP3A4,) influencing drug serum values.^{5,6}

Neurological

Mental retardation (secondary to severe anaemia and hypoxia at an early age) can cause cooperation and consent issues.²

Skin

Bronze hyperpigmentation.⁵

Monitoring

B-thalassaemia does not affect the accuracy of pulse oximetry. In β -thalassaemia foetal haemoglobin is increased and the oxyhaemoglobin dissociation curve is shifted to the left leading to decreased unloading of oxygen to the tissues.

Positioning

Care must be taken with positioning of such patients as they are prone to fractures due to accelerated demineralisation and osteopenia. Iron deposition at the joints can cause arthritis affecting all joints.

Conclusion

We have presented a case report of a 51-year-old patient with β -thalassaemia major undergoing laparoscopic cholecystectomy. The patient was born in 1961 in Greece and was one of the first patients to be started on chronic hypertransfusion therapy. Never-

theless, it was not until her twenties that iron chelation therapy was introduced. Our patient exhibits an interesting pathophysiology, as she survived past childhood due to the initiation of chronic hypertransfusion therapy, but suffered almost all of the complications of iron overload due to delay in the initiation of chelating therapy in the 1960s when she was born.

The anaesthetic management of this severe form of β -thalassaemia requires multiple considerations including the airway, cardiovascular system, liver and coagulation system.¹¹ Anaesthetists should be aware of both the pathophysiology of the disease and the potential complications of its treatment. Meticulous consideration should be paid to each one of the systems involved in order to achieve the best possible outcome in these patients.

References

1. Firth P. Anesthesia and hemoglobinopathies. *Anesthesiology Clin.* 2009;27:321–36. <http://dx.doi.org/10.1016/j.anclin.2009.05.001>
2. Rinder C. Hematologic disorders. In: Hines R, Marscall K, editors. *Stoelting's anesthesia and co-existing disease*. 5th ed. Oxford: Elsevier; 2009. p. 414–5.
3. Mak P, Ooi R. Submental intubation in a patient with beta-thalassaemia major undergoing elective maxillary and mandibular osteotomies. *Br J Anaesth.* 2002;88(2):288–91. <http://dx.doi.org/10.1093/bja/88.2.288>
4. Orr D. Difficult intubation: a hazard in thalassaemia. A case report. *Br J Anaesth.* 1967;39(7):585–6. <http://dx.doi.org/10.1093/bja/39.7.585>
5. Shander A, Berth U, Betta J, et al. Iron overload and toxicity: implications for anesthesiologists. *J Clin Anesth.* 2012;24:419–25. <http://dx.doi.org/10.1016/j.jclinane.2011.12.005>
6. Taher A, Musallam K, Karimi M. Splenectomy and thrombosis: the case of thalassaemia intermedia. *J Thromb haemost.* 2010;8:2152–58.
7. Chou S, Liem R, Thompson A. Challenges of alloimmunization in patients with haemoglobinopathies. *Br J Haematol.* 2012;159:394–404. <http://dx.doi.org/10.1111/bjh.2012.159.issue-4>
8. Perez Ferrer A, Ferrazza V, Gredilla E, et al. Bloodless surgery in a patient with thalassaemia minor. Usefulness of erythropoietin, preoperative blood donation and intraoperative blood salvage. *Minerva Anesthesiol.* 2007;80(2):323–6.
9. Rund D, Rachmilewitz E. Beta-thalassaemia. *N Engl J Med.* 2005;353:1135–46.
10. Cao A, Galanello R, Rosatelli M, et al. Clinical experience of management of thalassaemia: the Sardinian experience. *Semin Hematol.* 1996;33:66–75.
11. Katz R, Goldfarb A, Muggia M, et al. Unique features of laparoscopic cholecystectomy in β thalassaemia patients. *Surg laparosc Endosc Percutan Tech.* 2003;13(5):318–21. <http://dx.doi.org/10.1097/00129689-200310000-00006>

Received: 12-03-2014 Accepted: 23-09-2014

The Anaesthetic Foundation Refresher Course

12-13 September 2015

14 CPD points including 4 Ethics

Doctors' Programme 2015

Topics & Speakers

- Anaesthesia for the Bariatric Patient
- Update on Starvation and RSI
- Perioperative Steroid Supplementation
- The Prolonged QT
- Update on Resuscitation
- Lung Separation
- What's New in ICU?
- Ultrasound for Vascular Access
- Novel Applications for Ultrasound
- Scams, Fraud and Security
- Anaesthesia Billing and the Law
- Anaesthesia and Loadshedding
- What's New in Cardiac Output Monitoring?

- Prof Analee Milner
- Prof Chris Lundgren
- Prof Ivan Joubert
- Dr Scott Bannan
- Dr Roger Dickerson
- Dr Nick Brouckaert
- Dr Bridget Madlener
- Dr Nathi Mdladla
- Dr Jonathan Sheldon
- Mr Kevin Hogan
- Dr Elsabe Klinck
- Dr Jates Oettle
- Dr Catherine Hosking

- Muscle Relaxants and Monitoring, a Practical Approach
- Analgesia in the Frail and the Elderly
- Assessment for Renal Access
- What's New in the Literature?
- Analgesia in ICU
- Epidural PCEA

- Dr Mike Morford
- Dr Erni Welch
- Dr Alex Dresner
- Dr Ahmad Alli
- Dr Mark Eager
- Dr Nick Brouckaert

Dimension Data Campus, The Forum, 57 Sloane St, Bryanston

Open to Anaesthetists, Registrars and Nurses.
For information and registration go to our website
www.anaestheticfoundation.co.za
or contact the Anaesthetics Help Line on 0794659949

