orphanesthesia

Anesthesia recommendations for patients suffering from

Beckwith–Wiedemann Syndrome

Disease name: Beckwith–Wiedemann Syndrome

ICD 10: 68730

Synonyms: Exomphalos-Macroglossia – Gigantism Syndrome (EMG Syndrome)

Beckwith-Wiedemann Syndrome (BWS) is a complex overgrowth disorder with an estimated incidence of 1:13700 live births. It is caused by a variety of genetic or epigenetic alterations within two domains of imprinted gene on chromosome 11p 15. Most of the BWS cases are sporadic (85%). Approximately 15% of the cases are familial forms. BWS is caused by various epigenetic or genetic alterations that regulate imprinted genes on chromosome 11p15.5.

The patients are usually presented in infancy with the symptom triad: exomphalos, macroglossia and gigantism. However, the clinical features of BWS are variable and include viseromegaly, neonatal hypoglycemia, ear creases pits, adrenocortical cytomegaly and renal immaturity. Because of viseromegaly, these patients have an increased risk of embryonal tumor development.

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

Association of cardiovascular anomalies is rare but can present difficulties during perioperative management. The diagnosis is mainly clinical and there are no absolute requisites for clinical diagnosis of BWS. It is generally accepted that the presence of at least three major findings, or two major and one minor findings support a clinical diagnosis. Molecular diagnosis is difficult, mostly because of large spectrum of genetic and epigenetic abnormalities. Death may be due to complications arising from hypoglycemia, prematurity, cardiomyopathy, macroglossia or tumors. Some of these patients require surgery for correction of macroglossia and associated abnormalities (eg. cleft palate,exomphalos or removal of embryonal tumors. Although BWS perse is only rarely associated with neurologic development abnormalities, hypoglycemic period can lead to varying degree of psychomotor retardation. Congenital cardiac problem may need corrective surgery under cardiopulmonary bypass. The main perioperative anaesthetic concern in the treatment of BWS patients is management of a difficult airway, recurrent hypoglycemia and electrolyte imbalance. The underlying cardiac disease may complicate the anaesthesia management further.

Typical surgery

Surgical correction of macroglossia, closure of abdominal wall defect and correction of omphalocele, orchidopexy, removal of embryonal tumors, surgical correction of posterior urethral valve, cleft palate (uncommon) and correction of congenital cardiac anomaly under cardiopulmonary bypass (rare).

Type of anaesthesia

There is definite indication for general anaesthesia.

No reports of regional or local anesthesia.

Premedication is usually avoided if there is a suspicion of possible airway compromise following sedation or small infant with congestive cardiac failure. However there are reports of scopolamine premedication without any complication. Inhalational induction is comparatively safe because of the fact that during mask ventilation overdose of sedatives may cause tongue to fall back into the retro lingual space leading to severe airway obstruction.

Awake tracheal intubation can be done safely. However this is particularly to be avoided in the presence of uncooperative cases and those in whom there is chance of precipitation of pulmonary hypertensive crisis secondary to discomfort and at times pain generated during the procedure.

There is no report of malignant hyperthermia.

There is no evidence supporting the use of conscious sedation for any diagnostic or therapeutic procedure in BWS patients.

Necessary additional diagnostic procedures (preoperative)

BWS is usually manifested during infancy. Because the clinical features of this syndrome are variable, it is generally accepted that diagnosis of BWS requires at least 3 clinical findings including at least 2 major findings. Diagnostic testing (cytogenetic analysis) is most useful for confirming the diagnosis of BWS and for defining recurrence risks rather than phenotype/genotype correlation and perioperative anaesthesia management. Proper documentation of hypoglycemia is essential. An acute insulin response testing should be performed to differentiate BWS from known form of congenital hyperinsulinism. Check for electrolyte, blood urea and creatinine are essential. All the patients should be screened for hypercalciuria. The importance of hypercalciurea is related to perioperative renal dysfunction. If there is a history or physical finding indicative of congenital heart disease, a comprehensive cardiologic examination is indicated. However without such signs there is no indication for nonstandard cardiac evaluation.

A preoperative chest radiograph is required not only to diagnose some evidence of cardiac anomaly but also to exclude thoracic neuroblastoma. Polycythemia and hypothyroidism though less common should be ruled out before surgery due to their adverse effect on perioperative events in terms of bleeding and delayed weaning from mechanical ventilation.

Comprehensive cardiac evaluation including ECG, echocardiography and CT angiography is only necessary when cardiac anomaly is suspected during clinical examination. Evaluation by a cardiologist is essential when a major cardiac problem exists.

Abdominal ultrasound is required to access for organomegaly, nephrocalcinosis, medullary sponge kidney and other structural abnormality. A preoperative CT or MRI examination of abdomen is essential to rule out the presence of any intra abdominal tumor mass only in cases where the ultrasonographic evidence for the same is present. Again adequate screening (if indicated at all) should be left to the expertise of the pediatrician /geneticist and is not the task of preoperative screening.

Particular preparation for airway management

Because of the macroglossia mask ventilation without an oro or nasopharyngeal airway device may be difficult. Since the tongue can be easily displaced, endotreacheal intubation or laryngeal mask placement is in most cases possible with conventional techniques. However, one should be prepared for a difficult airway in all patients with BWS. A detailed oral examination to be performed to rule out cleft palate or closed cleft palate as nasotracheal intubation can threaten the abnormal palatal anatomy.

Patients with macroglossia at times require either awake tracheal intubation or awake vocal cord inspection. This can be facilitated by using topical anesthesia. If glottis can be viewed than either an intravenous induction or inhalational induction may be undertaken. In case of pre-existing airway obstruction, inhalational induction may be undertaken. A nasopharyngeal airway formed from an endotracheal tube is useful in relieving obstruction as the anesthesia depth deepens. A breathing circuit may than attached to the endotracheal tube being used as a nasopharyngeal airway for delivery of anaesthetic gases and oxygen during intubation attempts. Another maneuver that can improve ventilation is forward and downward traction on the tongue.

In case of a planned glossectomy, nasotracheal intubation is advantageous for the surgeon and can in most cases be performed conventionally with the aid of Magill forceps. Cuffed endotracheal tube is preferred because the size of trachea is not easy to predict in BWS patients (larger size trachea in BWS), further to avoid risks incurred during changing of tracheal tube (in situation of difficult endotracheal intubation) and finally to avoid blood aspiration during oropharyngeal surgery.

A nasopharyngeal airway is useful in relieving the postoperative airway obstruction in conditions where edema of the tongue occurred after manipulation.

Glidescope is another good option to manage the difficult airway in these groups of cases.

Particular preparation for transfusion or administration of blood products

There may be a higher requirement of blood and blood products if patient to undergo a corrective cardiac surgery. Neonatal BWS patients may have polycythemia. There may some derangement of platelet function and coagulation abnormalities when congenital cyanotic heart disease co-exists. Adequate amount of blood and blood products to be kept ready when cardiac surgery under cardiopulmonary bypass is planned. Only two reports showed a higher perioperative blood and blood product requirement.

Particular preparation for anticoagulation

There is no evidence to support the need for particular anticoagulation. These patients can tolerate systemic anticoagulation by heparin while undergoing cardiopulmonary bypass.

Particular precautions for positioning, transport or mobilisation

Not reported.

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

Not reported.

Anaesthesiologic procedure

There is no contraindication for any of the anaesthetic agents.

Nitrous oxide is to be avoided if a cardiac surgical correction is required. Inhalational induction is better suited for the cases in those anticipated difficulty in airway management is present.

Opiates should be used cautiously to avoid postoperative airway obstruction and apnea.

All the neuromuscular blocking agents can be safely used unless there is a general contraindication (renal of hepatic insufficiency). Reversal of neuromuscular blockade is safe with neostigmine. There is no report about the use of sugammdex.

Prophylactic postoperative ventilation may be necessary in post cardiac surgical patients and few patients with glossectomy.

Particular or additional monitoring

Invasive arterial blood pressure and central venous pressure monitoring is essential in all major surgeries where massive fluid shift occurs (cardiac surgery).

No report exists showing the essentiality of cardiac output monitoring.

Placement of a pulmonary artery catheter is needed if monitoring is required to adjust the dose of pulmonary vasodilator (eg.nitric oxide).

Routine monitoring of neuromuscular function is not required.

Measurement of depth of anaesthesia by BIS is not obligatory.

Monitoring of blood gas, blood sugar and electrolytes at a regular interval is a must to prevent major emergencies.

Though installment of external defibrillation pads is not in reports, availability of the same as well as an internal defibrillation pad to be confirmed in BWS patients with coexisting cardiac problem or if open heart surgery is required.

Possible complications

Patients with BWS can be at risk for preoperative hypoglycemia especially in the neonatal period and shortly there after with concurrent major electrolyte disturbances. Regular checking of blood glucose, electrolyte and intravenous infusion of dextrose in fasting period can overcome this problem in the neonatal period and in patients with persistent hypoglycemia. As the application of glucose varies from country to country and hospital to hospital, it should be left to local practice how to give sugar.

An acute episode of hypoglycemia during intra or postoperative period needs bolus administration of dextrose followed by infusion. The episode of hypoglycemia is dramatic, difficult to correct and more problematic when the patient has to undergo cardiopulmonary bypass. After the initial bolus treatment of 10% dextrose followed by infusion of 5% dextrose along with lactated Ringer's solution throughout the perioperative period is adequate enough to keep the blood sugar and serum electrolytes within normal limits by overcoming metabolic stress response and electrolyte shift during perioperative period.

Premedication is usually avoided if a suspicion of respiratory insufficiency exists.

Presence of a large tongue and distorted airway might cause damage at the circoid ring in the presence of a cuffed endotracheal tube. As cricoids ring is a complete ring of cartilage, even a small amount of edema will result in significant narrowing, a very large increases in resistance to air flow, laryngospasm and subsequent hypoxemia. Cuffed endotracheal tube can cause compression of the mucosa between the tube and the circular cricoids cartilage leading to necrosis, ulceration. This compression pressure increases further in the presence of a large tongue that usually fallen back towards the vocal cord once the patient is anesthetized. To avoid this complication, we anaesthesiologist should follow the well known formula that is the correct size tube should pass through larynx without resistance and should have a slight leak at an inflation pressure of 20-25 cm of water.

Post operative tracheomalacia and failure to extubate can happen in some cases and the main reason is damage to the cricoids ring which is caused by the pressure necrosis secondary to the presence of a tight fitting/cuffed endotracheal tube and a large tongue or prolonged mechanical ventilation. Use of a correct size endotracheal tube, avoidance of excessive cuff pressure and plan for an early extubation are the different modalities that can be followed to avoid this complication.

Overdose of sedatives and /or opiates during induction may cause the tongue to fall back into the pharynx especially during postoperative period leading to severe airway obstruction, hypoxemia and sudden precipitation of pulmonary artery hypertensive crisis in cases with congenital heart disease with co existing pulmonary artery hypertension.

Awake intubation may increase in intracranial pressure which may contribute to additional neurological injury in patients undergoing cardiopulmonary bypass.

BWS patients are more prone for metabolic stress response and electrolyte shift during peroperatives period. This may contribute to high rise of pulmonary artery pressure and pulmonary artery hypertensive crisis.

Postoperative care

The postoperative care defends upon the age of the child, type of surgery performed, underlying cardiac problem, and presence of hyaline membrane disease. Patients who under went a partial glossectomy, the tongue may swell postoperatively possibly obstructing the upper airway. However, a large case series showed that anterior wedge tongue reduction does not need postoperative tracheal intubation.

Careful management of glucose and electrolyte homeostasis is mandatory in selected cases.

pulmonary Avoid hypoxia, hypercarbia, acidosis and pain as these may lead to ventricular fibrillation and reactionary artery hypertensive crisis.

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 diseases, e.g.:

Intractable hypoglycemia during perioperative period and upper airway obstruction due to macroglossia are the real emergencies. Abdominal viseromegaly can aggravate the respiratory insufficiency. Post glossopexy airway obstruction leading to respiratory arrest may happen and this can be prevented by insertion of a safe nasopharyngeal airway.

Fluid and electrolyte disturbance leading to acute cardiovascular emergency can happen.

Ambulatory anaesthesia

Probably have no role in managing BWS patients when a surgical correction of the upper airway is planned. Without a history of upper airway obstruction or persistent hypoglycemia minor operations outside the airways might be done as day care cases.

Obstetrical anaesthesia

New born and premature with severe BWS are at risk of early death due to complications arising from hyporglycemia, prematurity cardiomyopathy and macroglossia. Prognosis is generally good in patients who survive child hood. The anaesthesia management may be similar to any other pregnant patient when corrective surgery has already been done for the existing airway problem. Special emphasis has to be given for management of glucose and electrolytes in patients with persistent hypoglycemia. However, no information exists regarding this context.

Literature and internet-links

1. Beckwith JB. Extreme cytomegaly of the adrenal cortex, omphalocele, hyperplasia of kidneys and pancreas and Leydig cell hyperplasia: another syndrome? Presented at Annual meeting of the Western Society for Pediatric research; 1963: Los angels.
2. Cohen P, Shim M. Hyperpituitarism, tall stature, and overgrowth syndromes. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia, Pa: Saunders Elsevier; 2007: chap 561.
3. Elliott M, Bayly R, Cole T, Temple IK, Maher ER. Clinical features and natural history of Beckwith-Wiedemann syndrome: presentation of 74 new cases. Clin Genet. 1994; 46(2):168-74.
4. Palladino AA, Bennett MJ, Stanley CA. Hyperinsulinism in infancy and childhood: when an insulin level is not always enough. Clin Chem. 2008; 54(2):256-63.
5. Weksberg R, Shuman C, Smith AC. Beckwith-Wiedemann syndrome. Am J Med Genet C Semin Med Genet. 2005; 15 :(137C) 12-23.
6. Goldman M, Smith A, Shuman C,et al. Renal abnormalities in Beckwith-Wiedemann syndrome are associated with11p 15.5 uniparenteral disomy. J Am Soc Nephrol. 2002; 13:2077-2084.
7. Weksberg R, Shuman C, Beckwith JB. Beckwith-Wiedemann syndrome. Eur J Hum Genet.2012; 18:8-14.
8. Choufani S, Shuman C, Weksberg R. Beckwith Wiedemann-syndrome. Am J Genet. 2010;151C: 343-354.
9. Nargozian C. The airway in patients with craniofacial abnormalities. Paediatr Anaesth. 2004; 14(1):53-59.
10. Bingham RM, Proctor LT. Airway management. Pediatr Clin North Am. 2008; 55(4):873-886.
11. Kimura Y, Kamada Y, Kimura S. Anesthetic management of two cases of Beckwith-Wiedemann syndrome. J Anesth. 2008; 22(1):93-95.
12. Kim Y, Shibutani T, Hirota Y, Mahbub SF, Matsuura H. Anesthetic considerations of two sisters with Beckwith- Wiedemann syndrome. Anesth Prog. 1996; 43(1):24-28.
13. Rudolph AM, Yuan S. Response of the pulmonary vasculature to hypoxia and H+ ion concentration changes. J Clin Invest 1966; 45:399-411.
14. Hickey PR, Hansen DD, Wessel DL, Lang P, Jonas RA, Elixson EM. Blunting of stress responses in the pulmonary circulation of infants by fentanyl. Anesth Analg 1985; 64:1137-42.
15. Morray JP, Lynn AM, Mansfield PB. Effect of pH and PCO2 on pulmonary and systemic hemodynamics after surgery in children with congenital heart disease and pulmonary hypertension. J Pediatr 1988; 113:474-9. Kato T, Ochiai Y, Naganawa Y, Maki I, Ozawa Y, Ohnishi M, Hata T.Anesthetic management for partial tongue resection in a patient with Beckwith-Wiedemann syndrome. .Masui. 1992; 41:861-3. Japanese.
16. Gurkowski MA, Rasch DK. Anesthetic considerations for Beckwith-Wiedemann syndrome .Anesthesiology. 1989; 70:711-2.
17. Naguib M, Redwan A, Khawaja S. Anesthetic considerations in Beckwith-Wiedemann syndrome. Middle East J Anesthesiol. 1987; 9:127-33.
18. Kotoku R, Kinouchi K,Fukumistu K,Taniguchi A. A neonate with Anesthetic considerations for Beckwith-Wiedemann syndrome who developed upper airway obstruction after glossopexy. Mausi 2002; 51:46-8.
19. Hickey PR, Retzack SM. Acute right ventricular failure after pulmonary hypertensive responses to airway instrumentation: effect of fentanyl dose. Anesthesiology 1993; 78:372-6.
20. Munns CF, Batch JA. Hyperinsulinism and Beckwith- Wiedemann syndrome. Arch Dis Child Fetal Neonatal Ed. 2001; 84:F67-F69.
21. Song Lou, Fan Ding, Cun Long, Jinping Liu, Ju Zhao, Zhengyi Feng. Effect of perioperative glucose levels on adverse outcomes in infants receiving open heart surgery for congenital heart disease with cardiopulmonary bypass. Perfusion. 2011; 26:133-9.
22. Eaton J, Atiles R, Tuchman JB. GlideScope for management of the difficult airway in a child with Beckwith-Wiedemann syndrome.Paediatr Anaesth. 2009;19:696-8.doi:10.1111/j.1460-9592.2009.03031.x

23. Wabuchi I, Kagawa T, Oonishi H, Ueshima E.[Anesthetic management of a pediatric patient with Beckwith-Wiedemann syndrome accompanied by macroglossia.Masui. 2008; 57:464-6. Japanese.
24. Kimura Y, Kamada Y, Kimura S.Anesthetic management of two cases of Beckwith-Wiedemann syndrome.J Anesth. 2008;22:93-5. doi: 10.1007/s00540-007-0571-5.
25. Buyukcelik M, Satar N, Dursun H, Bayazit Y, Bayazit AK, Soran M, Noyan A, Anarat A. A child with Beckwith-Wiedemann syndrome and posterior urethral valves. Genet Couns. 2005; 16:41-4.
26. Celiker V, Basgul E, Karagoz AH.Anesthesia in Beckwith-Wiedemann syndrome. Paediatr Anaesth. 2004; 14:778-80.
27. Laroche C, Testelin S, Devauchelle B. Cleft palate and Beckwith-Wiedemann syndrome Cleft Palate Craniofac J. 2005 Mar;42(2):212-7.
28. Anraku S, Ushijima K, Terasaki H. Propofol-fentanyl anesthesia for a 13-year-old patient with Beckwith-Wiedemann syndrome. Masui. 2001; 50:1224-6. Japanese.
29. Nargozian C.The airway in patients with craniofacial abnormalities. Paediatr Anaesth. 2004; 14:53-9. Review.
30. Kim Y, Shibutani T, Hirota Y, Mahbub SF, Matsuura H. Anesthetic considerations of two sisters with Beckwith-Wiedemann syndrome.. Anesth Prog. 1996 Winter; 43:24-8.
31. Thomas ML, McEwan A. The anaesthetic management of a case of Kawasaki's disease (mucocutaneous lymph node syndrome) and Beckwith-Weidemann syndrome presenting with a bleeding tongue.Paediatr Anaesth. 1998; 8:500-2.
32. Takamatsu I. Bilateral vocal cord paralysis in children].Nihon Jibiinkoka Gakkai Kaiho. 1996; 99:91-102. Japanese.
33. Atkins BZ, Danielson DS, Fitzpatrik CM, Dixen P, Peterson RP, Carpenter AJ. Modified ultrafiltration attenuates pulmonary derived inflammatory mediators in response to cardiopulmonary bypass. Interact Cardiovasc Thorac Surg.2012; 11:599-603.
34. Suan C, Ojeda R, García-Perla JL, Pérez-Torres MC. Anaesthesia and the Beckwith-Wiedemann syndrome.Paediatr Anaesth. 1996; 6:231-3.
35. Choudhury M , Malik M, Singh P,Kiran U.Anesthesia for an infant with Anaesthesia and the Beckwith-Wiedemann syndrome who underwent open heart surgery for complete atrio ventricular canal defect. Accept (28-Jun-2012). Pediatric anesthesia.
36. Fujita A, Okutani R, Fukuda T, Fu K, Okamoto T. Anesthetic management in a patient with Beckwith-Wiedemann syndrome. Masui. 1994; 43:1389-91. Japanese.
37. Tobias JD, Lowe S, Holcomb GW 3rd.Anesthetic considerations of an infant with Beckwith-Wiedemann syndrome.J Clin Anesth. 1992 -; 4:484-6.
38. ShunmanC, Beckwith JB, Smith AC, Weksberg R. Beckwith-Wiedemann Syndrome in Pagon RA, Adam MP, Bird TD, Dolan CR, Fong CT, Stephens K. editor in GeneReviews Seattle WA. 2010.
39. Gardner K, Chitayat D, Choufani S, Shuman C, Blaser S, Terespolsky D, Farell S, Reiss R, Wodak S, Pu S, Ray PN, Baskin B, Weksberg R. Brain abnormalities in patients with Beckwith-Wiedemann syndrome. Am J Med Genet A. 2012; 158:1388-94.

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