Anesthetic consideration in downs syndrome-a review

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ABSTRACT

Downs syndrome constitutes to be the most common chromosomal disorder. Patients with Downs's syndrome are posted for several surgeries including dental procedures and even for facial reconstruction. They are associated with several congenital anomalies in different organ system. There is also increased incidence of atlanto axial instability and risk of spinal cord injury. These children are susceptible to infection and they are also considered to be hypersensitive to the effect or atropine. These all factors modify the anesthetic implication and also anesthetic management in these cases. We have highlighted all these factors and reviewed the anesthetic implication of these child posted for several procedures under anesthesia.

Keywords: Downs syndrome, anesthesia and surgery.

INTRODUCTION

Downs syndrome, also known as Trisomy 21 is the commonest of congenital anomalies occurring 1 in 800 live births.[1] It is characterized by dysmorphic facies. The incidence of Downs's syndrome increases as the age of mother increases. The syndrome was first described by Dr. John Langdon Down in 1866.[2] It is the best known chromosomal disorder in man.

Pathophysiology

The extra copy in chromosome 21 affects all the organ systems and results in a wide spectrum of phenotypic consequences. This extra copy of the proximal part of 21q22.3 appears to result in the typical phenotype, mental retardation, hand anomalies and heart defects.[3] The DSCR 1 gene is responsible for the heart and brain involvement in this syndrome, resulting in heart defects and mental retardation.[3] There is increase in the incidence of Down's syndrome if the maternal age exceeds 35, exposure to pesticides or electromagnetic fields, exposure to anesthetic agents, drinking alcohol and caffeine containing beverages.[3] Other features associated with Downs's syndrome include macroglossia, microcephaly, endocardial cushion defects, ventricular septal defects, duodenal atresia, and atlantoaxial instability and supraglottic stenosis. [3] All these results in unique sets of challenges to the anesthesiologists - so each of these shall be discussed in detail.

1. Atlanto axial instability

Atlanto axial instability is characterized by excessive movement at the junction between the atlas (C_1) and axis (C_2) vertebrae, due to either bony and or ligamentous laxity. Neurological symptoms may occur if spinal cord is involved.[4] It is estimated that two percent of children with Downs's syndrome have cord compression producing symptoms, whereas about 20 percent have laxity without any symptoms, which is also known as asymptomatic atlantoaxial instability.[4] Instability may be due to excessive laxity of the posterior transverse ligament of atlas and malformation of odontoid bone.[4] In 1984, the American Academy of Pediatrics issued its first position statement on atlantoaxial instability in Downs's syndrome.[5] For the diagnosis of atlantoaxial instability, lateral radiographs of cervical spine in flexion, extension and neutral position are sufficient. Atlantoaxial-dental interval of 3-5 mm is considered to be borderline; where as the values of 12 -13 mm is usually associated with symptoms.[6] For all the reasons above, positioning of head and neck during anesthetic management may place the spinal cord at risk if ligamentous instability is present, so the patients are recommended to undergo radiological evaluation of cervical spine before anesthesia.[7] In addition, assessing the laxity of other joints such as fingers, thumb, elbows and knees tend to correlate well with presence of atlantoaxial dislocation.[8] The priority lies in the documentation of neurological disability prior to the procedure; any changes are to be documented in anesthetic record.

The signs and symptoms of atlantoaxial instability include easy fatigability, difficulty in walking, abnormal gait, neck pain limiting neck mobility, torticollis, incoordination and clumsiness, sensory deficits, spasticity, hyperreflexia. These signs and symptoms remain stable for months or years; occasionally they progress and may result in hemiplegia, quadriplegia and death.[9]

Due to the risk associated with Downs's syndrome, perioperative care needs to focus on the likelihood of cervical spine instability. Great care must be taken to maintain the neck in neutral position. If atlantoaxial instability is revealed in the radiographic examination, the child should be referred to a neurosurgeon and orthopedic surgeon for further evaluation and stabilization of cervical spine is necessary before any surgery is undertaken.[6]

2. Cardiac anomalies

The incidence of cardiac anomalies in Downs's syndrome ranges up to 40 percent. The genetic band in 21q22 critical region is considered responsible for the cardiac malformations in this syndrome.[6]

i.Endocardial Cushion Defects

Three percent of general population has endocardial cushion defects. Of these, fifty percent are associated with Downs's syndrome. It includes a range of defects characterized by involvement of atrium septum, ventricular septum, and one or more AV valves.[10]

As superior and inferior cushion do not fuse, this results in intra atrial communication of the septum, thus shunting blood form left side to right side. This is called ostium primum defect.

In complete defect, large ventricular septal defect as well as valvular defect may occur, resulting in volume overload of both the right and left ventricles. This on long term results in pulmonary overload, resulting in pulmonary vascular disease and congestive heart failure.[10]

Other cardiac anomaly may include

ii. Atrial septal defect

iii. Teratology of fallot

iv. Persistence of ductus arteriosus

All the aforementioned conditions lead to increased blood flow to the pulmonary vasculature; thus there is a tendency of children with Downs's syndrome to develop pulmonary vascular disease independent of cardiac anomalies.[11]

Apart from the preanesthetic evaluation, it is important to note whether any surgical correction or other invasive procedures have been performed for cardiac anomaly. The patients who have had corrective cardiac surgery may be asymptomatic whereas the others may have residual defects which may result in limitation of activity and increase the anesthetic risk.[12] Repaired AV canal, TOF and VSD may result in the fibrosis of the tract; thus atrial rhythm anomalies are common after the repair of transposition of great vessels with an atrial baffle.[13,14]

Prophylactic antibiotics are indicated in patients who had aortic valvulotomy, resection of coarctation of aorta, pulmonary valvulotomy and any valve replacement of great vessels.[15]

If there is any doubt regarding the cardiovascular status of the patient then elective surgery is to be postponed till further cardiac lesions are sorted out and all the patients should receive prophylaxis for infective endocarditis.

3. Tracheal Stenosis

The upper airway has been frequently recognized as a source of obstruction.[16] Some authors reported small series in which congenital subglottic stenosis,[17-19] tracheal stenosis,[20,21] and tracheal bronchus[22] were related to DS children. Others[23-25] studied the hypo plastic tracheal size in patients with Down's syndrome, who underwent anesthetic procedures in order to provide adequate intubation guidelines; however, the real frequency of airway anomalies, specifically in the lower airway, is unknown.

Endotracheal intubations may lead to chronic inflammation and scarring of the subglottic airway; patients with Downs's syndrome should be intubated with an endotracheal tube 0.5–1.0 mm diameter smaller than the standard age-appropriate endotracheal tube size. There are the likely components of both congenital and iatrogenic stenosis contributing to subglottic pathology in these patients.[25]

An association of congenital ''hour-glass" tracheal stenosis with Down's syndrome has been described in four patients by Wells and coworkers. [22] Other studies of asymptomatic patients with Down's syndrome have shown that tracheal diameters are reduced compared with controls.[23-25] Associated anomalies including vascular rings and a hypoplastic aortic arch have been reported in up to 50.0% of patients with congenital tracheal stenosis. A right tracheal lobe bronchus and tracheoesophageal fistula have also been described.

Bronchoscopy is indicated in patients suspected of having tracheal stenosis. The area of stenosis can be visualized, and complete tracheal rings can be identified, if present. This shall not only help during the intubation, but also in the management of the stenotic lesions.[25,26]

Early diagnosis may help avoid respiratory complications that can necessitate complex medical and surgical treatment. Taking in consideration the chances of tracheal stenosis these patients are intubated with a

smaller sized endotracheal tube than the usual size for the age and sex.

4. Respiratory complications

There is increased incidence of respiratory complications in children with Downs's syndrome. Upper and lower airway problems exist in this subset of the population which is attributed to hypotonia, relative obesity, cardiac disease, small upper airway, degree of pulmonary hypoplasia, congenital anomalies of airway.[28] These are linked to the cardiovascular anomalies.[29] This recurrent infection may be also due to immune deficiency.[30]

Factors affecting the upper airway include hypotonia, obesity, midfacial hypoplasia, relative glossoptosis, small upper airway volume (T!rd of the normal), increased secretions and large adenoids and tonsils.

They have increased chances of developing pulmonary vascular disease.[31-32] The causes include chronic hypoxemia secondary to pulmonary infection, hypoventilation due to muscle hypotonia[33] and obstructive sleep apnea.[34]

These children are also prone to have obstructive airway disease. Symptoms include snoring, unusual sleeping position, increased fatigue during day time and behavioral changes. There is also incidence of sleep induced ventilatory dysfunction in patients with Down's syndrome and this may be exaggerated by narcotic induced sedation and residual anesthetic concentration in the body.

Development of Eisenmenger syndrome is accelerated in children with Downs's syndrome as compared with children without trisomy 21.[29] During the preoperative period, these symptoms are to be analyzed and paramount importance should be given to the preoperative evaluation of the respiratory system which will result in smoother intraoperative course.

5. Immune system

There is also increased incidence of pulmonary infections and relative frequency of positive hepatitis-associated antigens.[35] This may also be due to thymus dependent immune system depression than humoral in children with Downs's syndrome.[36] It's advisable to take strict aseptic precautions during intravenous cannulation and central venous cannulation. Central venous cannula is advisable to be removed immediately after the surgery.[8]

If the patients are planned for central venous access, complete asepsis is necessary and it should be removed as soon as possible. Peripheral lines may be the source of infection so the lines are not to be kept in place for long periods of time.

6. Hematological system

Polycythemia with haematocrit values of more than seventy percent has been reported in children with Downs's syndrome. Hematocrit value more than eighty percent implies an indication for immediate phlebotomy for preventing circulatory failure.[8] Polycythemia may potentiate these patients for circulatory failure; so preoperative haematocrit is to be taken and phlebotomy if needed is to be done without fail.

7. Thyroid and endocrine system

Antithyroid antibodies are found in children with Downs's syndrome. In patients who reach adulthood there is about fifty percent chance of developing hypothyroidism.[37]

Patients with hypothyroidism are prone to have hypothermia and there are chances of delayed recovery pertaining to the thyroid status of these patients. Although the effect of neuromuscular blocking agents is not prolonged in this group of patients they may have delayed recovery due to hypothermia or other reasons pertaining to hypothyroidism.

8. Atropine response

The reported atropine sensitivity in patients with Downs's syndrome is important for anesthesiologists. Both exaggerated mydriatic response to ocular atropine[38] and an increased response to heart rate to parental atropine have been documented,[39] but some studies have failed to show the cardiovascular response.[40]

Although there is increased incidence of atropine hypersensitivity, it is advisable to use vagolytic dose of atropine as these patients have decreased sympathetic activity.[41]

9. Volatile anesthetic agents

Decreased CNS catecholamine levels have been demonstrated in children with Downs's syndrome, which may result in decrease in MAC of inhaled anesthetic agents.[40] During anesthesia, heart rate and blood pressure are stable in all these patients and this finding suggests that deeper level of anesthesia is achieved with the same MAC of inhaled anesthetic agents.[8] Levels of Dopamine â hydroxylase do not increase in the plasma of patients with Downs's syndrome following stress tests.[42] The blood pressure is lower in patients with Downs's syndrome as compared to normal children or other retarded children.[43-44]

So volatile anesthetic agent requirements in these patients are less than normal patients. Keeping in mind the possibility of awareness of anesthesia, BIS monitoring may be used if available.

10. Other organ systems

Gastro-esophageal reflux disease (GERD) is more prevalent in children with Downs's syndrome. The symptoms to be assessed preoperatively include vomiting, oesophagitis, respiratory symptoms like apnea, wheezing and aspiration pneumonia.[29]

Aspiration prophylaxis with modified rapid sequence induction may be used along with the agents to decrease the pH in the stomach. The agents that are used may vary in individual institutional basis.

CONCLUSION

Downs syndrome continues to be the most common congenital anomaly. Its incidence is growing due to increasing age of the mothers in developed and developing countries. So more of these patients will present for several reconstructive surgeries. Anesthetic management is different in these patients due to the airway anomalies, congenital heart disease and endocrine anomalies. These patients are also prone to have hypothermia during surgery. Post-operative respiratory complications are also more common. All these considerations are to be taken care of during and after anesthesia and extra vigilance are to be maintained in these patients during the intraoperative and post-operative period.

REFERENCES

1. Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Downs's syndrome in USA from 1983-1997: a population based study. *Lancet* 2002; 359: 1019-25.
2. National downs syndrome society. When was the downs syndrome discovered? 2003; available at: http://www.ndss.org/content.cfm?fuseaction=InfoResGeneralarticle&article=196 accessed: March 2007.
3. e-medicine: World Medical Library. Downs syndrome: Pathophysiology article by James Bowman, MD. Available at http://www.emedicine.com/ped/topic615.html accessed on November 2006.
4. William C. Atlantoaxial Instability: What Next? *Arch Pediatr Adolesc Med* 1998: 152; 119-22.
5. Harley EH, Collins MD. Neurological Sequelae secondary to atlantoaxial instability in Down's syndrome. *Arch Otolaryngol Head Neck Surg* 1998: 120; 159-65.
6. e-medicine: World Medical Library. Atlantoaxial Instability in individuals with Down syndrome: Article by Norberto Alvarez MD. Available at http://www.emedicine.com/20NEURO/topic554.html accessed on November 2006.
7. Pushchel SM, Findley TW, Furia J, Gallaghar PL, Scola FH, Pezzullo JC. Atlantoaxial instability in Downs's syndrome: roentgenographic, neurological and somatosensory evoked potential study. *J Pediatr* 1987; 110: 515-52.
8. Martin K, Creighton RE, Steward DJ. Anesthetic Considerations in Down's syndrome: Experience with 100 Patients and a Review of Literature. *Canadian Anaesths Soc J* 1982: 29; 593-9.
9. National Downs Syndrome Website. Atlantoaxial Instability in Down syndrome: Controversy and Commentary by Dr. Len Leshin available at http://www.ds-health.com/aai.htm accessed on November 2006.
10. e-Medicine: World Medical Library. Endocardial Cushion Defects: Article by Mary C Mancini MD PhD. available at http://www.emedicine.com/med/topic670.htm accessed on November 2006.
11. Stoelting RK, Dierdof SF. *Anesthesia and Co-existing disease* 4th Ed 2002 New York NY Churchill Livingstone.
12. Finesilver C. A new age for childhood diseases. *Downs Syndr Res Pract* 2002; 65: 980-3.
13. Downing JW, Kaplan S, Bove KE. Postsurgical left anterior hemiblock and right bundle branch block. *Brit Heart J* 1972; 34: 263-70.
14. Scott JG, Allan D. Anesthesia for dentistry in children: a review of 101 surgical procedures. *Canadian J Anaesth* 1970; 17: 391-402.
15. Kaplan, S. The adolescent with operated or unoperated congenital heart disease. *Postgrad Med* 1974; 56: 147-52.
16. Jacobs IN, Gray RF, Todd NW. Upper airway obstruction in children with Down syndrome. *Arch Otolaryngol Head Neck Surg* 1996; 122: 945–50.
17. Richardson MA, Cotton RT. Anatomic abnormalities of the pediatric airway. *Pediatr Clin North Amer* 1984; 31: 821–34.
18. Miller R, Gray SD, Cotton RT, Myer CM, Neterville J. Subglottic stenosis and down syndrome. *Amer J Otolaryngol 1990*; 11: 274–7.
19. Myer CM. Smaller average caliber of the subglottic region in children with Down's syndrome. *Clin Pediatr (Phila)* 1991; 30: 646.
20. Shapiro NL, Huang RY, Sangwan S, Willner A, Laks H. Tracheal stenosis and congenital heart disease in patients with Down syndrome: diagnostic approach and surgical options. *Int'l J Pediatr Otorhinolaryngol* 2000; 54: 137–42.
21. Wells TR, Landing BH, Shamszadeh M, Thompson JW, Bore KE, Caron KH. Association of Down syndrome and segmental tracheal stenosis with ring tracheal cartilages: a review of 9 cases. *Pediatr Pathol* 1992; 12: 673–82.
22. McLaughlin FJ, Strieder DJ, Harris GB, Vawter GP, Evaklis AJ. Tracheal bronchus: association with respiratory morbidity in childhood. *J Pediatr 1985*; 106: 751–5.
23. Jong AL, Sulek M, Nihill M, Duncan NO, Friedman EM. Tenuous airway in children with trisomy 21. *Laryngoscope* 1997; 107: 345–50.
24. Shott SR. Down syndrome: analysis of airway size and guide for appropriate intubation. *Laryngoscope* 2000; 110: 585–92.
25. Townsend A, Mohon TR. Congenital tracheal stenosis in a patient with Down's syndrome. *Pediatr Pulmonol* 1997; 23: 460–63.
26. Pablo B, Hector N, Solange C, Nils H, Ignacio S. Airway anomalies in children with Down's syndrome: Endoscopic findings. *Pediatr Pulmonol* 2003; 36: 137–41.
27. Aboussouan LS, O'Donovan PB, Moodie DS, Gragg LA, Stoller JK. Hypoplastic trachea in Down's syndrome. *Amer Rev Respir Dis* 1993; 147: 72-5.
28. Doull I. Respiratory disorders in downs syndrome: Overview with diagnostic and treatment options, *UK Downs Syndrome Medical Interest Website* available at www.dsmig.org.uk. Accessed on Feb 2007.
29. Cohen WI. Healthcare Guidelines for child with downs syndrome. *Downs Syndr Q June* 1996; 12: 1-11.
30. Ablin RJ. Immunity in Down's syndrome. *Eur J Pediatr* 1978;

127: 149-52.

31. Chi T, Krovetz LJ. The pulmonary vascular bed in children with Down syndrome. *J Pediatr* 1975; 86: 533-8.
32. Wilson SK, Hutchins GM, Neill CA. Hypertensive pulmonary vascular disease in Down's syndrome. *J Pediatr* 1979; 95: 722-6.
33. Rosengart RM, Isabel JB. Pulmonary vascular involvement in Down syndrome. *J Pediatr* 1976; 88: 161-2.
34. Clark RW, Schmidt HS, Schuller DE. Sleep-induced ventilatory dysfunction in Down's syndrome. *Arch Intern Med* 1980; 140: 45-50.
35. Sutnick AI, London WT, Blumberg BS, Gerstley BJS. Anicteric hepatitis with Australia antigen in patients with Down's syndrome. *Amer J Clin Pathol 1972*; 57: 2-12.
36. Levin S, Schlesinger M, Handzel Z *et al*. Thymic deficiency in Down's syndrome. *Pediatrics* 1979; 63: 80-7.
37. Baxter RG, Larkins RG, Martin FIR, Heyma P, Myles K, Ryan L. Down syndrome and thyroid function in adults. *Lancet* 1975; 2: 794-6.
38. Berg JM, Brandon MWG, Kirman BH. Atropine in mongolism. *Lancet* 1959; 2: 441-2
39. Harris WS, Goodman RM. Hyper-reactivity to atropine in Down's syndrome. *New Engl J Med* 1968; 279*:* 407-10.
40. Mir GH, Cumming GR. Response to atropine in Down's syndrome. *Arch Dis Child* 1971; 46*:* 61-5.
41. Keele DK, Richards C, Brown J, Marshall J. Catecholamine metabolism in Down's syndrome. *Amer J Ment Defic* 1969; 74: 125-9.
42. Coleman M, Campbell M, Freedman LS, Roffman M, Ebstein RP, Goldstein M. Serum dopamine-â-hydroxylase levels in Down's syndrome. *Clin Genet* 1974; 5: 312-5.
43. Murdochs JC, Rodger JC, Rao SS, Fletcher CD, Dunnigan MG. Down's syndrome: an atheroma-free model? *Brit Med J* 1977; 2: 226-8.
44. Richards BW, Enver F. Blood pressure in Down's syndrome. *J Ment Defic Res* 1979; 23: 123-35.