Pediatric Anesthesia

Pediatric Anesthesia ISSN 1155-5645

SPECIAL INTEREST ARTICLE (REVIEW)

Preoperative evaluation and comprehensive risk assessment for children with Down syndrome

Amy Feldman Lewanda[1], Andrew Matisoff[2], Mary Revenis[3], Ashraf Harahsheh[4], Craig Futterman[5], Gustavo Nino[6], Jay Greenberg[7], John S. Myseros[8], Kenneth N. Rosenbaum[1] & Marshall Summar[1]

1 Division of Genetics & Metabolism, Children's National Health System, Washington, DC, USA
2 Divisions of Anesthesiology, Sedation, and Perioperative Medicine, Children's National Health System, Washington, DC, USA
3 Division of Neonatology, Children's National Health System, Washington, DC, USA
4 Division of Cardiology, Children's National Health System, Washington, DC, USA
5 Division of Critical Care Medicine, Children's National Health System, Washington, DC, USA
6 Divisions of Pulmonary Medicine and Sleep Medicine, Children's National Health System, Washington, DC, USA
7 Divisions of Hematology and Oncology, Children's National Health System, Washington, DC, USA
8 Division of Neurosurgery, Children's National Health System, Washington, DC, USA

Keywords
Down syndrome; trisomy 21; surgery; anesthesia; perioperative; preoperative

Correspondence
Amy Feldman Lewanda, Division of Genetics & Metabolism, Children's National Health System, 111 Michigan Ave. NW, Washington, DC 20010, USA
Email: alewanda@childrensnational.org

Section Editor: Britta von Ungern-Sternberg

Accepted 1 December 2015

doi:10.1111/pan.12841

Summary

Down syndrome is a common chromosome disorder affecting all body systems. This creates unique physiologic concerns that can affect safety during anesthesia and surgery. Little consensus exists, however, on the best way to evaluate children with Down syndrome in preparation for surgery. We review a number of salient topics affecting these children in the perioperative period, including cervical spine instability, cardiovascular abnormalities, pulmonary hypertension, upper airway obstruction, hematologic disturbances, prematurity, low birth weight, and the use of supplements and alternative therapies. Recommendations include obtaining a complete blood count to detect an increased risk for bleeding or stroke, and cardiology evaluation to identify patients with pulmonary hypertension, as well as undiagnosed or residual heart disease. Pediatric cardiac anesthesiologists and intensivists should be involved as needed. The potential for cervical spine instability should be considered, and the anesthesiologist may wish to have several options available both for the medications and equipment used. The child's family should always be asked if he or she is on any nutritional supplements, as some products marketed to families may have secondary effects such as inhibition of platelet function. Using this evaluation in presurgical planning will allow physicians to better consider the individual circumstances for their patients with Down syndrome. Our goal was to optimize patient safety by choosing the most appropriate setting and perioperative personnel, and to mitigate those risk factors amenable to intervention.

Introduction

Down syndrome (DS) is the most common chromosome disorder in live born infants. It occurs in approximately 1/700 births, affecting roughly 5400 of the nearly 4 million infants born yearly in the United States (1,2). It is caused by the inheritance of an additional chromosome 21, usually by nondisjunction. DS is associated with a high rate of congenital heart disease and lesser but significant rates of gastrointestinal malformations including duodenal atresia and annular pancreas, which often require surgery within the first days to weeks of life. Other surgical conditions that occur at higher rates include Hirschsprung disease, polydactyly, cleft palate, and cataracts. Some patients have multiple malformations, and the repair of one needs to be considered in light of other existing abnormalities.

Due to more frequent major and minor malformations, individuals with DS have more surgeries than those without, and require special consideration to maximize safety before, during, and after surgery (3,4). A large retrospective study to quantify risk found the incidence of anesthesia-related complications to be significantly higher in DS patients (5). We formed a working group of pediatric specialists from Genetics, Anesthesia, Cardiology, Pulmonology, Critical care, Neonatology, Hematology, Otolaryngology, Neurosurgery, and Radiology at Children's National Health System in Washington, DC to consider these concerns. We recognize that no current consensus exists regarding the evaluation and management of these issues, perhaps most notably cervical spine instability. Our proposed evaluation is not intended to be definitive, but an attempt at evaluating children with DS in light of their unique physiology. Suggested risk classes for conditions such as pulmonary hypertension are those used in our facility to plan for potential perioperative problems. Our goal was to consider the special needs of this patient population and ensure the safest surgical experience.

Cervical spine instability

Potential instability of the cervical spine in DS patients has long been recognized and was highlighted by the 1983 Special Olympics policy (6) requiring evaluation prior to participation. Hata and Todd published a thorough review of this topic in 2005 (7). Unfortunately, predicting the likelihood of instability in any given patient can be difficult. Information regarding the evaluation for and incidence of cervical spine instability (CSI) is notably diverse. Authors cite the rate of atlantoaxial, atlantooccipital, or craniocervical instability, leading to wide variation in numbers. Tassone *et al.* (8) lists the frequency of atlantoaxial and atlantooccipital instability at 15%, while a later review found craniocervical instability reported in 8–63% of patients with DS (9). The frequency of os odontoideum (separation of the odontoid process from the body of the axis), which could contribute to instability, may be as high as 6% (9). Relying on symptomatology to identify patients with CSI is problematic, as it is estimated that only 1–2% will actually show significant symptoms (10,11). This implies that a large number of patients with some form of CSI may not be detectable on history and physical exam alone.

Radiologic assessment of cervical spine stability is challenging. In young children, (typically under age 3) the spine is often inadequately ossified to allow good measurements. However, a 16-day-old symptomatic baby was reported in whom cervical spine films revealed atlantooccipital instability (12). Behavioral issues in children with intellectual disability/mental retardation can complicate positioning for imaging. Some suggest using a wedge-shaped neck support with the patient supine to assure proper positioning (13). The measurement most commonly used to determine CSI is the atlantodens interval (ADI). The ADI changes with neck position, and is typically greater in flexion than extension. However, the reported upper limit of normal ranges from 4 to 5 mm (14). Excessive increase in ADI between the two views also raises concern for instability. Tassone *et al.* (8) notes that several authors consider the spinal (or neural) canal width along with the ADI to give the best risk prediction.

Another consideration is whether the structural integrity of the cervical spine changes over time. This is relevant when considering if radiographs taken at age 3 are still valid for a patient undergoing anesthesia and surgery at age 10. A 5-year study found a reduction in the atlantoaxial distance over time; none of the subjects with normal cervical spine X-rays had developed instability 5 years later (13). The exception was a child who was felt to have an acute rotary dislocation at the atlantoaxial joint after anesthesia and ear, nose, and throat surgery. As this child previously had normal films with an atlantoaxial gap of 3 mm (which increased to 7 mm postoperatively), the authors highlight that normal screening radiographs do not guarantee against injury. All DS patients in their facility are therefore fitted with soft collars prior to anesthesia, alerting staff of the potential for cervical spine injury.

The American Academy of Pediatrics (AAP) previously endorsed obtaining one set of lateral cervical spine X-rays for children with DS between 3 and 5 years of age. As noted above, more recent studies show such films do not provide usable information on which patients are actually at risk (15). The newest AAP guidelines no longer recommend routine cervical spine X-rays for asymptomatic children with DS (16). This means that over time, fewer children over the age of 3 years presenting for surgery will have had a previous cervical spine evaluation.

We found that even within the same institution, the approach used by individual practitioners regarding anesthesia for a child with DS varies widely. In some cases anesthesiologists were comfortable in proceeding without preoperative X-rays, yet surgeons would not operate without them. For a child with an increased atlantoaxial distance, some anesthesiologists use fiberoptic intubation, others feel that inline stabilization of the neck provides adequate protection of the cervical spine. Litman *et al.* surveyed pediatric anesthesiologists regarding evaluation and management of patients with

potential CSI (17). Of 171 respondents, only 18% obtained preoperative radiographs and/or subspecialty consultation (9%) in asymptomatic children with DS. For symptomatic children, 64% obtain radiographs and/or preoperative consultation (74%). They concluded that most respondents base their evaluation on the patient's signs and symptoms; an approach supported by the literature but contrary to recommendations made in some reports.

All individuals with DS should be treated as having potential for an acute dislocation, and have a basic neurologic exam to assure equal movement and strength of the limbs. A repeat assessment is important postoperatively to identify any patient that might have sustained a cervical spine injury. Positioning for intubation and surgery should be given additional consideration. Common procedures in children with DS include tonsillectomy and tympanostomy tube placement, both requiring more extensive manipulation of the neck than do general surgical procedures. At least one center has adopted a procedure for doing myringotomies which is to securely strap the patient to the operating table, place supports alongside the head, and roll the table to the side, rather than turning the head (7).

It seems that the probability of a spinal injury from intubation or surgery in a patient with DS is low, but consequences of an adverse event may be severe. As there is not enough evidence on which to base guidelines at this time, the decision of whether or not to obtain preoperative X-rays remains at the discretion of the anesthesiologist and surgeon. Future studies of practices at other facilities would be extremely helpful in creating best practice guidelines in this area.

Cardiovascular abnormalities

The most prevalent malformations associated with DS are those of the cardiovascular system, with the incidence of heart malformations ranging from 42 to 48% (18–21). A fetal study (22) found the rate to be even higher, at 56%. These numbers are not inconsistent given the higher loss rate of chromosomally abnormal fetuses. In both populations, the most common finding was an atrioventriculoseptal defect, although a wide range of cardiac malformations are reported.

Congenital heart disease is an important preoperative consideration. Assignment of risk must consider the severity of the lesion(s), the status of repair, including whether the defect was completely or partially repaired (as in a staged surgical correction), and whether any residual defect remains. Assessing surgical risk related to the repair of congenital heart disease is complex, and several scoring systems, including Aristotle (23) and RACHS-1 (24) have been proposed. These products evaluate risk for all pediatric patients, not just those with DS. The newest American Heart Association guidelines (25) should determine which children require antibiotic prophylaxis for subacute bacterial endocarditis.

Children with DS are significantly more likely to experience bradycardia during and after sevoflurane induction. In a study of 11 201 pediatric anesthetics, the incidence of age-defined bradycardia after sevoflurane anesthesia was 28% in DS patients compared to 9% in controls. In the majority of cases, the heart rate was corrected by decreasing the volatile agent and airway instrumentation. Despite the bradycardia, there was no difference in hypotension, pharmacologic interventions, or outcomes (26). The authors suggest that having anticholinergic agents such as atropine available during induction with sevoflurane seems prudent.

Pulmonary hypertension

Pulmonary artery hypertension (PAH) poses a significant risk during anesthesia and surgery. It is defined as a mean pulmonary artery (PA) pressure over 25 mmHg at rest along with the absence of left atrial hypertension (with a pulmonary capillary wedge pressure below 15 mmHg) (27,28). This definition was based on adult physiology. Tulloh (27) proposes that most pediatricians would accept a systolic pulmonary artery pressure of greater than 50% of systemic pressure as diagnostic for pulmonary hypertension.

The development of PAH is reviewed by King and Tulloh (28). Increased pulmonary flow intensifies the shear stress on pulmonary endothelial cells, triggering a progressive intimal fibrosis. Untreated, the fibrosis will narrow and then obstruct the arteries, further increasing the pulmonary vascular resistance. In a review of patients with pulmonary hypertension undergoing noncardiac surgery or cardiac catheterization, the risk of major complications including cardiac arrest or pulmonary hypertensive crisis was 4.5% (29). Those with baseline suprasystemic pulmonary artery hypertension were at highest risk.

We classify patients with PA pressure <30% of systemic (no PAH) as low risk; those medicated to keep their PA pressure <50% systemic as moderate risk, and those with PA pressure equal to or >50% of systemic (regardless of medication status) as high risk. The risk category for nonmedicated patients with PA pressures between 30 and 49% systemic is individually determined, and is influenced by factors such as right ventricular function and the presence or absence of a shunt to

allow 'pop-off' for maintaining cardiac output in the event of a PAH crisis. At our institution, all moderate or high-risk patients are evaluated by a pediatric cardiac anesthesiologist, even if the planned surgery is not cardiac in nature. If appropriate, the cardiac anesthesiologist assumes care for the patient during surgery.

The causes of PAH are numerous in children. However, many of these risk factors are themselves more frequent in those with DS. It is not surprising, then, that the incidence of PAH in children with DS is higher than those without. The high prevalence of congenital heart disease is a significant contributor. Chi and Krovetz (30) found higher rates of PAH in children with an atrial septal defect (ASD) and DS (4/5) as compared to those with an ASD without DS (1/41). The increase in PA pressure was not related to increased pulmonary blood flow; instead, an increase in pulmonary vascular resistance was the inciting factor. In a population of children with congenital heart disease, those with DS had a significantly higher mean PA pressure (51 vs 26 mmHg) and rate of PAH (51.4% vs 18.4%) (31). PAH also develops significantly earlier in those with DS (32,33).

PAH from congenital heart disease develops over time, and is not expected within the newborn period. It is significant, then, that there is an increased incidence of persistent pulmonary hypertension of the neonate (PPHN) in babies with DS (34,35). Cua (35) reports the incidence of PPHN in the general population to be 0.1%, compared to 1.2% in those with DS; Weijerman *et al.* (19) reported the incidence of PPHN in babies with DS to be 5.2%.

This would seem to imply that there are reasons intrinsic to the anatomy, biochemistry, or physiology of children with DS predisposing them to develop PAH. While congenital heart disease with a left to right shunt may be the most obvious, there are many causative factors affecting the upper or lower airway. A number of physical features associated with DS can contribute to upper airway obstruction and predispose to PAH. These are considered an independent risk factor for surgery and anesthesia, discussed in the upper airway obstruction section.

Lower airway abnormalities in DS have been extensively studied. Lung hypoplasia and highly typical abnormalities in the DS patients whose lungs were examined posthumously have been reported (36). The features were so consistent that DS was suspected in one individual well before the karyotype result was available. They noted that the terminal lung units (acini) contained too few alveoli, leading to spacious alveolar ducts that opened into a reduced number of large, well-formed alveoli. A double capillary network was seen in the alveolar septa and free walls in several patients, a finding the authors confirmed in a later study (37). They concluded that the diminished alveolar count significantly reduced the internal surface area of the lung and of the vascular bed itself, contributing to the early development of PAH. Others report several abnormalities in lung morphology, with no single pattern being characteristic. Schloo *et al.* (38) found that reduced airway branching was common. The number of airway generations in DS patients was reduced to approximately 75% of that expected; in some, that number was 60% or less. The reduction in branching indicated impaired growth as early as 10–12 weeks of gestation. Inflated lung volumes, however, were normal until 6 months of age, after which a significantly reduced volume was seen in DS patients. Abnormal lung development, then, has both prenatal and postnatal components.

Upper airway obstruction

The upper airway of an individual with DS is impacted by anatomic and functional abnormalities, including a flattened nasal bridge, macroglossia, shallow hypopharyngeal dimensions, tracheal and congenital subglottic stenosis, and airway malacia (39,40). These features are compounded by pharyngeal muscle hypotonia, hypertrophy of tonsillar and adenoid tissue, increased secretions, and frequent infections. Children with DS tend to have multiple sites of airway obstruction (39). Even after surgery to address an upper airway problem, they may have residual symptoms of obstruction and the insidious development of PAH.

Several features deserve particular attention. Subglottic stenosis occurs more frequently in patients with DS. This may be congenital, or as a result of previous intubation for respiratory issues or surgery. The use of a laryngeal mask airway should be considered for short procedures. If intubation is required, one should initially use an endotracheal tube at least two sizes smaller than would otherwise be predicted (41). Some practitioners use a small cuffed tube, which allows successful intubation, yet avoids an unacceptably large air leak. Obstructive sleep apnea is common in patients with DS (42–44). Obesity, particularly if extreme, can involve soft tissues of the upper airway and affect oxygenation and ventilation during and after anesthesia.

Hematologic disturbances

The presence of an additional chromosome 21 has a significant effect on blood cell precursors, especially in early life. Up to 80% of newborns with DS have neu-

trophilia, up to 66% have thrombocytopenia, and up to 34% have polycythemia (45,46). These occur most frequently within the first month, but the increased risk remains during the entire first year. A simple blood count will identify these disorders, so they may be addressed before surgery. Significant cytopenias or peripheral blasts require appropriate evaluation, including a bone marrow examination prior to any elective surgery.

Approximately, 10% of neonates with DS will have transient myeloproliferative disorder, also known as transient megakaryoblastic leukemia (47,48). This generally resolves within the first 3 months of life. However, if surgery is needed within the first days or weeks, special precautions may be needed. The two main issues are the very high white blood cell count (which in severe cases can increase the risk for thrombosis and stroke), and the decrease in other hematologic cell lines, producing anemia or thrombocytopenia. Plasmapheresis can lower the white cells to an acceptable range, but is generally considered only when the count is extremely high, perhaps over 125 000 per microliter. Red blood cell or platelet transfusion may be indicated to correct anemia or inadequate clotting.

Prematurity/Very low birth weight

Frid *et al*. (49) evaluated the rates of preterm birth and low birth weight in babies with DS over two periods (1973–1980 and 1995–1998). The rate of preterm (here defined as <36 week) delivery was constant over time. In those with DS, the rate was 25%, compared to 6.3% in the general population. The proportion of babies with DS and low birth weight (<2500 g) was also significantly increased in both study periods. In fact, the average birth weight of babies with DS was 450 g lower than those without. Overall, 14.2% of babies with DS were low birth weight, compared with 4.2% of the general population. Rasmussen *et al*. (50) evaluated the survival of babies with DS in Metropolitan Atlanta between 1979 and 1998. The incidence of low birth weight and prematurity (<37 weeks) in this population was 23.6% and 20.0%, respectively.

The physiology of a newborn differs from that of an older child. Fluctuation and equilibration of pulmonary artery pressure and blood circulation require consideration, and are magnified in premature babies. Not only is the infant's size an issue, but also the exaggerated response to stressors such as hypothermia, sepsis, aspiration of meconium or amniotic fluid, polycythemia, or other metabolic disturbances complicates surgical management. Infants who have normalized their PA pressure can develop acute neonatal pulmonary hypertension when stressed. In our experience, infants with DS are even more sensitive to these stressors than those without. For these reasons, infants who are preterm and/or low birth weight at the time of their surgery are at higher risk than full-term infants or older children.

Use of dietary supplements and alternative therapies

The use of alternative therapy to address the cognitive aspects of DS has existed for many years. It began with the recommendation for megadoses of vitamins in the 1950s (51), continued with commercially available 'high achievement potential' or HAP-Caps (52), and persists today with a large number of products marketed directly to the families of children with DS. These include carnitine, curcumin, folic acid, ginkgo biloba, piracetam, MSB Methyl Plus (Nutrichem Pharmacy, Ottowa, ON, Canada), NuTriVene (International Nutrition, Middle River, MD, USA), and Speak (NourishLife, Lake Forest, IL, USA). It is important to inquire regarding the use of supplements, as many parents feel they are not prescribed medications and do not need to be reported. There are potential problems, however, if a patient is using supplements unbeknownst to the surgical team. For example, piracetam, promoted as a substance to enhance cognitive function, also acts as a platelet inhibitor (53). If a child undergoes surgery while using piracetam, there may be an increased risk for bleeding. Some supplements such as NuTriVene contain over 40 ingredients, including vitamins, minerals, and antioxidants. Partner NuTriVene products also include enzymes and amino acids (54). None of these products are endorsed by the main advocacy organizations for Down syndrome patients, including the National Down Syndrome Congress (51,55) or the National Down Syndrome Society (56). While it is difficult to assign a specific risk for patients taking one or more of these products, it is important to be aware of their use so appropriate recommendations, including perhaps discontinuing them several days before surgery, be considered.

Conclusions

The anatomy and physiology of children with Down syndrome raises a number of concerns for safety during anesthesia and surgery. Consideration of these factors in presurgical planning will identify patients at increased risk for anesthetic complications and poor outcome. Steps can then be taken to identify appropriate personnel and equipment to maximize safety. Multiple

comorbidities would be expected to increase overall risk. This may suggest the need for the procedure to take place in a specialized pediatric hospital, and/or include an overnight stay for observation after surgery. Presurgical evaluation should include the following:

Consider combining two or more compatible surgical procedures under one anesthesia event, which decreases the potential complications of anesthesia induction, emergence from anesthesia, extubation, and postoperative pain control.

A recent evaluation by cardiology with an echocardiogram should be considered in all patients to assess for undiagnosed or residual heart disease and the presence of pulmonary hypertension. This allows for the selection of appropriate facilities and personnel. Specifically, a pediatric cardiac anesthesiologist may be the best choice for a patient with PAH or unrepaired congenital heart disease, even if the surgery is noncardiac. The procedure may best performed as an inpatient, to allow close monitoring postoperatively. For patients considered moderate to high risk, the services of pediatric intensivists should be available as needed.

Consider potential cervical spine instability. All patients with DS should be considered at increased risk for potential instability, and have basic pre- and postoperative neurologic examinations. Obtaining routine cervical spine X-rays in flexion and extension before surgery remains controversial and is at the discretion of the operative team.

Have a variety of options available for anesthesia at the time of surgery. A patient with Down syndrome may react differently to anesthetic agents, such as sevoflurane. A laryngeal mask airway for short procedures may be a good option. Those who do require intubation often benefit from smaller endotracheal tubes than would be predicted by age.

Inquire whether the patient is currently on any dietary supplements or neutraceuticals.

Obtain a screening CBC and platelets. This allows correction of hematologic abnormalities prior to surgery, lessening the risk of bleeding, abnormal clotting, and potential stroke.

Acknowledgments

The authors acknowledge the contributions of Laura Abate of the Himmelfarb Health Sciences Library for editorial and reference assistance, Dr. Diego Preciado for expertise in otolaryngology, and Dr. Dorothy Bulas for expertise in radiology.

Conflict of interest

The authors report no conflict of interest.

Funding

The study received no external funding.

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