Seminars in Anesthesia, Perioperative Medicine and Pain (2006) 25, 136-141

ELSEVIER

Seminars in Anesthesia, Perioperative Medicine and Pain

Anesthesia considerations in children with Down syndrome

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KEYWORDS:
Anesthesia;
Pediatric;
Genetic disease;
Down syndrome

The anomalies associated with Down syndrome present some interesting challenges for the anesthesiologist. Airway difficulties, a potentially unstable cervical spine, and a high incidence of congenital heart disease all require careful consideration. Impaired immune function predisposes to chronic infections and demands attention to asepsis during invasive procedures. Finally, there is the very considerable challenge of providing kind and considerate anesthesia care and effective postoperative pain management for a cognitively impaired child.

The incidence of Down syndrome (DS) is linked to maternal age; the risk being 1 in 385 at age 35 years, but increasing to 1 in 30 by age 45 years. The reason for this is not understood at present. The overall frequency in USA is about 1 in 800 live births, and approximately 6000 children with DS are born there each year.

Down syndrome was first described in 1866 by John Langdon Down in the *London Hospital Reports*.[1] He listed many of the features of the condition which are now well recognized, and also stressed the social and behavioral aspects. He noted that these patients were ". . .humorous, and a lively sense of the ridiculous often colours their mimicry." He also noted that their mental capacity varied and that they "very much repay judicious treatment." He went on to describe the now well recognized facial features of this condition. "The face is flat and broad . . . the hair of brownish colour, straight and scanty . . . the eyes obliquely placed and the internal canthi more than normally distant from one another . . . the lips are large and thick . . . the tongue is long, thick and much roughened."

Almost 100 years later in 1959, the genetic basis of the disease was explained as due to trisomy 21 by Jacobs et al.[2] in the USA and independently by Lejeune[3] in France. The extra chromosome causes a variety of anomalies and associated conditions in a number of organ systems, as listed in Table 1.

Some of these abnormalities are of particular importance when planning anesthesia care:

(a) In the central nervous system, moderate to severe mental retardation is present, with an I.Q. varying from 25 to 85. Early intervention programs aimed at optimizing personal and social development achieve considerable success in some children. These individuals may be capable of competently undertaking routine tasks as they get older. Seizure disorder occurs in 5-10% of patients and will require anticonvulsant medication. Most patients are warm, cheerful, gentle, and tolerant, but a few are stubborn and anxious. Autism and attention deficit may occur in childhood, and obsessive compulsive disorder, Tourette syndrome, or depression may occur as the child grows into an adult. Hearing loss is common, often secondary to chronic otitis media.

(b) The cardiovascular system is affected in 40-50% of all children with DS, but is present in approximately 70% of DS patients seen in hospital series.[4,5] Congenital heart defects include endocardial cushion defects (43% of lesions, 65% of all cases of complete AV canal occur in DS patients), ventricular septal defect (32%), and atrial septal defect (10%). Isolated patent ductus arteriosus occurs in about 4% of patients. Children with DS are particularly prone to develop pulmonary hypertension, either in associ-

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doi:10.1053/j.sane.2006.05.001

Table 1 Abnormalities associated with Down syndrome

General	Short stature and obesity are very common
Nervous system	Moderate to severe mental retardation (I.Q. 25–85) Seizure disorder (5–10%) Moya Moya disease (Rare)
Psychiatric	High risk for autism and attention deficit Hyperactivity and conduct disorder Depressive disorder (Older patients) Tourette syndrome (Rare)
Skull	Brachycephaly and microcephaly Sloping forehead and flat occiput Late closure of large fontanelles Patent metopic suture Absent frontal and sphenoid sinuses Hypoplasia of maxillary sinuses Hypoplastic nasal bone
Eyes	Slanted palpebral fissures with epicanthal folds Strabismus (45%), nystagmus (20%) Stenotic nasolacrimal ducts with tearing Congenital cataracts (3%)
Mouth and teeth	Large fissured tongue Angular cheilitis Teeth; agenesis or delayed eruption Microdontia (35–50%), malocclusion
Ears	Small with deformed helix Hearing loss common (65–85%) Chronic otitis media is common
Neck	Atlanto occipital and atlanto axial instability (15%) Spinal cord compression
Cardiovascular	Congenital heart disease (45–50%) Pulmonary hypertension
Gastrointestinal	Duodenal atresia or stenosis Gastroesophageal reflux Umbilical hernia Hirsprung disease (rare)
Urogenital	Renal hypoplasia Obstructive uropathy Undescended testis Testicular cancer
Musculoskeletal	Generalized hypotonia, hyperextensible joints Short broad hands, single flexion crease Clinodactyly of 5th finger. Increased space great toes to 2nd toes
Endocrine	Hypothyroidism (15–20%) Diabetes common later in life
Hematology	Increased risk of leukemia (10–15× normal) (acute lymphoblastic and myeloblastic) Polycythemia in neonates
Immunology	Relative immune deficiency Increased incidence Hepatitis B antigen +ve

ation with congenital heart disease (CHD) or as a result of chronic airway obstruction (see below).

(c) The respiratory system is compromised by an airway prone to obstruction; the nasal bone is flat secondary to mid face hypoplasia, the palate is short, the tongue is large, the tonsils are subject to hypertrophy secondary to chronic infection.[6] Sleep apnea is common. Subglottic stenosis may be present in children with DS[7] and due caution should be exercised during endotracheal intubation; many will require a tube of smaller than expected diameter.[8] Chronic sinus and middle ear infections are common and pneumonia may develop as a result of impaired cellular immunity.

(d) In the musculo-skeletal system, there is generalized hypotonia and also increased joint laxity. This latter feature may involve atlanto-axial and occipito-atlantal joints and lead to cervical spine instability which is usually reported to occur in 15% of patients, but may be more common.[9] These joints are particularly prone to subluxation during flexion and/or rotation. Neurologic sequelae secondary to spinal cord compression appear in a minority of children with DS. Such patients require surgery to stabilize the cervical spine, after which symptoms usually improve. The anesthesiologist must be concerned that manipulation of the neck during laryngoscopy or positioning for surgery might lead to subluxation and result in spinal cord compression. Such complications are very rare when compared with the large number of DS patients who are anesthetized but have been described following general anesthesia[10] and may be a consequence of positioning, particularly for ear surgery.[11]

(e) Immune deficiency predisposes to infections[12] and strict asepsis is essential during all invasive procedures. Children with DS and a history of hospitalization are at increased risk of hepatitis B carrier status. Leukemia develops in approximately 1 in 150 children with DS.

(f) Hypothyroidism occurs in 15-20% of young patients, and diabetes is common in later age. DS patients have been reported to have low catecholamine levels.[13]

(g) The gastro-intestinal system is affected in 12% of patients and many of these lesions require surgery; duodenal atresia, tracheoesophageal fistula, or omphalocele may present in the newborn. Umbilical hernia is common. Renal malformations, undescended testis, and hypospadius all occur with more frequency than in the general population.

Preoperative assessment and care

In the preoperative assessment of the patient with DS, particular attention should be directed to the airway, the cardiovascular system, and the neck. However, the overall health and emotional status of each child should be carefully noted bearing in mind what is known about the multiple manifestations of DS. During the physical assessment, it is important to gauge the likely responses of the child to the planned induction process and to gain whatever rapport is possible with the patient. The parents of the child with DS can often be most helpful in providing information about behavior and responses, and in most instances may provide valuable assistance during induction of anesthesia. This is especially pertinent when dealing with older children and adolescents.

The airway and respiratory system

The airway status should be assessed by first obtaining a detailed history from the parents, focusing particularly on symptoms of sleep apnea syndrome (snoring, restless sleep, daytime somnolence) or any past history of croup. The recent history of respiratory infections should be carefully noted. Upper airway post anesthesia complications are more common in children with DS, and it is wise to defer non-urgent surgery in any child with a dubious recent history of upper respiratory infection. The increased frequency of complications following ENT surgery also dictate that many patients with DS require hospital admission, and even ICU admission, after surgery which might be performed in the day care unit for normal children (eg, tonsillectomy and adenoidectomy).[14]

Examination of the head, neck, and oropharynx may suggest difficulty with the airway and intubation. It is wise to assume that any child with DS may be difficult to ventilate and intubate and the anesthesiologist must be suitably prepared. The large tongue, especially when combined with hypertrophied lingual tonsils, may cause unanticipated serious problems.[15] The chest should be carefully examined for any evidence of pulmonary disease, bearing in mind that pneumonia is relatively common in DS patients. Routine preoperative chest X-rays are not required.

The cardiovascular system

Most DS patients beyond the neonatal period will previously have been assessed by a cardiologist to exclude or diagnose cardiac disease. The American Academy of Pediatrics recommends that all infants with DS should have an echocardiogram before 6 months of age. Significant heart disease (eg, AV canal) may exist without an audible murmur. Any patient who has never had an echocardiogram should be referred for this to be performed preoperatively. A recent cardiac re-evaluation should be reviewed for those with heart disease, even if the lesion has been repaired. A clinical examination should be performed to exclude any evidence of cardiac failure, arrhythmia, or other disturbance which should be corrected prior to surgery. Pulmonary hypertension develops earlier in DS patients than in other children with comparable cardiac defects.[16] This may be a result of chronic airway obstruction but may also be due to an intrinsic anomaly of the pulmonary vasculature.[17] As pulmonary hypertension may have significant adverse effects on the perioperative course, it is important to document its presence. Some DS patients who have had repair of AV septal defects may be pacemaker dependent. In this case, the anesthesiologist should ensure that he is familiar with the type of pacemaker and its function. Discussion with a cardiologist may be indicated. All patients with cardiac disease or with repaired cardiac lesions (except ligated patent ductus or suture closed atrial septal defect) require prophylactic antibiotics prior to or at induction of anesthesia.

Table 2 Recommended procedure to assess the status of the neck[9]

1. Has the patient's behavior changed?
2. Has ability to ambulate worsened?
3. Has fine motor function decreased?
4. Any change in bowel or bladder control?
5. Any pain in head or neck?
6. Does patient refuse or is unable to turn neck?
7. Any episodes of syncope or dizziness?

A careful and gentle examination should then be made

8. Is there any abnormal range of head and neck movement?
9. Any neck tenderness? Abnormal Gait?
10. Is there weakness, spasticity, increased deep tendon reflexes, clonus or positive Babinski?

The cervical spine

The patient should be assessed to detect any evidence of cervical spine instability that is causing or might cause neurologic complications. A survey of the North American members of the Society of Pediatric Anesthesia in 1993[18] suggested that most respondents based the extent of their preoperative evaluation on the symptoms and signs of each patient. This approach seems to have stood the test of time. A recent recommendation[9] is that careful history should be obtained from the parents, followed by a physical examination as detailed in Table 2.

If any such symptoms or signs are found, elective surgery should be postponed for full cervical spine radiologic studies and evaluation by a specialist. For urgent surgery, the patient should be treated with appropriate cervical spine precautions.[9] Routine C-spine X-rays for asymptomatic patients, advocated by some writers, are not generally recommended.

Premedication

Most children with DS will benefit from sedative premedication to smooth the induction process. This should be ordered with due regard for any airway, sleep apnea, or cardiac considerations which may be present, for which the dosage should be adjusted accordingly. Oral midazolam 0.5-0.75 mg/kg is usually effective. The child should be observed in an appropriate setting by qualified experienced personnel once the medication has been administered in case of any airway problem or respiratory depression which might need the anesthesiologist's early intervention. In cases where the patient is extremely reluctant and induction promises to be a challenge, I found the use of a combination of oral midazolam 0.5 mg/kg with oral ketamine 2 mg/kg plus oral atropine 0.02 mg/kg (maximum of 0.6 mg) to be most effective.[19] The patient should be closely supervised by a member of the anesthesia team while this combination takes effect.

The possible sensitivity of DS patients to atropine has been the subject of some discussion. It was reported that the mydriatic effects of atropine were increased in DS patients,[20] and also that there was an increased heart rate response to parenteral injection of the drug.[21] Subsequent studies have not confirmed this effect on the heart rate and attest to the safety of atropine premedication for DS patients.[22] In our survey of the anesthesia course of 100 patients with DS, we detected no different response to IV atropine from that seen in normal patients.[4] Children with DS often have profuse secretions, and these in combination with a difficult airway may precipitate problems during induction of anesthesia; hence an antisialogue may be useful. In addition, the vagal blockade produced may be useful in DS children who have a reduced level of sympathetic nervous system activity and decreased circulating catecholamines.[23]

Induction of anesthesia

Unexpected airway problems may occur in DS patients during induction; before inducing anesthesia, the immediate availability of oropharyngeal airways, LMAs, and the pediatric difficult airway equipment should be ensured.

As stated earlier, many parents of DS children may be most helpful during this process, and, unless they are extremely anxious, it is usually beneficial to enlist their help. Sevoflurane has become the agent of choice for inhalational induction of anesthesia in children. It is reported that sevoflurane induction may produce bradycardia in infants and children with DS who did not receive anticholinergic premedication.[24] In a review of a large series of patients with DS, bradycardia during induction was demonstrated to be much more common than in other children.[5] Possibly, this is another manifestation of the lower sympathetic activity level in these patients and another indication to consider routine oral anticholinergic premedication. Once anesthesia is induced and deepened, it is not uncommon to have some difficulty in maintaining the airway, due to the large tongue and small mouth. Gentle jaw thrust and the insertion of a suitable sized oropharyngeal airway may be required. Be alert to the fact that joint laxity may result in subluxation of the temperomandibular joint during jaw thrust.

In older children, particularly if they are very anxious, an intravenous induction may be preferable, provided no extreme difficulty with the airway is anticipated. If an intravenous line is in place, then this may be used to induce anesthesia. Alternatively, preparation may be made to place an IV by applying EMLA® cream (Astra Zeneca) or Ametop® (Smith and Nephew) to a suitable site, preferably at least 1 hour in advance. The IV may then be placed in the sedated child with the parent applying suitable distraction and comfort measures.

The use of IM ketamine has been advocated by some, but I have never had to resort to this rather brutal approach, despite meeting with some really reluctant patients. Patience and gentle kindness plus the help of the parents will ensure success.

Airway management

If there is a history of croup, and the type and duration of surgery and other patient considerations are favorable, it is preferable to avoid endotracheal intubation and maintain anesthesia with a face mask or a laryngeal mask airway.

When endotracheal intubation is indicated, the tube should be cautiously placed with due regard for the possibility of subglottic stenosis. A size smaller than usual may be required. Check carefully that there is a leak when the circuit is pressurized to 20 cm water. If a cuffed tube is used, it should pass very easily through the larynx and subglottic space. In patients who have a history of previous repair of subglottic stenosis, extreme caution and planning is required. In such cases, consideration might be given to utilizing a regional analgesia technique (see below). In rare instances, other anomalies of the tracheo-bronchial tree may be present. Mid-tracheal stenosis in association with congenital heart disease has been described in a patient with DS.[25]

Maintenance of anesthesia

This may be conducted along the usual lines; there are no reports of any altered responses to anesthesia drugs or ancillary agents in patients with DS. The presence of hypotonia might suggest caution with dosage of relaxant drugs and close attention to a monitor of neuromuscular blockade. Special attention should be paid to patient positioning to ensure that the cervical spine is not subject to any unusual flexion, extension, or rotational stress. This requires particularly close supervision when positioning for ear surgery.

At the end of the surgery, unless there is a compelling contra-indication, it is recommended to extubate the patient when awake. In order to minimize coughing on the endotracheal tube, intravenous lidocaine, 1-1.5 mg/kg, may be administered as the general anesthesia agents are discontinued. A “No touch” technique may also be helpful to minimize airway complications. To accomplish this, the pharynx is suctioned while the patient is deeply anesthetized. The patient is then turned to the semi-prone recovery position and left intubated while awakening; during which time there is no stimulation or interference whatsoever. Once awake, the tube is carefully removed and a face mask gently positioned to administer oxygen.

The use of regional analgesia in DS patients has been limited by the need for the patient to cooperate and remain immobile during the surgical procedure. When indicated, however, a regional technique may be appropriate,[26] and can be accompanied by a very cautious low-dose propofol infusion, while monitoring the airway carefully.

Anesthesia-related complications

In a large study of DS patients having non-cardiac procedures,[5] the common complications were severe bradycardia (3.6%), airway obstruction (1.8%), postintubation stridor (1.8%), and bronchospasm (0.4%). Intubation was judged difficult in 0.5% of patients. An earlier review of 100 cardiac and non-cardiac procedures in DS patients[4] reported a similar incidence of post-intubation croup (2%), but did not report any instances of bradycardia. However, at the time of this review, it was the practice in that institution to administer IV atropine as a part of the induction sequence.

Following tonsillectomy and adenoidectomy (T&A) for sleep apnea, continuing episodes of apnea with desaturations were reported in 50% of the patients in one series.[14] A total of 25% of their patients required ICU admission for the management of significant continuing apnea. It was recommended that DS patients for T&A should be admitted to hospital,[14] and should be monitored with pulse oximetry for 24 hours postoperatively. Complications described after myringotomy and pressure equalization tube insertion (M&T) included upper airway obstruction and poor fluid intake,[6] and several children required overnight admission. It is not clear whether this report is from a children's hospital and whether pediatric anesthesiologists were involved in the care of these children. I have not seen such complications following routine M&T procedures, and it is not usually necessary to admit such patients. It is clear, however, that DS patients are particularly prone to postoperative airway problems, and demand a great deal of caution.

Postoperative care

The postoperative care of the DS patient should be planned with due regard for their propensity for airway complications. Generally, if extubation is planned, "awake" extubation is preferred, and an anesthesia technique to facilitate this should be chosen. Some patients may require an oropharyngeal airway after the endotracheal tube is removed. The recently extubated DS patient should be carefully positioned for transport to the post anesthesia care unit; the semi-prone position with the neck very gently extended is preferred. During transportation, oxygen should be administered by mask and the patient should be monitored with a pulse oximeter. Post intubation croup, if it occurs, often has an onset 20 to 30 minutes after the endotracheal tube is removed. The nurses in the PACU should be alerted to watch for this complication. The DS patient with a history of sleep apnea requires careful monitoring (including pulse oximetry) for at least 24 hours.

Pain management in the cognitively impaired patient may be particularly challenging for the anesthesiologist.[27] There have been several studies which aimed to determine the sensitivity to pain, its expression, and localization in DS patients. These patients have been reported to have limited capacity for verbal and behavioral expression in reaction to the pain of venepuncture.[28] It has also been reported that DS patients, although not insensitive to pain, express pain and discomfort more slowly and localize the stimulus less precisely than other patients.[29] The suggestions are made that this could relate to the higher levels of endogenous opioids in the frontal cortex of DS patients,[30,31] or to impaired somatosensory nerve function.[32] The DS patient, along with other cognitively impaired children, is obviously at risk for inadequate pain therapy. Indeed it has been shown that fewer cognitively impaired children may be assessed for pain postoperatively and that these patients may receive smaller opioid doses and less days of PCA therapy.[33]

However, DS patients are not insensitive to pain. Indeed in controlled studies, the heat pain threshold has been found to be lower than in normal controls.[34] Furthermore, another study has demonstrated higher morphine requirements of DS patients when compared with matched non-DS patients after pediatric cardiac surgery; the DS patients also required morphine for a longer period postoperatively.[35] Finally, the pain management of DS patients is further complicated by the fact that parents may be less able to recognize the level of pain experienced by their DS child than that experienced by normal siblings.[36]

It is clear from this discussion that much care is required when planning and supervising post operative pain management for DS children. The assessment of the intensity of the patient's pain cannot depend on self report, and indeed the parent's judgment may be less reliable. It must be carefully judged by recognized behaviors and objective physiological observations (eg, heart rate). Under these circumstances, regional analgesia techniques for the management of postoperative pain are particularly advantageous. Peripheral nerve and neuraxial blocks offer excellent pain relief and are not dependent on patient cooperation for their success. Methodology applied to other patients may be adapted to the special circumstances of the DS patient. The use of an epidural catheter positioned with electrostimulation of the nerve roots in a DS patient after thoracoabdominal surgery has been described.[37] Such imaginative approaches have particular application in cognitively impaired patients.

The patient with Down syndrome presents several unique challenges for the anesthesiologist. A knowledge of the pathophysiology of this condition together with careful attention to detail will ensure a smooth perioperative course, pleasing for the patient and parents, and rewarding for the anesthesiologist.

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