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EDITORIAL VIEW

Anesthesia in patients with unusual genetic diseases

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ABSTRACT

In the previous few decades a remarkable growth and development of anesthesiology and its related disciplines has been witnessed. Some specific publications by renowned authors have helped to document many genetic diseases and their perioperative anesthetic management. Also noteworthy are a number of case reports published in the major anesthesiology congresses and specialized journals on the subject. This has led to an understanding of the pathophysiology and the safe anesthetic management in patients with any of these diseases. However, some rare diseases always remain a challenge for the clinical anesthesiologists. It is of utmost importance to appreciate the pathophysiology of these diseases and to anticipate potential problems, as it will allow you to face situations of apprehension and decrease the associated risks to your patient.

Key words: Anesthesia; Anesthesia, General; Congenital Abnormalities; Genetic Diseases, Inborn

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As with the anesthetic procedures of all patients, the focus of effective perioperative care in a patient with coexisting unusual genetic disease begins with thorough preanesthetic evaluation and identification of comorbidities. Some factors may make evaluation more difficult; among them, lack of precise diagnosis, rarity, phenotypic variability and associations. Many congenital anomalies are interrelated. The presence of one anomaly should lead the anesthesiologist to look for others, and pattern recognition will help you plan the best anesthetic management.[1]

Genetic diseases include unique genetic disorders, polygenic disorders, chromosomal abnormalities, mitochondrial mutations, and multifactorial problems.[2] The term 'unusual' or 'uncommon' in the sense of infrequent, when related to disease may be relative only; since in some specific regions it may occur with higher frequency than others.

Not always a genetic disease will bring an important anesthetic implication, but as physicians we have an obligation to provide competent care to all who rely on our hands, no matter how rare their condition may be. Hence, it becomes imperative to know the disease, whose underlying pathophysiological processes can profoundly affect normal or 'routine' anesthetic management. Almost all anesthesiologists are taught and trained to deal with malignant hyperthermia, but very few will have the opportunity to come across such a case. As it is impossible for any clinician to know everything that might be needed to fulfill this responsibility, we have to depend upon quick access to a reliable knowledge source to successfully deal with such cases.

Many patients present for sedation and / or anesthesia and surgery, having been "labeled" with some eponym, acronym, syndrome or rare disease. Not infrequently the anesthesiologist is surprised by the expression: "Dr., the patient has the disease *"x"*. Every experienced anesthesiologist must have anesthetized many patients with chromosome 21 trisomy, and there are many, who may say that they know most of the important aspects of genetic alteration; however, there is an unknown number of unusual diseases, genetic or not, that can be found and have important and complex perioperative implications.[3-5]

Some newborns with genetic diseases are submitted just after birth to diagnostic and / or therapeutic procedures that require anesthesia.

Currently, some therapeutic procedures have been successfully performed *ex utero,* even before birth, to ensure the survival of the newborn. Due to multi-systemic impairment, anomalies and important pathophysiological changes, anesthesia in a large number of diseases presents high perioperative morbidity. It is important to analyze every individual case and evaluate the risk-benefit ratio in order to not to enhance the suffering of the patient.

In the preoperative clinical evaluation, the relatives are the first source of information about the patient and his illness. Some clinicians may be accustomed to manage certain diseases because these are directly related to their specialty; so they can provide valuable advice and guidance in the preoperative period.

The non-cooperative patient can also be a challenge, specifically those with mental disability, psychiatric diagnoses or aberrant behavior. Whenever possible, special attention should be paid to the safe administration of sedatives. Anxiety alleviation is a particularly important point for patients, since most have abnormalities of the central nervous system. In addition, hearing impairment and blindness are recognized features of various genetic diseases. Gaining confidence of the patient and the family will alleviate many of the problems. Exaggerated anxiety can lead to a lack of cooperation. However, in patients with limited lung reserves and increased sensitivity to respiratory depression, preoperative sedation should be avoided, despite being non-cooperative.

The need for a multidisciplinary team, or specialized equipment, or specific care in the perioperative period, or need of postoperative care in an intensive care unit, are factors to be analyzed in the planning of anesthesia and surgery. Emergencies and major surgeries always add to increased morbidity. Many patients are not eligible for outpatient procedures, and require hospitalization and specific care for any procedure. Preoperative evaluation of patients and identification of an abnormal respiratory pattern, hypercarbia in the preoperative blood gas analysis, history of recurrent pneumonia, presence of gastroesophageal reflux or swallowing problems may identify patients with a higher risk of perioperative respiratory complications.

In a comprehensive assessment the main problems related to unusual diseases are centered on airway abnormalities, congenital heart diseases, musculoskeletal disorders, neuromuscular disorders, mitochondrial diseases, metabolic diseases, coagulopathies, mental retardation and central nervous system disorders and restrictions or care with certain drugs. Hepatic and renal disorders rarely occur alone, but always in association with other systemic problems.

The airways and respiratory system are often involved as a result of upper or lower airway obstruction or defects, altered respiratory mechanisms caused by skeletal abnormalities, bronchopulmonary hypoplasia, altered respiratory drive, and gastroesophageal reflux. Careful intubation and rigorous airway monitoring are necessary to avoid serious complications or obstructions. The difficulty of adapting facial mask due to facial dysmorphia and the limitation of cervical mobility make it difficult to have a safe airway. The ability to perform adequate mask ventilation should be evaluated prior to the use of neuromuscular blocking agents. Appropriate equipment to handle the difficult airway should be readily available, including indirect laryngoscopy devices.

Other important factors found are vertebral and craniofacial anomalies caused by disorders of the skeletal or connective tissue. Proper positioning and care during intubation, such a axial traction, prevent maneuvers of hyperextension and hyperflexion of the cervical spine that could lead to cervical neurological damage.6 Every patient with a craniofacial anomaly presents a risk of difficult tracheal extubation.

Managing an airway can be further complicated by gastroesophageal reflux, resulting in an increased risk of aspiration. Drug prophylaxis and intubation in rapid sequence may be considered. In this configuration, a fast acting neuromuscular blocking agent may be required. However, an exaggerated and prolonged response may be observed in patients with neuromuscular disorders.[7]

When encountering a patient with cleft lip and/or palate, it is useful to know that 10% of isolated clefts, 25% for cleft lip and palate, and 45% of cleft palate alone are associated with other systemic abnormalities. In addition, a bilateral fissure is more frequently associated with other abnormalities than a unilateral fissure.[8]

Inefficient airway tone, including tracheomalacia and obstructive sleep apnea, may predispose to the development of postoperative respiratory failure. These issues may be exacerbated by preexisting respiratory dysfunction of hypotonia, coughing effort, chronic aspiration or recurrent pneumonia. An appropriate anesthetic technique should be selected, taking into account the risks.[9]

Cardiac lesions may be congenital or acquired. The prevalent lesions are atrial septal defects, followed by ventricular septal defects. Most of these lesions are not clinically detected. Complex heart diseases are rare but are usually debilitating and require early correction. Acquired lesions may be secondary to the primary condition, such as connective tissue disorders, osteogenesis imperfecta, and mucopolysaccharidosis.[10] The use of invasive monitoring will depend on cardiovascular impairment and the magnitude of the

surgical procedure. Special attention should be given to the antibiotic prophylaxis of bacterial endocarditis. Neuromuscular diseases are manifested as hypotonia, hypertonia, myotonia, muscular dystrophy and / or weakness due to disturbances in the muscle or nervous system.

Many patients may be using growth hormone, thyroid hormone, insulin, oral hypoglycemic agents and hypotensive drugs. It is important to know the pharmacological profile of these drugs and their possible interactions with anesthetics. Preoperative management to limit the potential for perioperative seizures includes optimizing and confirming therapeutic anticonvulsive levels prior to the surgical procedure. Known epileptogenic drugs should be avoided.[7]

Caution should be exercised with the use of specific drugs in patients with liver disease and those at risk of decreased clearance of the drug. Some drugs can lead to deleterious effects, including opioids, inhalation agents and neuromuscular blockers.

Adverse reactions to succinylcholine consist primarily of an extension of its pharmacological action and may cause prolonged muscle relaxation. Adverse reactions may include cardiac arrhythmias, malignant hyperthermia, hyperkalemia, respiratory depression, muscle fasciculation, and joint stiffness. Non-depolarizing muscle relaxants produce an exaggerated and prolonged response in patients with central nervous system disorders who are hypotonic.

Postoperative care should be individualized. Noninvasive techniques of respiratory support facilitate the postoperative management of many patients. Subjacent disorders may increase the need for a higher level of care after anesthesia. Analgesic techniques should be adapted to maximize effect, minimizing risks related to cardiorespiratory depression and anatomical defects.[9] As appropriate based on the surgical procedure, regional anesthesia may also be used as an adjunct to provide adequate postoperative analgesia, this will decrease the requirement for intraoperative anesthesia, including opioids, which may reduce the likelihood of postoperative respiratory depression.[7]

The vast majority of patients are children and young adults, who may present with minimal changes or are severely affected. Because many diseases impose a low life expectancy, any procedures, even diagnoses, should be evaluated for risk and benefit ratio. It is not uncommon for patients to present themselves in an emergency situation when there is insufficient time to fully investigate them.[7]

Patients undergoing craniosynostosis corrections should receive adequate vascular access, adequate ocular protection due to proptosis as well as strict monitoring of volume replacement, bleeding, temperature and electrolytes. These patients may present a risk of difficult extubation due to the presence of bone distractors for facial advancement surgeries.[7]

Any list of care in unusual genetic diseases will not be exhaustive, but it will guide a practical approach to approaching these patients. A brief search in the literature may clarify potential coexisting problems and perioperative recommendations, however, any orientation will not replace the individualized clinical evaluation of each case. The classical description of a disease may be greatly affected by phenotypic expression.

As we all know, anesthesia is nothing more than clinical pharmacology completely incorporated and crystallized in the real-time application to achieve very precise and results-oriented goals, in this direction the pharmacogenomics may assume a great future value in the context of anesthesia. Pharmacogenomics holds the promise that drugs can one day be made tailor-made for individuals and adapted to each individual's own genetic makeup.[2]

The study on this topic is not exhaustive, since there is an unlimited number of unusual genetic diseases. The recognition of certain diseases and the development of new treatments causes an increase in longevity and the possibility of procedures that require anesthesia in these patients. Recognizing unique considerations of anesthesia is an essential part of providing adequate healthcare for patients with genetic diseases and can serve as a means of avoiding morbidity and mortality.[6,7]

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REFERENCES

1. Bösenberg A. Anaesthesia for the "syndromic" child. South Afr J Anaesth Analg 2008;14(5):13-5.
2. Panditrao MM, Panditrao MM. Editorial: Anaesthesia and Genetics: Still, the Uncharted Territories!!. J Anesth Crit Care Open Access 4(1):2016. 00123. [Free full text]. DOI: 10.15406/jaccoa.2016.04.00123.
3. In CB, Choi YS, Park EY, Chang DJ, Lee SK, Choi H, Moon HS. Anesthetic management in patients suspected of Creutzfeldt-Jakob disease - A case report. Korean J Anesthesiol 2011;61(3):262-4. [PubMed] [Free full text]
4. Oliveira CRD, dos Santos FA, Nogueira CS, Mainardes EJ. Spinal anesthesia in a patient with congenital insensitivity to pain with anhidrosis. Anesth Analg 2007;104:1561-2. [PubMed]. DOI: 10.1213/01.ane.0000261247.53075.dd
5. Oliveira CRD, Paris VC, Pereira RA, Lara FST. Anestesia em paciente com insensibilidade congênita a dor e anidrose. Rev Bras Anestesiol 2009;59(5):602-9. [Free full text]
6. Butler MG, Hayes BG, Hathaway MM, Begleiter ML. Specific genetic diseases at risk for sedation/ anesthesia complications. Anesth Analg 2000;91:837-55. [Free full text]
7. Oliveira CRD, Nunes RR, Azevedo RA. Anestesia e doenças incomuns coexistentes. Rio de Janeiro: Sociedade Brasileira de Anestesiologia/SBA, 2017.
8. Maarse W, Rozendaal AM, Pajkrt E, Mermeij-Keers C, Mink van der Molen AB, van den Boogaard MJ. A systematic review of associated structural and chromosomal defects in oral clefts: when is prenatal genetic analysis indicated? J Med Genet 2012;49: 490-8.10.1136/ jmedgenet-2012-101013 [PubMed]
9. Bester K. The syndromic child and anaesthesia. South Afr J Anaesth Analg, 2014;20(5):197-20. [Free full text]. doi:97963310.1080/22201181. 2014.979633
10. Oyati AI, Danbauchi SS, Ameh EA, Mshelbwala PM, Anumah MA, Ogunrinde GO, Anyiam JO, Azuh PC. Echocardiographic findings in children with surgically correctable non-cardiac congenital anomalies. Ann Trop Paediatr 2009;29:41-4.10.1179/146532809X410359 [PubMed]