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OrphanAnesthesia – Getting the key points right for anaesthesia in patients with rare diseases

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ABSTRACT

Sooner or later, every anaesthesiologist will provide care for patients that suffer from a rare disease, be it from comorbidities related or unrelated to their special diagnosis. Syndromes may be accompanied by a phenotype prone to complications during anaesthesia, but expert knowledge on rare diseases is not a given - usually. Therefore in-depth preparation on these patients is essential. Literature regarding anaesthesia and rare diseases is limited and some might be of poor quality. In this article we reflect on different resources and strategies to prepare for anesthesia on patients suffering from a rare disease. Special focus will be laid on quality indicators for medical information and we will introduce OrphanAnesthesia, a growing database of high-quality, disease specific and practical recommendations for anesthetic procedures.

1. Introduction

Orphan diseases - a descriptive synonym for the term “rare diseases” - are diseases with a prevalence lower than 1 in 2000 citizens according to the definition formulated by European Union regulations [1]. Other countries have established alternative definitions, e.g. in the United States a rare disease is defined as a medical condition that affects fewer than 200,000 people within the U.S. [2]. However rare one single disease may be, the total number of about 8000 identified orphan diseases will lead to the seemingly paradox situation that a large percentage of the population, e.g. about 30 million within the European Union, are affected by one of those [3]. This calculation illustrates that it is anything but unlikely to be confronted with patients suffering from an orphan disease during every-day medical work.

Most orphan disease patients will have a dedicated disease specialist for their long-term, routine treatment. However, any anaesthesiologist may be confronted with this group of patients when diagnostic procedures require sedation or anaesthesia, or when a surgical intervention is necessary.

1.1. Anaesthesiologic pitfalls in syndromic patients

Surgery and anaesthesia might be linked to a pathology caused by an orphan disease. E.g. patients, who suffer from Stickler syndrome, which is a progressive hereditary arthro-ophthalmopathy with a prevalence of 1 in 7500, often require ocular surgery, cleft palate repair, orthopaedic treatment of femoral head failures, or spinal surgery due to scoliosis. Otherwise surgery independent of the orphan disease could be required, e.g. an appendectomy. In the case of a Stickler syndrome patient it would be essential for the anaesthesiologist to be aware that there are associations with, inter alia, hypertrophic cardiomyopathy, cervical spondylosis or Von Willebrand disease [4].

Speaking in more general terms, orphan diseases frequently lead to distinctive phenotypical anomalies, which challenge a safe anaesthesiological procedure. Butler at al. reviewed a large number of genetic diseases and identified seven recurring problems [5]:

- difficult airway
- altered respiratory mechanics
- gastric reflux
- cardiovascular disorders
- neuromuscular disorders
- liver disease and
- renal disorders

Ignorance of these pitfalls is a threat to patient safety and may lead to significant morbidity or mortality. Therefore, preparation for anaesthesia of a rare disease patient must include reading up on the disease in a way that allows to identify those aspects with

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relevance to anaesthesia and adapt one's individual procedural regime. This might be challenging due to multiple problems:

- Lack of time, in case of emergency treatment
- Small number of publications, by reason of small numbers of cases
- Existing data often with low level of evidence
- Literature might not focus on anaesthesiological aspects
- Disease experts are not available promptly in case of emergency treatment
- Disease experts not necessarily have competency in anaesthesiologic questions

1.2. Structured approach

Prottengeier et al. recommended a structured approach to prepare for anesthesia on a patient suffering from a rare disease [6]:

- Literature study on the orphan disease by means discussed later in this text.
- Screening of existing medical records and meticulous physical examination.
- Check of mental status, to verify if informed consent is possible, to assess the cooperativity of the patient and to plan appropriate premedication and guidance
- Request for additional examinations like electrocardiogram, echocardiogram or laboratory tests, if urgency of the procedure allows for it
- Investigate if perioperative feasting is possible, or if parenteral nutrition is necessary when a catabolic state has to be avoided
- Reflect, if there might be advantages of regional anaesthesia (e.g. in the case of a suspected difficult airway) or if general anaesthesia might be profitable (e.g. in the presence of musculoskeletal deformities impeding regional anaesthesia)
- Assessment of drug contraindications or interactions with long-term medication (e.g. NO propofol in some mitochondriopathies)
- Evaluation of a possible difficult airway, and planning of its management
- Evaluation of possible cardio-circulatory complications resulting from existing heart defects; consideration of extended hemodynamic monitoring and necessity of catecholamine therapy
- Inspection of musculoskeletal deformities, which will require the use of special tools for vascular access (ultrasound), alternative techniques for drug application (mucosal application, intraosseous application) etc.
- Plan for postoperative care and intensive care capacity, if necessary.

1.3. Quality requirements for medical information

An abundance of different resources is available to get informed on any orphan disease. It is essential to evaluate the quality of all sources to detect and avoid outdated, imprecise or simply false information. Lee et al. defined four dimensions of data quality in data management that should be checked to assess the quality of medical information: intrinsic information quality, contextual information quality, representational information quality and accessibility information quality. These four dimensions are detailed in table 1 .

1.4. Textbooks-the classical way

Medical textbooks are established sources of information. Well-known books covering the anaesthesiological treatment of rare disease patients are Baum's and O'Flaherty's "Anesthesia for Genetic, Metabolic, and Dysmorphic Syndromes of Childhood" [7], Fleisher's "Anesthesia and Uncommon Diseases" [8] and Bissonnette's "Syndromes: Rapid Recognition and Perioperative Implications" [9]. All of them present a multitude of rare diseases and their influence on anaesthesiological practice. They offer high intrinsic information quality. Concerning contextual information quality, any collection on orphan diseases, be it a textbook or an online source can hardly ever be complete, because of the continuing discovery of new syndromes and new aspects of treatment. An additional disadvantage of the medium textbook is that the integration of new facts is a time-consuming procedure, as the publication of a new updated edition may take several years. Representational information quality may be considered as high if the work has passed through peer review and the lectorate of a publishing house. Concerning accessibility, textbooks might not be available at every anaesthesiologic workplace promptly. This could be a problem in time-critical situations, when it is not possible to retrieve the necessary book from wherever it is stored.

1.5. Unlimited knowledge-searching the world wide web

The Internet is a vital medium for professionals to publish as well as to search for medical information. As computers or smartphones with Internet access might be present at most of our workplaces, it is reasonable to use these resources to get information about anaesthesia in orphan disease patients. Free search engines like Google may show a large number of results, but some important limitations have to be considered. We should be aware that the results and especially their order and make-up are not prepared by an editor with medical expert knowledge but rather produced by a non-transparent search engine algorithm and might by influenced by advertising interests and previous user preferences. Even a specialized scientific search engine like Google scholar does not solve the problem of unclear data quality: search results are composed by a computer program and medical expert review is not guaranteed.

Wikipedia is a freely accessible internet encyclopaedia with over 40 million articles in 299 different languages. Articles can be published and edited by any Internet user, even without registration in some languages [10]. A myriad of medical articles can be found, including on orphan diseases. However, the possibility that virtually everybody can create and edit articles leads to complete uncertainty concerning all four dimensions of data quality. Supporters of the wiki-principle may reply that errors or vandalism will be

Table 1
Dimensions of data quality, referring to [7]

Dimensions of data quality	Description
Intrinsic information quality	Accuracy or believability of data
Contextual information quality	Completeness, usefulness and relevance of information
Representational information quality	Understandability and Presentation
Accessibility information quality	Easy accessibility and security of data

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