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Denys-Drash Syndrome

orphan**a**nesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

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OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
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orphan^anesthesia

Anesthesia recommendations for Denys-Drash Syndrome

Disease name: Denys-Drash Syndrome

ICD 10: N04.1

ORPHAcode: 220

Synonyms: Drash Syndrome, Wilms tumor-DSD syndrome

Disease summary: Denys-Drash syndrome (DDS) is an uncommon genetic condition triggered by mutations in WT-1 (located on chromosome band 11p13), a gene known for its tumor-suppressing properties and involvement in gonadal development [1]. The exact incidence of DDS is not known but till date less than 300 cases have been reported in the literature [2]. It manifests as a combination of three disorders: ambiguous genitalia, nephrotic syndrome progressing to end-stage renal disease (ESRD), and Wilms' tumor [3]. Individuals affected by DDS typically exhibit renal histological characteristics aligned with diffuse mesangial sclerosis (DMS) or, in rare cases, focal segmental glomerulosclerosis (FSGS) [4]. Diagnosing DDS entails a comprehensive assessment of clinical features, genetic testing to identify WT1 gene mutations, and renal biopsy to evaluate kidney pathology [5]. Early detection of DDS is imperative to initiate timely management and minimize complications. Management strategies predominantly focus on supportive care, including pharmacological interventions to manage proteinuria and hypertension, dietary modifications, and renal replacement therapy for individuals with ESRD [6]. Regular imaging studies are also recommended for surveillance of Wilms' tumor to enable early detection and treatment. Despite advancements in medical management, individuals with DDS face considerable morbidity and mortality stemming from progressive renal dysfunction and the heightened risk of cancer. Early intervention with renal replacement therapy and vigilant monitoring for complications can enhance outcomes and quality of life for those affected by DDS [3].

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Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this guideline Perhaps new knowledge.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.



Find more information on the disease, its centers of reference and patient organizations on Orphanet: www.orpha.net

Emergency information

A	AIRWAY / ANESTHETIC TECHNIQUE	<p>Potentially difficult airway due to pediatric age group, generalized edema and scoliosis.</p> <p>Difficult airway cart along with fiberoptic bronchoscope should be available.</p> <p>Regional anesthesia techniques (especially under ultrasound-guidance) are favored to preserve renal function.</p>
B	BLOOD PRODUCTS (COAGULATION)	<p>Prone to anemia once renal function deteriorates.</p> <p>Heterologous blood transfusion should be avoided in view of any future need for renal transplantation.</p> <p>Preparations for autologous blood transfusion should be made if major intraoperative blood loss is expected. Coagulation profile and platelet function tests may be performed in the preoperative period.</p>
C	CIRCULATION	<p>Mean arterial pressure (MAP) should be maintained ≥ 65 mmHg to ensure adequate renal perfusion.</p> <p>Invasive hemodynamic monitoring in the form of central venous pressure and arterial blood pressure should be considered in major surgeries, especially for patients with compromised renal function.</p>
D	DRUGS	Nephrotoxic drugs should be avoided.
E	EQUIPMENT	Provision for renal replacement therapy should be available, depending upon the renal function of the patient.

Typical surgery and procedures

Surgical interventions for DDS encompass renal biopsy to assess renal dysfunction, nephrectomy for Wilms' tumor, and AV fistula creation for chronic renal replacement therapy (RRT). Renal transplantation becomes necessary for end-stage renal disease (ESRD). Genitoplasty addresses ambiguous genitalia, while gonadectomy prevents gonadal tumors in cases with dysgenetic gonads [7]. DDS patients can also present for any type of emergency surgery, which may not give adequate time for evaluation and optimization.

Type of anesthesia

To minimize the risk of adverse effects on renal function, anesthesia should prioritize agents and techniques with renal sparing properties. Regional anesthesia is favored wherever possible, as it offers effective analgesia while minimizing systemic effects and maintaining renal perfusion. Additionally, ultrasound-guided nerve blocks are valuable, serving not only for intraoperative anesthesia but also for postoperative analgesia. While using general anesthesia, all nephrotoxic drugs and agents should be avoided.

Necessary additional preoperative testing (beside standard care)

In addition to a comprehensive pre-anesthetic assessment, patients with DDS necessitate thorough nephrological evaluation, including renal function tests and kidney-ureter-bladder (KUB) ultrasonography, to gauge the extent of renal dysfunction and detect the presence of Wilms' tumor. Given the propensity for hypertension in DDS patients, a meticulous cardiovascular examination is essential. Utilizing tools such as a 12-lead electrocardiogram (ECG) and 2D-echocardiography can offer valuable insights into cardiac function. Moreover, considering the patient's age, assessment of developmental status, and cognitive function is imperative, as DDS individuals often contend with neurodevelopmental delays, necessitating tailored perioperative care. A chest X-ray is invaluable for identifying concomitant skeletal anomalies such as thoracic hemivertebrae, rib fusion or absence, and scoliosis. Should significant thoracic scoliosis be present, it is essential to assess the patient's respiratory reserve using pulmonary function tests (PFTs) in the preoperative period. Coagulation profile, bleeding time and platelet function tests may be helpful in detecting any associated bleeding disorder.

Particular preparation for airway management

Managing the airway in patients with DDS presents challenges, particularly due to factors such as their pediatric age, generalized edema, and potential presence of scoliosis. Scoliosis, if severe, can compromise respiratory reserve, increasing the risk of early desaturation during intubation. When anesthetizing DDS patients, preparation is the key. A difficult airway cart, complete with pediatric-sized equipment like video laryngoscopes and fiberoptic laryngoscopes, should be readily available. Adequate preoxygenation is crucial before attempting tracheal intubation, ensuring optimal patient safety throughout the procedure.

Particular preparation for transfusion or administration of blood products

Patients with DDS are often afflicted with end-stage renal disease (ESRD) and commonly experience anemia, necessitating potential blood transfusions during surgeries. However, given that many DDS patients eventually undergo renal transplantation, cautious consideration is warranted regarding blood transfusion. Transfusions may heighten sensitization to diverse human leukocyte antigens (HLAs), elevating the peril of graft failure [8]. Consequently, a meticulous risk-benefit assessment is imperative before administering blood to DDS patients. Alternative strategies such as preoperative optimization of

hemoglobin levels, intraoperative blood salvage techniques, and erythropoietin-stimulating agents may be considered to minimize the need for transfusion in these patients.

Particular preparation for anticoagulation

DDS patients may face a heightened risk of platelet dysfunction stemming from underlying renal disorders, potentially leading to uncontrolled bleeding. Additionally, the presence of vascular anomalies and nephrotic syndrome predisposes them to thrombotic events. As a proactive measure, preoperative evaluation may include assessing the coagulation profile, bleeding time, and platelet function tests. Identifying any abnormalities beforehand allows for timely correction and optimization, mitigating the risk of perioperative bleeding or thrombosis.

Particular precautions for positioning, transportation and mobilization

While specific precautions for positioning and transport of DDS patients may not be outlined, extra attention is warranted for those with significant scoliosis and bone demineralization. Gentle handling is paramount, with particular focus on padding joints and pressure points to minimize discomfort and the risk of injury. Ensuring optimal comfort on the operating table involves adequate cushioning of the scoliotic spine. These measures aim to promote patient safety and comfort during positioning and transportation, addressing the unique needs of DDS patients with skeletal anomalies.

Interactions of chronic disease and anesthesia medications

There are no reported interactions of chronic diseases and anesthesia medications in patients with DDS. However, considering the pediatric age group of most of these patients, all the drugs should be administered in a slow and titrated manner. It would be prudent to avoid the use of histamine releasing drugs and nephrotoxic agents.

Anesthetic procedure

Anesthesia management in DDS patients necessitates meticulous attention, particularly due to associated renal dysfunction, often progressing to ESRD. Maintaining optimal renal blood flow is paramount throughout the perioperative period, with strict avoidance of nephrotoxic agents. Patients undergoing RRT should undergo anticoagulant-free hemodialysis at least 6 hours preoperatively to stabilize fluid shifts, alongside optimizing serum electrolyte levels.

Given the frequent anemia seen in ESRD, hemoglobin levels should be optimized preoperatively, although blood transfusions are generally avoided to prevent HLA sensitization. Erythropoietin therapy may serve as an alternative. Managing hypertension can pose challenges, often requiring multiple antihypertensive agents. For major surgeries, intraoperative invasive arterial blood pressure monitoring may be warranted, with consideration given to omitting morning doses of ACE inhibitors and Angiotensin receptor blockers.

Identification and correction of underlying coagulopathies and platelet dysfunction are essential preoperatively [9], with intraoperative thromboelastography (TEG) potentially

employed for major surgeries. Given the potential for delayed gastric emptying, ensuring adequate fasting and considering agents to enhance gastric motility are advisable.

Difficult IV cannulation may be encountered, particularly in the presence of an AV fistula, necessitating careful limb management. Optimal glycemic control, sepsis prevention, and meticulous pressure point padding are crucial, alongside maintaining optimal temperature to prevent hypothermia.

Airway management can be challenging, warranting readiness of a difficult airway cart equipped with pediatric-sized fiberoptic laryngoscope and video-laryngoscope. While epidural analgesia is preferred, difficulties may arise in severe scoliosis cases during catheter placement. Vigilance and preparedness are key to ensuring safe anesthesia conduct in DDS patients.

Particular or additional monitoring

Apart from the standard ASA monitoring, central venous pressure and invasive arterial blood pressure monitoring are particularly beneficial in major surgeries, providing valuable hemodynamic insights. Given the underlying renal disorder, meticulous urine output monitoring is imperative.

Temperature monitoring holds significance, especially in pediatric cases, ensuring optimal thermal regulation throughout the procedure. For prolonged surgeries, serial arterial blood gas (ABG) monitoring aids in correcting electrolyte and metabolic imbalances promptly.

In cases of coagulopathy or platelet dysfunction, TEG emerges as a valuable tool in major surgeries, facilitating real-time assessment and management of clotting abnormalities.

Possible complications

Among the perioperative challenges encountered in patients with DDS, exacerbation of renal dysfunction leading to ESRD stands out as relatively common. Consequently, RRT may be required to manage this complication. Other potential complications encompass dyselectrolytemia, sepsis, coagulopathy, and uncontrolled bleeding.

Given the prevalence of pediatric cases, additional considerations arise, including challenges associated with airway management, susceptibility to hypothermia, risks of fluid overload, and the occurrence of intraoperative laryngospasm and bronchospasm.

Postoperative care

Vigilant monitoring of DDS patients must persist into the postoperative period as well. Rigorous input-output charting and vigilant blood pressure monitoring assume particular significance. Keeping the patient warm and promptly addressing fluid, electrolyte, and metabolic imbalances are paramount.

Effective pain management is essential, with careful avoidance of nephrotoxic agents. Timely removal of indwelling drains and catheters promotes patient comfort and facilitates recovery. Encouraging early mobilization and initiation of oral intake further contribute to a smoother postoperative course for DDS patients.

Disease-related acute problems and effect on anesthesia and recovery

DDS patients may encounter acute complications such as renal shutdown, profound metabolic and electrolyte disturbances, severe coagulopathy resulting in unmanageable bleeding, challenges with bag-mask ventilation and/or endotracheal intubation, and occurrences of intraoperative laryngospasm and bronchospasm [10]. These complexities render anesthesia administration particularly challenging and can prolong recovery in these individuals.

Ambulatory anesthesia

Given the complexity of DDS and the potential for associated complications, it is advisable to refrain from pursuing ambulatory surgeries in these patients. Instead, DDS patients warrant ample time for a gradual, secure, and complication-free recovery in the postoperative phase. Although, select patients with mild phenotype undergoing minor procedures may be appropriate candidates for ambulatory surgery, provided thorough preoperative evaluation and perioperative safeguards are in place. In general, however, a cautious approach favoring inpatient care remains prudent to ensure safe and complication-free recovery.

Obstetrical anesthesia

If a patient with DDS survives into the reproductive age group, pregnancy becomes a possibility. In such instances, anesthesia management can follow the guidelines outlined in preceding sections. However, special considerations must be made for potential challenges, including difficult airway management, scoliotic spine issues, renal function derangement and coagulopathy with platelet dysfunction. Early dialysis or RRT may be required in the perioperative period, with involvement of a multi-disciplinary team in the care of the obstetric patient is the corner stone of management [11]. Regional anesthesia is preferred, if coagulation optimization is ensured. Safe anesthesia administration keeping in mind the challenges outlined above ensures optimal outcomes for both the mother and the child.

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