

Anaesthesia recommendations for **Childhood nephrotic syndrome**

Disease name: Childhood nephrotic syndrome

ICD 10:

Synonyms: Idiopathic nephrosis

Disease summary: Idiopathic nephrotic syndrome is the most common chronic glomerular disease in children with an annual incidence ranging from 1.15 to 16.9 per 100 000 children, with a median age of 4 years of age and 88% between 2-10 years. Nephrotic syndrome (NS) in children is characterized by the presence of significant proteinuria, hypoalbuminemia, and oedema.

Most cases of nephrotic syndrome respond to steroid therapy and are classified as steroid-sensitive nephrotic syndrome. The most common complications are relapses, with risks of hypovolemia, acute kidney injury (AKI), thrombosis, infections (especially encapsulated bacteria, Varicella Zoster virus VZV and chickenpox) and complications of treatments. There is no risk of chronic kidney disease as long as the NS responds to treatment; nor pulmonary oedema, except in cases of inappropriate use of albumin infusions. Diuretics must be avoided due to the increased risk of hypovolemia, AKI and thrombosis.

Conversely, about 10% of children with idiopathic nephrotic syndrome fail to achieve complete remission. Approximately 50% of children with steroid-resistant and multi-drug resistant nephrotic syndrome progress toward kidney failure. This is also the case for hereditary nephrotic syndrome that may occur in early life as congenital or infantile nephrotic syndrome and can be associated with extra-renal features. Most of them do not respond to therapy and progress to kidney failure. Among them there are cases of congenital nephrotic syndrome of the Finnish type, Galloway-Mowat syndrome, and Denys-Drash syndrome. Depending on the severity, patients may have chronic kidney disease, oliguria or anuria, pulmonary congestion, and hypertension. Along with acute complications, mostly infections, thromboembolic events and AKI, chronic complications may also occur in steroid-resistant nephrotic syndrome including growth retardation, multifactorial anemia (especially iron deficiency anemia), hypothyroidism, hyperlipidemia and kidney failure. Children suffering from nephrotic syndrome may require surgical procedures over the course of their lives, mostly related to nephrotic syndrome and kidney failure.

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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Emergency information

A	AIRWAY / ANAESTHETIC TECHNIQUE	<p>Airway examination should focus on neck anatomy to evaluate potential airway problems. Pulmonary oedema might aggravate ventilation. Induction of anaesthesia should be performed with attention to cardio-pulmonary involvement. Peripherally inserted venous catheters and unnecessary venipunctures must be avoided if possible to preserve arteries and veins for the potential future creation of arteriovenous fistulae (in cases of SRNS).</p> <p>Central venous line insertion should be avoided owing to the high risk of thrombosis and the need to preserve the vasculature for future haemodialysis access. Preoperative laboratory analysis is recommended to identify patients with suspected or known impaired kidney function or coagulation disorder.</p>
B	BLOOD PRODUCTS (COAGULATION)	<p>Blood group testing is required prior to haemorrhagic surgery and kidney biopsy. Nephrotic syndrome patients may present abnormalities in platelet aggregation. No typical bleeding disorders were reported in nephrotic syndrome patients. Coagulation disorders are associated with risk factors of venous thromboembolism, including increased synthesis of factors V and VIII, decreased in antithrombin III, protein C and S, and altered fibrinolysis.</p>
C	CIRCULATION	<p>Preoperative cardiac ultrasound may prove useful in case of suspected cardiac dysfunction. Intraoperative cardiopulmonary evaluation might include invasive blood pressure and non-invasive cardiac output measurement (esophageal Doppler) for intra-operative fluid and blood pressure management. If volume expansion is needed, use albumin instead of 0.9% saline</p>
D	DRUGS	<p>Nephrotoxic drugs, especially non-steroidal anti-inflammatory drugs and drugs involving kidney metabolism must be avoided. Dose of drugs with kidney elimination need to be adapted to glomerular filtration rate, to avoid prolongation of half-life elimination.</p>
E	EQUIPMENT	<p>Do not monitor blood pressure on the arm of the arterio-venous fistula.</p>

Typical surgery and procedures

Surgical procedures related to nephrotic syndrome and its complications: central venous catheter insertion, implantable venous access device insertion, arteriovenous fistula for dialysis, renal biopsy, peritoneal dialysis catheter.

Nephrectomy / bilateral nephrectomies (open or minimally invasive surgery): considered in patients with severe complications, despite optimization of conservative treatment, and before transplantation.

Digestive endoscopy.

Emergency procedures, including the cure of intestinal intussusception, bacterial peritonitis.

Type of anaesthesia

Children with nephrotic syndrome require preoperative assessment and anesthesia care by a senior anesthetist. The potential involvement of different organs implies that preoperative assessment needs to be thorough and organ dysfunction should be assessed carefully (especially kidney, lung, and heart).

General anesthesia has only been described in few patients [1-4]. The use of sevoflurane, propofol, fentanyl and sufentanil has been reported as uneventful. Some studies suggest the use of succinylcholine in patients with renal failure is safe. However, cases of postoperative hyperkalemia following succinylcholine use warrant further investigation [5]. Other agents, such as atracurium and mivacurium, are minimally affected by impaired kidney function, whereas others, such as cisatracurium and rocuronium, can have altered clearance, necessitating dose adjustments in patients with renal failure [5]. In this situation, monitoring of the neuromuscular block depth is even more essential. In patients with preterminal or terminal kidney failure, a relevant prolongation of elimination times must be expected for certain drugs which undergo renal clearance.

Necessary additional pre-operative testing (beside standard care)

There is no general recommendation or protocol for an ideal preoperative assessment. In consideration of various manifestations and a peculiarity of symptoms, the preoperative assessment must identify the specific pattern of symptoms present in the individual patient. The assessment should focus on identifying organ dysfunction, particularly with special reference to lung, heart, kidneys and coagulation profile. Physical examination should at least include the assessment of blood pressure, volume status (signs of hypo- or hypervolemia), signs of oedema (e.g. ascites, pericardial and pleural effusions).

Preoperative laboratory analysis is recommended to identify patients with suspected or known impaired kidney function or coagulation disorder. Thus blood biochemistry must include: blood count, levels of sodium, chloride, potassium, calcium, magnesium, blood gas analysis, coagulation panel albumin, creatinine, urea, protein, albumin, and glucose. In addition, blood group testing is required prior to renal biopsy and to potentially hemorrhagic surgery. Determination of glomerular filtration rate as an indicator of the severity of renal function impairment could also be useful. Cardiac ultrasound may prove useful in case of suspected cardiac dysfunction. In case of suspected pulmonary involvement, chest Xray and lung function tests should be considered.

Particular preparation for airway management

Airway examination should be performed carefully and with particular attention to patient's anatomic features with focus on neck anatomy to evaluate potential airway problems [3]. In addition, pulmonary impairment, related to pulmonary oedema, might also aggravate ventilation.

A case of difficult airway has been reported in a 10-year-old boy with nephrotic syndrome presenting to the pediatric emergency with generalized anasarca, neck swelling and severe respiratory distress [3]. Neck swelling extended up to the sternal angle and his neck girth was 40 cm (normal: 27 cm). Due to increasing neck edema and impending respiratory failure, a difficult airway was anticipated. Despite severe glottic oedema with a narrow glottic opening, he was successfully intubated with a cuffed endotracheal tube using a video-laryngoscope in combination with a Frova introducer [3].

Overall, the evaluation and preparation for airway management in patients with nephrotic syndrome should follow common practice standards for airway management. Difficult airway management should be anticipated and strategies for airway management should be carefully planned in advance.

Particular preparation for transfusion or administration of blood products

Generally, avoid transfusion as much as possible in children with chronic kidney disease since it may lead to hyperimmunization, and compromise access to kidney allograft and increase the risk of rejection and graft loss.

Blood group testing is required prior to potentially hemorrhagic surgery as well as before kidney biopsy. In fact, post-renal biopsy hemorrhage requiring blood transfusion has been reported to complicate 3.2% (95% CI: 3.0%-3.5%) to 5.7% (95% CI: 5.3-6.0%) of adult patients [6]. Such data are not available in pediatric nephrotic patients. A careful discussion, case by case, about this problem must be done with the nephrologist thinking of the potential "immunization" of these patients and the possible future transplantations.

Nephrotic syndrome patients may present abnormalities in platelet aggregation [7]. However, these coagulation disorders are usually associated with risk factors of venous thromboembolism, including increased synthesis of prothrombotic factors (factors V and VIII), urinary loss of anticoagulant proteins (antithrombin III, protein C and S), altered fibrinolysis, and intravascular fluid depletion [7].

Particular preparation for anticoagulation

Nephrotic syndrome patients are subject to venous thromboembolism (VTE). The prevalence of symptomatic thromboembolic (TE) events in children with nephrotic syndrome has been evaluated as 3.60% (95% CI 1.95–5.63), which increased more than two-fold in children with congenital nephrotic syndrome to 8.70% (95% CI 5.11–12.96) [8]. In adult nephrotic syndrome patients, the KDIGO 2021 Clinical Practice Guidelines recommend prophylactic full-dose anticoagulation if serum albumin <20–25 g/L and if any of the following criteria is met: proteinuria >10 g/day, body mass index >35 kg/m², a genetic predisposition for TE, heart failure, recent surgery or prolonged immobilization [9].

The 2021 ESPN guidelines for congenital nephrotic syndrome recommend that preventive anticoagulation should be considered in all children with congenital nephrotic syndrome and/or a prior thrombosis and during states of increased thrombosis risk (i.e. acute illness, risk of dehydration, inserted central lines and/or thrombocytosis >750,000/ml). Infusion of antithrombin III (ATIII; 50 units/kg) before the placement of a central venous catheter is also recommended in cases of deficiency [10, 11]. Anticoagulation with low molecular weight

heparins may be ineffective owing to reduced antithrombin III levels, requiring also in this case an infusion of antithrombin III. Magnesium and calcium supplements should be given to children with congenital nephrotic syndrome when necessary to avoid very low levels that may promote thromboses [10-12].

In contrast to congenital nephrotic syndrome, for older children with steroid resistant nephrotic syndrome and with no prior history or risk of thrombosis the International Pediatric Nephrology Association has considered that there was insufficient evidence to recommend routine prophylactic anticoagulation [13]. Preventive anticoagulation with low molecular weight heparin or oral anticoagulants has been proposed, with a low level of evidence, in patients with a previous history of venous thromboembolic events, and consideration of treatment for those with additional risk factors.

In addition, mobilization of patients (as much as possible) with nephrotic syndrome has been suggested [13].

Particular precautions for positioning, transportation and mobilisation

No specific recommendations are given. Anyway, extreme positioning for specific operations, e.g. a (reverse) Trendelenburg positioning, might lead to hemodynamic impairment in case of severe cardiac involvement.

Interactions of chronic disease and anaesthesia medications

Drugs involving kidney metabolism or nephrotoxic, as well as potassium-based fluids should be avoided. Dose of drugs with kidney elimination need to be adapted to glomerular filtration rate. Peripherally inserted venous catheters and unnecessary venipunctures must be avoided if possible to preserve arteries and veins for the potential future creation of arteriovenous fistulae. Do not monitor blood pressure on the arm of the arterio-venous fistula.

Anaesthetic procedure

Preoperative Evaluation: see details above.

Patients under corticosteroids [14, 15]:

- In case of minor surgery (eg, tooth extraction under local anaesthetic), there is no need to change the usual steroid dose. Sick day dose should be given prior to procedure and return to usual dose immediately afterwards.
- In case of major surgery (eg, operation requiring general anaesthetic), sick day oral steroids is given on day of procedure, even when fasting. Intravenous hydrocortisone is administered a little before inducing anaesthesia (dose of 2 mg/kg intravenously, max 100 mg) and during surgery (1 mg/kg intravenously, max 50 mg, every 6 hours), and after surgery if needed. Alternatively, a hydrocortisone infusion can be used following the induction dose of hydrocortisone. For neonates it has been proposed to increase the doses (4 mg/kg at induction followed by 2 mg/kg intravenously every 6 hours).

Patients with an ongoing antithrombotic treatment should have their antithrombotic therapy stopped in the preoperative period and resumed in the postoperative period [16].

Premedication: might be performed, if clinically indicated (clinically relevant level of preoperative anxiety), weighing the benefits and risks in individual patients.

On the one hand, intraoperative difficulties may include difficult peripheral venous catheter insertion [2]. On the other hand, avoiding peripherally inserted venous catheters and unnecessary venipunctures if possible to preserve arteries and veins for the potential future creation of arteriovenous fistulae should be kept in mind [10, 11]. Also, insertion of central

venous line should be avoided/limited owing to the high risk of thrombosis and the need to preserve the vasculature for future haemodialysis access.

Regarding prophylactic antibiotic treatment, when surgically required, nephrotic syndrome patients rarely are on long-term antibiotic therapy, using oral penicillin or cotrimoxazole, to which a specific intra- and postoperative antibiotic treatment may be added. Despite these preventive measures, patients may present with a history of infection at the time of surgery, and an antibiotic therapy may already have been started before, or may be started during the surgery.

One of the primary strategies in the management of oedema is salt restriction, and fluid restriction in case of hyponatremia. Addition of a loop diuretic is restricted to severe symptomatic oedema, mostly during albumin infusion. Therefore, children may present at surgery with latent or patent hypovolemia. Symptoms that are suggestive of hypovolemia are abdominal discomfort, tachycardia, prolonged capillary refill time and hypotension [10, 11]. In this case, an infusion of albumin may be required before or during surgery. However, as most of the infused albumin is lost in the urine within hours, the purpose of albumin infusion is not to normalize serum albumin levels but to support intravascular volume and reduce extravascular fluid retention in patients with symptomatic hypovolemia. Management should be adapted to the clinical severity of the condition with the aim of maintaining intravascular euvoolemia.

Patient positioning and monitoring: act with caution due to hemodynamic impairment in case of severe cardiac and/or pulmonary involvement.

Anesthesia: induction of anesthesia should be performed with consideration of patient-specific risk factors and with attention to cardio-pulmonary involvement. With regard to physical features and pulmonary impairment, difficult airway management should be anticipated. Using established drugs (see details above) for induction and maintenance of anesthesia were reported as being uneventful. Total intravenous or balanced anesthesia using volatile anesthetics appears safe. The dosage of used drugs should be adapted to renal function.

There are no reports of regional or neuraxial anesthesia in patients with nephrotic syndrome disease. However, the use of regional anesthesia techniques might be favorable in patients with relevant organ disorders when applicable, in the absence of coagulation disorders (platelet dysfunction).

Particular or additional monitoring

A cardiopulmonary evaluation might include invasive blood pressure and non-invasive cardiac output measurement (transesophageal echocardiogram) for both intra-operative fluid management as well as blood pressure management as in other patients according to the patient's status and scheduled surgical procedure. However, the risk benefit ratio of inserting an invasive arterial line must be carefully evaluated and invasive arterial monitoring limited to clinically indisputable indication in order to preserve arteries for the potential future creation of arteriovenous fistulae [10, 11].

Neuromuscular block

Monitoring of the neuromuscular block depth is important given the increased risk of residual block due to altered drug metabolism in renal disease.

Possible complications

Perioperative complications are rather rare in children with steroid-resistant nephrotic syndrome operated on under general anesthesia. In a short series of nephrotic syndrome

children, no increase in thromboembolic, bleeding or infectious events were reported from the intraoperative period to the fifth postoperative day [2].

However, it should be noted that post-renal biopsy hemorrhage requiring blood transfusion may occur [6]. In addition, acute kidney injury (AKI) is recognized as the third most important complication in children treated in hospital with nephrotic syndrome [12]. Identified risk factors of AKI include mainly concomitant infections, use of nephrotoxic medications, and the use of diuretics in a child with hemoconcentration and intravascular volume depletion.

Post-operative care

Postoperative care should be tailored to the individual's disease severity and type of surgery. A stay in intermediate or intensive care unit is not always mandatory but might be reasonable if severe organ dysfunctions exist or postoperative dialysis is necessary.

Regarding postoperative pain management, one should keep in mind that patient with kidney failure may present a relevant prolongation of elimination half-life, especially for opioids like morphine. Therefore, morphine should be carefully titrated to avoid overdosage with the risk of respiratory depression.

In addition, non-steroidal anti-inflammatory drugs are also recognized as nephrotoxic medications and may contribute to AKI; they must be considered as contraindicated in nephrotic syndrome children [12].

Patients with an ongoing antithrombotic treatment should have their antithrombotic therapy resumed in the postoperative period [16].

Disease-related acute problems and effect on anaesthesia and recovery

No specific recommendations are given.

Ambulatory anaesthesia

Ambulatory anesthesia is possible and might be performed in institutions with adequate resources and expertise. Depending on pre-existing cardiac, respiratory and renal dysfunction and the procedure itself, this should be discussed on a case-by-case basis.

A longer period in the post anesthesia care unit (PACU) due to prolonged drug effects may be anticipated in case of renal dysfunction. There are no general recommendations regarding outpatient procedures due to a lack of reports in the literature.

Obstetrical anaesthesia

No specific recommendations are given.

References

1. Datt V, Tempe DK, Arora K, Virmani S, Joshi CS, Agarwal S. Anesthetic management of a child with nephrotic syndrome undergoing open heart surgery: report of a rare case. *Ann Card Anaesth* 2012;15:305-8.
2. Greff B, Faivre J, Carli PA, Niaudet P, Orliaguet GA. Intra- and postoperative adverse events in children with nephrotic syndrome requiring surgery under general anesthesia. *Paediatr Anaesth* 2012;22:244-9. Mahajan V, Saroa R, Singh T, Palta S. C-MAC video laryngoscopy in a difficult airway in a child with nephrotic syndrome with croup and severe neck oedema. *Indian J Anaesth* 2022;66:S129-S30.
3. Nammalwar BR, Vijayakumar M, Prahlad N. Experience of renal biopsy in children with nephrotic syndrome. *Pediatr Nephrol* 2006;21:286-8.
4. Radkowski P, Krupiniewicz KJ, Suchcicki M, et al. Navigating Anesthesia: Muscle Relaxants and Reversal Agents in Patients with Renal Impairment. *Med Sci Monit* 2024;30:e945141.
5. Charu V, O'Shaughnessy MM, Chertow GM, Kambham N. Percutaneous Kidney Biopsy and the Utilization of Blood Transfusion and Renal Angiography Among Hospitalized Adults. *Kidney Int Rep* 2019;4:1435-45.
6. Noone DG, Iijima K, Parekh R. Idiopathic nephrotic syndrome in children. *Lancet* 2018;392:61-74.
7. Dadgar K, Xue Y, Chung J, et al. Childhood nephrotic syndrome and the clinical profile of thromboembolism: a systematic review and meta-analysis. *Pediatr Res* 2023;93:1463-9.
8. Kidney Disease: Improving Global Outcomes Glomerular Diseases Work G. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int* 2021;100:S1-S276.
9. Boyer O, Schaefer F, Haffner D, et al. Management of congenital nephrotic syndrome: consensus recommendations of the ERKNet-ESPN Working Group. *Nat Rev Nephrol* 2021;17:277-89.
10. Boyer O, Schaefer F, Haffner D, et al. Publisher Correction: Management of congenital nephrotic syndrome: consensus recommendations of the ERKNet-ESPN Working Group. *Nat Rev Nephrol* 2021;17:434.
11. Monagle P, Cuello CA, Augustine C, et al. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. *Blood Adv* 2018;2:3292-316.
12. Trautmann A, Vivarelli M, Samuel S, et al. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome. *Pediatr Nephrol* 2020;35:1529-61
13. McKenna M, McBay-Doherty R, Heffernan E. Emergency and perioperative management of adrenal insufficiency in children and young people: BSPED consensus guidelines. *Arch Dis Child Educ Pract Ed* 2024;109:127-30.
14. Mushtaq T, Ali SR, Boulos N, et al. Emergency and perioperative management of adrenal insufficiency in children and young people: British Society for Paediatric Endocrinology and Diabetes consensus guidance. *Arch Dis Child* 2023;108:871-8
15. Jabbour SA. Steroids and the surgical patient. *Med Clin North Am* 2001;85:1311-7.

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