

A&I

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Alport syndrome

Beals syndrome

orphan**anesthesia**

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 Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

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 Anästhesisten damit keine Erfahrungen gesammelt haben, so dass 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 ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass 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 common 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.

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orphananesthesia

Anaesthesia recommendations for Alport syndrome

Disease name: Alport syndrome

ICD 10: Q87.81

Synonyms: Hereditary nephritis

Disease summary:

The Alport syndrome is a rare inherited form of progressive renal failure with an incidence of one in 10,000 newborns. It is due to genetic mutations of the collagen IV $\alpha 3-4-5$ network that is the major collagenous constituent of basement membranes in glomerulus, cochlea, lens and retina. Inheritance is X-linked in 80% of affected patients, with a more severe clinical course in males. It can lead to end-stage renal disease requiring dialysis and transplantation. The prevalence of autosomal recessive and dominant variants is 15% and 5%, respectively. This low prevalence of dominant cases can be due to their highly variable manifestation in the phenotype, ranging from mild symptoms to clinical patterns comparable to the X-linked disease, although deterioration of renal function occurs more slowly, resulting in several unrecognised dominant cases. Loss of renal function – due to the progressive glomerulosclerosis and tubulointerstitial fibrosis – is the most important clinical manifestation of the syndrome with haematuria, proteinuria and hypertension. Sensorineural hearing loss and ocular abnormalities are common especially in X-linked and autosomal recessive forms of Alport syndrome. Leiomyomatosis in respiratory, gastrointestinal and female reproductive tracts is found in 2–5% of patients with an X-linked genotype. The main anaesthetic problems in the treatment of patients with Alport syndrome are related to chronic renal failure with haemorrhagic diathesis and abnormalities in heart conduction due to hyperkalaemia and altered calcium metabolism. Circulatory collapse or difficulties in ventilation due to the presence of mediastinal leiomyomas compressing heart, large vessels and airways is a possible risk as well as the presence of concomitant comorbidities.

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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

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Typical surgeries

Renal biopsy; renal transplantation; eye surgery; hearing aids implantation; removal of leiomyomas.

Type of anaesthesia

Both general and regional anaesthesia can be performed in cases of Alport syndrome.

Doses of sedatives (i.e. midazolam) and opioids should be reduced and titrated to effect in patients with renal failure, since these agents may have delayed metabolism and excretion. Moreover, distribution volume and plasma protein binding of anaesthetic drugs may be altered, resulting in plasma concentrations higher than expected.

Hypnotic agents (i.e. propofol) should be carefully administered as a bolus to avoid haemodynamic and myocardial impairment in these patients who are often hypovolaemic and with coexisting heart failure.

Succinylcholine can be safely used as a neuromuscular blocking agent only in the absence of electrocardiographic changes and if the serum potassium concentration is <5.5 mEq/L.

Regional anaesthesia may limit the risks of deep narcosis and the use of intravenous drugs in patients with multiple comorbidities. It can be performed taking into account: 1) the altered platelet function induced by renal failure; 2) the residual effects of heparin administered during dialysis.

If possible, monitored anaesthesia care (MAC) – in which patient undergoes a procedure in local anaesthesia plus sedation and analgesia – is preferred in patients with end-stage renal disease related to Alport syndrome.

Specific pain management methods do not exist. However, some adjustments are required in patients who develop renal impairment: 1) non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated; 2) opioids (i.e. tramadol) must be administered in lower doses to avoid plasmatic accumulation and subsequent respiratory depression.

Necessary additional pre-operative testing (beside standard care)

Alport syndrome is often associated with cardiovascular diseases (hypertension, arrhythmias, heart failure) and progressive renal failure; these possible pathologies must be specifically investigated:

1. Cardiac function test, such as electrocardiography and echocardiography, should be performed to exclude cardiomyopathy;
2. The pulmonary picture should be evaluated, at least with chest radiography, to exclude oedema or pleural effusion;
3. Renal function, serum electrolytes and acid–base balance should be always evaluated to assess the degree of renal failure, the need of perioperative dialysis and to early adjust electrolytic and acid-base disorders;
4. Standard coagulation tests should always be performed, since haemorrhagic diathesis is a known risk. In end-stage renal disease patients, the use of thromboelastography (TEG) or rotational thromboelastometry (ROTEM) could be particularly indicated.

Particular preparation for airway management

No defined guidelines referring to the patient's airway management and position exist.

Major attention should always be given to airway management in patients with X-linked Alport syndrome due to the high incidence of upper airway lesions that characterise these patients. A preoperative careful airway assessment, possibly benefiting from a more specific examination by otorhinolaryngologist, is hence crucial in planning the best approach for anaesthesia induction.

In patients undergoing oesophageal leiomyoma removal surgery – a frequent complication of Alport syndrome – the lateral position could be particularly indicated to avoid the compression of tracheal and major vessels during the induction of anaesthesia. Fibrobronchoscopy could help in performing oro-tracheal intubation.

Since a case report describing a bilateral vocal cord paralysis following coronary artery aneurysmectomy in Alport syndrome has been published, pointing out the neural vulnerability in all renal failure patients, but especially in those with Alport syndrome, it is advisable for the surgeons to pay close attention to the risk of vocal cord damage.

Particular preparation for transfusion or administration of blood products

Alport syndrome patients developing renal failure may have an elevated risk of intraoperative bleeding due to the altered coagulation process and inhibited platelet function induced by uraemia, impaired vessel reactivity and anaemia. Consequently, a higher need of blood products could be observed during surgery.

Preoperative dialysis has been reported to improve platelet function in patients with end-stage renal disease, reducing the bleeding risk during surgery. In case that there is no time for dialysis, desmopressin could be useful to facilitate platelet aggregation.

Major attention should always be paid to residual heparin in the four hours following dialysis. Protamine could help to reverse heparin in case of emergency surgery.

Even in absence of definite recommendations for an administration of blood products in patients with Alport syndrome, all uraemic and actively bleeding patients should be treated with platelet concentrates immediately before or during surgery, regardless of the platelet counts.

Particular preparation for anticoagulation

If heparin has been used in patients with Alport syndrome on dialysis, normalisation of the coagulation parameters, usually lasting four hours, should be awaited before surgery. Protamine can anyhow reverse the heparin effect.

Particular precautions for positioning, transport or mobilisation

Patients with important oesophageal leiomyomas associated to Alport syndrome should be subject to cautious postural changes and remain in the lateral position to avoid airway, heart and major vessels compression by the mediastinal masses.

Other suggestions for positioning, transport or mobilisation have not been reported.

Interaction of chronic disease and anaesthesia medications

In dialysis-dependent patients with Alport syndrome, the recommendations concerning the use of anaesthetic agents are comparable to those of patients with end-stage renal disease.

Anaesthetic procedure

In patients with renal failure due to the Alport syndrome:

1. Midazolam and opioids (especially morphine) should be avoided or titrated to effect due to their delay in metabolism and excretion possibly resulting in prolonged respiratory depression;
2. Hypnotic agents (i.e. propofol) and volatile agents must be carefully administered in patients with myocardial impairment and/or at risk of hypovolaemia due to dialysis;
3. Non-depolarising neuromuscular blocking agents (NMBA) – such as atracurium and cisatracurium – should be preferred to succinylcholine, whose metabolism by cholinesterase is reduced in end-stage renal disease. Rocuronium may be used in longer surgery or if sugammadex is available, since it is eliminated partially by the kidney and its clearance could be reduced because of renal failure.

In patients requiring rapid sequence of induction and intubation, succinylcholine could be used if serum potassium concentration is <5.5 mEq/L and electrocardiographic alterations are not evident.

In patients requiring total intravenous anaesthesia (TIVA), such as in neurosurgery, continuous infusion of propofol and short-acting opioids (i.e. remifentanyl) is not contraindicated.

Regional anaesthesia is safe and feasible, when appropriate, in patients with Alport's syndrome considering that the onset of action of local anaesthetics is slower in end-stage renal disease due to low serum bicarbonate levels and reduced protein binding.

Particularly suggested is the use of combined spinal-epidural anaesthesia to perform renal transplantation in Alport syndrome patients. In fact, a low dose of intrathecal heavy bupivacaine in addition to an epidural volume extension of analgesia during and after the procedure has been reported to provide the necessary motor block and the best pain management, with a low risk of adverse events and no impact on haemodynamic and respiratory muscle activity.

Particular or additional monitoring

Due to the high risk of arrhythmias possibly induced by elevated serum potassium, at least 5-lead, better 12-lead, electrocardiogram (ECG) should be used during surgery in patients with Alport syndrome.

Non-depolarising muscular blockage should be always monitored due to the variability in the pharmacokinetics of NMBAs in end-stage renal disease patients.

In case of high-risk surgery, invasive tools and monitoring, such as arterial cannulation for invasive blood pressure measurement and central venous line placement, are recommended.

Possible complications

Severe cases of Alport syndrome are characterised by a high risk of fatal arrhythmias, hyperkalaemic cardiac arrest, heart failure and intraoperative bleeding. Over-administration of intravenous fluids during surgery may lead to pulmonary oedema, whereas under-administration may cause haemodynamic instability. Sedative drugs (i.e. midazolam) and NMBA's may induce severe and prolonged respiratory depression.

Post-operative care

Post-operative care and monitoring depends on patient and surgical characteristics.

The great majority of Alport syndrome patients could return home after outpatient procedures or be discharged to a regular surgical ward after inpatient surgery.

Admission to the intermediate or intensive care unit could be indicated in dialysis-dependent patients who are haemodynamically unstable after major surgical intervention, or if severe peri-operative comorbidities exist. All severe cases of Alport syndrome and all end-stage renal disease patients should be adequately monitored in the post-operative period due to the high risk of electrolytic disorders, pulmonary oedema and bleeding.

Major attention should be given to these patients when undergoing narcosis due to their slower drug metabolism and excretion, monitoring the breathing capacity.

Patients requiring dialysis should receive renal replacement therapy as soon as the risk of surgery-induced fluid shifts and bleeding has been reduced.

Post-operative analgesia should be guaranteed with a multimodal approach, such as regional anaesthetic techniques and wound infiltration with local anaesthetics in order to reduce the need of intravenous analgesics and to avoid NSAIDs.

Disease-related acute problems and effect on anaesthesia and recovery

The emergency-like situations in patients with Alport syndrome are fatal arrhythmias mainly related to end-stage renal disease.

There are evidences supporting the need of standby extracorporeal life support (ECLS) during surgery to remove oesophageal leiomyomas due to the risks of critical haemodynamic and/or breathing problems possibly induced by mediastinal mass compression on heart, major vessels and airway.

Ambulatory anaesthesia

Ambulatory anaesthesia is indicated during the early phases of Alport syndrome, taking into account renal function, electrolytic and acid-base balance and coagulation profile.

If outpatient procedures are necessary for patients with end-stage renal disease, anaesthesiologists should be aware of the recommendations on narcosis drugs and the potential complications detailed above.

Obstetrical anaesthesia

Not specific recommendations are reported.

Since X-linked inheritance is the most frequent form, females with Alport syndrome have often a disease phenotype less severe than males. It is uncommon for end-stage renal disease due to X-linked Alport syndrome to characterise pregnant women, since the risk of severe renal failure increases with increasing age, achieving a 30% probability at the age of 60. On the contrary, the chronic kidney disease and consequent myocardial impairment may occur in women with autosomal dominant forms during childbearing age.

However, central neuraxial block (spinal or epidural) may be safely used for labour analgesia and caesarean surgery in patients on dialysis.

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