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Stickler syndrome

Stiff Man Syndrome

orphanaesthesia

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

SUPPLEMENT NR. 13 | 2018

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 Orphan Anesthesia 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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

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 recommenations 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.

A survey of until now in A&I published guidelines can be found on:

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orphananesthesia

Anaesthesia recommendations for patients suffering from

Stiff Man Syndrome

Disease name: Stiff man syndrome / stiff person syndrome

ICD 10: G25.8

Synonyms: Moersch and Woltman syndrome, stiff limb syndrome, stiff trunk syndrome, PERM (progressive encephalomyelitis with rigidity and myoclonus)

A rare, disabling neurological disease characterised clinically by progressive muscle rigidity and painful spasms commonly affecting the axial and limb musculature. It was initially described by Moersch and Woltman in 1956. Its prevalence is said to be around 1/1,000,000.

It is observed to be twice more common in females. It is presently recognized as having 3 different forms: classic stiff man syndrome - also known as autoimmune - affects most of the body; limited stiff man syndrome - also called paraneoplastic - usually affects a particular region of the body (stiff limb, stiff body etc.) and is usually associated with paraneoplastic cancer conditions; PERM (progressive encephalomyelitis with rigidity and myoclonus) is a rapidly progressive form with diffuse central nervous system findings.

The autoimmune variety, accounting for around 60% of cases, is characterised by the presence of circulating anti-glutamic acid decarboxylase antibodies (anti-GAD). Although the exact aetiology is unknown, the autoimmune nature of the disease is supported by its association with other autoimmune disorders such as diabetes (30%), thyroiditis (10%), pernicious anaemia, cerebellar ataxia, and its response to immunotherapy. GAD is an essential, rate-limiting enzyme in the synthesis of GABA (gamma-aminobutyric acid). Due to the disinhibition from higher centres, there is exaggerated activity at the peripheral motor unit causing stiffness and rigidity.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

▶ **Citation:** Shanthanna H: Stiff Man Syndrome. Anästh Intensivmed 2018;59:S510-S518.
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Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

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Disease summary

Electrophysiologically, there is continuous and simultaneous activation of the agonist and antagonistic muscles due to involuntary activation. Age of onset is usually in the 3rd or 4th decade with active progression over several years. Typically, the axial, proximal and lower limb muscles are affected initially, later the disease spreads to the distal and upper limb musculature. Because of gait issues, the patients are susceptible to frequent falls. Clinical suspicion should be confirmed by laboratory testing for anti-GAD levels and electromyography testing. The seronegative disease is observed to be a paraneoplastic variety and the associated malignancies include breast, thymoma, lung, Hodgkin's lymphoma, multiple myeloma etc. The disease is treated by symptom modifying agents such as diazepam, baclofen and disease modifying agents such as steroids, plasma exchange and immunotherapy. Expected anaesthetic concerns involve the nature of the disease. The same applies to the associated therapy.

Typical surgery

There is no curative surgery involved. However, associated surgeries reported in literature include orthopaedic procedures, thymectomy, tumour resection surgeries, inguinal hernia, amputations, pregnancy C-sections, and heart valve replacement.

Type of anaesthesia and related concerns

Because of the rare nature of the disease, no specific technique has been recommended to be both safe and effective. A decision to employ either general anaesthesia (GA) or regional anaesthesia (RA) has to be made keeping in mind the type of surgery, the body region involved, the severity of the disease, the patient's preferences and the comfort level of the concerned anaesthesiologist.

The specific anaesthetic concerns are as follows. Case reports document significant hypotonia after GA. This could be due to the involved treatment with high dose benzodiazepines (diazepam) and muscle relaxants (baclofen). The use of muscle relaxants and inhaled vapours potentiates the hypotonia and may necessitate postoperative ventilation. Nevertheless, no prolongation of the muscular relaxant action has been demonstrated. It is also very important to continue with the treatment during the peri-operative period, so as not to precipitate any withdrawal. TIVA (total intravenous anaesthesia) has also been reported to be effective to minimise the risk of hypotonia.

Regional anaesthesia could be advantageous by providing effective and deep analgesia, without necessitating the use of muscle relaxants and inhalational agents. Safety and an effective use of RA has been demonstrated in several cases reported in the literature. Potential challenges to use of RA include patient positioning during the procedure, difficult anatomical landmarks, incidences of painful spasms and rigidity induced by the needle and the unpredictable nature of a spinal block due to alterations in spinal curvature. The presence of an intrathecal pump may necessitate a fluoroscopy-guided neuraxial procedure.

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Necessary additional diagnostic procedures (preoperative)

SMS is a progressive neurological disorder affecting the skeletal muscles. The necessary preoperative workup includes investigations to confirm the disease and also to know the extent of severity.

It is diagnosed by noticing symptoms of rigidity and spasms affecting the axial musculature and proximal muscles. Involvement of distal, especially calf and foot muscles should lead to suspicion of the paraneoplastic (anti-GAD-negative) disease. This necessitates a workup to rule out possible malignant conditions.

All SMS patients should have their anti-GAD levels checked to know the severity of the disease and the possible response to medications, including immunotherapy.

There are no reports of the disease's association with any cardiorespiratory disorder. It would be prudent to perform a pulmonary function test as it may help to assess the preoperative respiratory insufficiency, if any, and also guide postoperative respiratory support, if necessary.

Patients should have a complete blood work including electrolyte levels. Patients should also have a coagulation screen to help decide on a neuraxial procedure.

The appropriate working condition of an intrathecal pump, if available, should be assessed and documented.

Particular preparation for airway management

There are no reports on difficult airway primarily due to SMS. Patients with SMS are particularly sensitive to sudden stimulation and sounds, which may lead to spasms. One should take care to deepen the anaesthetic before any attempt at airway manipulation is made. This is of greater relevance in a patient with a known or suspected difficult airway.

Particular preparation for transfusion or administration of blood products

There are no specific recommendations regarding blood transfusion in stiff man syndrome.

Particular preparation for anticoagulation

There are no specific recommendations regarding anti-coagulation prophylaxis. However, it would be appropriate to consider them under high risk due to the nature of the disease and the associated mobility issues.

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Particular precautions for positioning, transport or mobilisation

Patients with SMS can have hyperlordotic spine with limited flexibility along with incomplete resolution of lordosis, when lying supine or bending forward from the waist. Because of this, there needs to be an individual specific adjustment of patient positioning using appropriate aids or pillows. It could be particularly challenging for RA procedures. Any voluntary movement, emotional upset or unexpected auditory or somatic stimuli can precipitate superimposed spasms.

Precautions must be considered to maintain a calm surrounding with appropriate level of sedation to limit any sudden stimuli.

Probable interaction between anaesthetic agents and patient's long term medication

For patients with SMS, there could be any or several of the following medications: diazepam, clonazepam, vigabatrin, baclofen, gabapentin, venlafaxin, plasma exchange, high-dosed corticosteroids, or intravenous gamma globulin. It is better to schedule a plasma exchange or IV globulin therapy close to the surgery to help decrease the level of anti-GAD antibodies. It is important to cover with steroid prophylaxis to supplement for the possible cortisone suppression. Diazepam and baclofen therapy are to be continued during the perioperative period. Any discontinuation can precipitate withdrawal and the anaesthetist must be aware of its possibility and the necessary treatment.

Baclofen withdrawal can cause increased spasticity, fever, labile heart rate and blood pressure, confusion, sweating, hallucinations and seizures. One needs to rule out acute autonomic dysreflexia, sepsis, serotonergic syndromes, illicit drug abuse, neuroleptic malignant syndrome, and malignant hyperthermia. Treatment may necessitate urgent neurocritical care, including oral baclofen therapy.

Muscle relaxants are best avoided as they act synergetic and can potentiate the hypotonia brought about by the use of medications. Any use of muscle relaxants needs monitoring and small titrated doses of a short-acting relaxant. There is insufficient information about the use of succinylcholine. Case reports on infants with stiff baby syndrome document both resistance to its effect and normal responses.

Both, inhalational agents and intravenous agents, have the potential to cause hypotonia based on GABA antagonism.

Anaesthesiologic procedure

There are no contraindications to any anaesthetic agents or procedure. However, due to the potentiation of muscle relaxation by anaesthetic agents, patients will have to be carefully monitored for hypotonia and the chances of supportive ventilation in the postoperative period. The mechanism of action of most anaesthetic drugs involves blockade of GABA receptors at various sites. This results in potentiation of muscle relaxation brought about by

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the use of ongoing therapy in SMS (1). Even intravenous agents involve GABA blockade and may potentiate muscle relaxation (2). In most published case reports the duration of the effects of skeletal muscle relaxants was found to be normal and as predicted. However, there are reports indicating that the duration of the second dose of pancuronium was longer than usual during cardiac surgery (3). In this regard, the following must be noted: There is no direct effect of SMS or its therapy on the neuromuscular junction and hence on the actions of non-depolarising relaxants. However, inhalational anaesthetics and intravenous agents can increase the proportion of densitised neuromuscular receptors and this can result in a non-competitive blockade and hence prolonged duration of action (4). Although no direct proof exists, this hypothesis may explain the conflicting observations reported (5). Hence it is suggested that the depth of neuromuscular blockade should be closely monitored and the muscle paralysis adequately reversed, keeping in mind that the there could be no correlation between the depth of muscle paralysis and hypotonia observed.

It is important to continue the regular medications and perhaps also to supplement any steroid therapy if the patient is on long-term steroid medication.

Particular or additional monitoring

Apart from routine monitoring which includes blood pressure, oxygen saturation, ECG and end-tidal CO_2, the following monitoring must also be done.

Neuromuscular paralysis.

Bispectral index: to be kept within a range of 40-60, indicating the depth of anaesthesia.

Temperature monitoring: Although no association with malignant hyperthermia is suspected, it allows us to differentiate the possible complications, including balcofen withdrawal and neuroleptic malignant syndrome.

Patient positioning and safety: Make sure that a patient prone to sudden spasms and rigidity is well supported.

Other invasive monitoring as demanded by the nature and duration of surgery.

Possible complications

Prolonged hypotonia

Intraoperative rigidity and spasms (not under general anaesthesia)

Needle trauma due to regional anaesthesia procedures

Baclofen withdrawal

Potential for respiratory insufficiency due to muscular rigidity.

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Postoperative care

Similar precautions as above have to be taken. Patient may need supportive ventilation.

Information about emergency-like situations / Differential diagnostics

caused by the illness in order to distinguish between a side effect of the anaesthetic procedure and a manifestation of the diseases, e.g.:

A SMS patient receiving a high-dose baclofen therapy is always prone to withdrawal symptoms. The patient must have a pocket card mentioning the daily dose and emergency contact details.

There are no emergency surgical indications specific to the disease.

Ambulatory anaesthesia

Regional anaesthesia has several advantages. However, it must be considered in the light of its practical applicability. Patients with SMS may not be appropriate candidates for ambulatory surgery.

Obstetrical anaesthesia

It is difficult to predict the changes associated with pregnancy in patients with SMS. However, the existing case reports suggest that these patients should continue to maintain their therapy during pregnancy. One patient had a spasm during episiotomy despite being on epidural (6). Other case reports also suggest an incomplete control of muscle spasms and disease symptoms when diazepam is withdrawn from treatment (7). Introduction of baclofen therapy could decrease the requirement for diazepam and thereby limit its deleterious effects on the baby. There is one case report of disease remission at 2 weeks postpartum (8). There is no consensus on the preferred route of delivery.

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