

Anesthesia 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 characterized 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 1/1000000.

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-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 etiology is unknown, the autoimmune nature of the disease is supported by its association with other autoimmune disorders such as diabetes (30%), thyroiditis (10%), pernicious anemia, cerebellar ataxia, and its response to immunotherapy. GAD is an essential, rate limiting enzyme in the synthesis of GABA (gamma amino butyric 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



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

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 which later spreads to 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 eletromyography 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, plama exchange and immunotherapy. Expected anesthetic concerns involve the nature of the disease and also by the associated therapy.

Typical surgery

There is no curative surgery involved. However associated surgeries reported in literature include orthopedic procedures, thymectomy, tumor 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, involved body region, disease severity, patient preference and the comfort level of the concerned anaesthesiologist.

Specific anaesthetic concerns are as follows. Case reports document significant hypotonia after GA. This could be due to the involved treatment by high dose benzodiazepines (diazepam) and muscle relaxants (baclofen). Use of muscle relaxants and inhaled vapours potentiate 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 chances 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 effective use of RA has been demonstrated through several case reports in literature. Potential challenges to use of RA include patient positioning during the procedure, difficult anatomical landmarks, chances of painful spasms and rigidity induced by the needle and the unpredictable nature of spinal block due to alterations in spinal curvature. Presence of intrathecal pump may necessitate a fluoroscopy guided neuraxial procedure.

Necessary additional diagnostic procedures (preoperative)

SMS is a progressive neurological disorder affecting the skeletal muscles. Necessary preoperative work up 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 axial musculature and proximal muscles. Involvement of distal, especially calf and foot muscles should lead to suspicion of paraneoplastic (anti-GAD negative) disease. This necessitates workup to rule out possible malignant conditions.

Any SMS patient should have their anti GAD levels checked to know the severity and possible response to medications, including immunotherapy.

There are no reports of its association with any cardiorespiratory disorder. It would be prudent to perform a pulmonary function test as it may help 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.

Appropriate working condition of intrathecal pump, if any, should be assessed and documented.

Particular preparation for airway management

There are no reports of 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 anesthetic before any attempt at airway manipulation is made. This is of greater relevance in a patient with 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 nature of the disease and the associated mobility issues.

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 individual specific adjustment of patient positioning using appropriate aids or pillows. It could be particularly challenging for RA procedures. Any voluntary movement, emotional upsets or unexpected auditory and 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

Patients of SMS could be on any one or more of the following medications: diazepam, clonazepam, vigabatrin, baclofen, gabapentin, venlafaxin, plasma exchange, high-dose 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 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 can potentiate, acting synergistically, the hypotonia brought about by the use of medications. Any use of muscle relaxants needs monitoring and small titrated doses of short acting relaxant. There is insufficient information about the use of succinyl choline. Case reports of infants with stiff baby syndrome document resistance to its effect or normal response.

Both inhalational agents and intravenous agents have the potential to cause hypotonia by causing GABA antagonism.

Anaesthesiologic procedure

There are no contraindications to any anesthetic agents or procedure. However due to the potentiation of muscle relaxation due to 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 the use of on going therapy in SMS (1). Even intravenous agents involve GABA blockade and may potentiate the muscle relaxation (2). In most published case reports the duration of

effect of skeletal muscle relaxants were found to be normal and as predicted. However there are reports that the duration of the second dose of pancuronium was longer than the usual time range during a 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 nondepolarising relaxants. However inhalational anaesthetics and intravenous agents can increase the proportion of sensitised 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 be closely monitored and the muscle paralysis must be adequately reversed, keeping in mind that there could be no correlation between the depth of muscle paralysis and hypotonia observed.

One must keep in mind to continue the regular medications and also possibly to supplement any steroid therapy if the patient is on long term steroid medication.

Particular or additional monitoring

Apart from the routine monitoring which includes blood pressure, oxygen saturation, ECG and endtidal CO₂ the following monitoring must also be done.

Neuromuscular paralysis.

Bispectral index: to be kept within 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 baclofen withdrawal and neurolept malignant syndrome.

Patient positioning and safety: to make sure that a patient prone for 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.

Postoperative care

Similar precautions as above need 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.:

Patient on SMS with high dose baclofen therapy is always prone for 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 must be considered in light of its practical applicability. Patients of SMS may not be appropriate candidates for ambulatory surgeries.

Obstetrical anaesthesia

It is difficult to predict the changes associated with pregnancy in patients of SMS. However the existing case reports suggest that the 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 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 post partum (8). There is no consensus on the preferred route of delivery.

References indicated in the manuscript

- 1) Johnson JO, Miller KA. Anesthetic implications in stiff-person syndrome. *Anesth Analg* 1995;80:612- 3
- 2) Garcia PS, Kolesky SE, Jenkins A. General anesthetic actions on GABA(A) receptors. *Curr Neuropharmacol*. 2010 Mar;8(1):2-9.
- 3) Ferrandis R, Belda J, Llau JV, Belda C, Bahamonde JA. Anesthesia for cardiac surgery on a patient with stiff person syndrome. *J Cardiothorac Vasc Anesth*. 2005 Jun;19(3):370-2.
- 4) Jonas Appiah-Ankam and Jennifer M Hunter. Pharmacology of neuromuscular blocking drugs *Contin Educ Anaesth Crit Care Pain* (2004) 4 (1): 2-7.
- 5) Elkassabany N, Tetzlaff JE, Argalious M. Anesthetic management of a patient with stiff person syndrome. *J Clin Anesth*. 2006 May;18(3):218-20.
- 6) Weatherby SJ, Woolner P, Clarke CE. Pregnancy in stiff-limb syndrome. *Mov Disord* 2004;19:852–4.
- 7) Amyradakis G, Carlan SJ, Bhullar A, Eastwood J. Pregnancy and stiff person syndrome. *Am J Med*. 2012 Mar;125(3):e1-2.
- 8) Cerimagic C, Bilic E. Stiff-person syndrome first manifesting in pregnancy. *Gynecol Obstet Invest* 2009;67:134–6.

Additional literature links

- 1) Dalakas MC, Fujii M, Li M, McElroy B. The clinical spectrum of anti-GAD antibody-positive patients with stiff-person syndrome. *Neurology* 2000;55:1531-55.
- 2) Levy LM, Dalakas MC, Floeter MK. The stiff-person syndrome: an autoimmune disorder affecting neurotransmission of gamma-aminobutyric acid. *Ann Intern Med* 1999;131:522 – 530.
- 3) Brown P, Marsden CD. The stiff man and stiff man plus syndromes. *J Neurol* 246:648-652.
- 4) Armon C, McEvoy KM, Westmoreland BF, McManis PG. Clinical neurophysiologic studies in stiff-man syndrome: use of simultaneous video-electroencephalographic–surface electromyographic recording. *Mayo Clin Proc*. 1990;65(7):960-967.
- 5) Lorish TR, Thorsteinsson G, Howard FM Jr. Stiff-man syndrome updated. *Mayo Clin Proc*. 1989;64(6):629-636.
- 6) Shaw PJ. Stiff-man syndrome and its variants. *Lancet*. 1999;353: 86-87.
- 7) <http://www.ninds.nih.gov/disorders/stiffperson/stiffperson.htm>
- 8) Iwata T, Inoue K, Mizuguchi S, Morita R, Tsukioka T, Suehiro S. Thymectomy for paraneoplastic stiff-person syndrome associated with invasive thymoma. *J Thorac Cardiovasc Surg*. 2006 Jul;132(1):196-7.
- 9) B Bouw J, Leendertse K, Tijssen MA, Dzoljic M. Still person syndrome and anesthesia: case report. *Anesth Analg* 2003;97:486- 7.
- 10) Ledowski T, Russel P. Anaesthesia for stiff person syndrome: successful use of total intravenous anaesthesia. *Anaesthesia* 61: 725.
- 11) Murphy C, Shorten G: Train of four fade in a child with stiff baby syndrome. *Paediatr Anaesth* 10:567-569,2000.
- 12) Haslam N, Price K: Anaesthesia for stiff-person syndrome. *Anaesthesia* 57:298-299, 2002.

Last date of modification: January 2014

This guideline has been prepared by:

Author

Harsha Shanthanna, anaesthesiologist, Health Sciences Centre, Ontario, Canada
harshamd@gmail.com

Peer revision 1

Raquel Ferrandis, anaesthesiologist, Hospital Clínic Universitari de València, Valencia, Spain
raquelferrandis@gmail.com

Peer revision 2

Jennifer Goldkamp, Department of Obstetrics, St Louis University School of Medicine, St Louis, Missouri, USA
jgoldka2@slu.edu
