

Anaesthesia recommendations for **Hereditary spastic paraplegia**

Disease name: Hereditary spastic paraplegia (HSP)

ICD 10: G11.4

Synonyms: Strumpell-Lorrain disease (designating one type of HSP called SPG4); Familial spastic paraplegia

Disease summary: Strumpell-Lorrain disease or Hereditary spastic paraplegia describes a group of rare and heterogeneous genetic neurological disorders [1]. In Europe, HSP is estimated to affect 1 to 9 per 100,000 individuals [2–6].

HSP is an inherited neurodegenerative group of disorders which mainly affects primarily the corticospinal tract with a distal to proximal retrograde axonal degeneration. For this reason, in the so-called pure HSP cases, the clinical picture is characterized mainly by a progressive spasticity of the lower limbs leading to paraparesis or paraplegia affecting several members of the same family. Many patients experience only stiffness and weakening of the leg muscles; a few require the use of a wheelchair. Progression of the disease to the rest of the corticospinal tracts, to peripheral nerves, to the cerebellum or to the brain explains the other additional symptoms commonly found in complicated or complex HSP cases: cerebellar ataxia, dysarthria, extrapyramidal disorder, mental retardation, dementia, epilepsy, retinopathy, deafness, axonal or demyelinating neuropathy and eventually systemic signs. Clinical diagnosis is based on four criteria [7]: exclusion of differential diagnoses, compatible family history (although not obligatory), progressive disturbance of gait and corticospinal tract deficits in the lower limbs with hyperreflexia.

Spinal cord atrophy is a common finding in HSP [8]. Conventional brain magnetic resonance imaging findings are usually normal in patients with HSP but multiple diffusion tensor indices can be disrupted [9]. It can disclose different findings in complicated or complex HSP, such as thin corpus callosum, leukoencephalopathy and hyperintensity sign in the corticospinal tract.

Diagnosis must be confirmed by DNA analysis. The most commonly involved genes are the SPG4 and SPG3A respectively encode for the proteins spastin and atlastin. Transmission of HSP can be autosomal dominant, autosomal recessive, X-linked or maternally inherited (mitochondrial inheritance [10]). Mutations in more than 80 distinct loci and more than 50 mutated gene products have been identified in patients with HSP [11,12]. The main pathogenetic mechanisms underlying the clinical phenotype include membrane trafficking disturbance, impairment of organelle transport, morphogenesis and distribution in neuronal cells, and mitochondrial dysfunction. Membrane trafficking and organelle morphogenesis and distribution are important for axonal development, maintenance and degeneration [1,13].

There is no specific pharmacological treatment. Treatment is symptomatic and includes physical therapy, benzodiazepines, oral or intrathecal baclofen [14] and injections of Botulinum toxin [15] to reduce spasticity. By blocking potassium channels, prolonging action potentials and thereby increasing neurotransmitter release at the neuromuscular junction, dalfampridine may be useful in the treatment of HSP [16,17].

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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Typical surgery

Patients are frequently evaluated for surgeries related to spasticity control, including selective dorsal rhizotomy, tenotomy and other procedures.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia.

Six case reports involving the use of general anaesthesia have previously been published [18–22]. In all these case reports, no complications from hypnotic or opioid drugs were reported.

Some authors prefer regional spinal anaesthesia to general anaesthesia [23–25]. HSP is not known to increase local anaesthesia drug toxicity, and no complications have been reported.

Necessary additional pre-operative testing (beside standard care)

No specific diagnostic procedure is required preoperatively.

Particular preparation for airway management

No specific preparation is required for airway management.

Particular preparation for transfusion or administration of blood products

No specific preparation is required for administration of blood products.

Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. Except is case of impaired mobility of advanced stage patients: it may suggest a higher risk of postoperative thrombosis [26].

Particular precautions for positioning, transportation and mobilisation

No specific preparation is required for positioning, transport or mobilisation.

Interactions of chronic disease and anaesthesia medications

Interferences are possible between baclofen and curare and general anaesthetics. They may be responsible for neuromuscular block augmentation, heart rhythm disorders, arterial hypotension or increased sedation but weaning is much more dangerous [27–30]. To avoid the emergence of weaning, it is recommended not to interrupt intrathecal baclofen.

No interaction between anaesthetic agents and dalfampridine had been described in clinical practice. Dalfampridine (4-aminopyridine or 4-AP) selectively blocks voltage-gated potassium channels, prolongs the action potential, increases calcium influx, and subsequently, enhances interneuronal and neuromuscular synaptic transmission. The 4-AP is used in animal models to increase the release of GABA and to study the action of GABAergic antagonists. The CAM of halogens is often used as an endpoint. It is assumed that the 4-AP does not modify the CAM in these models [31]. Clinical cases of poisoning reveal that its mechanism of action has cholinergic characteristics [32]; propofol sedation was then used without complication. The central cholinergic action produces antagonism to ketamine anaesthesia in rats [33,34]. This effect was also observed in pediatric anaesthesia [35]. The 4-AP has been used as an antidote for a rohypnol coma induced [36]. It also reduces morphine-induced respiratory depression but the antinociceptive activity of morphine is unaffected [37,38]. The antagonization of anaesthetic drugs is described for doses higher (0,3 to 1,0 mg/kg i.v.) than that used in the treatment of the disease (a tablet of 10 mg per twelve hours). By precautionary principle, Dalfampridine should be interrupted on the morning of surgery.

An overdose may be observed in patients with postoperative acute renal failure [39]. Dalfampridine is contraindicated in pregnant or nursing women [39].

Anaesthetic procedure

There are no data in the literature to support a recommendation of TIVA or inhalatory anaesthesia. The problem is that HSP is a heterogeneous group of genetic diseases and there is no certainty that anaesthetic drugs will have the same action in all variants. Depth of anaesthesia monitoring may be the best approach in HSP patients.

The choice of neuromuscular blocking agents must be made with extreme care in HSP. The use of succinylcholine is contraindicated in HSP as it may induce hyperkalaemia due to upregulation of nicotinic acetylcholine receptors [40]. Non-depolarizing muscle relaxants carry a risk of an exaggerated muscle relaxant response. The use of rocuronium had been described in most of cases [22,41,42] and sugammadex had been used in three cases due to the presence of moderate neuromuscular block at the end of surgery. After the use of sugammadex, no re-curarization was observed. Rocuronium appears to be the best choice when muscle relaxation is indicated, due to the possibility of antagonizing its effects with sugammadex. Long-acting neuromuscular blockers should be avoided and a train of four ratio over 0.9 must be obtained before extubating. Recovery with neostigmine may expose to re-curarization.

Particular or additional monitoring

Monitoring of the neuromuscular blockade is strictly recommended if any neuromuscular blocking agent is used: it is useful to obtain baseline values before injection the non-

depolarizing neuromuscular blocking agent. The rocuronium–sugammadex association seems to be the most secure.

Depth of anaesthesia monitoring is strongly recommended in case of general anaesthesia.

Possible complications

Patients with HSP are at risk for hyperkalaemic cardiac arrest with the use of succinylcholine.

The neuromuscular block duration is increase when neuromuscular blocking agents are used.

There is no evidence of an elevated risk of malignant hyperthermia.

Post-operative care

Degree of postoperative monitoring is depending on surgical procedure and preoperative condition of the patient. Intensive care is not mandatory.

Disease-related acute problems and effect on anaesthesia and recovery

Disease triggered emergency-like situations are not common in HSP.

Ambulatory anaesthesia

Ambulatory anaesthesia (according to common guidelines) is probably possible in HSP patient with early disease and low risk surgery.

Obstetrical anaesthesia

Caesarean section under general anaesthesia or spinal anaesthesia have already been described without complication [19,23]. Childbirth or caesarean section have not been described under epidural analgesia/anaesthesia. HSP is not known to increase local anaesthesia drug toxicity, and no complications have been reported. The risk/benefit report should be evaluated with the neurologist's opinion.

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