

orphananesthesia

Anaesthesia recommendations for patients suffering from **Homocystinuria**

Disease name: Homocystinuria

ICD 10: E72.11

Synonyms: Homocystinemia, classical homocystinuria, cystathionine b-synthase deficiency, CBS deficiency

Classical homocystinuria is a rare autosomal recessive inherited disorder. It is caused by a deficiency of the enzyme cystathionine- β -synthase leading to accumulation of homocysteine and methionine. High levels of plasma homocysteine are associated with vascular injury via mechanisms of oxidative damage, vascular smooth muscle proliferation, promotion of platelet activation and aggregation, and disruption of normal procoagulant-anticoagulant balance favouring thrombosis. The current cumulative detection rate of CBS deficiency is 1 in 344,000. Classical homocystinuria involves four major organ systems: eye, skeletal, central nervous system and cardiovascular system. It can also involve liver, skin and hair. The diagnosis is usually confirmed by the presence of elevated levels of total homocysteine and methionine in plasma. Diagnosis at early age should aim to prevent ocular, musculoskeletal and intravascular complications and to ensure normal development. However, late diagnosis should focus at reducing life threatening thromboembolic events. There is no cure for homocystinuria. One third of the patients with CBS deficiency are vitamin B6 responsive, and they do not need other treatments. Patients with BCS not B6 responsive are treated with a low-methionine diet, vitamin B6, vitamin B12, folic acid and betaine. These patients most commonly present for ophthalmic surgeries for ectopia lentis. Fatal episodes of thromboembolic phenomena may occur in these patients following general anaesthesia if not diagnosed before or if there is poor metabolic control. To minimize these risks we suggest good compliance to diet and treatment, avoidance of dehydration and hypoglycemia, reduction in blood viscosity and platelet aggregation by medication (if poor metabolic control), and the maintenance of good venous return, avoidance of nitrous oxide and the postoperative early ambulation of the patient.

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Typical surgery

Ocular surgery for unilateral or bilateral lens extraction for ectopia lentis.

Type of anaesthesia

Surgery can be performed under local or general anaesthesia. Due to the increase in risk of thromboembolic episode with general anaesthesia, local anaesthesia is the preferred choice for ocular surgery. However, due to occurrence of mental retardation and uncooperative behaviour in some of these patients, general anaesthesia may be necessary.

Regional anaesthesia also carries a risk of thromboembolic event as spinal anaesthesia can promote peripheral vascular stasis secondary to the sympathetic blockade produced. Epidural anaesthesia also carries the same risk but to lesser extent.

Any nerve block performed in the immediate vicinity to large- and medium-sized vessels, e.g., brachial plexus block, could initiate vascular damage culminating in thromboembolic phenomena.

The goals of anaesthetic management should be:

- (a) maintenance of high cardiac output and rapid circulation time
- (b) prevention of thromboembolism
- (c) reduction of peripheral vascular resistance and improvement of peripheral perfusion
- (d) avoidance of dehydration and hypoglycaemia
- (f) rapid recovery and early ambulation.

Nitrous oxide should be avoided because of an increase in blood homocysteine level due to the inhibition of methionine synthase enzyme by nitrous oxide.

Titrated use of short acting sedative drugs in these patients has found no contraindication until now. However, use of narcotics or drugs causing respiratory depression leading to delayed ambulation should be avoided.

Necessary additional diagnostic procedures (preoperative)

Diagnosis is made by the analysis of plasma amino acids (elevated methionine and low cysteine) and plasma total homocysteine (elevated).

In addition to routine investigation, the haematocrit, clotting time, prothrombin time, and partial thromboplastin time and platelet count should be determined.

Blood glucose level is checked to avoid hypoglycaemia in these patients.

Echocardiography and electrocardiography should be done to rule out any cardiac abnormality, as many case reports have found valvular heart disease in these patients.

Particular preparation for airway management

Although there can be difficulty in airway management in these patients due to occurrence of high arched palate and Marfanoid habitus, no data regarding difficult airway managements has been published until now.

Particular preparation for transfusion or administration of blood products

Not reported until now.

As most common surgeries in these cases are ophthalmic surgeries, which are associated with minimal blood loss, there is less likely requirement of any transfusion.

Particular preparation for anticoagulation

Preoperative measures include:

- a) Good treatment and diet compliance to lower or control serum methionine and total homocysteine levels (<45 $\mu\text{mmol/l}$ according to Carrillo-Carrasco et al. 2012)
- b) Adequate preoperative intravenous hydration
- c) Pharmacological measures described in the literature are: low dose aspirin (100 mg/day), dipyridamole (100 mg four times a day) and low molecular weight heparin intraoperatively, but no formal recommendations exist. The need of such treatment should be assessed on an individual basis. Drugs that predispose to a hypercoagulable state (e.g. oral contraceptives) should be avoided.

Intraoperative measures include:

- a) Maintenance of intraoperative cardiac output
- b) Pneumatic stockings to prevent peripheral stagnation of blood
- c) Use of dextran 40 to diminish platelet adhesiveness
- d) Use of glucose solutions to avoid hypoglycaemia.

Postoperative - early ambulation.

Particular precautions for positioning, transport or mobilisation

Not reported.

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

There is no evidence of interaction of anaesthetic agents with patient's long-term medication.

Anaesthesiologic procedure

Preoperatively prolonged fasting hours leading to dehydration should be avoided.

Use of various preventive measures to prevent thromboembolism before surgery including adequate intravenous hydration and pharmacological measures including administration of antiplatelet and anticoagulants have been described in anaesthesia literature. Some authors have successfully used Dextran 40 and compression stocking during general anaesthesia to increase venous return and to prevent venous stasis.

Use of nitrous oxide (N₂O) should be avoided in these patients as N₂O causes increase in the levels of plasma total homocysteine by inhibiting methionine synthase.

Anaesthetic agents having vasodilator action like halothane should be preferred.

Short acting anaesthetic drugs associated with rapid recovery are beneficial in these cases.

Intraoperative dextrose infusion can be used to minimize risk of hypoglycaemia which is commonly found in these patients due to increase in insulin level.

Particular or additional monitoring

Not reported until now.

Possible complications

Patients with homocystinuria are prone to develop spontaneous thromboembolic phenomena. Serious complication of thromboembolism includes optic atrophy, hemiparesis, hypertension due to renal infarcts, focal seizures and fatal pulmonary embolism.

Use of nitrous oxide can increase the platelet adhesiveness leading to thromboembolism.

Hypoglycaemia can occur due to alteration in insulin release associated with high methionine levels. This can be avoided with exogenous glucose during periods of fasting.

Postoperative care

Postoperatively patients should be monitored for 48-72 hours for any thromboembolic event.

Subcutaneous low-molecular-weight heparin could be administered postoperatively until ambulation is possible.

Monitor blood glucose level to prevent hypoglycaemia. Adequate hydration should be maintained.

Early ambulation is demanding in these cases if possible.

Continue anticoagulant and antiplatelet drug after discussion with surgical team for risk of bleeding.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Not reported.

Ambulatory anaesthesia

Ambulatory anaesthesia is demanding in these patients as it decreases the risk of thromboembolic event.

Obstetrical anaesthesia

Pyridoxine-responsive women have better outcome pregnancies. There is much less experience of outcome in nonresponsive women. Thromboembolism and cerebrovascular accident are main concern in these patients. As normal pregnancy itself causes hypercoagulable state, these patients may require anticoagulant, e.g. unfractionated heparin or low-molecular-weight heparin antenatally. Some patients described in the literature received low-molecular-weight heparin during the last two weeks of pregnancy and the first six weeks in the postpartum period. Aspirin in low doses was also given. Regional anaesthesia can be performed after stopping low-molecular-weight heparin or unfractionated heparin for recommended time if needed.

Literature and internet links

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This guideline has been prepared by:

Author

Kewal Krishan Gupta, Anaesthesiologist, GGS Medical College & Hospital,
Faridkot, Punjab, India
doc.krishan31@yahoo.co.in

Peer revision 1

Nuria García Segarra, Centre des maladies moléculaires (CMM), Clinique Infantile 02-32
Lausanne, Switzerland
Nuria.Garcia-Segarra@chuv.ch

Peer revision 2

Sufin Yap, Consultant Paediatrician in Metabolic Medicine, Sheffield Children's Hospital,
NHS Foundation Trust, Sheffield, United Kingdom
Sufin.Yap@sch.nhs.uk

Peer revision 3

John Walter, Honorary Clinical Professor of Inherited Metabolic Medicine,
Central Manchester University Hospitals NHS Foundation Trust. Saint Mary's Hospital,
Manchester, United Kingdom
john.walter@cmft.nhs.uk