



## ANAESTHETIC MANAGEMENT OF A PATIENT WITH HYPERHOMOCYSTEINEMIA FOR TOTAL ABDOMINAL HYSTERECTOMY

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**ABSTRACT** Hyperhomocysteinemia is a disorder caused by a disruption of any of the enzymes or cofactors involved in the pathways of homocysteine metabolism. The resultant high plasma levels of homocysteine increase the risk for thromboembolic events. These patients are frequently anticoagulated in the perioperative setup. Interruption of anticoagulant therapy may subject the patient to an increased risk of thrombosis, infarction, and death. Neuraxial anaesthesia techniques may be relatively contraindicated in anticoagulated patients and nitrous oxide may exacerbate the condition by inhibiting the conversion of homocysteine to methionine. We describe a case of the anaesthetic management of a unique case of hyperhomocysteinemia with multiple recent thrombotic episodes proposed for total abdominal hysterectomy conducted under general anaesthesia, the intraoperative and postoperative monitoring and considerations.

**KEYWORDS :** Hyperhomocysteinemia, thromboembolism, general anaesthesia, nitrous oxide.

### INTRODUCTION

Homocystinuria is a rare inherited metabolic disorder with an incidence of about 1 in 300000 live births.<sup>1</sup> It is associated with substantial elevations in plasma and urine homocysteine levels due to deficient activity of enzyme cystathionine- $\beta$ -synthase. Clinical manifestations of homocystinuria include developmental delay, marfanoid appearance, osteoporosis, ocular abnormalities, thromboembolic disease, and severe premature atherosclerosis.<sup>2</sup> Hyperhomocysteinemia is a related but similar entity with a less marked increase in plasma levels of homocysteine. Although unassociated with the clinical stigmata, it is an independent and modifiable risk factor for atherosclerotic vascular disorders affecting coronary, cerebral and peripheral vascular systems ultimately leading to stroke and other vascular events.<sup>3</sup> Although this disorder is rare, surgical intervention and anaesthetic requirements are frequently needed in these patients, especially for ophthalmic and skeletal abnormalities and to a lesser extent for other gynaecologic and urologic indications. It is associated with a high incidence of adverse events and mortality during the perioperative period. Here we describe the anaesthetic management of a patient with a large uterine fibroid with abnormal uterine bleeding for total abdominal hysterectomy.

### CASE REPORT

A 46-year-old female, presented to gynaecology department with a history of heavy menstrual bleeding for the past 6 months with severe anemia (Hb 3.7gm/dl). She is a known case of peripheral occlusive vascular disease for 7 years on irregular medication. She was diagnosed with hyperhomocysteinemia, 6 months back while being evaluated for acute cerebellar infarction and upper limb ischemia. The patient was on dual antiplatelets, direct-acting factor Xa inhibitor-Rivaroxaban, and platelet aggregation inhibitor-Cilostazole. Additionally, she was started on vitamin supplements like pyridoxine, folic acid, and methylcobalamin. She is a known case of hypothyroidism on hormone supplements. She has a history of multiple blood transfusions.

Airway examination revealed a normal study. There was no evidence of marfanoid habitus. During the investigation, for prothrombotic state, the homocysteine level was 5  $\mu$ mol/L and within the normal limits (3-18  $\mu$ mol/L) before surgery. Haemoglobin was corrected to 10.4 gm/dl before taking up for surgery. Other haematological investigations and coagulation profile were essentially normal. An earlier MRI brain taken 6 months prior showed a subacute infarct involving the left cerebellar hemisphere. CT angiogram showed an unstable thrombus involving the left subclavian artery and total luminal occlusion of radial artery. Recent arterial doppler however reported a thrombus in the mid-brachial artery causing only moderate luminal narrowing with no evidence of vascular compromise distally. ECG, chest radiograph, renal, liver, and thyroid function tests

were unremarkable. Echocardiography was done to rule out any cardiac anomaly and revealed a normal study.

Preoperatively, dual antiplatelets and rivaroxaban were stopped 5 days before surgery and bridged to LMWH 40 IU s/c twice daily. Cilostazole was withheld 2 days prior to surgery. The patient was advised 8 hours of fasting for solid foods and encouraged to take clear oral fluids upto 2 hours prior to surgery. She was started on intravenous fluids to avoid dehydration. After shifting the patient to the theatre, all standard monitors were attached and basal vital parameters were recorded. However, radial pulse volume was feeble on the left side and was documented. Mechanical thromboprophylaxis (compression stockings) was applied on both lower limbs. Care was taken during patient positioning to avoid inadvertent injuries.

The patient was induced with fentanyl, propofol and vecuronium as per institutional protocol after adequate preloading. Anaesthesia was maintained with oxygen, isoflurane, air, and intermittent vecuronium boluses. Nitrous oxide was avoided. Euvolemia and normal haemodynamics were maintained. Blood glucose level was monitored at regular intervals. There was a single episode of hypoglycemia which was promptly corrected with 5% dextrose infusion. The intraoperative course was uneventful. After surgery, a bilateral transverse abdominus plane block was given with 20 ml of bupivacaine 0.25% on each side for postoperative analgesia. Residual neuromuscular blockade was reversed and the patient was extubated after achieving adequate respiratory efforts. Intravenous fluid was continued into the postoperative period until oral intake was appropriate. Adequate analgesia was maintained with paracetamol and tramadol. High doses of narcotics and drugs causing respiratory depression were avoided to promote early ambulation. Rivaroxaban was resumed within 24 hrs post surgery after ensuring renal function and adequate hemostasis. She was started on LMWH. Other antiplatelets were resumed on the third postoperative day. After 3 days of stay in ICU patient was shifted to the ward and discharged after seven days.

### DISCUSSION

Hyperhomocysteinemia is a condition characterized by an elevation of homocysteine levels in the blood due to genetic or acquired changes in the metabolic pathway. It may be acquired as a result of deficiencies of vitamin B12 and folate B9.<sup>2</sup> The hereditary defect lies within the methionine-homocysteine pathway.<sup>4</sup> In both ways there is disruption of the normal procoagulant anticoagulant balance favoring thrombosis due to the increasing plasma levels of homocysteine.

Vitamin B supplements, folic acid, and anticoagulant therapy to prevent vascular thrombosis comprise the conventional treatment for hyperhomocysteinemia. Vitamin supplements are indicated to normalize the levels of homocysteine before surgery (ideal

perioperative levels <50 μmol/L for patients with homocystinemia).<sup>5</sup>

Large bleeding uterine fibroids are an indication of hysterectomy. Patients with hyperhomocystinemia are on anticoagulant therapy which may further exacerbate the abnormal uterine bleeding. These patients pose a unique challenge to anesthesiologists when it comes to choosing a type of anesthesia. Surgery may be done under general or regional anesthesia. General anesthesia itself has got thrombotic risks, but it may be necessary in certain circumstances. Regional anaesthesia also carries a risk of thromboembolic events as spinal anaesthesia can promote peripheral vascular stasis secondary to sympathetic blockade thereby increasing thrombotic risk.<sup>6</sup>

The goals of our anaesthetic management were maintenance of high cardiac output and rapid circulation time, prevention of thromboembolism<sup>7</sup>, reduction of peripheral vascular resistance and improvement of peripheral perfusion, avoidance of dehydration, avoidance of hypoglycemia<sup>8</sup>, and early ambulation.

Our case is peculiar because the patient was on multiple anticoagulants with a recent history of multiple thrombotic episodes. She had a Caprini Risk Score of 7 and belonged to the high risk category for venous thromboembolism, necessitating early resumption of anticoagulant therapy.<sup>9</sup> High risk of cerebral infarction and dislodgement of thrombus warranted the use of a safe technique that could help control hemodynamics precisely. If nitrous oxide is not used then general anaesthesia is considered a safe solution as we did in our case. Nitrous oxide slows the conversion of homocysteine to methionine by irreversibly inhibiting methionine synthetase which leads to an increase in the level of homocysteine. It not only exacerbates homocystinemia but also impairs endothelial function and promotes procoagulant activity such as platelet adhesiveness, factor 5 activation, protein C inhibition, and prothrombin and plasminogen activator binding.<sup>10</sup>

The mechanism of hypoglycaemia is due to an increase in methionine level which stimulates the pancreatic cell to release more insulin.<sup>11</sup> Our patient had fairly normal blood sugar levels except for a single episode of low normal value which was picked up by hourly glucose monitoring. Care was taken at the time of positioning as these patients have increased risk of osteoporosis. Adequate analgesia, thromboprophylaxis, and euglycemia ensured uneventful post-operative recovery.

## CONCLUSION

It is reasonable to assume that both general as well as regional anaesthesia may be used in patients with hyperhomocystinemia, but the core tenets of anaesthetic management has to be followed in either method. The choice of anaesthesia should be based on the specific patient factors and coagulation status. Finally, due to the inherent risk of thromboembolic complications, proper preparation of the patient and perioperative thromboprophylaxis becomes essential.

## Declaration Of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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**Conflicts Of Interest:** There are no conflicts of interest

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