

## Hyperhomocysteinemia: Anesthetic concerns

Sir,

Homocystinuria is an inherited autosomal recessive metabolic disorder, which occurs due to deficiency of enzymes (methionine synthase, cystathionine  $\beta$  synthase) involved in methionine metabolism.<sup>[1]</sup> Homocysteinemia, a separate, but related entity, may be due to similar genetic pre-disposition or in association with chronic renal failure, hypothyroidism, malignancies, methotrexate treatment, oral contraceptive use, and smoking. Hyperhomocysteinemia predisposes to coronary and cerebrovascular thrombotic disease.<sup>[2]</sup>

A 28-year-old male patient presented to us with jejunal obstruction and was subsequently posted for laparotomy. He was a known case of coronary artery disease (CAD), but was not receiving any medications and his Echocardiography showed CAD, dilated left ventricle (LV) with regional wall motion abnormalities in left anterior descending

and left circumflex territories, severe LV dysfunction with ejection fraction of 30-35%. During investigation, for prothrombotic state following values were noted: Homocysteine levels of 25.37  $\mu\text{mol/l}$  (3.7-13.9  $\mu\text{mol/l}$ ), factor VIII levels 396% (70-150%), C-reactive protein levels of 22.5 mg/l (0-5 mg/l), protein C (78.1%), protein S (92%), factor V Leiden (148%), and factor IX (98.4%). Lipid profile, coagulation profile, and lower limb venous Doppler study was normal.

Pre-operatively, he was started on aspirin, atorvastatin, carvedilol, folic acid, pyridoxine, methylcobalamin, and enoxaparin. Adequate hydration and ambulation were also assured. In the operation theater, other than routine monitors, invasive blood pressure, and cardiac output monitoring using the flotrac/vigileo™ device (Edwards Lifesciences, Irvine, CA, USA) was carried out continuously. Pneumatic compression devices were applied on both legs.

Modified rapid sequence induction of anesthesia was carried out with fentanyl, propofol, and rocuronium. He received oxygen, air, sevoflurane for maintenance. Induction was marked by hypotension and decrease in cardiac output and was managed by lactated ringer, intermittent boluses of mephentermine and dopamine infusion, titrated according to stroke volume variation, systemic vascular resistance index, and cardiac output respectively. One episode of hypoglycemia was also noted despite continuous infusion of 25% dextrose. After completion of resection and anastomosis and tracheal extubation, dopamine could be tapered off. In post-operative period, adequate analgesia was ensured, invasive and glucose monitoring, deep venous thrombosis (DVT) prophylaxis and all his pre-operative medications were continued. His further stay in the hospital was uneventful.

Homocysteinemia is associated with thromboembolic complications by causing endothelial dysfunction, increasing procoagulant activity and decreasing antithrombotic effect. It decreases protein C activation rate, resistance of endothelium to thrombosis and reduces vasodilatory effect of nitric oxide and thereby promotes thrombosis.<sup>[3]</sup> It increases chances of premature atherosclerosis involving cardiovascular system, central nervous system, renal vein, and peripheral veins.

Challenges related with our case were history of CAD with poor myocardial function, a prothrombotic state necessitating perioperative anticoagulation, increased risk of perioperative adverse cardiovascular or cerebrovascular events and need to bring down homocysteine levels pre-operatively to decrease thrombotic complications. There was an added risk of aspiration and urgency for surgery due to nature of disease.

DVT prophylaxis, active ambulation, and good hydration used pre-operatively decreased risk of perioperative thromboembolic complications. Oral pyridoxine, folic acid, and vitamin B12 were given as they have been known to decrease rise in homocysteine levels.<sup>[4]</sup> Intraoperative steps taken were maintenance of euvoledmia and hemodynamics. Nitrous oxide was avoided as it inhibits the enzyme methionine synthase and leads to accumulation of homocysteine. Badner *et al.*<sup>[5]</sup> compared

patients anesthetized with and without nitrous oxide and found 12-24  $\mu\text{mol/l}$  increase in plasma homocysteine levels. He also observed significantly increased incidence and duration of post-operative ischemia in patients' anesthetized with nitrous oxide. Hypoglycemia is a known complication as methionine causes insulin release. Care was taken at the time of patient positioning as these patients have increased risk of osteoporosis. Adequate analgesia, thromboprophylaxis, and euglycemia ensured uneventful post-operative recovery.

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