Integration of monitoring aids: A scientific approach for better patient outcome during hyperthermic intraperitoneal chemotherapy

Sir,

Hyperthermic intraperitoneal chemotherapy (HIPEC) is a new therapeutic modality for management of malignancy with peritoneal seedlings, these procedures often had wide dissections, large denude raw areas, leading to major fluid shifts, and hemodynamic alterations. The mechanism behind the altered hemodynamic changes might be due to substantial fluid shifts, release of inflammatory mediators, bacteremia, tumor lysis, cytotoxic drugs, and coagulopathy. The reported incidence of perioperative complications was high (40%), leading to increased morbidity and mortality, mostly in form of pulmonary and cardiac complications. Being an emerging modality with limited clinical experience, standard monitoring guidelines yet to be defined. In spite of using standard and advanced monitoring aids, hemodynamics can swing. To overcome such swings, timely detection and interventions are required, which demands integration of one or more advance monitoring assistances (flow derived hemodynamic monitoring [stroke volume variation/pulse pressure variation (SVV/PPV)], extravascular lung water monitoring, lung ultrasound (LUS), and transoesophageal echocardiography [TEE]). Most common reasons outlined for these complications are inappropriate fluid transfusion along with the release of inflammatory mediators, bacteremia, and cytotoxic medications. To minimize such complications, intraoperative intravascular volume should be assessed regarding severity of the American Statistical Association physical status of patients, complexity of surgery, and extent of major fluid shifts. Unresolved outlook on gold standard intraoperative hemodynamic monitoring for borderline patients persists regarding adequacy of intravascular fluid volume and outcome. Minimally invasive hemodynamic monitoring devices reflect left ventricular filling pressure and volume indices more accurately over static devices in various surgical patients, and are used to guide decisions for volume replacement, monitoring the effect of given fluid therapy and to gauge the degree of fullness of intravascular compartment. Maximal cardiac output is dependent on preload in a normal functional heart but becomes independent to preload in failing heart and thus PPV/SVV cannot be a sole marker to guide decisions of fluid transfusion, hence echocardiography transthoracic echocardiograms (TTE/TEE) should be combined to assess global left and right ventricular functions. Even though these patients may be at responsive part of Fick’s cardiac output curve, they can still have leaky lung capillaries and are unable to tolerate the transfused fluid. In these patients, LUS can detect leaky capillaries as B lines, hence extravascular lung water. Thus, it detects pulmonary edema much earlier before the patient desaturates or exhibits clinically evident heart failure. Hence, LUS can act as defender for each point of fluid transfused and keeps strict vigilance on fluid transfusion and its tolerance, and hence prevents many pulmonary and cardiac complications, and thus the morbidity and mortality.

Apart from the fluid overload, altered hemodynamics might result from myocardial insult in the form of arrhythmias, myocardial stunning, myocardial ischemia, or infarct and pulmonary edema. Intraoperative, these cardiac complications can be detected and managed by TEE. Apart from the liberal fluid transfusion, liberal blood product transfusion may be warranted, with excessive bleeding. Such massive transfusions can provoke transfusion reactions, coagulopathy, DIC, venous stasis, thromboembolism, and strokes. Routinely used lab parameters (prothrombin time/partial thromboplastin time test kaolin, platelet count) of coagulation profile do not detect all factors of coagulation cascade, hence give ambiguous reports, leading to injudicious over-or under-corrections of blood components. Thromboelastography guided transfusion is presently the most rational and cost-effective approach for transfusing blood products. Urine output ≥400 ml/h has been advocated during HIPEC, to prevent acute tubular necrosis and requirement of renal replacement therapy, can be reduced to 200 ml/h in patients with compromised cardiac functions. Peak glucose level, peak core temperature, end-of-case central venous pressure, pH, and lactate levels do not appear to be relevant for adverse postoperative events. To sum up, each patient should be assessed individually for the requirement of advanced monitoring aid integration of various monitoring to reduce complications, and hence morbidity and mortality.

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Conflicts of interest
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Vorapaxar: The missing link in antiplatelet therapy!

Sir,

Patients with atherosclerotic disease (coronary, cerebrovascular, and peripheral vascular) are prescribed with dual antiplatelets (DAPs) along with statins. DAP constitutes aspirin along with thienopyridine derivative (clopidogrel, prasugrel, and ticagrelor). Aspirin inhibits cyclooxygenase-I irreversibly that prevents generation of thromboxane A2 by platelets leading to antithrombotic effect. Thienopyridines inhibit P2Y12 receptors irreversibly that prevent adenosine diphosphate-induced platelet aggregation, thus preventing thrombosis.

In spite of regular use of DAP by patients, recurrent cardiovascular events still occur. Researchers realized that there is some other mechanism leading to thrombosis which is not addressed by conventional DAP. This led to the development of agents that act at the thrombin-mediated pathway.

Vorapaxar belongs to protease-activated receptor-1 (PAR-1) inhibitor group. It is the first PAR-1 inhibitor approved by the United States Food and Drug Administration in coronary and peripheral vascular disease in May 2014. It was approved after the results of thrombin receptor antagonist in secondary prevention of atherothrombotic ischemic events-thrombolysis in myocardial infarction 50 trial were released.

The results revealed that vorapaxar reduced the rate of the combined endpoint of cardiovascular death, myocardial infarction, stroke, and urgent coronary revascularization when used along with aspirin and/or clopidogrel in patients without previous history of stroke. However, patients with history of stroke suffered with intracranial hemorrhage 2 years after starting vorapaxar. Therefore, the drug is not recommended in patients with history of stroke, transient ischemic attack, or a previous intracranial hemorrhage.

PAR receptors are a super-family of G-protein-coupled receptors which are expressed throughout the body and are involved in platelet activation along with thromboxane A2 and P2Y12 through a different pathway. PAR receptors have a significant contribution to the pro-inflammatory response occurring due to atherosclerosis and thrombotic events. Vorapaxar is a competitive, reversible antagonist of PAR-1 receptor that acts by blocking thrombin-induced platelet activation. Vorapaxar binds to PAR-1 reversibly, but due to a long half-life (terminal half-life of approximately days), the final effect is irreversible.

Vorapaxar is completely absorbed when consumed orally and attains a peak plasma concentration within 1–2 h. Oral bioavailability is not affected when consumed with food. The mean...