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Our clinical practice and clinical studies have been focused on (1) anesthetic management in patients undergoing major surgery including joint arthroplastic surgery for hemophilia patients, variable surgical procedures for translational researches (2) assessment of functional failure of the internal valve of anesthesia machine (3) assessment of reliability of cardiac output measurements (4) risk management of medical electronic devices in Research Hospital. (5) Bioactive lipids and the mechanism of pain

1. Anesthetic management for carrier hemophilia.

Hemophilia is X-linked gene disease with the activity abnormality of the coagulation factor. The hemophilia A is caused by factor VIII abnormality, and the hemophilia B is caused by factor IX abnormality. Careful hemostatic management is required in perioperative care of the hemophilic patients. It is usually recommended that we perform coagulation factor replacement therapy and hemostatic monitoring.

We experienced anesthesia management of the orthopedic surgery of patients with hemophilia B that underwent living-donor liver transplantation for cirrhosis due to the hepatitis C virus this time. We carried out hemostatic monitoring and perioperative management, but did not require coagulation factor replacement therapy. There were no complications such as postoperative bleeding and infection.

Female hemophilia patients are often not informed as carriers themselves, and there is a possibility that medical practice may be performed without recognizing them as hemophilia patients. We experienced anesthesia of female hemophilia patients and safety managed anesthesia with appropriate hemostatic management.

2. Assessment of functional failure of the internal valve applying maximum and positive end-expiratory pressure of anesthesia machine

Equipment-related complications, whatever its cause, should be prevented by checking the breathing system prior to general anesthesia. We found irregularities with some of the anesthesia machines at our department, which was related to a ventilator-related problem that recurred after application of positive end-expiratory pressure (PEEP) during general anesthesia.

The issue with the PEEP/Pmax valve, which can lead to changes in flow and pressure during mechanical ventilation, could go unnoticed because the valve is encased inside the breathing circuit, and requires disassembly for close inspection. Our findings highlight the importance of keeping the anesthetic circuit, including the internal components of the PEEP/Pmax valve, free of unexpected contamination through more thorough preventive maintenance cycles.

3. Assessment of reliability of cardiac output measurements.

Knowing a patient's cardiac output (CO) could contribute to a safe, optimized hemodynamic control during surgery. Precise CO measurements can serve

as a guide for resuscitation therapy, catecholamine use, differential diagnosis, and intervention during a hemodynamic crisis. Despite its invasiveness and intermittent nature, the thermodilution technique via a pulmonary artery catheter (PAC) remains the clinical gold standard for CO measurements. LiDCO rapid™ (LiDCO, London, UK) and FloTrac/Vigileo™ (Edwards Lifesciences, Irvine, CA) are less invasive continuous CO monitors that use arterial waveform analysis. Anesthesiologists use FloTrac/Vigileo™ in our operating room.

We found both devices tended to underestimate the calculated CIs when the CIs were relatively high. These proportional bias produced large percentage errors in the present study.

4. Risk management of medical electronic devices and endoscopic surgery support robot for laparoscopic surgery

As a certified proctor of robot-assisted surgery, surgeon actively perform minimally invasive surgery.

We engage in preventive maintenance and care of the life support machines including instruments for mechanical ventilation or blood purification and robot systems for laparoscopic surgery. We also super-

vised physicians during clinical usage of these instruments. We have promoted dual-directional information system with the Division of Clinical Trial Safety Manage on malfunctions or incidents of the rest of medical electronic devices in this hospital in collaboration.

5. Bioactive lipids and the mechanism of pain

Postoperative incisional pain is characterized by persistent acute pain at the site of tissue injury and is associated with local inflammation. Various bioactive lipids such as Prostaglandins and Leukotrienes were synthesized at injured tissue and involved in acute inflammation and nociceptive pain.

Leukotriene B₄ (LTB₄) is a potent lipid mediator of inflammation and its biological effects are mediated primarily through the high affinity receptor BLT1. We investigated the role of LTB₄-BLT1 signaling in inflammatory pain. We defined the transient increase of LTB₄ production in local incisional site in the quite early stage. We found that LTB₄-BLT1 signaling exacerbates pain responses by promoting local infiltration of inflammatory monocytes and cytokine production. LTB₄-BLT1 axis is a potential target for therapeutic intervention of acute pain induced by tissue injury.

Publications

Asahara M, Ito N, Hoshino Y, Sasaki T, Yokomizo T, Nakamura M, Shimizu T, Yamada Y. Role of leukotriene B₄ (LTB₄)-LTB₄ receptor 1 signaling in post-in-

cisional nociceptive sensitization and local inflammation in mice PLoS One. 2022 Oct 20;17(10):e0276135. doi: 10.1371/journal.pone.0276135.