SOME malignancies of the extremities can be treated by hyperthermic isolated limb chemotherapy. This procedure involves arterial and venous cannulation of the affected limb and isolated perfusion using a bypass pump.1–3 When a steady state is reached, the blood is warmed and oxygenated, and a chemotherapeutic agent (e.g., melphalan) is added and circulated in the limb for up to 1 h. Because the limb is theoretically isolated, large doses of the chemotherapeutic drugs may be used, sometimes as much as 10 times a systemic dose.4 However, there is an ever-present danger of leak from the limb to the rest of the body. This is termed a “systemic leak,” and it is potentially hazardous to the patient. The continued integrity of limb isolation during the bypass period is therefore critical.

Various methods of limb isolation5 have been described, ranging from tourniquet occlusion to more sophisticated systemic or limb flow and pressure manipulations. Regardless of the technique, monitoring for a leak in real-time has proved to be difficult. We describe a new technique to monitor for limb-to-systemic leak during hyperthermic isolated limb chemotherapy.

Case Report

A 38-yr-old man with recurrent melanoma of the right leg was scheduled for hyperthermic isolated limb chemoperfusion. Anesthesia was induced with 2 mg/kg intravenous propofol, 5 μg/kg fentanyl, and 50 mg rocuronium. The patient’s trachea was intubated, and anesthesia was maintained with nitrous oxide 50% in oxygen and a propofol infusion. No volatile anesthetic agent was administered. Arterial cannulae were placed in the right dorsalis pedis and left radial arteries. A right internal jugular cannula was also inserted to monitor the central venous pressure and to administer vasopressor agents. Temperature was monitored centrally and peripherally in the affected limb by a number of tissue probes placed in the skin and muscle. Other monitoring included continuous electrocardiography, pulse oximetry, and continuous inspired and expired gas analysis, using an Ohmeda 5310 respiratory gas monitor infrared monitoring system (Datex-Ohmeda, Tewksbury, MA). The femoral vessels were identified and cannulation was performed according to a previously described technique.1–3 The perfusion circuit consisted of the perfused limb, arterial and venous cannulae, Baxter Durollo heparinized tubing (Baxter Health System, Deerfield, IL), a Stocker roller pump (Munich, Germany), a Baxter Univox oxygenator, and a Datex-Ohmeda Tec 6 desflurane anesthetic vaporizer. The oxygen flow rate through the circuit was 200 ml/min. The patient underwent anticoagulation with 7,000 units heparin before the bypass circuit was established. The pump flow rate was 900–1,000 ml/min, and the mean limb arterial and venous pressures were in the region of 60 and 9 mmHg, respectively. Systemic mean arterial and venous pressures were 80 and 11 mmHg, respectively. Systemic arterial and central venous pressures were manipulated with the use of intravenous fluids or with the vasoconstrictor phenylephrine. A gradient of approximately 20 mmHg was maintained between the systemic arterial diastolic pressure and the limb mean arterial pressure. A gradient of approximately 2 mmHg was maintained between the central venous pressure and the limb venous pressure. When a steady state was reached, with stable limb and systemic hemodynamics, 3% desflurane was introduced into the bypass circuit. No desflurane was detected in the expired breath for a period of 3 min. A limb-to-systemic leak was deliberately induced by partially clamping the venous return to the pump. This allowed the limb venous pressure to increase above the systemic venous pressure. Within 50 s (six breaths of mechanical ventilation), desflurane appeared in the expired breath at a concentration of 0.2%. The nonleak hemodynamics were then restored, and a steady state was again achieved. The desflurane rapidly disappeared from the expired breath. Fluorescein dye was then injected into the perfusion circuit. The skin of the trunk and extremities proximal and distal to the level of the cannulation was observed
under a Wood lamp. Luminescence was detected appropriately distal to the cannulation site and was absent in the rest of the body. This “one-shot” test appeared to confirm a leak-free circuit. At this point, the calculated dose of melphalan was injected into the pump and circulated for 1 h. Administration of 3% desflurane was continued in the bypass circuit, and on three occasions, a transient 0.1% desflurane concentration was detected in the expired breath. Each time, this disappeared within seconds of minor adjustments to the bypass pump flow rate and restoration of a systemic-to-limb pressure gradient. After 1 h, the chemotherapy perfusate was drained and the circuit was flushed with Plasmalyte A (Baxter Health System). The blood in the perfused limb was replaced with melphalan-free, low-molecular-weight dextran. The patient’s recovery was uneventful. Postoperatively, results of the patient’s complete blood count and liver function tests were normal, showing no signs of acute, significant, chemotherapeutic toxicity.

Discussion

A number of methods has been described to monitor for circuit-to-systemic leak during high-dose, limb-perfusion chemotherapy. A traditional method involves injection of fluorescein dye into the limb circuit before introduction of the chemotherapeutic agent. The limb isolation can then be confirmed by examination of the limb using a Wood lamp to delineate bypassed tissues and to confirm a line of demarcation at the level of vascular cannulation. The disadvantage of this technique is that it is a one-time test and does not ensure continued circuit integrity during the period of high-dose chemotherapy administration. Another method is to monitor for an increase in body temperature, which would indicate a leak. This method can be insensitive because a large and potentially dangerous leak may have occurred already, before the core temperature changes enough to be detected. A more sophisticated test is injection of radio-labeled erythrocytes or albumin into the limb circuit and continuous monitoring of the patient’s heart for detection of the labeling isotope. This system is hard to standardize and is costly and cumbersome.

Concerns regarding limb-to-systemic leak from inadequately compressed, deep collateral vessels led to a change from methods of tourniquet occlusion to more sophisticated flow-balance techniques. By manipulating limb venous drainage and limb mean arterial, central venous, and systemic arterial pressures, adequate flow can be maintained while ensuring a systemic-to-limb arterial and venous gradient. As with all dynamic systems, however, real-time monitoring is desirable to adjust technique and to reduce complications.

Desflurane is a relatively new volatile anesthetic agent with very low blood-gas solubility. Relatively small amounts of desflurane in the blood show up in large volumes in the alveoli. Its pharmacokinetics are well-described, and, similar to all volatile anesthetics, it has mild vasodilator properties. With the addition of desflurane to the bypass circuit and with the use of a nonvolatile anesthetic technique for the procedure, any expired desflurane detected in the expiratory gases must have originated from the limb, therefore indicating a limb-to-systemic leak. The vasodilator properties of the agent in the limb may also convey an increased perfusion benefit, although this is only speculative. The respiratory gas monitor has an accuracy of ± 0.2% for a range of 0 to 5% for desflurane, and the low blood–gas coefficient of this agent makes it ideal for rapid detection in expired gas. When a small leak was detected using this method, small manipulations of pump flows and pressures were able to abolish end-tidal desflurane within a few breaths. The machines used for hyperthermic isolated limb perfusions usually are the same models that are used more commonly for cardiac surgery; most already will have volatile anesthetic vaporizers in circuit, and therefore no modifications are necessary. The anesthetics administered may vary, however, and, although all agents would be detected in a similar way, the use of more blood-soluble volatile agents, such as isoflurane, may marginally increase the response time needed to detect a leak.

In summary, this technique appears to be a simple and inexpensive means of detecting limb-to-systemic leak during high-dose limb-perfusion chemotherapy. Further studies are ongoing to more precisely determine the dynamics of this monitoring system, in particular, to quantify the relation between desflurane and melphalan levels.

References

Right Atrial Membrane Interfering with Insertion of Pulmonary Artery Catheter

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An 81-yr-old man (105 kg, 180 cm) presented for a coronary artery bypass grafting procedure. Preoperative cardiac catheterization revealed severe three-vessel occlusive coronary artery disease. Left ventricular function was estimated to be normal, with an ejection fraction of 60%. Cardiac output was 4.8 l/min, with an index of 2.1. Pulmonary artery pressure, measured via the femoral vein to the inferior vena cava route, was normal. Results of a physical examination were remarkable only for a plethoric purplish red face, which the patient has had for many years. Results of other laboratory tests and of chest radiography were noncontributory.

On the morning of surgery, the patient was brought to the operating room, routine monitors were placed, intravenous access was obtained, and a radial arterial catheter was inserted. General anesthesia was induced, and an endotracheal tube was inserted without difficulty. The right internal jugular vein was identified, and an 18-gauge catheter was inserted. Catheter position was verified by blood aspiration and by pressure transduction to rule out arterial insertion. A wire was passed through the catheter but met with resistance at a depth of 15–20 cm. Several attempts to reposition the wire, including reinsertion of the catheter by several experienced operators from the anesthesia and surgery team, were also met with resistance.

A right-sided subclavian approach was attempted, but, again, it was met with the same resistance at similar depths. Subsequently, the left subclavian vein was cannulated after a wire was passed without resistance. Multiple attempts to float a pulmonary artery catheter were unsuccessful, without sight of a right ventricular pressure trace. The catheter was left at a depth of 20 cm, and preparation for surgery continued.

Transesophageal echocardiography was performed. The transesophageal echocardiography revealed a long right atrial membrane that extended from the lower portion of the interatrial septum, above the tricuspid valve, which divided the right atrial lumen into anterolateral and posteromedial chambers (fig. 1). The membrane appeared to be mobile in its center but fixed by its margins. A microbubble imaging contrast test performed by injecting agitated saline via the central line port showed filling of the postero-medial portion first and a rapid propagation into the anterolateral portion via what appeared to be a single opening in the membrane close to the interatrial septum.

No right-to-left shunts in the form of an atrial septal defect or a patent foramen ovale were shown. Results of the rest of the transesophageal echocardiography examination were normal. After the patient’s chest was opened, the surgeon noted that the venous system draining into the right atrium was exceptionally dilated. Because of these findings, the right atrium was opened during the cardiopulmonary bypass period of the procedure, and the membrane was identified and resected. The transesophageal echocardiography...