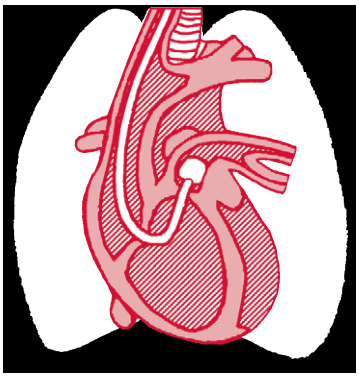

CASE CONFERENCE

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CASE 3—2008
The Use of Acute Normovolemic Hemodilution During Cardiac Surgery in a Patient With Human Immunodeficiency Virus Infection

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HUMAN IMMUNODEFICIENCY VIRUS (HIV) infection is characterized by a chronic disease process with systemic multiorgan involvement.[1] Since the first reported description in 1981,[2] the management of the HIV-positive patient has, in effect, become a medical subspecialty. HIV-positive patients undergoing surgery, particularly cardiac surgery, present multiple challenges to anesthesiologists in that neurologic, pulmonary, cardiovascular, and hematologic abnormalities may impact the delivery of anesthesia.[3-5] Because HIV is transmitted parenterally, patients with HIV infection are ineligible to serve as allogeneic blood donors.[6] However, with perioperative autologous blood techniques, no restrictions or contraindications exist because the autologous blood products pose no increased infectious risk to the patient. Unfortunately, very little is known about the use of autologous blood in HIV-positive patients; a paucity of reports have addressed this topic.

Acute normovolemic hemodilution (ANH) is a blood conservation modality in which autologous whole blood (AWB) is collected intraoperatively in blood bags containing anticoagulant before the commencement of surgery.[7] This AWB product may be transfused contemporaneously when need for red blood cells or coagulation factors occurs later during the surgical procedure.[8] ANH is effective in reducing the need for allogeneic blood products during surgery and also is associated with decreased postoperative surgical hemorrhage.[7,8] In this report, an HIV-positive patient undergoing cardiac surgery is described in which ANH was used to assist in the perioperative blood management.

CASE REPORT*

A 52-year-old, 87-kg, HIV-positive man who presented with severe substernal chest tightness at rest, diaphoresis, and a positive stress test was scheduled for coronary artery bypass graft (CABG) surgery. Cardiac catheterization revealed multivessel coronary artery disease including segmental stenosis (80%) of the left anterior descending coronary artery (CA), 70% stenosis of the first obtuse marginal CA, 80% stenosis of the right CA, and a left-ventricular ejection fraction of 45% with mild hypokinesia of the basal and midanterolateral myocardial segments. Comorbid factors included a 15-year history of HIV disease, 40-pack year history of smoking, prior cerebrovascular accident, diabetes, and a splenectomy 20 years previously for thrombocytopenia. Although the patient had experienced past episodes of pneumocystis carinii, HIV encephalopathy, and cytomegalovirus retinitis, antiviral therapy for 8 years (atazanavir, tenofovir, abacavir, and ritonavir) had effectively suppressed progression of any HIV-infective symptoms (recent CD4 T cell count 1008 cells/mL, HIV RNA $<$ 50 copies/mL). Baseline laboratory findings revealed a hemoglobin concentration ([Hb]) of 14.3 g/dL, hematocrit of 43%, and platelet count of 102,000/μL. Electrolytes, blood urea nitrogen, serum creatinine, and coagulation function tests were all normal.

Antiviral therapy was continued preoperatively until the time of surgery. After sedation with intravenous midazolam, the patient was transported to the operating room where a radial arterial catheter was placed before the induction of anesthesia. After anesthesia induction and endotracheal intubation, additional monitoring modalities were inserted, including a pulmonary artery catheter (PAC) and transesophageal echocardiography (TEE) probe. The PAC revealed pulmonary hypertension (pulmonary artery pressure 35/19 mmHg). TEE revealed biventricular hypertrophy, mild right ventricular enlargement, a tricuspid annular plane of systolic excursion of 1.5 cm, a left ventricular ejection fraction of 40% with hypokinesia of the basal and midanterior and anterolateral myocardial segments, and trace mitral regurgitation and tricuspid regurgitation.

The AWB volume to be collected using ANH was calculated by using the standard ANH equation[8]:

$$WB_{ANH} = EBV \times \left(\ln\left[Hb_i/Hb_t\right]\right),$$

where WB_{ANH} is the volume of whole blood collected using ANH (mL), EBV is the estimated blood volume (75 mL/kg), ln is the natural logarithm, Hb_i is the initial/baseline hemoglobin (g/dL), and Hb_t is the target hemoglobin concentration (g/dL). Second-phase hemodilution during cardiopulmonary bypass (CPB) was projected using the following equation[9]:

$$Hb_{CPB} = HB_t \times \left[EBV/\left(EBV + PV\right)\right],$$

where Hb_{CPB} is the projected Hb during CPB and PV is the prime volume of the extracorporeal circuit. These calculations indicated that for this 87-kg patient, the EBV was 6,525 mL, the PV was 1,500 mL, the Hb_i was 14.3 g/dL, and the Hb_t was 11 g/dL. A collection of approximately 1,600 mL of whole blood would thus produce an Hb_{CPB} of approximately 9 g/dL, which was deemed a safe and acceptable lower limit of anemia during CPB in this patient.

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1053-0770/08/2203-0026$34.00/0

doi:10.1053/j.jvca.2008.03.011

Key words: acute normovolemic hemodilution, cardiac surgery, human immunodeficiency virus

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ANH was commenced by attaching 450-mL blood-collection bags containing citrate-phosphate-dextrose anticoagulant to a high-flow port in the patient's PAC introducer. Blood was allowed to drain passively via gravity into the blood collection bags. The blood-collection bags were manually agitated every minute to ensure adequate admixture of blood and anticoagulant. After 1 blood bag was filled, a subsequent bag was connected (a total of 3 blood-collection bags were collected). Each unit of AWB was placed in a kidney dish, labeled, and placed on a separate tray and kept adjacent to the anesthesia work area in full view of the anesthesiologist. As blood was being collected, normovolemia was maintained by infusing crystalloid and colloid. For each 1.0 mL of blood collected, 1.5 mL of replacement was infused. ANH was well tolerated by the patient. Systemic and pulmonary artery pressures remained within normal limits, heart rate and cardiac index increased slightly with progressive hemodilution, and new wall motion abnormalities were not detected on TEE. The patient was then heparinized (300 U/kg), producing an activated coagulation time of greater than 450 seconds, and myocardial revascularization was performed (4 bypass grafts) with assistance of CPB. Antifibrinolytic therapy (epsilon-aminocaproic acid) also was used during the procedure including a loading dose of 100 mg/kg with heparinization followed by an infusion of 10 mg/kg until admission to the intensive care unit (ICU). The AWB was reinfused after termination of CPB and protamine administration. Blood remaining in the extracorporeal circuit was subjected to centrifugation in an autotransfusion device and subsequently reinfused. On arrival in the ICU, the patient's laboratory findings were Hb of 11.3 g/dL, hematocrit of 34%, platelet count of 87,000/μL, prothrombin time of 14.7 seconds, partial thromboplastin time of 29.9 seconds, and an international normalized ratio of 1.4. The patient was extubated 4 hours after ICU arrival and made an uneventful recovery. Allogeneic blood products were not transfused during the postoperative course, and he was discharged on postoperative day 6. During eventual follow-up in the cardiac surgery clinic, the CD4 T-cell count was 1,127 cells/mL, and HIV RNA was $<$50 copies/mL.

DISCUSSION

HIV is classified as a member of the genus *Lentivirus*, part of the family of Retroviridae. Lentiviruses have many common biological properties and characteristically produce long-duration illnesses with a long incubation period.[10] Two species of HIV infect humans: HIV-1 and HIV-2. HIV-1 is more virulent, easily transmitted, and is the cause of the majority of HIV infections globally.[10] HIV-2 is less transmittable and is largely confined to West Africa. Untreated, HIV infection deteriorates into a well-defined condition termed "acquired immunodeficiency syndrome" (AIDS).[1] Antiviral therapy has rapidly evolved over the last 10 years and includes nucleoside and nonnucleoside reverse-transcriptase inhibitors (interrupt an early stage of the virus making copies of itself), protease inhibitors (interrupt the virus from making copies of itself at a later step in its life cycle), and fusion inhibitors (interfere with HIV-1's ability to enter into cells by blocking the merging of the virus with the cell membranes).[11] Because HIV can become resistant to any of these drugs, combination therapy will effectively suppress the virus. When multiple drugs (3 or more) are used in combination, it is referred to as highly active antiretroviral therapy (HAART) and are indicated for patients who are newly infected with HIV as well as people with AIDS.[12] HAART is credited as being a major factor in significantly reducing the number of deaths from AIDS. Although HAART is not a cure for AIDS, it has greatly improved the health of many people with AIDS and reduces the amount of virus circulating in the blood to nearly undetectable levels, as seen in the previously mentioned patient.[12]

This report describes the successful application of ANH in an HIV patient undergoing cardiac surgery and the perioperative avoidance of all allogeneic blood products. The decision to use ANH in any HIV-infected patient should take into consideration the effect of the disease on the cardiovascular system. Patients who are HIV positive manifest a higher degree of cardiac dysfunction secondary to the effects of the chronic viral infection, coinfection with other pathogens, antiviral therapy, and immunosuppression.[13] HIV infection is associated with cardiomyopathy, right ventricular dysfunction, myocarditis, and pericardial effusion.[14] For this reason, a PAC and TEE were used in the present patient to closely monitor ventricular function and detect any new wall motion abnormalities during ANH. Although HAART may attenuate the severity of the cardiovascular disease, the incidence and severity of coronary artery disease associated with HAART are increasing.[15] Antiviral therapy produces dyslipidemia (increased low-density lipoprotein cholesterol, decreased high-density lipoprotein cholesterol, and increased serum triglycerides).[15] HIV-positive patients also manifest several hematologic abnormalities, of which the cytopenias are the most common.[16,17] Anemia and neutropenia are primarily caused by the suppression of bone marrow by the HIV infection, although opportunistic infections, antiviral therapy, or malignancies also may be contributory. Thrombocytopenia is caused by immune-mediated destruction of platelets and inadequate platelet production.[16,17] HAART has reduced the frequency of these hematologic complications.[16] However, anemia, if present, is a relative contraindication to ANH because subsequent hemodilution may be associated with unacceptably low levels of hemoglobin during CPB. Fortunately, in the previously mentioned patient, preoperative Hb and platelet count were within normal limits.

ANH is thought to exert its blood conservation effects by decreasing Hb secondary to hemodilution. Thus, relatively smaller quantities of hemoglobin are subsequently lost via surgical hemorrhage.[7] In addition, AWB serves as an intraoperative source of fresh red blood cells, platelets, and coagulation factors for the patient.[8] Several studies have shown that ANH is associated with avoidance or near-avoidance of allogeneic blood during cardiac surgery and reduced surgical blood loss.[18-20] Unfortunately, ANH is still regarded as a controversial blood conservation modality. Some individual clinical studies are thought to have methodologic design flaws, whereas meta-analysis suggests that definitive conclusions regarding clinical utility of the technique are lacking.[21,22] However, recent guidelines published jointly by the Task Force of the Society of Thoracic Surgeons (STS) and the Society of Cardiovascular Anesthesiologists (SCA)[23] suggest that ANH be used as part of a multimodality approach to blood conservation. When combining ANH with other perioperative tools, such as antifibrinolytic therapy and autotransfusion, as shown in the present patient, the efficacy of the individual methodologies may be augmented.

Currently, experience with autologous blood techniques in HIV-positive patients is limited. Vanston et al[24] analyzed the days of life saved by autologous blood from noninfected versus HIV-infected individuals and concluded that use of autologous