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Case Report

The Utilization of Conventional Ultrafiltration as a Blood Conservation Technique in Three Human Immunodeficiency Virus-1 Seropositive Patients Undergoing Aortic Root Surgery

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Abstract

Background: HIV-seropositive patients are increasingly undergoing open-heart surgery in the 21st century. This case series evaluates three HIV-seropositive patients who underwent aortic root surgery with the concomitant utilization of conventional ultrafiltration during cardiopulmonary bypass (CPB) as a blood conservation technique.

Methods: IRB approval was obtained for this case report. Three males (ages 44, 34, and 58) presented for surgical correction of aortic dilation; the patients underwent Bentall procedure, David procedure with Shafer repair and David procedure with hemi-arch repair, respectively. Patients underwent uneventful anesthesia induction and initiation of CPB. During cardiopulmonary bypass, conventional ultrafiltration was initiated as an additional blood conservation maneuver in an effort to avoid allogenic blood transfusion; all three patients were successfully weaned from cardiopulmonary bypass.

Results: Conventional ultrafiltration was implemented for all three patients. No blood products were transfused intra-operatively or post-operatively. All of the patients were successfully discharged home with no complications.

Conclusion: This case series demonstrates that conventional ultrafiltration may be a useful adjunct for blood conservation during cardiothoracic procedures requiring CPB in HIV-seropositive patients. Although conventional ultrafiltration is classified as a class IIb intervention by the Society of Thoracic Surgeons, this modality should be considered as part of the multi-modal approach for blood conservation in HIV-infected patients undergoing aortic root surgery.

ABBREVIATIONS

HIV: Human Immunodeficiency **V**irus, **CPB:** Cardiopulmonary Bypass, **CUF:** Conventional Ultra Filtration, **ANH:** Acute Normovolemic Hemodilution

OVERVIEW

Thirty years ago, the Human Immunodeficiency Virus-1 (HIV) was first identified as the pathogen that eventually leads to the Acquired Immune Deficiency Syndrome (AIDS). Since that time, breakthroughs in the understanding of the pathophysiology of HIV has allowed scientists and physicians to develop highly active anti-retroviral therapy (HAART) that effectively suppresses HIV replication. As a result of the efficacy of HAART, patients with HIV/AIDS are living longer and now presenting to the operating room for a wide variety of surgical procedures, including cardiothoracic surgery [1,2]. In the 21st century, patients with HIV/AIDS may require cardiac surgery for the same reasons as non-HIV-infected individuals, as well as due to HIV-related pathology, infections, HAART-related co-morbidities, or from accelerated aging due to HIV infection itself. Although specific clinical guidelines or paradigms for optimally managing patients with HIV/AIDS undergoing cardiac and thoracic surgery are still evolving, multiple studies have demonstrated that patients with HIV/AIDS can safely undergo major cardiothoracic procedures, including aortic surgery [3].

While cardiothoracic surgery has become more common

in HIV-infected patients, management strategies addressing the unique concerns of this patient population remain poorly studied and specific blood conservation techniques for HIV-infected patients are almost-non-existent. Administration of packed red blood cells, and other blood products are associated with increased morbidity and mortality in the non-HIV-infected population undergoing cardiothoracic surgery [4,5]. The deleterious effects of transfusion are potentially more significant in HIV-infected patients [6]. Current clinical practice recommendations by the Society for Thoracic Surgeons (STS) suggest various modalities for blood conservation, however, many of the specific interventions are not necessarily practiced in many settings [7]. With regard to the management of HIV+ patients in the cardiac suite, only one case report has delineated a specific approach for blood conservation in an HIV-infected patient undergoing coronary artery bypass grafting [8].

Conventional ultrafiltration (also known as hemoconcentration) is a Class IIB recommendation for blood conservation during cardiac surgery in adult patients undergoing cardiopulmonary bypass (CPB) [7], however, the literature evaluating its utility is quite limited [9-12]. The specific use of conventional ultrafiltrationin HIV-infected adult patients undergoing cardiothoracic surgical procedures has never been evaluated. In this case series, three HIV-infected patients without AIDS-defining diagnoses undergoing aortic root surgery underwent conventional ultrafiltration during CPB as a method to minimize operative blood loss. This retrospective case series was approved by the Institutional Review Board at Cedars-Sinai Medical Center.

DESCRIPTION

Patient A - Background

A 44 year-old, Asian male with body surface area (BSA) of 1.64 m^2 was initially seen for evaluation of a deep venous thrombosis (DVT) and underwent a comprehensive computed tomography (CT) scan. During work-up of the DVT, CT revealed a 5.4 centimeter (cm) aneurysm of the aortic root and ascending aorta. Co-morbidities included an 18-year history of HIV-infection and Hepatitis B disease, childhood tuberculosis treated with antibiotics, past history of treated syphilis infection, asthma, hypothyroidism, and hypogonadism secondary to anabolic steroid use. The patient also had a family history significant for amyloidosis and premature coronary artery disease. The patient complained of associated decreased exercise tolerance over the past year. HAART was initiated four years after his initial HIV diagnosis when his CD4 T-lymphocyte (CD4+) cell count reached approximately 225 cells/milliliter^3; therapy was shortly thereafter discontinued due to severe side effects including exacerbation of his Hepatitis B. HAART was restarted a year later, and he remained compliant with medications since that time. Electrolytes, blood urea nitrogen, serum creatinine, and coagulation function studies were all normal.

See Table 1 for summary of HIV history, immune function studies and baseline laboratory values. TEE confirmed the presence of severe aortic root dilation with measurement of the Sinuses of Valsalva to be 5.4 cm. Initial central venous pressure was 5 mmHg, and pulmonary artery systolic pressure was 27 mmHg. Surgical repair consisted of a Bentall procedure with implantation of a bioprosthetic valve.

Patient B – Background

A 34-year-old, Caucasian man with a BSA of 1.92 m^2 was hospitalized for right lower extremity pain noted to be secondary to pelvic abscess with concomitant bacteremia with methicillin resistant *Staphylococcus aureus* (MRSA). During the course of the evaluation, chest CT revealed an incidental finding of a 5.6 centimeter (cm) ascending aortic root aneurysm at the sinus of Valsalva. Co-morbidities included a 14-year history of HIV-infection with adherence to HAART, hypertension, personality disorder, depression and history of drug use (crystal methamphetamine, marijuana). Electrolytes, blood urea nitrogen, serum creatinine, and coagulation function studies were all normal.

See Table 1 for summary of HIV history, immune function studies and baseline laboratory values. TEE confirmed the presence of severe aortic root dilation with measurement of the Sinuses of Valsalva to be 5.6 cm. Surgical procedure consisted David procedure (valve-sparing aortic root replacement) and Shafer repair of non-coronary cusp of aortic valve.

Patient C – Background

A 58-year-old, Caucasian man with a BSA of 2.06 who was admitted for repair of aortic root aneurysm and proximal ascending aorta. Co-morbidities included a known history of bicuspid aortic valve and a 12-year history of HIV-infection. The patient had been maintained on HAART with full immune reconstitution. Electrolytes, blood urea nitrogen, serum creatinine, and coagulation function studies were all normal. See Table 1 for summary of HIV history, immune function studies and baseline laboratory values. TEE confirmed the presence of severe aortic root dilation with measurement of the Sinuses of Valsalva to be 5.4 cm. Surgical procedure consisted of David procedure (valve-sparing aortic root replacement), subannular commisuroplasty and hemi-arch reconstruction with total circulatory arrest.

Anesthetic Management

All three patients in this case series received similar anesthetic techniques. After initial sedation was achieved with midazolam in the pre-operative holding area, each patient was transported to the operating room where a radial artery catheter was inserted prior to anesthesia induction. Anesthesia was induced with a balanced anesthetic technique consisting of etomidate, fentanyl and rocuronium and maintained with fentanyl, cisatracurium and sevoflurane. Additional monitoring consisted of central venous monitoring, bispectral index, cerebral oximetry and TEE. Antifibrinolytic therapy consisted of tranexamic acid 1 gram intravenously prior to incision.

Ultrafiltration Technique during Cardiopulmonary Bypass

Cardiopulmonary bypass (CPB) was conducted per the standard procedure at our institution. The system components include a SORIN S5 heart lung machine, SORIN 3T cooler-heater (SORIN Group USA, Inc., Arvada, CO), Terumo CDI500

Table 1: Summary of Patient Information and Pertinent Laboratory Studies.

	Patient A	Patient B	Patient C
Age	44	34	58
Procedure	Bentall procedure (biologic valve)	David procedure with Shafer Repair	David procedure with hemiarch Repair
Years of HIV Infection	18	14	12
History of treated syphllis Infection	Yes (18 years prior)	Yes (18 years prior)	Yes (11 years prior)
AIDS-defining diagnosis at time of surgery	No	No	No
AIDS-defining diagnosis in past (if yes, number of years prior to surgery)	No	No	Yes (12 years prior)
Type of HAART regimen	Lopinivir Ritonavir Emtricitabine Tenofovir	Darunovir Ritonavir Emtricitabine Tenofovir	Lamivudine Nevirapine Raltegravir
Years of HAART	15	7	12
Hx Drug Use	None	Crystal Meth	Crystal Meth Coacaine
Pertinent Labs on Day of Surgery			
Hemoglobin(G/DL)/ Hematocrit(%)	13.9 41	12 36.1	14.1. 42.4
BUN (MG/DL)/ Creatinine (MG/DL)	19 1.2	20 1.0	19.1 1.1
Alkaline phosphatase (U/L)	N/A	86	79
Aspartate Transaminase (U/L)	N/A	111	107
Total Protein (G/DL)	7.4	7.3	7.0
CD4+ cell count (cells/ml^3)	860 (day of surgery)	628 @6 months prior to surgery	750 (day of surgery)
HIV viral load (RNA-PCR; copies/mL)	<48	<48	<48

Table 2: Summary of Cardiopulmonary Bypass (CPB) Data.

	Patient A	Patient B	Patient C
Body Surface Area (m^2)	1.64	1.92	2.06
Minutes of Cardioplumonary Bypass (CPB)	176	212	153
Minutes of Aortic Cross Clamp	115	167	131
Total Circulatory Arrest If yes, minutes	No	No	Yes
Mean arterial pressure on CPB	72 mmHg	65 mmHg	70 mmHg
Pump Prime: *Crystalloid* *Albumin* *Sodium Bicarbonate* *Mannitol*	800 ml 250 ml 30 ml 40 ml	1000 ml 250 ml 50 ml 50 ml	700 ml 250 ml 35 ml 67 ml
Total ultrafiltrate	1050 ml	1200 ml	1100 ml
Cell-salvage volume	250 ml	1000 ml	1200 ml
Antifibrinolytics given pre- and during-CPB	Tranexamic acid 2 grams	Tranexamic acid 2 grams	Tranexamic acid 2 grams
Desmopression	None	20 mcg	20 mcg
Blood products given during CPB	None	None	None
Hct @ onset of CPB	38	33	39
Hct @ end of CPB	28	24	29
Urine Output on CPB	260 ml	228 ml	426 ml

monitor (Terumo Cardiovascular Systems, Ann Arbor, MI) and Haemonetics Elite cell saver (Haemonetics Corporation, Braintree, MA). Perfusion was accomplished utilizing a roller pump and an open system Medtronic Affinity NT membrane oxygenator (Medtronic, Minneapolis, MN). See Table 2 for pump prime information.

After median sternotomy and prior to aortic cannulation, all three patients received a heparin dose, based on the patient's own dose response to heparin, intravenously via central venous catheter with subsequent measurement of activated clotting time (ACT) yielding greater than 500 seconds and a minimum heparin concentration of 3 mg/kg. Anticoagulation management was monitored with the Medtronic HMS (Medtronic, Minneapolis, MN) for both ACT and heparin concentration.

The myocardial protection strategy included an initial arresting dose of blood cardioplegia which was delivered in an antegrade manner followed by a slow continuous infusion of Plegisol crystalloid cardioplegia delivered retrograde via a coronary sinus cannula throughout the aortic cross clamp period; all doses of cardioplegia were cold. Topical hypothermia (ice) was also used in the myocardial protective strategy.

Alpha-stat blood gas management was the technique employed during the period of cardiopulmonary bypass. All patients were cooled to a bladder temperature of 32 degrees Celsius unless the circulation was going to be ceased; if circulatory arrest was utilized the temperature was reduced to 18 degrees Celsius. All patients were rewarmed to a bladder temperature of 36 degrees Celsius before terminating cardiopulmonary bypass. Normal vascular resistance was maintained by the administration of phenylephrine boluses as necessary. Anesthesia maintenance was achieved with sevoflurance and cisatracurium.

The ultrafiltration device utilized during all three cases was a SORIN SH14 hemoconcentrator (SORIN Group USA, Inc., Arvada, Colorado). As per our institutional protocol, the hemoconcentrator was placed in a parallel orientation in the extracorporeal circuit. The inlet to the hemoconcentrator was attached from the arterial side of the circuit, and the outlet was connected to an inlet on the cardiotomy/venous reservoir. The effluent side was connected to a suction canister that was open to the atmosphere.

In all three cases, the process of ultrafiltration was initiated after the aortic cross clamp was placed and continued throughout the period of cardio-pulmonary bypass. Fluid was removed during the entire CPB period while maintaining a safe operating level in the venous reservoir as recommended by the manufacturer. The perfusionist continued to remove volume throughout the case ensuring that adequate volume remained necessary to adequately load the patient at the termination of CPB. Blood pressure was maintained with intermittent boluses of phenylephrine as per usual protocol. Of note, the amount of ultrafiltrate removed included not only the volume total that was given in intravenous fluids, cardioplegic solutions and irrigation from the surgical field, but also included any extra-circulating volume from the patient. The total volume of ultrafiltrate removed during the three cases and details regarding CPB are summarized in Table 2.

After the surgical procedure was completed, all three patients were successfully separated from cardiopulmonary bypass without any difficulty and without utilization of inotropic agents or pressors. In addition to continuous ultrafiltration as a means of blood conservation, any shed blood during the case was collected and deposited into a cell-salvage receptacle for processing and subsequent infusion to the patient. Each patient received processed autologous blood during the period of bypass (see Table 2).

Post-Operative Course

All three patients were transported to the Cardiovascular Surgical Intensive Care Unit (CSICU) uneventfully. The patients were weaned from mechanical ventilation and extubated as per protocol at Cedars-Sinai Medical Center within 3.5 to 6 hours after arrival in the CSICU. HAART was restarted in all three patients within twenty-four hours of admission as per the original dosing regimen and schedule. The patients were subsequently discharged to home with follow-up in the cardiac surgery clinic.

Two patients (patient A and Patient B) developed pericardial effusions on post-operative days 26 and 8, respectively. Management consisted of surgical drainage of the pericardial effusion for Patient A and conservative management for Patient B. None of the three patients received any blood products during the perioperative period or readmission period (see Table 3).

DISCUSSION

During the past decade patients infected with HIV have been presenting for surgery, including cardiothoracic surgery, at an increasing rate. Blood conservation and avoidance of blood product transfusion is a major goal during the performance of major cardiothoracic surgery [7]. Although blood conservation has been a major focus of surgical care, especially during cardiothoracic surgery, the incidence of blood transfusion at many institutions continues to increase. The administration of allogenic blood products during cardiac surgery is a common practice; practice history, low transfusion triggers, and lack of formal institutional practice guidelines are among the reasons for current high transfusion rates. Extracorporeal cardiopulmonary bypass contributes to morbidity after cardiac surgery by adversely affecting various physiologic mechanisms, including but not limited to, systemic inflammatory response syndrome (SIRS), hematologic variations, and the adverse effects of hemodilution.

Patients infected with HIV remain a particularly unique sub-category of patients undergoing cardiothoracic surgery. Despite the increase in HIV+ patients undergoing cardiothoracic surgery over the past fifteen years, there is a paucity of defined paradigms for blood conservation in HIV+ patients undergoing cardiothoracic surgery. Only one case report has described a specific intervention, acute normovolemic hemodilution (ANH), and its utility in blood conservation in an HIV+ patient undergoing multiple coronary artery bypass grafting [8]. Further aggravating the clinical scenario for HIV-infected patients undergoing surgery is the existing debate over whether patients infected with HIV should donate blood for autologous use. In this context, we reviewed a small series of three HIV+ patients who

Table 3: Summary of Intensive Care Unit (ICU) Data.

	Patient A	Patient B	Patient C
Mean arterial pressure on arrival to ICU	72mmHg	68 mmHg	74mmHg
Time to extubation (minutes)	183	320	222
Blood products given in ICU	None	None	None
Need for re-intubation	No	No	No
6 hours post-surgery WBC Hematocrit (G/DL)/ Hemoglobin(%)	 11.9 9.2 27	 8.9 11.5 34.8	 9.1 10.2 31.4
Post-Op Day #1 WBC Hematocrit (G/DL)/ Hemoglobin (%)	 10.7 9.7 30.1	 6.8 9.6 28.3	 7.0 11.3 33.7
24 Hours post-surgery HIV viral load (RNA-PCR; copies/mL)	<48	< 48	<48
Blood products transfused in ICU within 24 hours post-surgery	250 ml Cell-salvage (collected during CPB)	1000 ml Cell-salvage (collected during CPB)	1200 ml Cell-salvage (collected during CPB)
Total blood products received during entire ICU admission	None	None	None
Total blood products received during entire hospital admission	None	None	None

underwent aortic root surgery with application of conventional ultrafiltration during CPB and did not subsequently receive any blood products in the perioperative period.

HIV infection, especially left untreated, impacts the hematologic system by diminishing its ability to produce hematopoetic cells. In addition, HAART may act to impair the hematopoietic system further exacerbating anemia in HIV-infected individuals. Therefore, many HIV+ patients possess chronic anemia, and this is observed in 10% to 20% of patients at time of HIV diagnosis. In the non-surgical literature, studies have indicated that anemia and resultant transfusions are associated with accelerated morbidity and mortality in HIV+ patients. Additionally, the administration of allogenic red blood cell products during surgery in HIV+ patients may have serious consequences, including increased mortality. Some studies have also indicated that transfusion of allogenic red blood cells may contribute to generalized immune suppression in patients-at-large, however, in patients who are HIV+, transfusion of red blood cells may create more serious immunodulatory disturbances even in patients who are on HAART [13]. In addition, HIV seropositive patients may experience transient but significant increases in HIV virion production in vivo following exposure to allo-antigens. HIV-infected patients in the perioperative period possess a high likelihood of receiving allogenic blood transfusions due to preexisting anemia coupled with complex surgery; therefore, efforts should be made to identify novel methods to reduce blood administration in HIV+ patients during surgery.

Conventional ultrafiltration (CUF) is a technique capable of removing large amounts of fluid (isotonic plasma water) while reducing inflammatory mediators complicating CPB procedures in pediatric patients undergoing cardiac surgery. While not as well studied in adults, multiple investigators have evaluated CUF's utility in adult patients undergoing cardiac surgery [10,14]. Conventional ultrafiltration is useful in removing exogenous fluid related to CPB priming volumes and anesthesia administration. When CUF is applied during the early phase of CPB, it possesses the ability to elevate hematocrit, remove excessive prime volume and concentrate plasma proteins without jeopardizing hemodynamic stability. One of the major concerns regarding the utilization of CUF is the potential occurrence of renal compromise and/or development of acute renal failure. However, this issue has been extensively evaluated and does not appear to be a significant contributor to renal dysfunction [9]. However, it is important to carefully review the laboratory studies of an HIV-seropositive patient who is being considered for major cardiac surgery, especially in African-American patients due to their increased risk for renal failure.

Ultrafiltration offers several advantages to ANH and may establish itself as a viable option in various scenarios for HIV+ patients undergoing cardiothoracic surgery with CPB. Unlike ANH, ultrafiltration does not require the perfusionist and/or anesthesiologist to perform additional maneuvers during the period after induction. While ANH may be useful in patients infected with HIV, its application is limited in the presence of anemia which commonly occurs in this patient population; in contrast, ultrafiltration is not limited by anemia. Another potential benefit as a result of the utilization of conventional ultrafiltration is a reduction in inflammatory mediators resulting from CPB. HIV+ patients, in general, have a heightened state of inflammation from HIV infection itself. Even after HAART is initiated, general and specific inflammatory markers (hs-CRP, D-dimer, IL-6) remain elevated.

This case series demonstrates that conventional ultrafiltration may be a useful adjunct for blood conservation during cardiothoracic procedures requiring CPB in HIV-seropositive patients. Although conventional ultrafiltration is classified as a class IIb intervention by the Society of Thoracic Surgeons, this modality should be considered as part of the multi-modal approach for blood conservation in HIV-seropositive patients. The HIV+ patient population presents unique challenges and

opportunities for the perfusionist during cardiac surgery. Further studies are warranted to evaluate more detailed benefits and risks of all types of ultrafiltration (conventional, modified or zero-balance) in this particular patient population in an effort to optimize blood conservation and overall management during cardiopulmonary bypass.

DISCLOSURE

This case report was presented as an abstract at the 35th Annual Meeting of the Society of Cardiovascular Anesthesiologists, Miami, Florida, 2013 [15].

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