

Heart retransplantation in children without the use of blood product

Retransplante cardíaco em criança sem o uso de hemoderivados

Antonio Alceu dos Santos¹, José Pedro da Silva², Luciana da Fonseca³, José Francisco Baumgratz⁴

DOI: 10.5935/1678-9741.20120051

RBCCV 44205-1388

Abstract

This article reports a case of a cardiac retransplantation without the use of blood products, in a 6 year old child, with severe dilated cardiomyopathy after chronic graft rejection and refractory to clinical treatment. To avoid a blood transfusion in this surgery a multidisciplinary approach was planned, which involved the use of preoperative erythropoietin, acute normovolemic hemodilution and intraoperative cell salvage with autologous blood recovery system, as well as a meticulous hemostasis and reduced postoperative phlebotomy.

Descriptors: Heart transplantation. Child. Erythropoietin. Blood transfusion, autologous. Graft rejection.

Resumo

Este artigo relata um caso de retransplante cardíaco sem o uso de hemoderivados, em uma criança de 6 anos, com miocardiopatia dilatada grave, após rejeição crônica do enxerto e refratária ao tratamento clínico. Para evitar transfusão sanguínea nessa cirurgia, foi realizado planejamento multidisciplinar, que envolveu o uso de eritropoietina no pré-operatório, hemodiluição normovolêmica aguda e recuperação de sangue autólogo no intraoperatório (*cell saver*), bem como hemostasia meticolosa e redução de flebotomias no pós-operatório.

Descritores: Transplante de coração. Criança. Eritropoietina. Transfusão de sangue autóloga. Rejeição de enxerto.

INTRODUCTION

Medicine is one of many areas of knowledge related to the maintenance and restoration of health. It works in a broad sense, with the prevention and cure of human and animal diseases in a medical context. This became evident in 1967 when it performed the first heart transplant between humans, by Barnard [1]. That same year, Kantrowitz et al. [2] tried, unsuccessfully, the first transplant in newborn patients with Ebstein anomaly. Only in 1984, after the introduction of cyclosporine in the handling of rejection,

which Bailey et al. [3] performed the first transplant in a child with the hypoplastic left heart syndrome (HLHS).

In children with severe cardiomyopathy refractory to medical treatment, as in the case of non-compacted myocardium [4], or cardiogenic shock [5], heart transplantation is imposed as saving measure. The first heart transplant in an adult without use of blood transfusion occurred in 1985 [6]. At the Congress of the Brazilian Society of Cardiology (CSBC), 2009, a heart transplant was reported in a child 2 years and 9 months, without the use of blood products [7]. Neonatal and infant

1. Specialist in Cardiology, Hospital Beneficência Portuguesa of São Paulo, Assistant Team Physician Dr. José Pedro da Silva, São Paulo, Brazil.
2. PhD in Cardiovascular Surgery, Hospital Beneficência Portuguesa of São Paulo, São Paulo, Brazil.
3. PhD in Cardiovascular Surgery, Hospital Beneficência Portuguesa of São Paulo, São Paulo, Brazil.
4. Specialist in Cardiovascular Surgery, Hospital Beneficência Portuguesa of São Paulo, São Paulo, Brazil.

Work performed at Hospital Beneficência Portuguesa of São Paulo, São Paulo, Brazil.

Correspondence address: Antonio Alceu dos Santos
Rua Maestro Cardim, 769 – Bela Vista – São Paulo, SP
Brasil – CEP: 01323-001
E-mail: antonioalceu@cardiol.br

Article received on January 22nd, 2012
Article approved on April 23rd, 2012

Abbreviations, acronyms & symbols	
CPB	Cardiopulmonary bypass
CSBC	Congress of the Brazilian Society of Cardiology
ANH	Acute normovolemic hemodilution
NYHA	New York Heart Association
rHuEPO	recombinant human erythropoietin
HLHS	Hypoplastic Left Heart Syndrome

cardiac transplantation has enabled survival and improved quality of life in children with severe myocardial dysfunction [8]. The graft failure occurs in approximately 7% of heart transplants in children [9] and in these cases, retransplantation becomes the only therapeutic option. Well-defined strategies have enabled to reduce the use of blood transfusions in cardiac surgery [10,11]. The treatment by cardiac retransplantation, particularly for pediatric patients, is what has reduced prospects for organ procurement in a timely manner, especially at the lower weight and reduced availability of compatible donors. Recently, we discovered, after research in national and international literature, which had not yet been reports of retransplantation in children without the use of blood transfusion. Thus, we report a case of cardiac retransplantation in a 6 year old child without blood transfusion.

The study was approved by the Ethics Committee in Research of the Hospital Beneficência Portuguesa of São Paulo (São Paulo, SP, Brazil).

CASEREPORT

One child, female, with a diagnosis of HLHS at birth, was submitted initially to the first (04/11/2003) and second (03/19/2004) stage of the correction protocol Norwood. After 2 years and 4 months, she developed severe myocardial dysfunction, cardiac transplantation is necessary, performed on 29.07.2006, without the use of blood products [7].

The patient was uneventful until 2009, when she was again admitted to the Hospital Beneficência Portuguesa of São Paulo, with 6 years, weight 16.6 kg and body surface area of 0.69 m², respectively, diagnosed with congestive heart failure functional class IV according to New York Heart Association (NYHA), and ventricular tachycardia in severe chronic rejection refractory to immunosuppressive therapy (cyclosporine, mycophenolate, methylprednisolone), as well as the use of vasoactive drugs (dobutamine, milrinone, norepinephrine), evolving with rapid clinical deterioration, even to cardiogenic shock, requiring mechanical ventilation. A transthoracic echocardiogram revealed poor left ventricular function to a significant degree, with delta D of 16%. Due to this large hemodynamic instability without

response to medical treatment, he was appointed the new heart transplant.

For religious reasons, parents requested that staff apply in this case the protocol management and conservation of blood to serious and complex heart surgery, the team created especially for surgery in adults but also in some cases in children, as shown in the CSBC, in 2011 [12]. With a more restrictive conduit for blood transfusion [13], this surgery was accepted.

Preoperatively, the child showed normal levels of hemoglobin (13.0 g / dl), hematocrit (38 mL / dL) and platelets (146 mil/mm³), nevertheless, we promptly began treatment with recombinant human erythropoietin (rHuEPO 600 IU / kg / week), ferrous sulphate (10 mg / kg / day), folic acid (5 mg / day), and cyanocobalamin (vitamin B12 5000 IU / day) because the optimum result of the stimulus erythrocytes occurs later after the first week [14].

With a schedule of any team (surgeon, physician, anesthesiologist, intensive care), was performed orthotopic cardiac retransplantation, on 12/13/2009, successfully and without administration of blood products. The total time of ischemia was 180 minutes. For surgery, we mini-circuit (mini-SCC) without human albumin in the priming, controlled hypotensive anesthesia, normothermia, acute normovolemic hemodilution (ANH) and, crucially, intraoperative recovery of cells (cell saver), and meticulous hemostasis.

Postoperatively, the child was kept normotensive and normothermic and also minimized the phlebotomy. rHuEPO were reintroduced, iron, vitamin B12 and folate and the beginning of immunosuppressants. The dose of cyclosporine was controlled according to their serum by means of radioimmunoassay method, maintaining the level of 300-400 ng / mL. The dose of mycophenolate sodium was 11.2 mg / kg / day. The lowest level of hemoglobin after surgery was 9.7 g / dl. Patient was discharged 40 days after transplantation and with normal levels of hemoglobin (Figure 1).

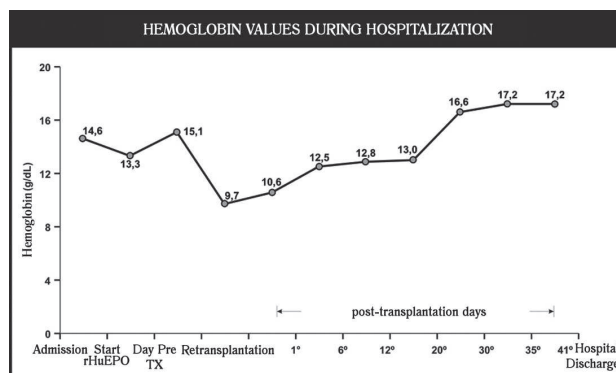


Fig.1 - Hemoglobin levels during hospital stay

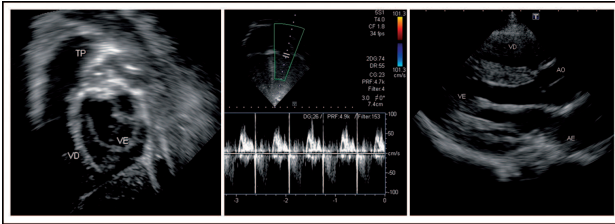


Fig.2 - Doppler echocardiogram showing normal biventricular cardiac function

Since the retransplantation by that date, the child is in excellent general condition with normal biventricular cardiac function at the Doppler echocardiography (Figure 2), with no sign of rejection and lack of toxicity by immunosuppressants.

DISCUSSION

Since the first reported case of retransplantation in 1977 [15], experience with this procedure is still limited, especially in children. Vasculopathy and acute or chronic rejection of the graft represent the main indications [16]. In 1964, we performed the first heart surgery in the world without blood transfusion [17], and since then several other similar cases have been described in the literature [18]. Although some studies show, first, that surgery with massive bleeding not treated with blood transfusions increase the risk of death [19], which actually has been observed in the last decade, several studies showing increased morbidity [20], and fundamentally increase in mortality related to the practice of blood transfusions [21,22]. Another extension problem worldwide is the shortage of blood, raising great concern. In a situation of increasing demand for blood and blood products, with a stationary trend of donations, the emphasis is on lack of stocks in several countries [23]. In Brazil, the demand for blood increases 1% per year, while expectations for growth of blood donations ranging from 0.5% to 0.7% per year [24]. All this has contributed to seek medical treatment options [11] and more restrictive strategies [25] to avoid or minimize blood transfusions.

We have many protocols in the literature for performing pediatric heart surgery free of homologous blood transfusion, first, we mention the proposed by Gomez et al. [26], who enumerated several strategies in pre-, intra- and postoperatively. In 2008, other authors confirmed the efficacy and safety of these programs [27]. Another protocol considers the pre-autologous blood donation associated with the administration of erythropoietin [28].

Similarly, since 2002, also developed a program of management and conservation of homologous blood for cardiac surgery, which basically boils down to increase red

cell mass (iron, folate and rHuEPO) [29,30], and the HNA, the Intraoperative recovery of cells [27] and, crucially, the surgical technique with meticulous hemostasis. Thanks to this program, multiple blood transfusions have been reduced or even avoided, especially in case of retransplantation.

CONCLUSION

It was possible to perform a cardiac retransplantation without the use of homologous blood in a child with severe dilated cardiomyopathy after chronic graft rejection and irreversible drug therapy, using a program management and conservation of blood, and rigorous multidisciplinary planning. Blood transfusions can be avoided or reduced when it is meant to preserve the autologous blood.

REFERENCES

1. Barnard CN. The operation. A human cardiac transplant: an interim report of a successful operation performed at Groote Schuur Hospital, Cape Town. *S Afr Med J*. 1967;41(48):1271-4.
2. Kantrowitz A, Haller JD, Joos H, Cerruti MM, Carstensen HE. Transplantation of the heart in an infant and an adult. *Am J Cardiol*. 1968;22(6):782-90.
3. Bailey LL, Nehlsen-Cannarella SL, Concepcion W, Jolley WB. Baboon-to-human cardiac xerotransplantation in a neonate. *JAMA*. 1985;254(23):3321-9.
4. Croti UA, Braile DM, Moscardini AC, Kozak ACLFBM. Transplante cardíaco em criança com miocárdio não compactado. *Rev Bras Cir Cardiovasc*. 2010;25(2):261-3.
5. Jatene MB, Miana LA, Pessoa AJ, Riso A, Azeka E, Tanamati C, et al. Transplante cardíaco pediátrico em vigência de choque cardiogênico refratário: análise crítica da viabilidade, aplicabilidade e resultados. *Arq Bras Cardiol*. 2008;90(5):360-4.
6. Corno AF, Laks H, Stevenson LW, Clark S, Drinkwater DC. Heart transplantation in a Jehovah's Witness. *J Heart Transplant*. 1986;5(2):175-7.
7. Santos AA, Silva JP, Fonseca L, Baumgratz JF, Lianza AC, Lima DLC, et al. Transplante cardíaco sem uso de hemotransfusão em criança com hipoplasia de coração

- esquerdo. Arq Bras Cardiol. 2009;93(3 supl 1):29. Disponível em: http://www.arquivosonline.com.br/2009/9303/pdf/Resumo_Comunicacoes_64CBC.pdf Acesso em: 6/4/2012.
8. Barbero-Marcial M, Azeka E, Camargo PR, Riso A, Jatene M, Soares J, et al. Transplante cardíaco neonatal e infantil. Arq Bras Cardiol. 1996;67(3):165-70.
 9. Mahle WT. Cardiac retransplantation in children. *Pediatr Transplant*. 2008;12(3):274-80.
 10. Souza HJB, Moitinho RF. Estratégias para redução do uso de hemoderivados em cirurgia cardiovascular. *Rev Bras Cir Cardiovasc*. 2008;23(1):53-9.
 11. Mackenzie CF, Shander A. What to do if no blood is available but the patient is bleeding? *South Afric J Anaesth Analg*. 2008;14(1):39-43.
 12. Santos AA, Silva JP, Fonseca L, Baumgratz JF, Freire R, Castro RM, et al. Protocolo de gerenciamento e conservação do sangue em cirurgias cardíacas graves e complexas. *Arq Bras Cardiol*. 2011;97(3 Supl.1):59. Disponível em: <http://www.arquivosonline.com.br/2011/9703/pdf/TL-66-CBC.pdf> Acesso em 6/4/2012.
 13. Lacroix J, Hébert PC, Hutchison JS, Hume HA, Tucci M, Ducruet T; TRIPICU Investigators; Canadian Critical Care Trials Group; Pediatric Acute Lung Injury and Sepsis Investigators Network, et al. Transfusion strategies for patients in pediatric intensive care units. *N Engl J Med*. 2007;356(16):1609-19.
 14. Aguiar IFVP, Krebs VLJ, Gualandros SFM, Silveira PAA, Vaz FAC. Efeitos da eritropoetina recombinante humana em recém-nascidos pré-termo com doenças infecciosas. *Rev Assoc Med Bras*. 2007;53(1):90-4.
 15. Copeland JG, Griep RB, Bieber CP, Billingham M, Schroeder JS, Hunt S, et al. Successful retransplantation of the human heart. *J Thorac Cardiovasc Surg*. 1977;73(2):242-7.
 16. Richmond ME, Addonizio LJ, Hsu DT, Mital SR, Mosca RS, Quaegebeur JM, et al. Cardiac retransplantation in high risk pediatric patients. *Pediatr Transplant*. 2007;11(6):615-23.
 17. Cooley DA, Crawford ES, Howell JF, Beall AC Jr. Open heart surgery in Jehovah's Witnesses. *Am J Cardiol*. 1964;13:779-81.
 18. Ott DA, Cooley DA. Cardiovascular surgery in Jehovah's Witnesses. Report of 542 operations without blood transfusion. *JAMA*. 1977;238(12):1256-8.
 19. Benson KT. The Jehovah's Witness patient: considerations for the anesthesiologist. *Anesth Analg*. 1989;69(5):647-56.
 20. Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. *J Am Coll Surg*. 2006;202(1):131-8.
 21. Ergoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. *Ann Thorac Surg*. 2002;74(4):1180-6.
 22. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Crit Care Med*. 2008;36(9):2667-74.
 23. Sojka BN, Sojka P. The blood donation experience: self-reported motives and obstacles for donating blood. *Vox Sang*. 2008;94(1):56-63.
 24. Novaretti MCZ. Importância dos carreadores de oxigênio livre de células. *Rev Bras Hematol Hemoter*. 2007;29(4):394-405.
 25. Hajjar LA, Vincent JL, Galas FR, Nakamura RE, Silva CM, Santos MH, et al. Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. *JAMA*. 2010;304(14):1559-67.
 26. Gomez D, Olshove V, Weinstein S, Davis JT. Blood conservation during pediatric cardiac surgery. *Transfus Altern Transfus Med*. 2002;4(1):27-33.
 27. Jonh T, Rodeman R, Colvin R. Blood conservation in a congenital cardiac surgery program. *AORN J*. 2008;87(6):1180-6.
 28. Komai H, Naito Y, Okamura Y, Fugiwara K, Suzuki H, Uemura S. Preliminary study of autologous blood predonation in pediatric open-heart surgery impact of advance infusion of recombinant human erythropoietin. *Pediatr Cardiol*. 2005;26(1):50-5.
 29. Shannon KM, Keith JF 3rd, Mentzer WC, Ehrenkranz RA, Brown MS, Widness JA, et al. Recombinant human erythropoietin stimulates erythropoiesis and reduces erythrocyte transfusions in very low birth weight preterm infants. *Pediatrics*. 1995;95(1):1-8.
 30. Maier RF, Obladen M, Scigalla P, Linderkamp O, Duc G, Hieronime G, et al. The effect of epoetin beta (recombinant human erythropoietin) on the need for transfusion in very-low-birth-weight infants. European Multicentre Erythropoietin Study Group. *N Engl J Med*. 1994;330(17):1173-8.