The Effect of Normothermic Cardiopulmonary Bypass on Postoperative Bleeding in CABG

Saeed Hoseini MD, Nasrin Elahi MSc RN, Sepideh Sobhani MSc RN, Seyyed Mohammad Bagher Tabatabaee MD, Ali Sadeghpoor Tabaie MD, Ali Yaghoubi MD, Masoud Shafiee MD, Mahsa Firoozi RN, Mohammad Hosein Yousefzadeh RN, Maryam Moetamedkhah RN, Hamid Reza Davoudi RN and Zohre Gholami, RN

Abstract

Background- CABG is the most common type of cardiac surgery which generally is done under cardiopulmonary bypass (CPB). Hypothermic CPB was introduced in cardiac surgery in order to protect organs against hypoperfusion. Hypothermia is associated with many adverse effects on the vital organs, which result in impairment of organ and systemic function. Normothermia on the other hand is more in agreement with the physiology of human organs. The aim of this study is to evaluate the effect of body temperature during CPB on postoperative bleeding.

Methods- One hundred patients were randomized into normothermic (35-37º C, N=50) and mild hypothermic (28-32º C, N=50) CPB groups and compared with respect to blood loss, transfusion requirements and platelet level in primary coronary artery bypass grafting. The patients' hemoglobin levels, leukocyte counts and platelet counts were measured before operation, immediately upon arrival in the intensive care unit, 4 hours afterwards and 6 days after surgery. The volume of blood shed through mediastinal and pleural drainage tubes were recorded at 6, 12 and 24 hours after operation.

Results- There were no differences in preoperative characteristic including patient age, sex, number of occluded vessels, weight, height, hemoglobin and hematocrit level, platelet and WBC levels. Normothermic patients tended to bleed less at 24 hours (warm, 288±30ml vs. cold, 580±100ml). Platelet levels were preserved better in normothermic patients than in hypothermic patients. The warm group had a reduced blood loss by 40 percent after 6, 34% after 12 and 30% after 24 hours as compared with blood loss in hypothermically-perfused patients.

Conclusion- These data suggest that normothermic systemic perfusion reduced postoperative blood loss and preserved platelets ***(Iranian Heart Journal 2006; 7 (2):31-36)***.

Key words: normothermia ▪ bleeding ▪ coronary artery bypass grafting ▪ hypothermia

Both cardiopulmonary bypass and hypothermia contribute to bleeding after cardiac operations.

Cardiopulmonary bypass activates platelets, leading to platelet degranulation, deposition and depletion. [1-5]

Impaired platelet function increases postoperative blood loss. Hypothermia induces a reversible platelet membrane dysfunction, activates the fibrinolytic cascades and inhibits activated clotting factors.

Received Aug 1, 2006; Accepted for publication Oct 20, 2006
From the Dept. of Cardiovascular Surgery, Shaheed Rajaee Cardiovasclar Medical Center, Mellat Park, Vali Asr Ave. Tehran, Iran.
Correspondence to: Saeed Hosseini MD; Dept. of Cardiovascular Surgery; Shaheed Rajaee Cardiovascular Medical Center, Mellat Park, Vali Asr Ave. Tehran, Iran

Patients undergoing the combinations of systemic hypothermia and cardiopulmonary bypass may aggravate postoperative platelet dysfunction.

A retrospective review undergoing isolated coronary artery bypass grafting at our institution between 2004 and 2005 showed that normothermic systemic perfusion was associated with reduced postoperative blood loss.

To better evaluate the effect of normothermic systemic perfusion on postoperative blood loss, we reviewed bleeding in patients in an ongoing randomized clinical trial comparing the normothermic technique of heart surgery with mild hypothermic systemic perfusion. The primary goal of this ongoing clinical trial is reducing perioperative morbidity and mortality.

Methods

One hundred consecutive patients undergoing isolated primary coronary artery bypass grafting from 2004 to 2005 participated in our study of normothermic versus hypothermic heart surgery. Patients were randomly assigned either to receive warm systemic perfusion (warm group, 35 to 37º C, N=50) or to receive mild systemic hypothermia (cold group, 28 to 32º C, N=50). Antifibrinolytic agents were given to most patients without a specific protocol. Perfusion temperature was assigned by the perfusionist during operation according to a randomization table without regard to drug treatment. Cardiopulmonary bypass was established with a single two stage right atrial cannula and an ascending aorta cannula. During bypass, the hematocrit value was maintained between 18% and 25%, pump flows between 2 and 2.5l/min/m2 and mean arterial pressure between 50 and 60 mmHg.

Transfusions of blood products were ordered by the surgeon or by the anesthetist in the intensive care unit who was not aware of the randomly assigned perfusion temperature. Patients considered to be at greater risk for preoperative morbidity and mortality (patients 70 years or older or those undergoing urgent operation for unstable angina, 39/100 patients, 39%) were given packed red blood cells to maintain postoperative hemoglobin values greater than 8.0g/l. Low risk patients (younger than 70 years and undergoing elective or semi-elective surgery, 61/100 patients, 61%) received transfusions to maintain intraoperative hematocrit values greater than 18% and postoperative hemoglobin levels greater than 7.5g/l. The distribution of high and low-risk patients did not differ between groups. Platelet concentrates were administered to correct significant thrombocytopenia (<70×10^3cells/L) associated with increased postoperative bleeding (>200 ml/hr) or a platelet count of less than 50×10^3cells/ L in the absence of increased blood loss.

The volume of blood shed through mediastinal and pleural drainage tubes was recorded at 6, 12 and 24 hours after operation.

The frequency of transfusion of erythrocytes preparations was recorded, as were the numbers of units of packed blood cells, platelet concentrates, plasma and cryoprecipitate administered.

The patients' hemoglobin level, leucocyte count and platelet count were measured before operation, immediately on arrival in intensive care unit, 4 hours after operation in the morning and at 6 days after operation of the first postoperative day at 6, 12, 24, 48 hours for Hgb and one time for other values.

Statistical analyses were carried out with SPSS v.11. Initial comparisons were made between warm and cold techniques with unpaired t tests and x^2 analysis.

Ten patients who were returned to the operating room for exploration and had a surgical source of bleeding identified were excluded from the study. Among these patients, four were in the warm group.

Results

There were no differences in preoperative characteristics including patient age, sex, number of occluded vessels, weight, height, hemoglobin/hematocrit level, platelet and WBC levels. There was no difference in preoperative clinical information in warm and cold groups (Table I).

Table I. Preoperative clinical data in warm and cold groups.

Clinical Data	Cold group	Warm group	P value
Age	59.85	57	0.234
Height	170.11	169.26	.765
Weight	72.59	72.89	0.491
Graft number	3.74	3.04	0.054
Hgb preop	13.94	13.64	0.978
Platelet preop	247,926	234,250	0.167
PT preop	13.93	13.39	0.153
PTT preop	42.704	42.607	0.970

The systemic perfusion temperature had a significant effect on the volume of blood loss after 6, 12 and 24 hours ($p<0.05$): the warm group bled significantly less after 6 and 12 hours than did the cold group of patients ($p<0.05$, Fig.1).

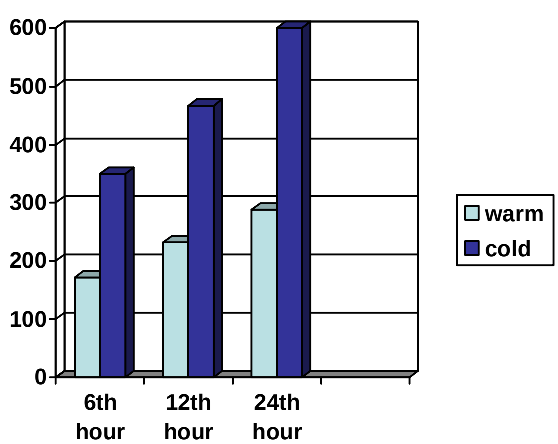

Fig. 1. Bleeding comparison in warm and cold groups.

Of 100 patients, 26 received transfusions of packed red blood cells. The frequency of erythrocyte transfusion differed between perfusion temperature groups (cold, 18% vs. warm, 8%). Platelet levels fell immediately after operation in both temperature groups. However, platelet levels were significantly higher after operation in the warm group than in the cold group ($P<0.05$, Fig.2).

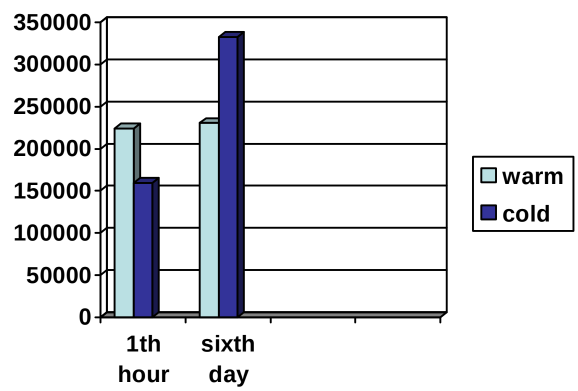

Fig. 2. Platelet count in warm and cold groups.

Hemoglobin levels fell from a preoperative value of 13.5±0.1g/l for all patients to a low of 9.0±1g/l ($P<0.05$) immediately after operation, and levels reached 11.71±1g/l in the warm vs. 8.3±1g/l in the cold group after 6 days ($P<0.05$). Thus there was a significant difference between warm and cold groups with regard to hemoglobin level at 6, 12, 24, 48 hours and at 6 days after operation (Fig. 3). The operation resulted in an elevation of leukocyte counts, from $7.5\pm0.2\times10^3$cell/l before operation to a high of $10.1\pm0.2\times10^3$cell/l on the morning of the first postoperative day ($P<0.05$). By 6 days after operation leukocyte counts had declined to $8.5\pm0.2\times10^3$cell/l but were still significantly elevated from preoperative levels ($P<0.05$). Temperature of perfusion had no influence on leukocyte counts during this period.

Discussion

Concern with transfusion-related morbidity and death has led most cardiac surgeons to initiate blood conservation programs. We randomly assigned patients undergoing coronary bypass grafting in our ongoing trial to warm or cold perfusion surgical groups.

We expected normothermia to exert a larger effect on postoperative blood loss. The warm group had a reduced blood loss by 40% after 6 hours, 34% after 12 hr and 30% after 24 hours as compared with blood loss in patients perfused hypothermically. Del Rosis et al. and Natan et al. attributed a reduction of 30% and 28% in the volume of blood shed during 24 hours to warm groups. Horrow and colleagues found that warm group has a reduced blood loss at 12 hours by 34%.

Patients who received normothermic perfusion bled less than the those in the cold perfusion group ($P<0.05$). The reduction in blood loss was probably related to perfusion temperature. In this study, systemic perfusion at 35 to 37º C rather than 28 to 32º C reduced blood loss at 6, 12 and 24 hours after operation. Patients receiving warm perfusion had lower frequency of red blood cell transfusions and received a lower number of units of packed red blood cells per patient, so warm perfusion is effective in reducing blood loss and transfusion requirements. Both groups had a significant drop in circulating platelet counts after intraoperative hemodilution. Administration of normothermia resulted in significantly higher platelet counts than those found in control patients at postoperative measurement periods. In Horrow and coworkers' study, the perfusion temperature had no effect on postoperative platelet counts, however the patients in the study of Horrow and coworkers had a higher frequency of platelet transfusion than did the patients in our study; this may have been responsible for their platelet counts. The platelet counts in the first hour after operation in the warm group was 223,928/ml and 159,333/ml in the cold group the difference being significant between groups ($P< 0.05$).

Therefore, we conclude that increasing systemic perfusion temperature from 28-32º C to 35-37º C resulted in greater preservation of platelets postoperatively. The reduction of postoperative bleeding by warm perfusion may be due in part to increased levels of circulating platelets.

The platelet counts often 6 days in the warm group was 230,428/ml and 332,629/ml in the cold group, that is not a significant difference between groups because the defect in platelet function is enhanced by warm perfusion, because the defect in platelet membrane function induced by hypothermia is rapidly reversible, and alterations in platelet function may affect blood loss during the first hours but should have diminishing effects at 12 hours after operation.

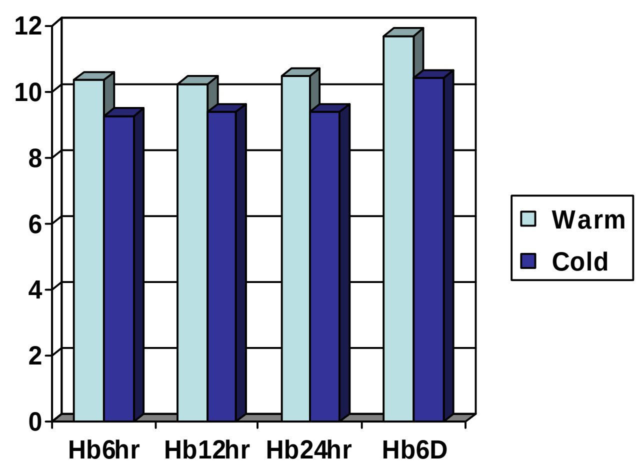

Fig. 3. Hemoglobin levels in warm and cold groups.

References

1. Nathan HJ, Parlea L, et al. Safety of deliberate intraoperative and postoperative hypothermia for patients undergoing coronary artery surgery. J Thorac Cardiovasc Surg 2004; 127(5): 1270-1275.

2. Swan H. Thermoregulation and bioenergetics. Patterns for vertebra survival. 3rd edition. Elsevier Publishing, 1984, pp. 429-430.

3. Gross RE, Hubbard J. Surgical ligation of patent ductus arteriosus: Report of first successful case. JAMA 112; 1980: 720.

4. Nathan HJ, Wells GA, et al. Neuroprotective effect of mild hypothermia in patients undergoing coronary artery surgery with cardiopulmonary bypass. Circulation. 2001; 104 (12 suppl 1): 185-191.

5. Slavik J, Medek K, et al. Normothermia in cardiac surgery with extracorporeal circulation. Center of cardiovascular .

6. Voorhees WD, Abendschein DR, Tacker WA. Effect of whole-body hypothermia on myocardial blood flow and infarct salvage during coronary artery occlusion. American Heart Journal 107; 1984: 945-9.

7. Shumway NE, Lower RR. Topical hypothermia for extended period of anoxic arrest. Surgical Forums 10; 1959: 945-9.

8. Griepp RB Stinson EB, Shumway NE. Profound local hypothermia for myocardial protection during open heart surgery. J Thorac Cardiovasc Surg 1973; 66: 731 - 7.

9. CJ O'Conner, WE McCarthy, Ivankovish AD. Multivariate proctors of bleeding and transfusion in reoperative CABG surgery. Anesthesiol Analgesia 1997; 84: S1-S5, 99.

10. Leslicate MB, Sessler D. Implication of hypothermia for early tracheal extubation following cardiac surgery. J Cardiothorac Vasc Anesthesia Dec 1998; 12 (6) suppl 2: 30-34.

11. Caspi Y, Safadi T, Ammar R, Elamy A, Fishman NH, Merian G. The significance of bundle branch block in the immediate postoperative electrocardiograms of patients undergoing coronary artery bypass. Journal Thorac Cardiovasc Surg 1987; 93: 442-6.

12. Chu A, Califf RM, Pryor DB, McKinnis RA, Harrel FE, Lee KL, Curtis SE, Oldham HN, Wagner GS. Prognostic effect of bundle branch block related to coronary artery bypass grafting. Amer J Cardiol 1987; 59: 798-803.

13. Bigelow WG Lindsay RC, Harrison RC, Gordon RA, Greenwood WF. American J Physiol 160.1980; 160:125-37.

14. Bigelow WG, Lindsay WK, Greenwood WF. Hypothermia: its possible role in cardiac surgery: an investigation of factors governing survival in dogs at low body temperature. Annals Surg 1989; 132 (s): 849-65.

15. Buckberg GD. Myocardial temperature management during aortic clamping for cardiac surgery: protection, preoccupation and perspective. J Thorac Cardiovasc Surg 1991; 102: 849 - 65.

16. Lehot JJ, Villad J, et al. Hemodynamic and hormonal responses to hemodynamic and normothermic cardiopulmonary bypass. J Cardiothorac Vasc Anesthesia 1992; 6: 132-9.

17. Valeri CR, Khabbaz K, Khuri SF, et al. Effect of skin temperature on platelet function in patients undergoing extracorporeal bypass. J Thorac Cardiovasc Surg 1992; 104: 108-16.

18. Robber MJ, Natale AM. Effect of hypothermia on the coagulation cascade. Critical Care Medicine 1992: 1402-5.

19. Lichtenstein SV, Ash E, Dalati H, Cusimano RJ, Panos A, Slutshy AS. Warm heart Surgery. J Thorac Cardiovasc Surg 1991; 101: 269-74.

20. Blair E. Clinical Hypothermia. New York, McGraw-Hill; 1964.

21. Kentaro D, Roger W, VanWinkle D. Hypothermia increases the threshold for ischemic preconditioning. J Thorac Cardiovasc Surgery Aug1998; 8: 319-325.

22. Engelman R, Pleet B. Influence of cardiopulmonary bypass perfusion temperature on neurologic and hematologic function after coronary artery bypass grafting. Annals Thorac Surg 1999; 67: 1547 - 56.

23. Bachet J, Guilment D, Goudot B, et al. Cold cerebroplegia: a new technique of cerebral protection during operations on the transverse aortic arch. J Thorac Cardiovasc Surg 1991; 102: 85-93.

24. Engelman R Pleet AB, Rousou JA, Deaton D, Cheryl GA, Pekow P. What is the best perfusion temperature for coronary revascularization? J Thorac Cardiovasc Surg

Dec 1996; 12: 1622-1633.

25. Christakis GT, Koch JP, Deemer KA, et al. A randomized study of the systemic effects of warm heart surgery. Ann Thoracic Surg 1992; 52: 449-59.

26. Massimino RJ, Steanns GT, Gough JD, Martin J, Singh AK. Moderate hypothermic versus normothermic total cardiopulmonary bypass for coronary artery surgery. J Extracorporeal Technology 1994; 23: 5-8.

27. Leurs PB, Mulder AW, Fiers HA, Hoorntje SJ. Renal failure in the perioperative patient. In: Advances in Cardiac Surgery. Vol. 3, St. Louis, Mosby Yearbook, 1992, pp. 313-27.

28. Mazer CD, Hornstein A, Freedman J. Platelet activation in warm and cold heart surgery. Ann Thoracic Surg 1995; 59:1481-6.

29. Mazer CD, Byrick RJ. Warm heart surgery in patients with perioperative renal dysfunction. Canadian Journal Anesthesiology (Abstract) 1993; 40: A46.

30. Cheng D, et al. Plasma catecholamine responses during normothermic and hypothermic cardiopulmonary bypass surgery. Canadian Journal Anesthesia (Abstract) 1993; 40: A47.

31. Engelman RM, Rousou JA, Flack JE III, et al. Fast-track recovery of coronary bypass patients. Ann Thoracic Surg 1994; 58: 1742-6.

32. Boyle EM, Verrier ED, Spies BD. Endothelial cell injury in cardiovascular surgery: the procoagulant response. Ann Thoracic Surg 1996; 62: 1549-57.

33. Jett JR, Kuritsky JN, Homburger HA. Acqirred immunodeficiency syndrome associated with blood-products transfusion. Ann Internal Med 1983.

34. Hazz K, Hiramon K, Sumiyoshi T, et al. Current status and problems in long-term management of patients undergoing coronary artery bypass surgery in Japan. Japanese Circulation Journal 1986; 50: 895-902.

35. Nightingale R, Deckers J, et al. Quality care and cost-effectiveness: an organized approach to problem solving. Ann Surg 1987; 122: 451-456.

36. Yoshihara H, Yamamoto T, Mihara H. Changes in coagulation and fibrinolysis occurring in dogs during hypothermia. Circulation 1985: 503-512.

37. Reed RI, Bracey AW, Hudson JD, Miller TA, Fisher RP. Hypothermia and blood. Circulation 1990; 32: 141-152.

38. Yau M, Terrence, et al. The effect of warm heart surgery on postoperative bleeding. J Thorac Cardiovasc Surg 1992; 103: 1155-1163.

39. DelRossi, et al. Prophylactic treatment of post-perfusion bleeding. Chest 1989; 96: 27-30.

40. Engelman R, et al. Fast-track recovery of the coronary bypass patient. Ann Thorac Surg 1994; 58: 1742-6.

41. Chang D. Impact of early tracheal extubation on hospital discharge. J Cardiothorac Vasc Anesthesia suppl 2 (Dec) 1998; 12 (6): 35-40.

42. Smeltzerc S, Bare GB. Textbook of Medical Surgical Nursing. 9th edition, Philadelphia, Lippincott, Williams and Wilkins, 2000.

43. Gravlee P. Glenn’s Cardiopulmonary Bypass. Second edition. Philadelphia, Lippincott, Williams and Wilkins, 2000.

44. Salero AT. Warm Heart Surgery. First edition, Cambridge, Holer Headline Group, 1995.

45. Kirklin JW, Barratt-Boyes B. Cardiac Surgery. Third edition, USA, Elsevier Scientific Press, 2003.

46. Lewis FJ, Tauffic M. Closure of atrial septal defects with the aid of hypothermia. JAMA 1953; 153: 1081-1085.

47. Abendschein DR, Tacker WA, Babbs CF. Protection of ischemic myocardial blood flow and infarct salvage during coronary artery occlusion in dogs. Amer Heart J 1984; 107: 945-9.