

# INDUCED MODERATE HYPOTHERMIA FOR LOW CARDIAC OUTPUT AFTER PEDIATRIC CARDIAC SURGERY

P. Akbari-Asbagh\*<sup>1</sup> and M. A. Navabi<sup>2</sup>

1) Department of Pediatric Cardiology, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

2) Department of Pediatric Cardiosurgery, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

**Abstract-** Postoperative low cardiac output states are a major cause of postoperative mortality in infants and children following corrective cardiac surgery or congenital heart defects. Whole body hypothermia has been used since 2001 in the management of these low output states when they are refractory to conventional modes of therapy. From December 2001 to April 2006, 25 cases were included in this study. The median (range) age of patients was 36.6 months (1 mo-19 y) with a median weight of 12.2 kg (3.5-44 kg). Following cooling, there was a decrease in heart rate ( $P < 0.001$ ), an increase in mean arterial pressure ( $P < 0.001$ ) and a decrease in mean arterial pressure ( $P < 0.001$ ). Significant increases in pH and urine output were also noticed, the increase in urine output being greater in the surviving group ( $P = 0.02$ ). A decrease in platelet count was occurred ( $P < 0.001$ ) but WBC count remained unchanged ( $P = 0.18$ ). Fifteen of 25 patients survived to leave hospital. Induced hypothermia does not appear to be associated with any complications and after the failure of all conventional treatments, it seems likely that the technique may have been beneficial to outcome in some patients.

© 2008 Tehran University of Medical Sciences. All rights reserved.

*Acta Medica Iranica* 2008; 46(4): 299-302.

**Key words:** Cardiac surgery, hypothermia, low cardiac output, pediatric surgery

## INTRODUCTION

Induced hypothermia is a well-established technique used primarily during operation involving cardiopulmonary bypass in order to reduce tissue oxygen demand and provide a degree of cellular protection against ischaemia (1-7).

In the postoperative period, low cardiac output states refractory to conventional treatment continue to cause significant morbidity and mortality. In an attempt to treat these patients, induced hypothermia has been used in the postoperative period and has

been described for the treatment of intractable heart failure in children following surgery for complex congenital heart disease (5), uncontrollable supraventricular tachycardias (8) and respiratory distress syndrome in a child (9).

We performed this study to evaluate the effect of moderate hypothermia in the management of low output states after cardiac surgery.

## MATERIALS AND METHODS

From December 2001 to April 2006, patients having a low cardiac output state unresponsive to conventional treatment were included in the study. The study was approved by Ethics Committee of Tehran University of Medical Sciences. Written informed consent was obtained from all parents.

A low cardiac output state was diagnosed by persistent unresponsive hypotension, poor peripheral

Received: 2 Mar. 2008, Revised: 3 May 2008, Accepted: 30 Jun. 2008

### Corresponding Author:

Parvin Akbari-Asbagh, Department of Pediatric Cardiology, Imam Khomeini Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran  
Tel: +98 21 88907062  
Fax: +98 21 88907241  
Email: akbari\_asbagh@sina.tums.ac.ir

## Moderate hypothermia for postoperative low output

perfusion, a widening core/peripheral temperature difference, oliguria in the presence of normal (or increased) right atrial pressure and a developing base deficit despite optimization of pharmacological support and biochemical and hematological parameters. Inotropic support such as adrenaline, dobutamine, dopamine and nitrates was instituted in all patients with low cardiac output states as thought necessary. All patients were intubated and their lungs were mechanically ventilated with optimization of their blood gases; the inspired fraction of oxygen being kept to a minimum level to ensure an adequate arterial partial pressure of oxygen.

Positive end-expiratory pressure and inverse ratio ventilation were used if appropriate. All patients were sedated. Hemodynamic indices were optimized using vasodilators and fluid resuscitation as appropriate. Metabolic abnormalities such as acidosis, electrolyte imbalance and anemia were corrected as far as possible.

Patients in a cardiac rhythm other than sinus were paced using sequential atrioventricular pacing through wires that were placed routinely at the time of surgery. Regular post operative echocardiography was performed to exclude any potentially correctable mechanical defect and to exclude the presence of cardiac tamponade. Biochemical, hematological and clotting studies were performed at least once every 24 h, together with routine bacteriological screens for sepsis. Electrolytes, acid-base status and hematocrit were optimized as far as was possible. Oliguria (< 0.5 ml/kg/h), unresponsive to both adequate atrial pressure and diuretics, was managed by peritoneal dialysis.

Hypothermia was induced using a thermostatically controlled water-filled cooling blanket placed under the child and usually took about one hour to achieve. Body temperature was measured with a rectal thermistor. Although we are aware of limitation of using this site as an indication of core temperature, we believe it to be suitable for the management of postoperative cooling and monitoring of a steady state. Peripheral temperature was measured using a skin thermistor placed on the big toe.

Hemodynamic parameters were measured over a 4-hour period before cooling and were compared

with another 4-hour period 6 hours after the start of cooling. This 6 hours interval was chosen to allow adequate cooling of all tissues and the alignment of a physiological steady state. Parameters measured were heart rate, right atrial pressure, systemic arterial blood pressure, urine output and core/peripheral temperature difference. The blood gases and acid-base status were also measured. Platelet count and white blood cell count were measured before cooling and 48 hours after cooling (or before rewarming if this occurred earlier) and were compared with the values recorded before cooling. Survival was defined as the child leaving hospital.

## RESULTS

A total of 25 patients who had a refractory low cardiac output state unresponsive to conventional treatment were treated with moderate hypothermia and cooled to 32-33° C in the postoperative period. Fifteen of these survived to leave the hospital.

Median (range) age at time of surgery was 36.6 months (1 month to 19 years). Median weight was 12.2 (3.5-44) kg. Underlying disorders are shown in Table 1. The time after surgery that cooling was started ranged from 0 to 120 hours. The duration of cooling ranged from 1.5 to 72 hours. There was no significant difference in these values between surviving and non surviving groups. The physiological changes observed after cooling are presented in Table 2.

**Table 1.** Underlying diseases of the patients who developed low output states

Diagnosis	Procedure	No
Tetralogy of Fallot (VSD, PA)	Total correction	8
TGA, VSD, PS	Rastelli procedure	4
TGA	Arterial switch	2
VSD	Closure	4
Aortic stenosis	Ross procedure+ Repair	2
TAPVC	Total repair	1
CAV-Canal	Total repair	1
Other	-	3

Abbreviations: VSD, ventricular septal defect; PA, pulmonary atresia; TGA, transposition of great vessels; PS, pulmonic stenosis; AS, aortic stenosis; TAPVC, total anomalous pulmonary venous connection; CAV canal, common atrioventricular canal.

**Table 2.** Changes in measured variables noted 6 h after the start of cooling\*

Variable	Before cooling	After cooling	P value
Heart rate (beats/min)	175	139	0.001
Mean arterial blood pressure (mm Hg)	46	65	0.001
Mean right atrial pressure (mm Hg)	13	10	0.001
Toe-core temperature difference (°C)	6.3	6.1	0.72
Arterial pH	7.37	7.45	0.001
Plasma bicarbonate (mmol/L)	18	23	0.028
Urine output (ml/kg/h)	1.0	2.8	0.004
Platelet count; ( $\times 10^9/L$ )	220	70	0.001
White blood cell count ( $\times 10^9/L$ )	11.200	10.8	0.19

\* Data are given as mean (SD).

There was significant increase in mean arterial pressure, arterial pH, plasma bicarbonate and urine output ( $P < 0.05$ ). Also, there were significant decreases in heart rate, mean right atrial pressure and platelet count ( $P < 0.05$ ). There were no significant changes in toe-core temperature difference or white blood cell count. There was a significant difference between survivors and non survivors in only one variable: urine output. Surviving patients had a significantly higher mean urine output than non surviving patients.

Peritoneal dialysis was required in 21 of the 25 patients before cooling. No marked metabolic acidosis seen during subsequent gradual rewarming. Thrombocytopenia was treated with platelet transfusions although no fixed limit was used below which transfusion was instigated. There was no evidence of DIC (disseminated intravascular coagulation) in any child. The observed decrease in platelet count was not associated with increased bleeding.

## DISCUSSION

Induced hypothermia is now a well-established technique used in several forms of surgery to provide tissue protection during periods of ischemia. The technique is used most commonly during cardiac surgery when the myocardium is subjected to periods of circulatory standstill. The protective effects of hypothermia were initially thought to be due to a decrease in metabolic rate associated with a slowing of temperature-dependent enzymatic reaction (1). Oxygen consumption decreases by  $\approx 8\%$  for each degree centigrade decrease in temperature

and at core temperature of  $28^\circ\text{C}$  oxygen demand is halved (1, 10). The cytoprotection is seen at moderate hypothermia ( $33\text{-}35^\circ\text{C}$ ) (15).

Deep hypothermia and cardiac standstill has been used to facilitate cardiac surgery for many years. In 1959, Drew and Anderson described three such cases (7) and in 1967, a large team from the University of Kyoto in Japan described their experience (14). Barrat-Boyes also used deep hypothermia and circulatory arrest in the repair of cardiac defects in infancy (6) and in the Wessex Cardiac Unit profound hypothermia was used, along with its advantages and problems, over a 6 year period (15).

The success of operative hypothermia led to the suggestion that hypothermia may be of benefit to patients with primary myocardial failure in the postoperative period. We have used the technique of induced hypothermia after failure of conventional treatment and when a relentless downhill course with a fatal outcome seemed inevitable. We are not in a position to say whether cooling affected the outcome in these cases because, in our view, a controlled study would present serious ethical problems. It is our belief that the use of moderate hypothermia has played a significant part in reducing the mortality in this group of critically ill patients.

Despite the known detrimental effects of cooling the technique appears to be safe. The only adverse change we noted was a decrease in platelet count that was treated by platelet transfusions when the platelet count decreased to  $50 \times 10^3$  and was not associated with increase mortality or morbidity from bleeding.

In conclusion, moderate hypothermia is a helpful therapeutic modality for patients with low cardiac

## Moderate hypothermia for postoperative low output

output. It may give us time to recognize and correct inadequate repair. Cooling may be more effective when LV dysfunction is causing low cardiac output. Transient, post re-warming neurologic and behavioral disorder maybe be the result of 1) non homogenous cooling, 2) inadequate paralysis, and 3) sedative accumulation. Persistent adequate diuresis may indicate good response to cooling and patients' weight is definitely a limiting factor for cooling. There are still a lot to be learned from effect of moderate hypothermia

### Conflict of interests

The authors declare that they have no competing interests.

## REFERENCES

1. Fairley HB. Metabolism in hypothermia. *Br Med Bull.* 1961 Jan;17:52-55.
2. Dill DB, Forbes WH. Respiratory and metabolic effects of hypothermia. *Am J Physiol.* 1941; 132: 685-692.
3. Salisbury PF, Cross CE, Rieben PA. Integrative study of the circulation in moderate hypothermia. *Am J Cardiol.* 1963 Aug;12:184-193.
4. Badeer HS. Effect of hypothermia on the contractile "capacity" of the myocardium. *J Thorac Cardiovasc Surg.* 1967 May; 53(5):651-656.
5. Moat NE, Lamb RK, Edwards JC, Manners J, Keeton BR, Monroe JL. Induced hypothermia in the management of refractory low cardiac output states following cardiac surgery in infants and children. *Eur J Cardiothorac Surg.* 1992;6(11):579-584
6. Barratt-Boyes BG, Simpson M, Neutze JM. Intracardiac surgery in neonates and infants using deep hypothermia with surface cooling and limited cardiopulmonary bypass. *Circulation.* 1971 May; 43(5 Suppl):I25-30.
7. Drew CE, Anderson IM. Profound hypothermia in cardiac surgery: report of three cases. *Lancet.* 1959 Apr 11;1(7076):748-750.
8. Reasbeck PG, Edwards JC, Monroe JL. The treatment of intractable myocardial failure after open-heart surgery by whole body hypothermia. *J Cardiovasc Surg (Torino).* 1980 Jan-Feb; 21(1):91-94.
9. Pilkington S, Edwards JC, Monroe JL, Salmon AP. Hypothermia and respiratory distress syndrome. *Pediatr Cardiol.* 1996 Nov-Dec;17(6):390-392.
10. Balaji S, Sullivan I, Deanfield J, James I. Moderate hypothermia in the management of resistant automatic tachycardias in children. *Br Heart J.* 1991 Sep; 66(3):221-224.
11. Phoon CK. Deep hypothermic circulatory arrest during cardiac surgery: effects on cerebral blood flow and cerebral oxygenation in children. *Am Heart J.* 1993 Jun;125(6):1739-1748.
12. Ahn DS, Lee YH, Kang DH, Kang BS. Effect of hypothermic cardioplegia on cardiac protection--I. Effect of hypothermic cardioplegia on the cytosolic Ca<sup>2+</sup> concentration in rat ventricular myocytes. *Yonsei Med J.* 1994 Jun; 35(2):162-176.
13. Krivosic-Horber R. [Mild hypothermia and cerebral protection]. *Ann Fr Anesth Reanim.* 1995;14(1):122-128. French.
14. Hikasa Y, Shirotani H, Mori C, Kamiya T, Asawa Y. Open heart surgery in infants with an aid of hypothermic anesthesia. *Nippon Geka Hokan.* 1967 Jul 1;36(4):495-508.
15. Manners JM, Monroe JL, Edwards JC. Corrective cardiac surgery in infants. A review of 136 patients including the contribution of postoperative ventilation. *Anaesthesia.* 1980 Dec; 35(12):1149-1156.
16. Boyer NH, Gerstein MM. Induced hypothermia in dogs with acute myocardial infarction and shock. *J Thorac Cardiovasc Surg.* 1977 Aug; 74(2):286-294.
17. Goldberg LI. Effects of hypothermia on contractility of the intact dog heart. *Am J Physiol.* 1958 Jul; 194(1):92-98.
18. Prec O, Rosenman R, Braun K, Rodbard S, Katz LN. The cardiovascular effects of acutely induced hypothermia. *J Clin Invest.* 1949 Mar; 28(2):293-300.
19. Suga H, Goto Y, Igarashi Y, Yasumura Y, Nozawa T, Futaki S, Tanaka N. Cardiac cooling increases E<sub>max</sub> without affecting relation between O<sub>2</sub> consumption and systolic pressure-volume area in dog left ventricle. *Circ Res.* 1988 Jul; 63(1):61-71.
20. Cooper KE. The circulation in hypothermia. *Br Med Bull.* 1961 Jan; 17:48-51.
21. Bay J, Nunn JF, Prys-Roberts C. Factors influencing arterial PO<sub>2</sub> during recovery from anaesthesia. *Br J Anaesth.* 1968 Jun; 40(6):398-407.