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Simple deep hypothermia with a large amount of fentanyl anesthesia in neonates undergoing correction for total anomalous pulmonary venous return

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Introduction

Total anomalous pulmonary venous return (TAPVR) is a congenital heart disease. Since no effective palliative treatment has been established, radical open heart surgery must be performed during the early period after birth. Although cardiopulmonary bypass (CPB) is generally used during surgery, many problems remain with respect to its use in neonates, and the prognosis has not been satisfactory. We had been performing simple deep hypothermia under deep ether anesthesia for radical surgery in neonates and younger infants with TAPVR. However, due to cardiac insufficiency, the infants' hemodynamics could not be stabilized under deep ether anesthesia. From 1989 to 1996, simple deep hypothermia was performed for radical surgery in ten neonates with TAPVR using a large amount of fentanyl instead of ether, and it was observed that the hemodynamics during surgery were stable and that the outcome improved. The present paper discusses several problems concerning this anesthetic and surgical procedure in comparison with CPB.

Patients and methods

Severe cyanosis, hypoxia, cardiomegaly, and congestive lungs were detected in all patients from the time of birth. Five patients underwent artificial ventilation, and no cardiotonics or diuretics were administered. The diagnosis of TAPVR was based on an ultrasonographic cardiography.

The patients were placed supine on the special operating table for hypothermia as shown in Fig. 1. Routine monitoring included electrocardiography (ECG), electroencephalography (EEG), and recording of arterial blood pressure (ABP), heart rate (HR), central venous pressure (CVP), arterial blood gas analysis, rectal and esophageal temperature, and urine volume.

Anesthesia was induced with 100 μg fentanyl IV without premedication. Endotracheal intubation was performed with 1 mg vecuronium bromide IV, and ventilation was controlled in fractional inspiratory oxygen (F_{IO_2}) 1.0 during anesthesia. Nine patients (patients 1–9) were managed with α-stat, and patient 10 was managed under pH-stat according to decreasing ventilation volume during hypothermia. A total of 100 $\mu g \cdot kg^{-1}$ of fentanyl was administered. Each patient was then covered with a vinyl sheet and immersed in ice water by lowering the inner table. A low concentration of ether or 0.5% of isoflurane was inhaled by the patient intermittently with favorable hemodynamics. During the cooling period, 10 $ml \cdot kg^{-1}$ of 10% low-molecular-weight dextran in 5% dextrose (LMWD) and lactated Ringer's solution, and 10 $mg \cdot kg^{-1} \cdot h^{-1}$ of lidocaine were infused continuously; furthermore, 5–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dobutamine (DOB) was given continuously during all phases of the anesthetic course if necessary. At an esophageal temperature of 30°C, 100 units$\cdot kg^{-1}$ of heparin was administered IV. When severe hypotension was observed, 1 ml of cardiotonic cocktail (10 ml of 20% dextrose, 10 ml of 2% $CaCl_2$, and 1 ml of 0.01% norepinephrine in 21 ml solution) was bolus-administered IV. When the target body temperature was achieved, the ice water was removed, and surgery was started by raising the inner table to the operating level. After clamping of the venae cavae, pulmonary artery, and aorta, 10 ml of Young's solution (5 g potassium citrate, 12.3 g

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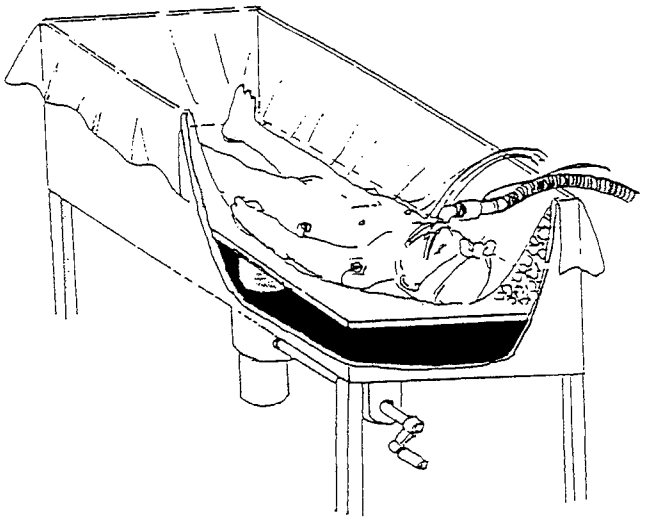

Fig. 1. Operating table for hypothermia used at Iwate Medical University. An inner table, within a tank-like tub filled with water, can be raised or lowered easily. The patient, when immersed in ice water for cooling or hot water for warming, is covered with a vinyl sheet. The operation can be performed by raising the inner table to the operating level

magnesium sulfate, and 5 mg neostigmine bromide in 500 ml solution) at room temperature was injected transaortically into the coronary artery to induce cardiac standstill. Intracardiac correction was then performed. During intracardiac correction under cardiac standstill, Young's solution was not supplemented.

After completing intracardiac correction, artificial ventilation was started, the clamps were removed from the large vessels (except for the aorta), and 10 ml of cardiotonic cocktail and autologous blood sucked from the aorta were pumped with a syringe several times into the coronary artery transaortically. Simultaneously with achievement of cardiac resuscitation, the aortic clamp was removed. The inner operating table, shown in Fig. 1, was lowered into 42°C water and the patient placed on the vinyl sheet was warmed without getting him or her wet. The acid-base balance (ABB) was corrected by a sodium bicarbonate solution after cardiac resuscitation. During rewarming, 5 $ml \cdot kg^{-1} \cdot h^{-1}$ lactated Ringer's solution and stored whole blood were infused to maintain the level of CVP at 10 mmHg, and 5–15 $\mu g \cdot kg^{-1} \cdot min^{-1}$ DOB was administered to maintain optimal ABP for body temperature. One milligram per kilogram protamine sulphate and 5 mg furosemide were administered to reverse the heparinization and for urination at 30°C esophageal temperature. Infusion of lidocaine was continued during cooling and circulatory arrest, and it was stopped after cardiac resuscitation. After rewarming to 36°C esophageal temperature, all patients were transported to the intensive care unit (ICU), where mechanical ventilation was performed.

Results

Fentanyl administration decreased the HR but also resulted in a slight decrease in ABP; both ABP and HR decreased gradually in parallel with the lowering of body temperature and recovered to control levels after rewarming at 36°C as shown in Table 1. Although supraventricular extrasystole was detected in the ECGs of a few patients at esophageal temperatures lower than 25°C, risky arrhythmia, such as ventricular tachycardia or extrasystole and an abnormal ST segment, was not detected during the course of anesthesia. The EEG showed a decrease in frequency and amplitude, and under 23°C esophageal temperature, including circulatory arrest, the EEG was flat. With cardiac resuscitation and rewarming, the EEG recovered to control at 36°C. No spike or wave discharge was detected in the EEG during anesthesia in spite of the administration of a large dose of lidocaine during cooling and circulatory arrest.

At the time of induced cardiac arrest, the body temperature at the esophagus ranged from 18.5 to 21.1°C (20.2 ± 0.9°C), and that at the rectum from 14.5 to 19.8°C (16.6 ± 1.5°C). The duration of cardiac arrest ranged from 36 to 83 min (56 ± 14 min). Upon artificial ventilation and after pumping the cocktail into the coronary artery without cardiac massage, the heart began to beat immediately in eight patients and within 5 min in two patients. Rectal temperature always fell earlier during cooling and rose during rewarming more than esophageal temperature. The difference in temperature between the esophagus and rectum was less than 1.7°C during the cooling and rewarming phases. However, the difference reached 3.6 ± 1.5°C between the end of cooling and the beginning of cardiac resuscitation.

Both respiratory alkalosis and metabolic acidosis were revealed by arterial gas analysis; 3.1 ± 1.2 $mEq \cdot kg^{-1}$ of sodium bicarbonate was administered during the course of anesthesia in 9 cases (patients 1–9) managed with α-stat. Patient 10, who was managed with pH-stat, showed slight metabolic acidosis and was administered 1.1 $mEq \cdot kg^{-1}$ of sodium bicarbonate.

The amounts of measured blood loss and of transfusions given are shown in Table 1. In patient 10, intracardiac blood was sucked into a device (Solcotrans, Solco Basle, Rockland, MA, USA) for the collection and reinfusion of autologous blood and was immediately transfused, making it possible to avoid alloblood transfusion.

The hemodynamics were stable during rewarming (Table 2). In several cases slight myocardial edema was

Table 1. Patients, perioperative condition, and surgical outcome

Case	Age	Weight	Type	P. con.	Venti. 1	E/R temp.	Occ. time	C/W time	Blood out/in	Venti. 2	Outcome
1	8	3.5	III	+++	Yes	18.5/16.0	58	75/110	180/300	5	Alive
2	3	2.0	III + Ib	+++	Yes	19.2/16.0	83	45/70	110/300	26	Dead
3	3	3.2	III	++	Yes	19.9/17.0	64	65/120	44/80	2	Alive
4	8	4.3	IIb + Ib	++	No	19.8/17.7	75	90/150	265/315	1	Alive
5	17	2.1	Ia	++	Yes	20.4/17.3	50	50/100	65/130	3	Alive
6	15	2.1	IIb + Ib	++	No	20.6/14.5	58	75/110	117/25o	2	Dead
7	9	3.0	IIa	++	Yes	19.9/17.0	41	95/120	473/560	2	Alive
8	30	3.2	IIa	++	No	21.1/14.7	48	130/180	38/60	1	Alive
9	6	3.0	III	+	No	20.8/16.2	45	75/110	48/160	2	Alive
10	11	2.5	III	++	No	21.8/19.8	38	60/110	6/0	2	Alive
Mean ± SD	11 ± 8	2.9 ± 0.7				E 20.2 ± 0.9 R 16.6 ± 1.5	56 ± 14	C 76 ± 23 W 118 ± 28	Out 135 ± 135 In 216 ± 156		

Age, age in days; weight, body weight (kg); type I, supracardiac type: A common pulmonary vein drains via a left vertical vein to the innominate vein (a), the superior vena cava (SVC) (b), and then finally to the right atrium; type II, cardiac type: A common pulmonary vein drains directly into the right atrium (a) or coronary sinus (b); type III, infracardiac type: A common pulmonary vein passes through the diaphragm at the esophageal hiatus, and the common vein drains into the portal vein, hepatic vein, or ductus venous; p. con., pulmonary congestion; venti. 1, artifical ventilation before surgery; E/R temp., esophageal and rectal temperature at induced cardiac arrest (°C); occ. time, circulatory occlusion time; C/W time, cooling and rewarming time (min); blood out/in, blood loss weight (g) and blood transfusion volume (ml); venti. 2, period of artificial ventilation after surgery (days).

Table 2. Hemodynamics and acid-base balance during deep hypothermia

	HR (beats·min^{-1})	SBP (mmHg)	DBP (mmHg)	pH	Pao_2 (mmHg) (Fio_2 1.0)	$Paco_2$ (mmHg)	BE (mEq·l^{-1})
Before anesthesia	166 ± 9	62 ± 10	39 ± 8				
After induction	137 ± 19	61 ± 9	38 ± 9	7.53 ± 0.11	96 ± 58	26 ± 8	+0.5 ± 2.4
30°C at esophagus	105 ± 12	51 ± 10	30 ± 7	7.43 ± 0.12	107 ± 58	24 ± 9	−1.1 ± 2.7
25°C	62 ± 6	50 ± 7	33 ± 5	7.60 ± 0.10	174 ± 96	18 ± 4	−0.5 ± 3.1
Lowest temperature	37 ± 6	39 ± 2	21 ± 4	7.58 ± 0.09	249 ± 87	18 ± 3	−2.2 ± 2.2
After resuscitation	24 ± 10	27 ± 6	17 ± 3	7.33 ± 0.11	423 ± 152	23 ± 6	−11.4 ± 4.3
25°C	50 ± 11	51 ± 13	31 ± 10	7.44 ± 0.20	466 ± 88	22 ± 7	−6.2 ± 8.8
30°C	88 ± 19	62 ± 13	40 ± 12	7.44 ± 0.06	360 ± 110	28 ± 10	−4.0 ± 5.6
36°C	120 ± 25	69 ± 13	44 ± 10	7.37 ± 0.01	393 ± 72	31 ± 9	−6.0 ± 2.1

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; Pao_2, partial pressure of arterial oxygen; Fio_2, fractional inspiratory oxygen; $Paco_2$, partial pressure of arterial carbon dioxide; BE, base excess.
Mean ± SD: data of 9 patients (patient 10, managed with pH-stat, was excluded).

detected during surgery. The sternum was able to be closed without difficulty in all cases. Anesthesia and operating time were 386 ± 77 min and 244 ± 62 min, respectively. The partial pressure of arterial oxygen (Pao_2) level in Fio_2 1.0 increased from 96 ± 58 mmHg before surgery to 393 ± 72 mmHg after surgery. After surgery, artificial ventilation was administered to all patients in the ICU. The results of surgery for eight of the patients were good, and 8 patients received artificial ventilation for up to 5 days. However, patient 2 died of pulmonary vein occlusion 42 days after surgery, and patient 6 died of congenital superior vena cava occlusion 39 days after surgery. No neurological disorders such as convulsions or prolonged obtundation were detected in any patients, including these two cases. To date all surviving patients have remained healthy.

Discussion

Because radical surgery for TAPVR should be performed soon after birth, the neonates are highly sensitive to surgical stress and the effects of accompanying procedures such as CPB and/or hypothermia. Although many institutions use CPB-induced deep hypothermia and circulatory arrest [1,2], there are numerous problems related to this procedure. CPB-induced hypothermia is effective in obtaining a bloodless surgical field [3]; however, there have been reports of renal failure [4], brain damage, and other organ failures [5,6]. In addition, cardioplegia and poor venous drainage from the vena cavae can easily cause myocardial edema in neonates that is too severe to permit closing their sternum [7]. Furthermore, perfusion with a high-osmotic solu-

tion increases the risk of intracerebral hemorrhage [8]. Elevation of the heart apex for surgical procedures results in poor coronary perfusion during CPB [9], and high arterial inflow frequently causes general edema [7]. To overcome the disadvantages of CPB for open heart surgery in neonates and younger infants, we have been utilizing simple deep hypothermia under deep ether anesthesia at about 20°C body temperature and obtaining satisfactory surgical results [10]. Even though in simple deep hypothermia, the cooling time to 20°C body temperature is longer, the difference between central and peripheral body temperature is smaller, the microcirculation is better, and metabolic acidosis occurs less frequently than in CPB.

Litasova et al. [11] combined light ether anesthesia and morphine to surface-cool the whole body to 30–32°C body temperature, and then achieved 24–26°C by cooling only the head, abdomen, and back to prevent risky arrhythmias.

Since TAPVR is always complicated by cardiac failure, deep ether anesthesia cannot be indicated; therefore, we used a large amount of fentanyl as a nonmyocardial depressant anesthetic. Since fentanyl anesthesia was suspected to be insufficiently deep to prevent the increasing irritability of the cardiac muscle caused by deep hypothermia, a large dose of lidocaine and low concentration of ether or isoflurane were combined. Consequently, risky arrhythmias were not detected on the ECGs; on the EEGs, no spike or wave discharge due to the administration of a large dose of lidocaine during cooling was detected.

Severe pulmonary congestion is also a complication in this disease. Administration of higher F_{IO_2} may further cause severe pulmonary congestion due to decreased pulmonary vascular resistance. It is therefore better to ventilate with as low F_{IO_2} as possible depending on hemoglobin oxygen saturation (S_{PO_2}) or P_{aO_2}. Since we do not have an appropriate anesthesia machine delivering either oxygen, air, ether, and/or isoflurane at the same time, ventilation was controlled with F_{IO_2} 1.0 as a second choice. Fortunately, no complications due to high F_{IO_2}, such as pulmonary edema, occurred.

The permissible time of circulatory arrest is considered to be 60 min at 20°C esophageal temperature, plus/minus 6 min for every drop/rise of 1°C in cases maintaining optimal circulatory dynamics during anesthesia [12,13]. In patients 2 and 4, although the duration of circulatory arrest greatly exceeded the permissible time, no brain damage was detected. The reason was thought to be that some margin in the calculated time existed [14] and that the patients were neonates or younger infants [15].

Cardiac resuscitation was accomplished by pumping the cocktail into the coronary artery and providing artificial ventilation. In the present study, cardiac resuscitation was easily achieved without cardiac massage in all cases. We never experienced any difficulties in cardiac resuscitation during simple deep hypothermia for these ten cases of TAPVR.

During rewarming, relative hypovolemia will occur due to expansion of the vascular bed. However, an appropriate level of ABP can be obtained by maintaining CVP at 10 mmHg by blood transfusion and/or fluid therapy.

Maintaining the acid–base balance (ABB) is important. The use of sodium bicarbonate solution is effective in cases of metabolic acidosis. Although bicarbonate therapy during cardiac arrest has several adverse effects, e.g., acidosis in the central nervous system due to increased partial pressure of arterial carbon dioxide (P_{aCO_2}), hyperosmolality, a left shift of the oxyhemoglobin dissociation curve, and a decreased arrhythmia threshold, there was no problem in administering sodium bicarbonate to correct the ABB after cardiac resuscitation. We were easily able to maintain optimal hemodynamics in heart rate and arterial blood pressure, and experienced no hypercapnia or intracerebral bleeding caused by bicarbonate therapy.

The difference in temperature between the esophagus and rectum is a valued index for the microcirculation. In this study, the small difference of less than 1.7°C during the cooling and rewarming phases may suggest a good microcirculation. In either a child or an adult, the esophageal temperature responds more quickly to cooling and rewarming than the rectal temperature, while the rectal temperature is more quick to respond in a neonate or infant than the esophageal temperature. It is suggested that in a neonate or infant, the space between the body surface and rectum is very small, and the rectal temperature is easily influenced by the environment, such as ice water or hot water during surface cooling and rewarming. The rectal temperature cannot be estimated in the same way as the cerebral temperature.

Disagreement does exist with regard to the appropriate level of P_{aCO_2} during deep hypothermia. When a blood gas sample is drawn from a hypothermic patient and sent to the blood gas laboratory, the sample is warmed to 37°C prior to measurement. The values obtained at 37°C are called the temperature-uncorrected values. When the pH and P_{CO_2} of a blood gas sample are measured at 37°C and then corrected to a lower temperature, the electrochemically neutral pH will be higher and the correct P_{CO_2} will be lower than the normal values at 37°C. Thus, electrochemical neutrality is maintained by keeping pH alkalotic in temperature-corrected gases and normal in temperature-uncorrected gases. This is known as α-stat regulation. For practical purposes it is easier to use uncorrected gases and keep pH and P_{CO_2} in the range considered normal at 37°C.

The pH-stat regulation refers to maintaining pH and Pco_2 at normal values for 37°C when temperature-corrected gases are used and at acidotic values when temperature-uncorrected gases are used. Cerebral vascular resistance and cerebral blood flow also depend on $Paco_2$ during hypothermia. Although cerebral blood flow is greater in pH-stat than in α-stat, brain edema easily occurs in pH-stat [16]. We had previously managed pH-stat in some cases and sometimes experienced therapy-resistant ventricular fibrillation. Therefore, we consider α-stat to be more appropriate during deep hypothermia. In this study, an anesthesiologist managed pH-stat for patient 10 to avoid metabolic acidosis and to keep the circulatory dynamics stable. Fortunately, the course of anesthesia proceeded without any trouble and the prognosis was good.

It has been confirmed that simple deep hypothermia has little negative influence on respiratory function [17,18]. In this study, artificial ventilation was utilized for less than 3 days in most cases after surgery.

Blood loss is influenced by the surgeon's skill and by hemostatic conditions. Especially in patient 10, the measured blood loss was only 6 g and blood transfusion could be avoided. Suzuki reported that platelet count, platelet functions, and partial thromboplastin varied with cooling, and all three factors recovered to pre-cooling values, by the end of rewarming at 36°C [19].

In the eight surviving patients, no neurological deficits due to circulatory arrest were detected after surgery, but this should be confirmed by neurological examinations including brain magnetic resonance imaging (MRI), brain computted tomography (CT) scan, EEG, an intelligence test, and assessment of social adaptation in daily life afterwards.

In conclusion, radical open heart surgery was performed in ten cases of TAPVR complicated by cardiac failure and hypoxia, without inducing complications such as neurological disorders and renal failure. By utilizing simple deep hypothermia and administering a large amount of fentanyl, favorable results were obtained.

For this surgery, simple deep hypothermia is better than a cardiopulmonary bypass. The reasons are as follows:

1. It allows surgery to be performed on a bloodless, dry, broader, stationary surgical field without blood drainage cannulae.
2. It is economical.
3. It does not incur a bleeding tendency.
4. The shift in the body fluid balance, such as in serum electrolytes and the acid–base balance, is minimized.
5. There is less probability of negatively affecting the respiratory function.
6. Blood loss is minimized and open heart surgery for neonates and younger infants can be performed without alloblood transfusion.

However, simple deep hypothermia for open heart surgery has a few weak points in that the heart must be resuscitated within the permissible time of circulatory arrest to prevent brain damage, and the hemodynamics depend on the patients' own pathological heart.

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