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Original Article

Relevance of the measurement of the concentration of lactate in the serum subsequent to the Fontan procedure in small children

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Abstract *Background:* To determine the clinical relevance of change in the level of lactate in the serum as a meanings of establishing the efficacy of the circulation immediately after the Fontan procedure in small children. *Methods:* We measured the concentration of lactate in the serum consecutively in 30 patients undergoing the Fontan procedure, without fenestration, under the age of 2 years. Of these, we did not use cardiopulmonary bypass in 13. *Results:* Concentrations gradually increased during the first several hours after establishment of the Fontan circulation, and then eventually decreased, reaching the normal range within 48 hours, with specific values of 0.9 plus or minus 0.3 pre-operatively, 2.3 plus or minus 1.1 immediately after creation of the Fontan circulation, 4.0 plus or minus 2.4 at 6 hours, 1.6 plus or minus 0.6 at 24 hours, and finally 1.3 plus or minus 0.4 millimoles per litre at 48 hours. This trend was irrespective of use or no use of cardiopulmonary bypass. The higher initial level in the intensive care unit was related to higher systemic venous pressure, higher transpulmonary pressure gradient, higher maximal level of alanine transaminase and blood urea nitrogen, and longer duration of peritoneal drainage, the latter as a monitor of sequestration of fluid rather than peritoneal dialysis. In patients with initial levels greater than 3.0 millimoles per litre, there was extended duration of endotracheal intubation. *Conclusions:* Postoperative changes in the levels of lactate in the serum subsequent to creation of the Fontan procedure were peculiar, not necessarily correlated with the cardiac output, but relevant to the clinical course.

Keywords: Congenital heart disease; postoperative care; functionally univentricular heart; off-pump

THERE ARE INCREASING PUBLICATIONS INDICATING the clinical importance of measuring the level of lactate in the serum, since this parameter can be a good predictor of morbidity and mortality in critically ill or injured patients.[1–3] During the postoperative period after cardiac surgery, similar information is available in adults as well as children.[4–10] Postoperative change in the concentration of lactate in the serum, nonetheless, has yet to be well documented after the Fontan procedure. In order to investigate the change of this parameter immediately after commencement of the Fontan circulation in small children, we carried out our study in a retrospective fashion.

Patients and methods

We included 30 consecutive children in this study, all undergoing total cavopulmonary connection without fenestration under 2 years of age at the National

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Cardiovascular Center of Japan between 1997 and 2000. Their age at operation ranged from 10 to 23 months, with a mean of 16 months, and body weight varied from 6.1 to 11.6 kilograms, with a mean of 8.6 kilograms. The predominant cardiac malformation was classical tricuspid atresia, seen in 8, mitral atresia in one, common or double inlet ventricle in 10, pulmonary atresia with intact ventricular septum in 4, and variants of double outlet right ventricle in 7. Of these, visceral heterotaxy was noted in 11 patients, with 10 having isomerism of the right atrial appendages, and 1 exhibiting left isomerism. The dominant ventricle was of the morphologically left type in 15, and of the morphologically right type in the other 15. The bidirectional Glenn procedure had been carried out in 10 patients as a staged procedure before completion of the Fontan circulation. There had been no palliative procedures in 7 patients. In the remaining 13, we had either constructed a systemic-to-pulmonary shunt, in 10, or banded the pulmonary trunk, in the other 3.

So as to establish the total cavopulmonary connection, we constructed the extracardiac channel using an expanded polytetrafluoroethylene tube graft in 12, and a tailored pedicled autologous pericardial roll[11] in 13. In another 4 patients, the pulmonary trunk could be directly anastomosed to the orifice of the inferior caval vein. In the remaining patient, an expanded polytetrafluoroethylene tube was placed within the atrial cavity.[12] Of all the 30 patients, cardiopulmonary bypass was used in a standard fashion in 17 patients, while the Fontan circulation could be established without use of cardiopulmonary bypass[11] in 13 patients, in whom no intracardiac manoeuvres were concomitantly needed. Cardiopulmonary bypass time in the initial 17 patients was 111 plus or minus 62 minutes. In none of these did we use modified ultrafiltration.

Dopamine was started routinely in all patients, with an initial dosage of 3 micrograms per kilogram per minute at the commencement of the Fontan circulation. All patients were transferred to the intensive care unit without extubating the endotracheal tube. In the intensive care unit, postoperative fluid balance was carefully managed, aiming towards early removal of the endotracheal tube. When urine output decreased to 1.0 millilitre per kilogram per hour or less, we infused furosemide at between 0.5 and 1.0 milligram per kilogram per hour. Irrespective of the amount of urinary output, we put a peritoneal drainage tube in patients in whom retention of fluid within the abdominal cavity was detected on echo, so as to monitor any change in the amount of ascites, and also to minimize the influence of any considerable amount of ascites on respiration. When the amount of drainage became less than 2 millilitres per kilogram per hour, peritoneal drainage was stopped.

We measured the concentration of lactate in the serum by sampling 0.4 millilitre of arterial blood into a heparinized blood gas syringe, and immediately making the analysis for lactate. Samples were taken just after induction of anaesthesia, immediately after commencement of the Fontan circulation, at the time of admission to the intensive care unit, every hour until extubation, soon after extubation, and every 2 hours between extubation and 12 hours after establishment of the Fontan circulation. A couple of further samplings were then added at 24 and 48 hours after establishment of the Fontan circulation.

The end point of this study was set to be one year after the Fontan procedure, or death of a patient if it occurred within the first postoperative year. Follow-up catheterization was carried out one year after the Fontan procedure, as a routine examination, in 20 patients. Cardiac output was determined by the so-called Fick method.

Values were described in a mean plus or minus standard deviation. Continuous variables were analyzed with unpaired t test in those data considered as showing a normal distribution. Otherwise, we used the Mann Whitney U test. Pearson's correlation co-efficient was calculated to evaluate any relationship between changes in the concentration of lactate and clinical outcome. Repeated measures of analysis of variance were used to compare consecutive changes in concentration in two groups. All these analyses mentioned were carried out using the software package Statview for Macintosh (Abacus Concepts, Berkeley, CA, USA). The p value was considered significant when smaller than 0.05.

Results

We lost one patient 30 days after the procedure because of mediastinitis. As other postoperative complications, chylothorax was noted in 5, arrhythmia in 4, liver dysfunction in 1, and palsy of the phrenic nerve was surgically treated in 1, as well as cardiac tamponade in another.

Overall change in concentration of lactate in the serum after total cavopulmonary connection

As a whole, concentrations gradually increased during the first several hours after the Fontan circulation, and then eventually decreased, returning to the normal range within 48 hours, irrespective of whether the procedure was performed with or without cardiopulmonary bypass (Fig. 1).

The maximal concentration in each patient was measured at 7.4 plus or minus 2.1 hours after

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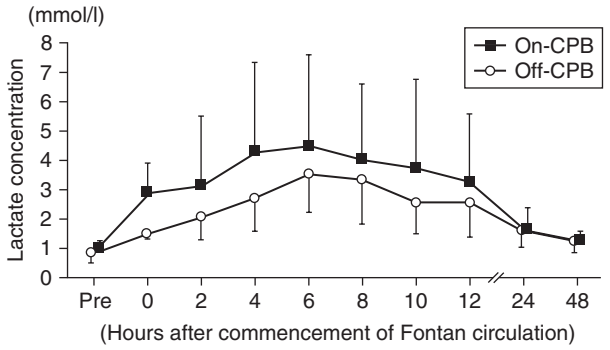

Figure 1.
Change in lactate concentration after the Fontan procedure. Levels of lactate in the serum gradually increased during the first 6 hours after commencement of the Fontan circulation, then decreased until reaching the normal range at 48 hours after the procedure. This trend was irrespective of use or no use of cardiopulmonary bypass. pre: just after induction of anesthesia (before surgical maneuvers), CPB: cardiopulmonary bypass; mmol/l: millimoles per litre.

commencement of the Fontan circulation, with its value being 4.8 plus or minus 2.3 millimoles per litre. At the time of admission to the intensive care unit, concentration was 3.2 plus or minus 2.4 millimoles per litre. This value was taken as a predictive representative of the maximal value, because of a coefficient 0.88 (p value less than 0.0001) between these values.

Characteristics of the patients and pre-operative catheterization data

The initial value for lactate at admission to the intensive care unit did not differ in terms of age at operation, body weight (Table 1), atrial arrangement, morphology of the dominant ventricle, or previous employment of the bidirectional Glenn procedure.

This initial value did not clearly correlate with pulmonary resistance, pulmonary arterial index measured according to the system of Nakata,[13] or the index of systemic flow derived from pre-operative catheterization (Table 1).

Peri-operative factors

Peripheral body temperature, a dose of fentanyl during operative procedures, or total time of the operation did not appear to be influential on the initial concentration of lactate as measured in the intensive care unit.

Postoperative clinical parameters

The initial value of superior caval venous pressure in the intensive care unit was weakly correlated with that of the level of lactate, with a coefficient of 0.4, p value equal to 0.03. This was not the case for the pressure measured in the atrial cavity connected to the systemic ventricle. Trans-pulmonary pressure gradients of 10 millimetres of mercury or greater, seen in 16, with 8 undergoing cardiopulmonary bypass and 8 not, of 30 patients, was more common in patients with higher initial concentrations of lactate measured in the intensive care unit, with a coefficient of 0.7, p value less than 0.0001.

Mechanical ventilation was weaned off at 10 plus or minus 13 hours after admission to the intensive care unit. The duration of endotracheal intubation was not significantly correlated with the initial level of lactate as measured in the intensive care unit (Table 1). In the subgroup of patients with this value greater than 3.0 millimoles per litre, nonetheless, the duration of endotracheal intubation was longer compared with the counterpart (p value equal to 0.008).

The base excess level at admission to the intensive care unit was significantly correlated to the initial level of lactate as measured in the intensive care unit, with a coefficient of −0.49, p value equal to 0.006. The duration of administration of dopamine was not correlated with the initial level as measured in the intensive care unit, regardless of use of cardiopulmonary bypass or peritoneal drainage. Neither the concentration of haemoglobin, nor the mixed venous saturation of oxygen, both as measured immediately after admission to the intensive care unit, was well correlated to the initial level of lactate measured in the intensive care unit.

Peritoneal drainage was employed prior to tracheal extubation in 10 patients. This was the case in 8 of 17 undergoing cardiopulmonary bypass, and 2 of 13 undergoing the off-pump procedure. Duration of peritoneal drainage ranged from 1 to 18 hours, with a median value being 4 hours. The initial concentration of lactate measured in the intensive care unit was related to duration of peritoneal drainage, with a coefficient of 0.7, p value less than 0.0001. Within the subgroup of patients undergoing cardiopulmonary bypass, moreover, the initial concentration was higher in 8 patients in whom peritoneal drainage was carried out than in the other 9. The p value for this difference is equal to 0.005.

The initial concentration of lactate correlated with maximal level of alanine transaminase in the serum, with a coefficient of 0.5, and p value equal to 0.004, and also with blood urea nitrogen, this having a coefficient of 0.4, giving a p value equal to 0.03.

Overall, the quantity or duration of pleural and pericardial drainages was not correlated with the initial level of lactate measured in the intensive care unit.

Table 1. Relationship between clinical parameters and the initial lactate concentration in the intensive care unit.

Characteristics of patients	*r*	p value	*n*
Age at Fontan procedure	0.03	0.88	30
Body weight	0.09	0.62	30
Preoperative catheterization data			
Pulmonary resistance	−0.13	0.50	30
Pulmonary artery index	0.22	0.24	30
Qs index	−0.18	0.35	30
Perioperative data			
Peripheral body temperature	−0.03	0.86	30
Total dose of Fentanest	0.27	0.15	30
Operation time	0.23	0.21	30
Early postoperative parameters			
SCVP	0.40	0.03	30
LAP	0.14	0.45	30
SCVP − LAP ⩾ 10 mmHg	0.70	<0.0001	30
SvO_2	0.31	0.09	30
Base excess	−0.49	0.006	30
Haemoglobin concentration (grams per decilitre)	−0.20	0.29	30
Duration of intubation	0.29	0.13	30
Duration of catecholamine administration	0.17	0.38	30
Duration of peritoneal drainage	0.67	<0.0001	30
Overall quantity of pleural effusion	−0.08	0.70	25
Duration of pleural and pericardial drainage	0.23	0.27	25
ALT concentration (international unit per litre)	0.50	0.004	30
BUN concentration (milligrams per decilitre)	0.39	0.03	30
Cr concentration (milligrams per decilitre)	0.25	0.19	30
Follow-up catheterization data at one year after the Fontan procedure			
Pulmonary resistance	−0.07	0.77	20
Pulmonary artery index	−0.17	0.59	20
Cardiac index	0.21	0.38	20

The initial concentration of lactate as measured in the intensive care unit had some clinical relevance to the early postoperative parameters, but not in terms of pre-operative and peri-operative factors

Qs: quantity of systemic flow; SCVP: pressure of the superior caval vein; LAP: pressure of the atrial cavity connected to the ventricular chamber (functionally left atrium); SCVP − LAP ⩾ 10 mmHg: SCVP minus LAP greater than or equal to 10 millimetres of mercury; SvO_2: mixed venous saturation; ALT: alanine transaminase; BUN: blood urea nitrogen; Cr: creatine

"*r*" is Pearson's correlation co-efficient and "*n*" is the corresponding sample size

Postoperative catheter parameters

Postoperative follow-up catheterization was carried out as a routine examination around one year after the procedure in 20 patients. Neither pulmonary resistance, ejection fraction of the dominant ventricle, pulmonary arterial index, or cardiac index in the intermediate term, correlated with the initial level of concentration of lactate in the serum as measured in the early phase after the procedure.

Discussion

Many recent articles have stated that the level of lactate measured in the blood could be relevant to some disorders and postoperative courses. As increased level of lactate in the serum was determined as an independent predictor of postoperative low cardiac output syndrome in patients undergoing coronary arterial bypass grafting,[10] and was held to be an early indicator for postoperative mortality and morbidity in patients with congenital cardiac disease.[5–9] This was because such levels sensitively reflected the state of systemic perfusion, be it adequate or impaired. With insufficient systemic perfusion, delivery of oxygen does not meet the demand from the bodily organs. This results in conversion of pyruvate into lactate under anaerobic conditions. In this setting, higher lactic acidosis is likely associated with either lower systemic venous saturation, or lower cardiac index.

In infants with respiratory distress syndrome, a higher level of lactate in the serum was regarded as a predictor of mortality.[2] Because of hypoxia, delivery of oxygen to the bodily organs becomes insufficient,

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enhancing the anaerobic metabolic cycle. Although extensive ventilatory support for respiratory distress, as well as high pulmonary vascular resistance, could make the overall circulation less effective, low cardiac output is not always the rule. An increased level of lactate in the serum was also regarded as an early indicator of sepsis.[1] In this instance, however, higher cardiac output, rather than low, is the case. Accordingly, an increased concentration is associated with elevated demand for oxygen in the bodily organs, or inappropriate extraction for the energy-producing cycle in the affected tissues. In other words, a change in the level of lactate in the serum is a useful means for assessing the clinical situation, but does not exclusively represent circulatory failure caused by impaired cardiac function.

The Fontan circulation is known to be characteristic, demonstrating a state of low cardiac output with elevated systemic venous pressure and non-pulsatile flow of blood to the lungs.[14] Seeking to estimate the efficacy of the Fontan circulation during the early postoperative phase, many surgeons and intensivists pay attention to the classical parameters, such as systemic venous pressure, saturation of oxygen in the systemic venous blood, systemic arterial pressure, pressure in the atrial chamber connected to the systemic ventricle, urinary output, and so on. We initially considered that the concentration of lactate in the serum could be another parameter clearly indicating the state of low cardiac output, even in those with the Fontan circulation. Although the lower initial level we measured was associated somehow with preferable haemodynamics, specifically lower systemic venous pressure and transpulmonary pressure gradient, the initial concentration failed to correlate with the level of mixed venous saturations of oxygen, generally held to be a good measure of cardiac output.[15] Moreover, during this period of time, before 2000, we employed peritoneal drainage, in addition to pleural drainage, as a monitor of fluid sequestration rather than as peritoneal dialysis for oliguria. Correlation between the duration of peritoneal drainage and the level of lactate implied that the concentration of the latter in the serum was another clinically relevant parameter indicating overall efficacy of the Fontan circulation beyond a specific parameter merely correlating to cardiac output.

In this respect, not only synthesis of lactate from pyruvate in an anaerobic condition, but also clearance of lactate by the liver and the kidney, and also by the skeletal muscles at rest, should be taken into account. Due to the elevated systemic venous pressure, these vital organs are greatly influenced in terms of their metabolic functions. In reality, hepatic enzymes and levels of blood urea nitrogen were higher when the initial concentration of lactate was raised. The change seen in our present study should reflect the balance between elevated synthesis and impaired clearance. The Fontan circulation in small children needs 6 to 8 hours to balance these two aspects, and 48 hours to adapt to an alternatively compensated state. The data available on preoperative catheterization provides useful information for the pulmonary circulation and ventricular pump function, but does not necessarily predict the process of adaptation in terms of other organs such as the liver and the kidney. The adaptation of the whole body to the Fontan circulation was needed irrespective of whether cardiopulmonary bypass was used or not. A difference between the two groups was only seen at the very beginning of the Fontan circulation. The off-pump procedure could just avoid a significant rise in the start point, but did not modify the whole process of adaptation, at least in the present series of small children.

On the basis of the present findings, we would promote early extubation for smooth postoperative course when the initial level of lactate was low in the intensive care unit. If we found it high, in contrast, more attention would be paid to control of body temperature and optimal management of fluids, under sedation and mechanical ventilation, until the level of lactate had passed its peak.

In conclusion, therefore, we are able to regard the level of lactate in the serum, and its consecutive changes, as a parameter composed of multi-factorial backgrounds, and as one of clinically pertinent measurements during the acute phase subsequent to establishment of the Fontan circulation.

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