Blood pressure and urine output during the first 120 h of life in infants born at less than 29 weeks’ gestation related to umbilical cord milking

S Hosono, H Mugishima, H Fujita, A Hosono, T Okada, S Takahashi, N Masaoka and T Yamamoto

Arch. Dis. Child. Fetal Neonatal Ed. 2009;94;F328-F331; originally published online 16 Feb 2009; doi:10.1136/adc.2008.142935

Updated information and services can be found at:
http://fn.bmj.com/cgi/content/full/94/5/F328

These include:

References
This article cites 15 articles, 4 of which can be accessed free at:
http://fn.bmj.com/cgi/content/full/94/5/F328#BIBL

Rapid responses
You can respond to this article at:
http://fn.bmj.com/cgi/eletter-submit/94/5/F328

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Topic collections
Articles on similar topics can be found in the following collections

- Hypertension (4539 articles)
- Child health (9108 articles)
- Infant health (2080 articles)
- Neonatal health (1127 articles)

Notes

To order reprints of this article go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to Archives of Disease in Childhood - Fetal and Neonatal Edition go to:
http://journals.bmj.com/subscriptions/
Blood pressure and urine output during the first 120 h of life in infants born at less than 29 weeks’ gestation related to umbilical cord milking

S Hosono,1 H Mugishima,1 H Fujita,1 A Hosono,1 T Okada,1 S Takahashi,1 N Masaoka,2 T Yamamoto2

ABSTRACT

Objective: To investigate the effects of umbilical cord milking on cardiopulmonary adaptation in very low birth weight infants.

Patients and methods: This was the secondary analysis of a randomised control study of the effect of umbilical cord milking in premature infants. Forty singleton infants born between 24 and 28 weeks’ gestation were randomly assigned to groups in which the umbilical cord was clamped either immediately after birth (control group, n = 20) or after umbilical cord milking (milked group, n = 20). Blood pressure, heart rate, urine output, fluid intake, and ventilatory index values in both groups were measured during the first 120 h after birth.

Results: There were no significant differences in gestational age or birth weight between the two groups. The initial haemoglobin value was higher in the milked group (mean (SD) 16.5 (1.4) g/dl in the milked vs 14.1 (1.6) g/dl in the control; p<0.01). During the first 12 h, blood pressure was significantly higher in the milked group. Urine output in the milked group was higher than that in the control group during the first 72 h. There were no significant differences in heart rate, water intake, or ventilatory index values between the groups.

Conclusion: Umbilical cord milking may facilitate early stabilisation of both blood pressure and urine output in very low birth weight infants.

The majority of term neonates successfully complete the postnatal transition from fetal to postnatal cardiopulmonary circulation. However, early postnatal adaptation to transitional circulation in low birth weight infants is frequently associated with low blood pressure and decreased blood flow to organs. Systemic hypotension during the first postnatal week is associated with a high likelihood of end-organ damage, resulting in death or long-term neurological impairment in the very low birth weight (VLBW) neonates.1 2 Although blood pressure may not directly correlate with tissue perfusion, it is frequently used as an index of haemodynamic status in neonates, in whom it is very difficult to measure cardiac output and vascular resistance. Because blood pressure is the product of cardiac output and vascular resistance, many of the cardiovascularily compromised neonates initially maintain normal blood pressure such as compensated shock. In the initial compensated phase, vital organ (brain, heart, and adrenal glands) perfusion and blood pressure are maintained by neuroendocrine compensatory mechanisms via the redistribution of blood flow from non-vital organs (eg, kidneys, intestine, liver, skin).3 On the other hand, there is no evidence that preterm infants with hypotension have lower blood volumes than normotensive infants.4 In addition, there is no evidence from randomised trials to support the routine use of early volume expansion in very preterm infants without cardiovascular compromise. There is insufficient evidence to determine whether infants with cardiovascular compromise benefit from volume expansion.4

A recent Cochrane Review demonstrated that infants who underwent delayed clamping were less likely to need a transfusion for low blood pressure at birth.5 Our previous retrospective study revealed that infants in the higher haemoglobin group had higher blood pressure during the first 24 h of life, as compared with the lower haemoglobin group.6 The initial study of this randomised control trial showed that initial blood pressure in the milked group was significantly higher than that in the control group.7 We hypothesise that increased circulating blood volume resulting from the umbilical cord milking might lead to increased systemic blood pressure and to decreases in the use of both inotropic agents and volume expanders. Thus, the purpose of this secondary analysis of data from our previous randomised control trial was to investigate the impact of umbilical cord milking on cardiopulmonary adaptations in premature infants during the first 120 h after birth.
MATERIALS AND METHODS
This study is the secondary analysis of the results of a randomised control study regarding the effect of umbilical cord milking in premature infants. The original study design was a randomised controlled trial with two treatment arms. This original randomised controlled trial was carried out in a single tertiary perinatal centre over a 24-month period from January 2001 to December 2002. Exclusion criteria were: (1) multiple births; (2) major congenital anomalies or chromosomal anomalies; and (3) hydrops fetalis. Women must have been admitted to the hospital at least 6 h before delivery to allow time for enrolment. The chief neonatologist decided whether to enrol the patients in the present study. For randomisation, we used serially numbered opaque envelopes that were opened by neonatology staff after enrolment and just before delivery. Subjects were randomly selected to have their umbilical cord clamped either immediately after birth or after umbilical cord milking. A neonatologist informed the obstetricians of the intervention type. Hence, the resuscitation and therapeutic teams were not blinded to the infants’ grouping.

Forty infants born at 24 to 28 weeks’ gestation were randomised and admitted to level III neonatal intensive care units.

Infants in the milked group were placed at or below the level of the placenta, and about 30 cm of the umbilical cord was vigorously milked towards the umbilicus two to three times before clamping the cord. The milking speed was about 10 cm/s.

Prenatal and delivery data were collected from the mother’s charts. Infants’ data were collected from the records.

Sixty-three fetuses were assessed for eligibility; 23 fetuses were excluded. Thus, 40 of the 63 VLBW infants born at between 24–28 weeks’ gestation were randomised and admitted to the level III neonatal intensive care unit at Nihon University Itabashi Hospital in Tokyo, Japan.

Informed consent was obtained from the parents after a full explanation of the procedure. This study was approved by the Research Review Board at Nihon University Itabashi Hospital.

We previously reported primary outcome measures such as the probability of not needing a transfusion and the number of red blood cell transfusions performed during the hospital stay. This study examined the secondary outcome variables. We focused on cardiopulmonary adaptations, which were indicated by blood pressure, heart rate, urine output, fluid intake, and ventilatory index (VI) values during the first 120 h after birth in the present report. All data were retrospectively obtained from a review of medical records.

A peripheral or umbilical arterial catheter was placed to obtain arterial pressure readings and blood samples. If it was difficult to place a peripheral artery catheter due to the very fragile skin of infants born prior to 25 weeks’ gestation, an umbilical arterial catheter was used. Blood pressure and heart rate were continuously monitored using a multichannel neonatal monitor (Siemens patient monitor SC7000; Siemens-Asahi Medical Technologies Ltd, Tokyo, Japan). Blood pressure values were recorded in medical records every hour. Extracted points were taken at admission and at 6, 12, 24, 48, 72, 96 and 120 h after birth. Blood pressure measurements were obtained each hour from the average value of three points. The arterial blood pressure gradient was calculated as the blood pressure at each time point in comparison to the initial blood pressure.

Fluid intake and urine output were determined every 24 h.

The VI was calculated as inspired oxygen × mean airway pressure/postdustal aortic oxygen tension.

Respiratory distress syndrome (RDS) was defined based on the basis of clinical and radiographic findings and a negative or weak microbubble test. Infants suspected to have RDS received surfactant (Surfactant; Mitsubishi Tanabe Pharma Corporation, Osaka, Japan). Extremely low birth weight infants received prophylactic indomethacin (Indacin; Banyu Pharmaceutical Co., Ltd., Tokyo, Japan) therapy within 12 h after birth.

STATISTICAL ANALYSIS

Normally distributed continuous outcome variables were compared with the unpaired student t test, and non-parametric continuous outcome variables were analysed with the Mann–Whitney U test. Categorical variables were compared using the χ² test. Fisher’s exact test was used for contingency tables showing expected cell counts <5. The data are expressed as the mean (SD). All analyses were conducted with two-tailed tests. p Values <0.05 were considered significant. Statistical analyses were carried out using Doctor SPSS II for Windows (SPSS, Japan Inc., Tokyo, Japan).

RESULTS

During the study period, 63 fetuses were eligible and 40 were then randomly selected. Twenty infants were allocated to the milked group and 20 to the control group. A total of 40 VLBW infants were admitted and were analysed for the present study. There was no protocol infraction in either group.

The mean (SD) haemoglobin value at birth of 16.5 (1.4) g/dl (range: 13.7–19.6 g/dl) measured at birth in the milked group was significantly higher than the mean (SD) haemoglobin value of 14.1 (1.6) g/dl (range: 12.2–16.9 g/dl) measured in the control group (p<0.01).

Table 1 shows the baseline characteristics of the infants. There was no significant difference in gestational age or birth weight between the two groups. No infants died within the early neonatal period in either group.

Figure 1 shows the changes in systolic and diastolic blood pressure of the neonates during the first 120 h after birth. During the first 12 h, both systolic and diastolic blood pressures in the milked group were higher than those in the control group. The mean (SD) arterial blood pressure gradient from birth to 24 h after birth in the milked group was significantly lower than that of the control group (1.3 (8.8) mm Hg vs 6.3 (6.2) mm Hg; p<0.05). The benefits of umbilical cord milking included better blood pressure and reduced needs for both volume expansion and inotropic support (table 2). There was no difference in the heart rate or mean fluid intake between the two groups. In contrast, during the first 72 h, mean urine output in the milked group was significantly higher than that in the control group (fig 2). The VI value was comparable in the two groups during the first 120 h.

Table 1  Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Milked group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=20</td>
<td>n=20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) gestational age (weeks)</td>
<td>26.6 (1.2) (24–28)</td>
<td>27.0 (1.5) (24–28)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mean (SD) birth weight (g)</td>
<td>846 (171) (587–1180)</td>
<td>836 (223) (494–1198)</td>
<td>0.43</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>13 (65)</td>
<td>10 (50.0)</td>
<td>0.26</td>
</tr>
<tr>
<td>Antenatal steroid, n (%)</td>
<td>7 (35.0)</td>
<td>7 (35.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Chorionicnitis, n (%)</td>
<td>11 (55.0)</td>
<td>10 (50.0)</td>
<td>0.50</td>
</tr>
<tr>
<td>Caesarean section, n (%)</td>
<td>14 (70.0)</td>
<td>14 (70.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>3 (15.0)</td>
<td>2 (10.0)</td>
<td>0.50</td>
</tr>
</tbody>
</table>
DISCUSSION

Circulating blood volume is an important variable, but is difficult to measure in VLBW infants. A severe volume deficit leads to recognisable clinical shock that requires rapid intervention. However, small volume depletions may have no noticeable effect on circulation and arterial pressure, because vasoconstriction assists in the redistribution of blood to vital organs. On the other hand, reduced blood flow to several organs, such as the skin, kidneys, and gastrointestinal tract, renders these organs ischaemic and unable to maintain a normal arterial pressure.8

The Joint Working Group of the British Association of Perinatal Medicine has recommended that the mean arterial blood pressure in mm Hg should be maintained at or greater than the gestational age in weeks.9 However, the diagnosis of hypotension and subsequent management are controversial with respect to the care of VLBW infants.10

This study revealed that the mean arterial pressure during the first 12 h in the milked group was higher than that in the control group, with lower pressure gradients from birth to 24 h after birth. In other words, the fluctuation of blood pressure in the milked group was less marked, and infants in the milked group achieved normotension within a brief period of time. Our previous reports revealed that the initial haemoglobin values are closely associated with both blood pressure during the first 24 h and the incidence of intraventricular haemorrhage (IVH) and that the high haemoglobin group exhibited a smaller pressure gradient from birth to 24 h afterwards.5 The recent meta-analysis showed IVH was higher in the immediate umbilical cord clamping group as compared with the delayed cord clamping group.11 Mercer reported that delayed cord clamping appeared to protect VLBW infants from IVH.12 Grönlund reported that elevated diastolic, mean and systolic blood pressures were significantly associated with peri-intraventricular haemorrhage in preterm newborn infants.13 In our study, despite a successful adaptation of the circulatory condition, there was no significant difference in the incidence of IVH in both groups in the first analysis. Adequate statistical power might reveal a lower incidence of IVH.

Tachycardia and increased cardiac contractility are two compensatory mechanisms that help to maintain cardiac output during shock. During the immediate postnatal period, hypotension and/or decreased systemic blood flow in extremely premature infants are often observed due to the inability of immature myocardium to effectively pump against the suddenly increased peripheral vascular resistance.14 The present study revealed that there was no difference in heart rate in different blood pressure groups. Oh et al have reported that, in spite of the lower systolic blood pressure observed in the early clamped group, there was no significant difference in the mean heart rate during the first 5 days between the early- and the late-clamped groups in term neonates.15 The results of Oh’s study and the present research indicate that the heart rate might be a limited index of compensatory mechanisms in hypotensive premature infants in days immediately after birth. In addition, some normotensive infants suffered from compensated shock that led to decreased end-organ perfusion.

Renal perfusion is one of the most frequently used indicators of circulatory function. This phase may be clinically best recognised by a decrease in urine output. Decreased urine output in the absence of known renal disease is a typical sign of hypovolaemia. Despite fewer interventions with volume load and inotropes, the present study found higher urine output during the first 3 days in the milking groups. This may indicate volume expansion due to placental transfusion following milking of the umbilical cord. In 1966, Oh et al reported that during the first 12 h of life, early-clamped infants had a significantly lower urine flow and lower effective renal blood flow as compared with late-clamped infants.16 On the other hand, the difference in urine output was observed during the
first 3 days in our study. The most likely explanation for the different findings may be the fact that Oh and colleagues’ study population consisted of term infants. Furthermore, positive correlations were demonstrated between blood pressure and haemoglobin values and between haemoglobin values and urine output in our study.

If shorter gestation infants cannot receive sufficient blood volume at birth, infants may run short of systemic circulatory blood volume for the following reasons. First, the transitional circulatory changes that occur within the first 72 h after delivery result in unique circulatory vulnerability for the extremely preterm infant. Pulmonary vascular resistance falls, but systemic vascular resistance rises. Moreover, the increase in cardiac output to the lungs from 8% during the fetal period to the 45% immediately after birth necessitates the transfer of an adequate volume of blood.17 When the cord is clamped before an adequate placental transfusion to the infant has occurred, pulmonary blood volume might be drawn out of systemic blood volume, resulting in relative systemic tissue hypoperfusion. Next, a process of fluid shift involving capillary fluid transudation from the vascular to extravascular spaces occurs during the first 4–6 h. Body fluid and electrolyte redistribution and glomerular and tubular functional adaptations might achieve the necessary adjustment required by the vascular distension and transudation resulting from placental transfusion at birth.18

In prematures, placental transfusion, including both delayed cord clamping and milking of the umbilical cord, is a sort of volume resuscitation. The Cochrane Reviews by Osborn showed that there is no evidence to support the routine use of early volume expansion in very premature infants without cardiovascular compromise.19 On the other hand, a recent Cochrane Review found that a brief delay in cord clamping time of at least 30 s improves the stability of the cardiovascular systems of infants during the first day of life, leading to a reduced requirement for volume therapy and inotropic support.3 This conflicting result may be based on the following reasons. Placental transfusions by delayed cord clamping and umbilical cord milking represent different methods of volume expansion. Volume expansion, in general, is performed after an effort has been made to establish proper breathing or after injection of the appropriate dose of epinephrine. That is to say, the technique is performed when the infant is in a state of decompensated shock. Moreover, the recommended volume expander for acutely treating hypovolaemia is 10 ml/kg of an isotonic crystalloid solution including normal saline or Ringer’s lactate over 5 to 10 minutes.19 In contrast, the composition of the placental transfusion is obviously fresh whole blood and infants receive a rapid and large volume expansion as compared with the recommended rate of administration and dose. Arguably, even in the absence of hypovolaemia or normotensive compensated shock, volume expansion by placental transfusion has the potential to increase cardiac output and blood pressure through the Frank–Starling mechanism and may therefore be a useful therapeutic strategy.

We conclude that umbilical cord milking may facilitate early stabilisation of both the blood pressure and urine output, as well as decrease the need for therapeutic intervention with regard to circulation after birth in VLBW infants.

Acknowledgements: We are very grateful to the obstetricians for their excellent technical assistance. We also thank the paediatricians (Dr Makimoto, Dr Kitamura, Dr Inami, Dr Chinen and residents) and nurses of the NICU. Finally, we thank the parents who consented to inclusion of their babies in this study. This study was supported by “The Mother and Child Health Foundation”.

Competing interests: None.

Ethics approval: This study was approved by the Research Review Board at Nihon University Itabashi Hospital, Tokyo, Japan.

Patient consent: Parental consent obtained.

REFERENCES