4 小児のメタボリックシンドロームへはどのように介入するか

1）食事療法の基本

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はじめに

メタボリックシンドロームを肥満，そして内臓脂肪の蓄積から始まる負の連鎖であるとするならば，その根本的な治療方法は肥満に導く生活習慣を改善することに尽きる．生活リズムを整えて成長と身体活動量に見合った食事摂取を心がけることである．しかしながら，日々の生活習慣の歪みは自覚しづらいばかりか，修正しようという意欲を消し去るほど根深いので，改善は容易ではない．したがって食事療法は単に摂取エネルギー量を決定し，それを指導するだけではなく，家庭環境や生活リズムを把握して生活特性に合わせた内容としなければならない．そして患児あるいは保護者をエンパワーメントしていく対応が必要である．

本項では小児の特徴を考慮した食事療法とその指導方法について述べたい．

1 食事療法の基本的な考え方

メタボリックシンドロームの源流にある内臓脂肪を減少させ，高血圧，高血糖や脂質異常を改善することが食事療法の最終的な目標である．しかし食事のみで内臓脂肪を選択的に減少させることはできないので，肥満の改善を目指すことが食事療法の実際の目標となる．さらに肥満の結果として現れる高血圧，高血糖や脂質異常に配慮した内容をそこに含めなければならない．

メタボリックシンドロームにはその最終的な帰結として虚血性疾患や脳血管疾患などの動脈硬化性疾患の発症が待ち受けている．したがって生活習慣の改善が小児期に留まらず成人期まで継続されることも重要である．このような観点から食事療法は短期的のみならず長期的な視点から立案していかなければならない．

さらに食事療法を小児に実施するときに配慮すべきことは指導内容が成長と発達を阻害してはならないことである．過度のエネルギー制限が成長障害を引き起こすことは明白である．アトピー性皮膚炎[1]や1型糖尿病で摂取エネルギー制限によって成長率が低下し，やせが進行した症例は後を絶たない．食事摂取基準[2]を参考に十分な摂取エネルギー量を維持する．

小児期は生活能力の低い乳幼児期から自我に目覚め自立していく思春期までを幅広く包含している．乳幼児期は保護者への指導が中心になるが徐々に自立を考えて指導の軸足

を患児自身に置いていかねばならない．その ような時期に患児が指導を十分に受容していなかったときは指導自体を拒絶することがある．一見指導を受け入れている場合でも抑圧から多食や大食などの食行動異常に傾いていくこともある[3]．指導内容を受容しているか，前向きに取り組んでいるかは食事指導を進めるうえで重要なチェックポイントとなる．

2 摂取エネルギー量

摂取エネルギー量は食事摂取基準（表 1）[2] を参考にして決定する．食事摂取基準には年齢と基準体位が記載されているので，年齢あるいは体位に対応したエネルギー量を摂取エネルギー量とする．肥満小児はしばしば身長が高いので，年齢よりも身長がどの年齢群の基準体位に相当するかをみてエネルギー量を決める．このときに身体活動レベルと肥満度を加味して指示する摂取エネルギー量を増減させなければならない．中等度以上の肥満を認める場合には摂取エネルギーの 10％程度，軽度肥満であれば 5％程度を減じる[4]．

指導を受けていない肥満小児ではいきなり標準的な摂取エネルギー量を指示しても継続することは難しい．1 カ月～数カ月の期間で標準領域に入るように，導入時には緩い指示の方が長期的には受け入れがよい．実際に厳しく制限しなくても生化学検査の異常値は改善することが多い．

一日の摂取エネルギー量が決まったら，各食事にどのように配分するかを決める．このときに夕食への配分を少なくするのが理想だが，現実的ではない．各家庭の食習慣や学校給食での摂取エネルギー量を考慮しながら，各食事へのエネルギー配分を決める．

学童期以降であれば間食は基本的に必要ないが，食事内容の理解度や年齢に応じて，やむを得ず一定期間導入する場合もある．その場合は一日エネルギー量の 10％以内とする．

高度肥満児の場合は入院管理下で low calorie diet（LCD）による短期での肥満改善を試みることもある．ただし LCD 療法には短期的な効果は期待できても，ただ実施するだけであれば長期的な意義には乏しい．患児と家族への教育および動機付けの機会とし，

表 1 食事摂取基準（文献 2）より引用・改変）

年齢	男性									女性								
	基準身長	基準体重	エネルギー kcal 身体活動レベル			不飽和脂肪酸 g/日		基準身長	基準体重	エネルギー kcal 身体活動レベル			不飽和脂肪酸 g/日	
	cm	kg	Ⅰ	Ⅱ	Ⅲ	n-3系	n-6系	cm	kg	Ⅰ	Ⅱ	Ⅲ	n-3系	n-6系
0～5(月) 母乳栄養児	62.2	6.6	−	600	−	0.9	4	61.0	6.1	−	550	−	0.9	4
0～5(月) 人工乳栄養児			−	650	−					−	600	−		
6～11(月)	71.5	8.8	−	700	−	1.0	5	69.9	8.2	−	650	−	1.0	5
1～2(歳)	85.0	11.9	−	1,050	−	1.1	6	84.7	11.0	−	950	−	1.0	6
3～5(歳)	103.5	16.7	−	1,400	−	1.5	8	102.5	16.0	−	1,250	−	1.5	7
6～7(歳)	119.6	23.0	−	1,650	−	1.6	9	118.0	21.6	−	1,450	−	1.6	8.5
8～9(歳)	130.7	28.0	−	1,950	2,200	1.9	9	130.0	27.2	−	1,800	2,000	2.0	10
10～11(歳)	141.2	35.5	−	2,300	2,550	2.1	11	144.0	35.7	−	2,150	2,400	2.1	11
12～14(歳)	160.0	50.0	2,350	2,650	2,950	2.6	13	154.8	45.6	2,050	2,300	2,600	2.1	10
15～17(歳)	170.0	58.3	2,350	2,750	3,150	2.8	14	157.2	50.0	1,900	2,200	2,550	2.3	11

減量が実行可能であることを示せなければ意味がない.

3 栄養バランスと栄養素の内容

三大栄養素の配分比については議論が多い. 疫学的には脂質摂取比の増加と肥満小児の増加が相関していたので, 脂質悪玉説が一般的であった. しかしアメリカにおいては小児肥満の増加が糖質摂取比の増加と関連していることが栄養調査で明らかにされた[5]. このように肥満小児の増加は一つの栄養素の摂取増加で単純に説明できるものではない.

このような背景もあって食事療法を行う際に三大栄養素をどのように配分するかについては明快な解答は導き出されていない. しかしながら成人で行われた, いくつかの研究からは炭水化物摂取の低減が重要であることが示されている[6]. このような点から炭水化物50〜55%, 蛋白質15〜20%, 脂質25〜30%前後を基本とするのが現段階では妥当と思われる.

さらに各栄養成分の内容について心掛けねばならない点を列記する. 炭水化物では単純糖質（砂糖など）がより血清中性脂肪の上昇効果が高いので複合糖質（米, 麦, 粟, キビ, ソバ, トウモロコシ, イモ類など）を選択すべきである. さらに摂取後の急激な血糖上昇を避けるために血糖上昇係数（Glycemic index ; GI）の低い食品（表2）を中心にした構成にした方がよい. GI が高い食品の場合には食物線維を同時に摂取するようにする.

脂質では飽和脂肪酸やトランス型脂肪酸を避け, 一価不飽和脂肪酸や n-3 系多価不飽和脂肪酸の摂取を心掛ける（表3）. “第6次改訂日本人の栄養所要量” ではこれらのバランスを 3:4:3 としているが, 食事摂取基準では小児について目安値を示すに留まっている（表1）. しかし実際の食事中に個々の食品に含まれる脂肪酸の種類を調べて調理するこ

表2 食品の血糖上昇係数

食品	係数	食品	係数
ブドウ糖	100	ぶどう	65
食パン	95	バナナ	60
蜂蜜	90	スパゲッティ	55
ジャガイモ	90	さつまいも	50
ポップコーン	85	玄米ご飯	50
コーンフレーク	85	乳製品	35
うどん	80	インゲン豆	30
もち	80	フルーツ類	30
ビスケット	70	大豆	15
とうもろこし	70	緑黄色野菜	<15
ご飯	70	きのこ	<15

血糖上昇係数は食後の血糖上昇をブドウ糖と比較し, ブドウ糖の曲線下面積に対する重複する部分の面積の割合で示す. この数値は被験者や食品など検査方法によって変化するので, 参考値である.

表3 脂肪酸の種類

不飽和脂肪酸	一価不飽和脂肪酸（オリーブオイルやサフラワー油など） 多価不飽和脂肪酸 n-3系：α-リノレン酸，EPA，DHA など （えごま油，なたね油や魚油に多く含まれる） n-6系：リノール酸，アラキドン酸 など （コーン油など植物油）
飽和脂肪酸	肉類の脂肪や乳製品の脂肪など
※トランス型脂肪酸	マーガリン，ファットスプレッドやショートニングに含有量が多い

表4 脂肪酸 100 g 当たりの多価不飽和脂肪酸含有量（g）

	n-6系多価不飽和脂肪酸		n-3系多価不飽和脂肪酸		
	リノール酸	アラキドン酸	リノレン酸	イコサペンタエン酸	ドコサヘキサエン酸
カステラ	16.5	0.2	0.5		1.7
かわらせんべい	22.5	1.4	0.9		1.4
あじ焼き	22.0	1.7	0.9	8.1	15.3
まいわし焼き	2.2	1.0	0.9	12.6	12.2
しらす干し	1.0	2.0	1.1	13.5	28.2
さけ新巻き焼き	1.0	0.7	0.5	8.3	16.8
さんま焼き	1.5	0.6	1.1	6.1	9.9
あさり生	0.8	4.3	0.5	7.0	11.3
いか焼き	0.0	2.8	0.2	14.0	37.9
えびあまえび生	1.0	1.9	0.1	21.9	18.1
鶏若鶏ささ身	14.7	2.5	0.5	0.7	3.6
豚肝臓	15.3	17.0	0.3	0.7	4.6
鶏卵全卵生	13.4	1.7	0.3	0.0	1.8
人乳（母乳）	15.0	0.5	2.1	0.1	0.5

とは難しい（表4）．現代の食生活では，肉類や乳製品などの飽和脂肪酸が多い食品やn-6系多価不飽和脂肪酸は過剰摂取傾向にあるので，どちらかというと肉や乳由来の動物性脂質に偏らないこと，不足しがちなn-3系多価不飽和脂肪酸を多く含む魚を摂取すること，そして植物性油で調理することを目標にする．

三大栄養素以外ではカルシウム，鉄やビタミン類の摂取に心掛ける．摂取エネルギー量の制限を開始すると栄養バランスがよくないままにこれらの摂取がさらに減少することがある．したがって意識的に摂取するように指導する．

これらに加えて塩分制限の重要性を強調すべきである．減塩によって血圧が是正されるのみではなく，過剰な摂食を抑制することができる．

4 食行動や食環境の是正と維持

食事内容に関する指導以上に大切なのは食行動や食環境の是正である．肥満小児は大食であるうえに早食いであることが多い．外で遊ぶべき時刻には室内でお菓子を口に運びながら静かに遊んでいる．夜遅くに帰宅する父親の晩酌に付き合っては酒の肴を一緒に食する．

このような点を改善するためにまず取り組むべきことは食環境の整備である．いつでもどこでも何かを食べられる状態にしておくことはダラダラ食いを助長する．食事と適度な間食以外には清涼飲料水を含めて取らせないように冷蔵庫を含めて目に付く場所に飲食物を置かない．さらに買い置きをしないことが大切である．

食事を用意するときには多めに作らず余計なおかわりをさせない．ご褒美として，あるいは子どもの機嫌をとるためにお菓子を与えることはやめる．

食事の取り方としてまず指導すべきことはゆっくりと食べさせることである．一口入れたら箸を置く，小皿に分けて盛りつける，茶碗を小さくする，よく噛むということを心掛けさせる．また食卓にはなるべく家族が揃って食事を取ることが重要である．子食や孤食は早食い，食べ過ぎやバランスの乱れにつながる．

子どもが置かれた心理状態に配慮することも肥満の発生を予防するという点では重要である．次の子どもが出生すると家族の注目がその子どもへと移るので，食べることに関心が向かうことがある．そのほかにも親が就労したとき，進学や転居による友人との別れ，本人あるいは家族の入院，親や祖父母の死去など寂しさが増したときにも食べることへと逃避することがある．このような心理的環境の変化にも配慮した対応が必要である．

またこれらはすべて祖父母を含めた家族や地域の協力なしには進まない．子どもを取り巻くすべての人が子どもを肥満にさせない環境作りに取り組めば肥満の改善あるいは肥満の予防という目標の達成は決して困難なことではないだろう．

5 外来での指導と評価

メタボリックシンドロームあるいは肥満の改善を求めて小児科外来を受診した際には生活環境，生活リズム，食行動と食事内容をチェックし，何が歪んでいるのかを把握する．

肥満小児はしばしば摂取食物が片寄っている．この偏りは大きく三つに分けることができる．ご飯太り，肉太りとお菓子太りである．どのようなタイプであるかは簡単な問診で明らかにすることができる．生活リズムや運動習慣を含めて生活習慣のチェックリスト（図 1）を使用して問題点を洗い出すという方法もある．チェックリストは自覚を促すのみならず，その後の経過観察にも使用できるので有用である．病院においてはさらに栄養士に食事や食習慣を評価してもらうとよい．

先に述べたように食事の内容と食行動について，問診あるいはチェックリストから浮かび上がった問題点の改善を目標にして外来での指導を開始する．指導内容はわかりやすくなければ意味がない．摂取エネルギー量を数字で示すのではなく，より具体的に表現する．たとえばご飯の盛りつけを2/3にする，一口減らすなどである．

食事療法の効果は最終的に内臓脂肪（腹囲）の減少や生化学的異常や高血圧の改善で

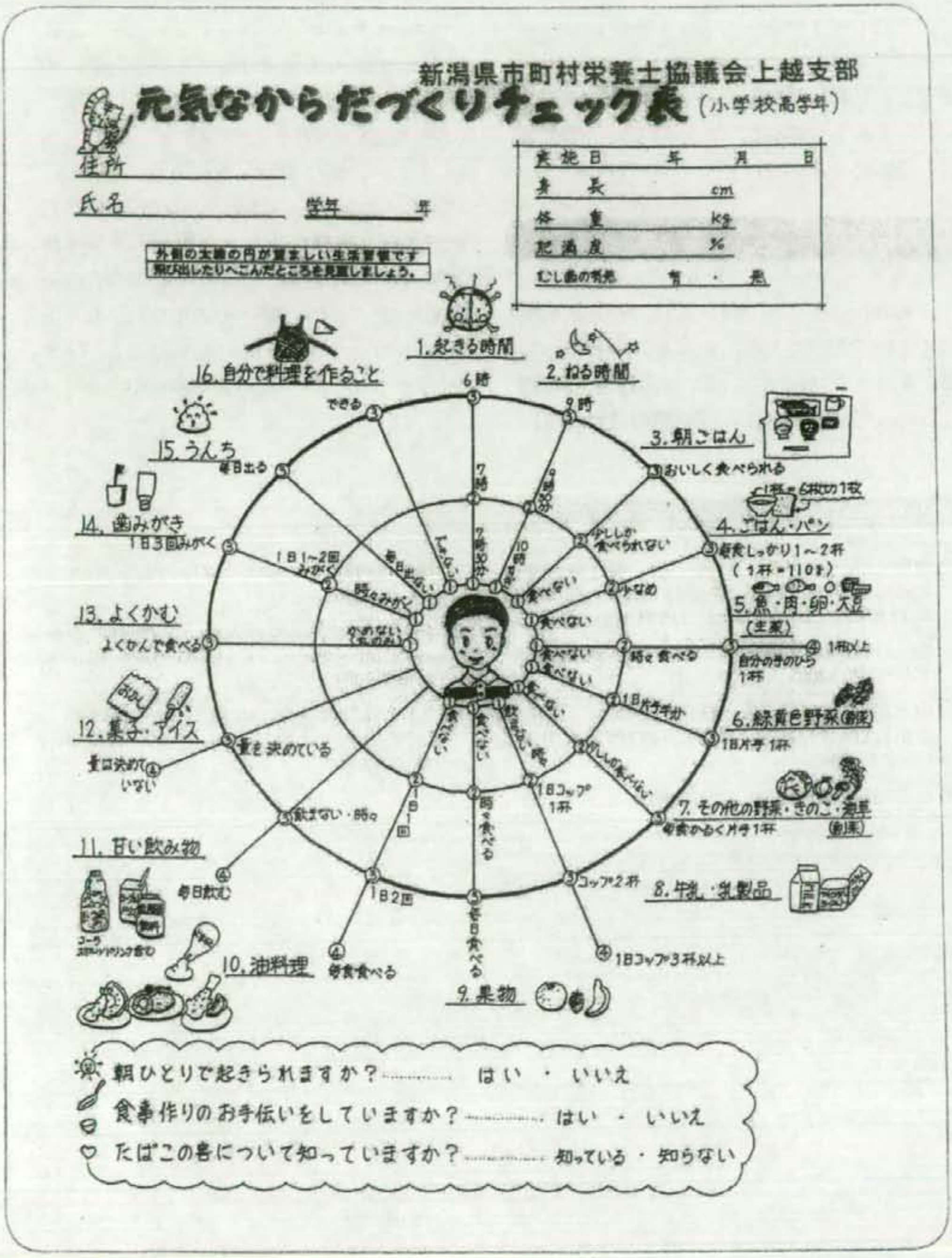

図1 生活習慣チェックリスト

評価されるべきである．しかし実際には指導に抵抗してこれらが改善しないことも多い．設定した目標に到達しないと医療者も指導を受けるものも意欲が低下するので，目標や評価の指標をできるだけ多くもつのがよい．

おわりに

メタボリックシンドロームにおける食事療法について述べてきた．食事を内容と量の両面からコントロールし，その食習慣を長期間にわたって維持することは至難の技である．したがって食事療法の継続をどのように支援するかが実際の現場では最も重要である．そのためには実行が難しい目標を強引に指導するよりも優しい励ましが効果的である．理解しやすい言葉（表現）を使うならば，「いつでも，どこでも，好きなものを好きなだけ」という環境に子どもを置かず，「食べ過ぎず，よく体を動かし，果物や野菜や全粒穀類を食べ，スナック菓子や清涼飲料水などのジャンクフードを控える」ということがメタボリックシンドロームの食事療法である．

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雑　誌

Blood pressure and urine output during the first 72 hours in infants born less than 29 weeks' gestation related to umbilical cord milking

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Blood pressure and urine output during the first 72 hours of life in infants born at less than 29 weeks' gestation related to umbilical cord milking

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Abstract

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

Patients and Methods: This study was the secondary analysis of a randomized 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 ventiratory index values in both groups were measured during the first 120 hours after birth.

Results: There were no significant differences in gestational age or birth weight between the two groups. The initial hemoglobin value was higher in the milked group (16.5 ± 1.4g/dl in the milked vs. 14.1 ± 1.6 g/dl in the control; p<0.01). During the first 12 hours, 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 hours. There were no significant differences in heart rate, water intake, or ventilatory index values between the groups.

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

Key words

Blood pressure
Delayed cord clamping
Hemoglobin level
Placental transfusion
Premature infants

Introduction

The majority of term neonates successfully complete the postnatal transition from fetal to postnatal cardio-pulmonary 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 directory correlate with tissue perfusion, it is frequently used as an index of hemodynamic 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 cardiovascularly 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 (e.g., 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 randomized 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 hemoglobin group had higher blood pressure during the first 24 hours of life, as compared with the lower hemoglobin group 6). The initial study of this randomized control trial showed that initial blood pressure in the milked group was significantly higher than that in the control group 7). We hypothesize 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 randomized control trial was to investigate the impact of umbilical cord milking on cardio-pulmonary adaptations in premature infants during the first 120 hours after birth.

Materials and Methods

This study is the secondary analysis of the results of a randomized control study regarding the effect of umbilical cord milking in premature infants 6). The original study design was a randomized, controlled trial with two treatment arms. This original randomized controlled trial was carried out in a single tertiary perinatal center over a 24-month period from January 2001 to December 2002. Exclusion criteria were i) multiple births, ii) major congenital anomalies or chromosomal anomalies, and iii) hydrops fetalis. Women must have been be admitted to the hospital at least 6 hours before delivery to allow time for enrollment. The chief neonatologist decided whether to enroll the patients in the present study. For randomization, we used serially numbered opaque envelopes that were opened by neonatology staff after enrollment 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 randomized 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 randomized 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 (RBC) transfusions performed during the hospital stay. This study examined the secondary outcome variables. We focused on cardio-pulmonary adaptations, which were indicated by blood pressure, heart rate, urine output, fluid intake, and ventilatory index (V.I.) values during the first 120 hours 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, 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 hours 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 hours.

The V.I. was calculated as inspired oxygen x mean airway pressure/ postductal 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 hours after birth.

Statistical analysis

Normally distributed continuous outcome variables were compared with the unpaired Student t test, and non-parametric continuous outcome variables were analyzed with the Mann-Whitney U test. Categorical variables were compared using the chi-square test. Fisher's exact test was used for contingency tables showing expected cell counts < 5. The data are expressed as the mean ± standard deviation. 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 7). Twenty infants were allocated to the milked group and 20 to the control group. A total of 40 very low birth weight infants were admitted and were analyzed for the present study. There was no protocol infraction in either group.

The hemoglobin value at birth of 16.5 ± 1.4 g/dl (range: 13.7-19.6g/dl) measured at birth in the milked group was significantly higher than the hemoglobin 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 hours after birth. During the first 12 hours, both systolic and diastolic blood pressures in the milked group were higher than those in the control group. The mean arterial blood pressure gradient from birth to 24 hours after birth in the milked group was significantly lower than that of the control group (1.3±8.8 mmHg vs. 6.3±6.2 mmHg $p<0.05$). The benefits of umbilical cord milking included better blood pressure and reduced needs for both volume expansion and inotropic support (Table2). There was no difference in the heart rate or mean fluid intake between the two groups. In contrast, during the first 72 hours, mean urine output in the milked group was significantly higher than that in the control group (Fig.2). The V.I. value was comparable in the two groups during the first 120 hours.

Discussion

Circulating blood volume is an important variable, but is difficult to measure in VLBW infants. A severe volume deficit leads to recognizable 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 ischemic 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 mmHg 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 hours in the milked group was higher than that in the control group, with lower pressure gradients from birth to 12 hours 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 hemoglobin values are closely associated with both blood pressure during the first 24 hours and the incidence of IVH and that the high hemoglobin group exhibited a smaller pressure gradients from birth to 24 hours afterward 6). The recent meta-analysis showed IVH was higher in the immediate umbilical cord clamping group as compared with the delayed cord clamping group 11). Meier 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 hemorrhage in preterm newborn infants13). 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 resistance14). 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 means 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 recognized clinically by a decrease in urine output. Decreased urine output in the absence of known renal disease is a typical sign of hypovolemia. Despite fewer interventions with volume load and inotoropes, 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 hours 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 hemoglobin values and between hemoglobin 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 hours 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 hours. 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 16).

In premature infants, 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 18). On the other hand, a recent Cochrane Reviews found that a brief delay in cord clamping time of at least 30 s improves the stability of the cardio-circulatory systems of infants during the first day of life, leading to a reduced requirement for volume therapy and inotropic support 5). 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 hypovolemia 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 to the recommended rate of administration and dose. Arguably, even in the absence of hypovolemia 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 stabilization of both the blood pressure and urine output, as well as decrease the need for therapeutic intervention with regard to circulation after birth in VLEW infants.

Table1 Baseline characteristics

	Control group n=20	Milked group n=20	p value
Gestational age (weeks)	26.6 ± 1.2 (24-28)	27.0 ± 1.5 (24-28)	0.14
Birth weight (g)	846 ± 171 587-1180	836 ± 223 494-1198	0.43
Male	13 (65.0)	10 (50.0)	0.26
Antenatal steroid	7 (35.0)	7 (35.0)	0.63
Chorioamnionitis	11 (55.0)	10 (50.0)	0.50
Caesarean section	14 (70.0)	14 (70.0)	0.63
Death	3 (15.0)	2 (10.0)	0.50

Table 2 Treatment for hypotension during the first 120 hours

	Control group n=20	Milked group n=20	p value
Hypotension at admission	12(60.0)	5(25.0)	0.03*
Blood transfusion for hypotension	0(0.0)	0(0.0)	-
Volume expander	8(40.0)	2(10.0)	0.03*
DOA+DOB ≤ 5 μg/kg/min	5(25.0)	4(20.0)	0.73
DOA+DOB > 5 μg/kg/min	12(60.0)	3(15.0)	<0.01**

Hypotension is defined as a mean arterial pressure (in mmHg) that is less than the gestational age (in weeks)

DOA:dopamine. DOB:dobutamine

Percentages, given in parentheses, are calculated as a proportion of the total number.

*p<0.05, **p<0.01

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