Journal of Tropical Pediatrics, 2019, 65, 63–70
doi: 10.1093/tropej/fmy012
Advance Access Publication Date: 23 March 2018
Original paper

OXFORD

An Open-label Randomized Controlled Trial to Compare Weight Gain of Very Low Birth Weight Babies with or without Addition of Coconut Oil to Breast Milk

Sumitha Arun,[1] Manish Kumar,[1] Thomas Paul,[2] Nihal Thomas,[2] Sarah Mathai,[3] Grace Rebekah,[4] *and* Niranjan Thomas[1]

[1]Department of Neonatology, Christian Medical College, Vellore, Tamil Nadu 632004, India
[2]Department of Endocrinology, Christian Medical College, Vellore, Tamil Nadu 632004, India
[3]Department of Child health, Christian Medical College, Vellore, Tamil Nadu 632004, India
[4]Department of Biostatistics, Christian Medical College, Vellore, Tamil Nadu 632004, India
Correspondence: Manish Kumar, Consultant Neonatologist, Christian Medical College, Vellore, Tamil Nadu, India.
E-mail <maneeshdr@gmail.com>

ABSTRACT

Background: Nutritional guidelines involving the feeding of very low birth weight babies (VLBW) recommend addition of Human Milk Fortifiers to breast milk. Owing to financial constraints, it is a practice in low- and middle-income countries (LMIC) to add coconut oil to aid better weight gain. There are inadequate data on improvement of growth parameters with oral coconut oil supplementation of breast milk.

Methods: In this randomized controlled trial, we measured growth parameters and body composition of 60 babies who received either breast milk with coconut oil or breast milk alone. Randomization was stratified according to intrauterine growth appropriate for gestational age ($n = 30$) and small for gestational age ($n = 30$).

Results: There was no difference in weight gain between the two groups. The weight gain velocity was 15 ± 3.6 and 14.4 ± 3.4 g/kg/day (p value $= 0.49$) in the breast milk alone and in the breast milk with coconut oil group, respectively. There was no difference in increase in head circumference and length. Triceps skinfold thickness ($n = 56$) was similar in both groups, but subscapular skinfold thickness was significantly more in the coconut oil group. Total body fat percentage did not differ between the groups (25.2 ± 4.3 vs. $25.5 \pm 4.3\%$, $p = 0.79$).

Conclusion: Oral supplementation of coconut oil along with breast milk did not increase growth parameters or result in change in body composition in very low birth weight (VLBW) babies.

KEYWORDS: preterm, postnatal growth, nutritional supplement, medium-chain triglyceride

INTRODUCTION

Very low birth weight (VLBW) babies constitute 3.4% of all live births in India [1]. The survival of VLBW babies is about 85% [2]. As all VLBW babies require neonatal ICU (NICU) care soon after birth, they form a significant proportion of NICU admissions.

Caring for VLBW babies involves several challenges, including providing optimal nutrition. Optimal nutrition is defined as achieving intrauterine growth rate and body composition as that of a normally growing fetus of similar gestational age [3]. Providing breast milk alone to these babies does not meet their nutritional requirements. Human Milk Fortifiers (HMFs) are added to breast milk to meet the recommended calorie and protein requirements. The approximate cost estimate of using HMF in India is 150–250 Rupees/day. Owing to cost constraints and nonavailability, it is a practice in low- and middle-income countries (LMICs) and in our neonatal unit to use coconut oil or medium-chain triglyceride oil (MCT oil) for improving weight gain [4].

Coconut oil is composed of 60% MCT. MCT is composed of C6-C12 fatty acids. They are more easily absorbed regardless of bile acid concentration and can enter portal circulation directly without forming chylomicrons [5]. This property of rapid absorption has made it useful as part of enteral nutrition.

The rate of weight gain with coconut oil is not well known, and there is only one published study in the literature [6]. Hence, we proposed this study to look at growth parameters and body composition after enteral coconut oil supplementation.

METHODS

The study was a randomized controlled trial conducted at a tertiary care center from April 2016 to December 2016. The study was approved by the institutional ethics committee (number 9879/20/1/16) and registered in the clinical trials registry of India (CTRI/2016/06/007037).

Study subjects

VLBW babies admitted in NICU were eligible for the study. On reaching 100 ml/kg/day of feeds, they were enrolled after obtaining written consent from parents. Babies with major congenital malformations, babies not reaching full feeds by Day 21 of life, babies who had NEC Stage 3 and those who refused consent were excluded from the study.

Randomization and allocation concealment

VLBW babies in NICU on reaching 100 ml/kg of feeds were enrolled and stratified into appropriate for gestational age (AGA) and small for gestational age (SGA) according to intrauterine growth. They were then randomized to breast milk alone or breast milk with coconut oil. A computer-generated block randomization was used with block sizes of 2, 4 and 6. Serially numbered opaque sealed envelopes were used for allocation concealment.

Intervention

Babies were given expressed breast milk (EBM) every 2–3 h. EBM included own mothers milk and donor milk. Feeds were progressed at the rate of 20–25 ml/kg/day upto a maximum feed volume of 180 ml/kg/day. The babies in the breast milk with coconut oil group were given 1 ml coconut oil mixed with EBM every 6 h (4 ml/day) till 40 weeks of corrected age. The intervention was given through nasogastric tube till 1.7 kg and through paladai (a beaked cup used locally) till 40 weeks of corrected age. The oil used was Parachute oil from Marico Industries. Once direct breast feeds were fully established, mother was taught to add 1 ml coconut oil in one paladai (10 ml) of EBM four times a day. They were discharged at 1.8 kg and corrected gestational age of >35 weeks. In case of discharge before 40 weeks, the intervention was continued at home. The discharge summary included proper instructions. Compliance was checked during follow-up visit in outpatient department (OPD).

Babies in both groups were supplemented with oral calcium, phosphate, vitamin D3, iron and multivitamins as per routine nursery practice. All babies <32 weeks or <1.5 kg receive TPN in our unit. On Day 1, amino acids are started at 2 g/kg/day and then increased by 0.5 g/kg/day till 3.5 g/kg/day. Lipid is started from Day 2 onward at 1 g/kg/day and then increased by 1 g/kg/day till a maximum of 3 g/kg/day. When baby received two thirds of total volume of feeds enterally, TPN is stopped.

Primary outcome

The primary outcome was weight gain up to 1.8 kg and 35 corrected weeks of gestation.

Secondary outcomes

Secondary outcomes increase in length and head circumference, skinfold thickness, total body fat percentage, lipid profile and length of hospital stay.

Weight was measured daily in grams using calibrated electronic weighing scale [Essae DS 852, Essae Teroka Limited India] with error ±5 g. The discharge criterion in our unit is 1.8 kg and >35 corrected weeks. Weight gain was calculated from randomization at 100 ml/kg/day of feeds till discharge. Length was measured in centimeters with infantometer, and head circumference was measured using non stretchable tape corrected to nearest 0.1 cm.

Length and head circumference were measured at recruitment and at 1.8 kg to calculate growth velocity in cm/week. Corrected age was defined as the corrected gestational age from the best obstetric estimate of gestational age at birth.

The study subjects were seen in follow-up OPD 2 weeks after discharge and monthly thereafter. At 40 corrected weeks, they were assessed for skinfold thickness, lipid profile and body composition by Dual Energy Xray Absorptiometry (DEXA) scan.

Skinfold thickness was estimated using Harpenden calipers, which can be read to 0.1 mm. Triceps skinfold was measured midway between acromion and olecranon in the posterior part of left arm with arms by the side of body and elbow extended. Subscapular skinfold was measured just below the angle of left scapula with the arm by the side of the body.

DEXA scans were done at 40 weeks corrected age using HOLOGIC QDR series Discovery A machine. Lipid profile was measured using Cobas 8000 automated chemistry Analyzer using colorimetric enzymatic end point with esterase, oxidase and peroxidase method.

Feed intolerance was defined as increase in abdominal girth > 2 cm from baseline or presence of gastric aspirate >50% of feed volume or altered color gastric aspirate [7].

Masking

Masking of the intervention was not possible given the nature of the intervention.

Sample size

In a study by Vaidya *et al.* [6], to detect a mean weight difference of 6 g/day between the two groups with a pooled SD of 6 g/day at 5% level of significance and 90% power, a sample size of 21($n = 21$where n is sample size) was needed in each arm.

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times 2 \times \sigma^2}{(\delta)^2}.$$

Standard normal value for 5% α error, $Z\neg\alpha/2 = 1.96$.

Standard normal value for 90% power, $Z\neg\beta = 1.28$.

Pooled SD, $\sigma = 6$.

Expected difference, $\delta = 6$.

Pooled SD was calculated from reference study, 8 g/day in coconut oil group and 6 g/day in breast milk alone group. Adjusting for 20% lost to follow-up, an additional nine cases were needed. Therefore, the total sample size was estimated to be 60 (30 in each arm).

Statistical analysis

Descriptive statistics using frequency and percentage were used for analyzing baseline characteristics. p-value of < 0.05 was taken as significant. Continuous variables were reported using mean and SD. The mean difference was assessed using Student's t-test in case of parametric variables and Mann–Whitney U test in case of nonparametric variables. Categorical variables are represented as frequency and percentages and the association assessed using chi-square test. Statistical analysis was done using stata version 16. An intention to treat analysis was done.

Results

In total, 84 neonates were eligible and 24 were excluded for various reasons (Fig. 1). In one case, protocol was broken, as the baby in control arm developed cholestasis and required MCT as treatment. Intention to treat analysis was done. The baseline characteristics of the groups were similar except in

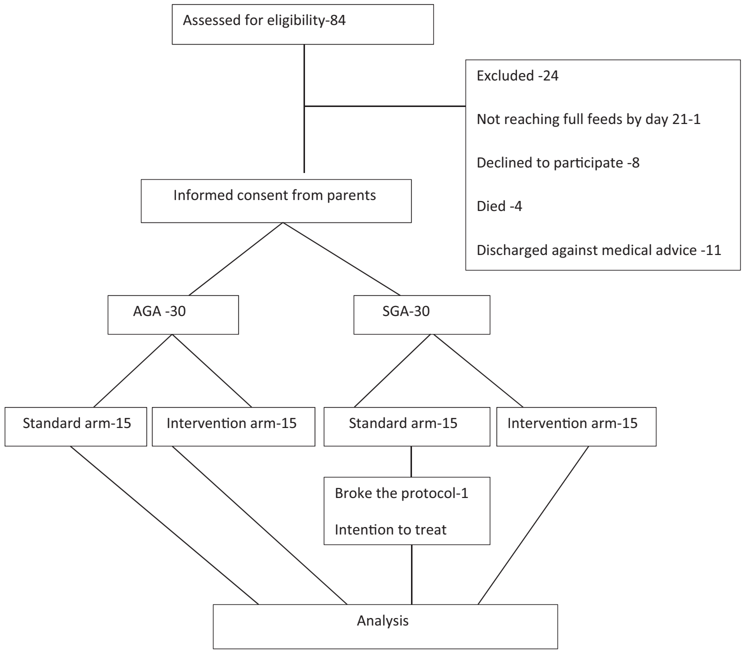

Fig. 1. Cohort flow diagram.

the AGA group where there was difference in length at birth (Table 1).

Weight gain was 14.4 ± 3.4 g/kg/day and 21.8 ±5.2 g/day in the breast milk with coconut oil group as compared with 15± 3.6 g/kg/day ($p = 0.49$) and 22.5 ± 7.9 g/day ($p = 0.70$) in the breast milk alone group. All the babies were off TPN at the time of randomization. There was no difference in gain in length and increase in head circumference between the groups.

In total, 56 babies were followed up till 40 weeks of corrected gestational age. Triceps skinfold thickness was similar in both groups. Subscapular skinfold thickness was significantly more in the coconut oil group (3.15 ± 0.71 vs. 2.71 ± 0.58 mm, p =0.02). The total body fat percentage was similar in both arms (Table 2). Subgroup analysis showed increased subscapular skinfold thickness in AGA group given coconut oil (3.4± 0.8 vs. 2.6± 0.5 mm), but no difference in total body fat (Table 3). Hypertriglyceridemia (TG > 150 mg/dl) was seen in more babies in the coconut oil group, but the difference was not statistically significant (Table 4).

DISCUSSION

It is well known that improved post-natal growth during NICU stay improves neurodevelopment outcomes in preterm and SGA babies [8–10]. Several nutritional practices like increasing volume of feeds (200–250 ml/kg/day) [11], oral MCT or coconut oil supplementation, addition of corn starch to breast milk [12], use of animal milk and massage therapy with coconut oil [13, 14] have been used to improve growth in resource-poor settings. In this study, we have looked at the effect of addition of coconut oil to breast milk.

Coconut oil is added to breast milk to increase the calories and to improve weight gain. In our unit, we have used coconut oil in the past in VLBW babies, and it was administered as 4 ml/day. Previously only one study has been done to assess weight gain with oral coconut oil. In that study by Vaidya *et al.*, they demonstrated a 7 g/day increase in weight with coconut oil. In our study, we could not demonstrate increased weight gain after supplementation of breast milk with oral coconut oil. There was no difference in rate of increase of length and head circumference among the two groups.

Table 1. Baseline characteristics of VLBW babies fed either breast milk and coconut oil or breast milk alone

	AGA		SGA	
Variables	Intervention	Control	Intervention	Control
Vaginal delivery	3 (20.0%)	2 (13.3%)	2 (13.3%)	4 (26.7%)
Apgar score at 5 minutes	8.6±0.9	8.0±0.9	8.9±0.9	8.8±0.8
Male	10 (66.7%)	9 (60%)	6 (40%)	8 (53.3%)
Gestational age (weeks)	29.8±1.7	29.9±2.1	33.2±1.6	33.1±1.4
Birth weight (grams)	1245.7±212.4	1124.7±235.2	1239.3±110.2	1257.3±131.5
HC at birth (cm)	26.4±1.9	26.1±1.6	27.7±0.8	27.6±0.9
Length at birth (cm)	38.0±2.5*	35.8±3.1	37.9±1.5	38.8±2.2
Weight at recruitment (grams)	1195.3±174.8	1051.3±202.1	1219.0±139.2	1210.7±143.2
HC at recruitment (cm)	26.9±1.3	27.1±3.8	28.4±0.7	28.1±1.1
Length at recruitment (cm)	39.1±2.0	37.0±3.5	39.5±1.3	39.6±1.7
Day of recruitment	11.4±5.2	10.3±3.6	9.8±3.2	9.7±2.5
HMD	7 (46.7%)	6 (40%)	0	2 (13.3%)
CPAP	7 (46.7%)	7 (46.7%)	0	2 (13.3%)
Ventilated babies	2 (13.3%)	2 (13.3%)	0	2 (13.3%)
PDA	5 (33.3%)	3 (20%)	0	1 (6.7%)
Feed intolerance	8 (53.3%)	4 (26.7%)	4 (26.7%)	6 (40%)
NEC	2 (13.3%)	1 (6.7%)	1 (6.7%)	1 (6.7%)
Blood culture-proven sepsis	0	1 (6.7%)	1 (6.7%)	1 (6.7%)
Duration of TPN	6.1±3.8	6.3±3.8	6.2±3.6	6.3±3.9

Note: Continuous variables are expressed as mean and SD. Categorical variables are expressed as frequency and percentage.
**p*-value for length at birth was significant (*p* ign.05) in AGA group.

Table 2. Growth parameters and body composition of infants fed breast milk with coconut oil or breast milk alone

Primary outcome	Breast milk with coconut oil	Only breast milk	*p*-value
	Mean±SD	Mean±SD	
Variable			
Weight gain velocity (g/kg/day)	14.4±3.4	15±3.6	0.49
Weight gain velocity (g/day)	21.8±5.2	22.5±7.9	0.70
Secondary outcome			
HC (cm/week)	0.79±0.21	0.74±0.17	0.29
Length (cm/week)	0.73±0.27	0.74±0.24	0.85
SFT mm (triceps)	2.94±0.65	2.65±0.65	0.13
SFT mm (subscapular)	3.15±0.71	2.71±0.58	0.02
Total body fat% (DEXA)	25.5±4.3	25.2±4.3	0.79
Duration of Hospital stay (days)	41.4±17.3	43.9±21.3	0.62

Table 3. Growth parameters and total body fat of VLBW babies fed either breast milk and coconut oil or breast milk alone based on subgroups—AGA vs. SGA

AGA	Breast milk with coconut oil	Only breast milk	p value
	Mean±SD	Mean±SD	
Weight gain velocity (g/day)	21.3±5.6	20.4±4.5	0.63
Weight gain velocity (g/kg/day)	13.8±3.6	13.9±2.7	0.94
HC (cm/week)	0.8±0.3	0.72±0.1	0.24
Length (cm/week)	0.76±0.3	0.74±0.2	0.78
Triceps skinfold thickness (mm)	3.1±0.7	2.5±0.5	0.05
Subscapular skinfold thickness (mm)	3.4±0.8	2.6±0.5	0.02
Total body fat% (DEXA)	26.2±3.9	24.7±3.9	0.28
SGA			
Weight gain velocity (g/day)	22.3±4.8	24.5±9.9	0.44
Weight gain velocity (g/kg/day)	14.8±3.2	16.0±4.1	0.36
HC (cm/week)	0.76±0.1	0.75±0.1	0.98
Length (cm/week)	0.69±0.3	0.74±0.3	0.63
Triceps skinfold thickness (mm)	2.7±0.4	2.7±0.8	1.0
Subscapular skinfold thickness (mm)	2.9±0.4	2.7±0.7	0.6
Total body fat % (DEXA)	24.7±4.6	25.8±4.8	0.55

Table 4. Lipid profile at 40 weeks of corrected age

Variable	Breast milk with coconut oil ($n=28$) Mean ± SD	Only breast milk ($n=25$) Mean ± SD	p-value
Total cholesterol (mg/dl)	99.5±35.3	88.0±26.4	0.18
Triglycerides >150 (mg/dl)[a]	16(57.1%)	11(44%)	0.33
HDL (mg/dl)	20.7±11.9	19.0±7.2	0.54
LDL (mg/dl)	43.3±28.3	40.4±21.3	0.67

[a]Triglycerides > 150 mg/dl expressed as frequency and percentage.

Feeding protocol in the study included 180 ml/kg/day of unfortified breast milk. The addition of coconut oil increased the total calorie intake by 32 kcal/day, but protein intake remained below recommended requirement. A previous study showed increased adherence of fat to gavage tube when MCT oil was mixed with formula feeds [15]. We do not know the amount of medium chain fatty acids that will adhere to gavage tube when coconut oil is given with breast milk. This may be a possible reason why addition of coconut oil did not result in improved growth parameters in our study. The two groups did not differ in weight, length and head circumference during subgroup analysis as AGA and SGA babies.

Normal body composition must be maintained in babies as they grow. Preterm and SGA babies have been found to have altered body composition in the form of increased adiposity compared with term and AGA babies [16, 17].

Alteration in body composition can lead to early onset of metabolic diseases like hypertension, insulin resistance, diabetes and cardiovascular illnesses. Increase in total body fat percentage is linked to early onset of these metabolic diseases. Increase in lean body mass is more desirable [18, 19]. This is the importance of knowing the effect of nutritional interventions on body composition. To date, to the best of our knowledge, no study has assessed the effect of oral coconut oil on body composition.

MCTs undergo obligatory oxidation in liver and have less tendency to be deposited as fat. This property has been studied to use it as a dietary intervention in adults [20]. On the other hand, it is also known that extra calories provided may be deposited as fat. To know the effect of coconut oil on body composition, we have measured skinfold thickness and performed DEXA scans.

Subscapular skinfold thickness at 40 weeks corrected age was significantly more in the intervention arm, and there was a trend to increased triceps skinfold thickness in the intervention group. Subgroup analysis showed that the difference was significant among AGA babies but not in SGA babies. Skinfold thickness has limitation as a measure of fat, and this finding should therefore be interpreted with caution [21].

The gold standard of measuring body composition in infants is DEXA scans. The radiation exposure per scan is 1/10th that of a chest radiograph. DEXA scans did not show a significant difference in total body fat percentage between the two groups.

There was no statistically significant difference in total body fat percentage in AGA and SGA babies in both groups.

One of the concerns of oral coconut oil is elevated triglycerides [22]. Unfavorable lipid profile including elevated cholesterol, triglycerides, LDL and low HDL is linked to metabolic diseases. Lipid profile done at 40 weeks corrected age showed increased cholesterol, LDL and triglycerides in the coconut oil with breast milk group. However, the difference was not statistically significant.

Enteral coconut oil supplementation in VLBW babies did not lead to improvement in weight, length or head circumference. There was a significant increase in subscapular skinfold thickness, but no difference in total body fat percentage.

Based on existing literature and our study, further studies will be required to justify the use of coconut oil as a routine supplementation in VLBW babies.

FUNDING

Fluid research grant from Institutional review board, CMC Vellore.

REFERENCES

1. Report of the National Neonatal Perinatal Database (National Neonatology Forum) 2002-03.
2. VLBW Infant Survival in Hospitals of India (VISHI) Study Investigators, Murki S, Kumar N, *et al*. Variability in survival of very low birth weight neonates in hospitals of India. Indian J Pediatr 2015;82:565–7.
3. American Academy of Pediatrics Committee on nutrition. Nutritional needs of low-birth-weight infants. Pediatrics 1985;76:976–86.
4. Patel Brijal S, KubavatAmita R, Sondarva Divyesh B, *et al*. Drug utilization study in neonatal intensive care unit at tertiary care hospital, Rajkot, Gujarat: a prospective study. World J Pharm Pharm Sci 2015;4:2034–42.
5. Schönfeld P, Wojtczak L. Short-and medium-chain fatty acids in energy metabolism: the cellular perspective. J Lipid Res 2016;57:943–54.
6. Vaidya UV, Hegde VM, Bhave SA, *et al*. Vegetable oil fortified feeds in the nutrition of very low birthweight babies. Indian Pediatr 1992;29:1519–27.
7. Bora R, Mukhopadhyay K, Saxena AK, *et al*. Prediction of feed intolerance and necrotizing enterocolitis in neonates with absent end diastolic flow in umbilical artery and the correlation of feed intolerance with postnatal superior mesenteric artery flow. J Matern Fetal Neonatal Med 2009;22: 1092–6.
8. Ehrenkranz RA, Dusick AM, Vohr BR, *et al*. Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. Pediatrics 2006;117:1253–61.
9. Belfort MB, Rifas-Shiman SL, Sullivan T, *et al*. Infant growth before and after term: effects on neurodevelopment in preterm infants. Pediatrics 2011;128:e899–906.
10. Ong KK, Kennedy K, Castañeda-Gutiérrez E, *et al*. Postnatal growth in preterm infants and later health outcomes: a systematic review. Acta Paediatrica 2015;104: 974–86.
11. Thomas N, Cherian A, Santhanam S, *et al*. A randomized control trial comparing two enteral feeding volumes in very low birth weight babies. J Trop Pediatr 2012;58:55–8.
12. Aborigo RA, Moyer CA, Rominski S, *et al*. Infant nutrition in the first seven days of life in rural northern Ghana. BMC Pregn Child 2012;12:76.
13. Sankaranarayanan K, Mondkar JA, Chauhan MM, *et al*. Oil massage in neonates: an open randomized controlled study of coconut versus mineral oil. Indian Pediatr 2005;42:877.
14. Salam RA, Das JK, Darmstadt GL, *et al*. Emollient therapy for preterm newborn infants–evidence from the developing world. BMC Public Health 2013;13:S31.
15. Mehta NR, Hamosh M, Bitman J, *et al*. Adherence of medium-chain fatty acids to feeding tubes of premature infants fed formula fortified with medium-chain triglyceride. J Pediatr Gastroenterol Nutr 1991;13:267–9.
16. Giannì ML, Roggero P, Taroni F, *et al*. Adiposity in small for gestational age preterm infants assessed at term equivalent age. Arch Dis Child Fetal Neonatal Ed 2009;94: F368–72.

17. Ibáñez L, Ong K, Dunger DB, *et al*. Early development of adiposity and insulin resistance after catch-up weight gain in small-for-gestational-age children. J Clin Endocrinol Metab 2006;91:2153–8.
18. Calkins K, Devaskar SU. Fetal origins of adult disease. Curr Probl Pediatr Adolesc Health Care 2011;41: 158–76.
19. Sipola-Leppänen M, Vääräsmäki M, Tikanmäki M, *et al*. Cardiometabolic risk factors in young adults who were born preterm. Am J Epidemiol 2015;181: 861–73.
20. St-Onge M-P, Jones PJH. Greater rise in fat oxidation with medium-chain triglyceride consumption relative to long-chain triglyceride is associated with lower initial body weight and greater loss of subcutaneous adipose tissue. Int J Obes Relat Metab Disord J Int Assoc Study Obes 2003; 27:1565–71.
21. Wells JC, Fewtrell MS. Measuring body composition. Arch Dis Child 2006;91:612–7.
22. Solanki K, Matnani M, Kale M, *et al*. Transcutaneous absorption of topically massaged oil in neonates. Indian Pediatr 2005;42:998.