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Efficacy of medium-chain triglyceride oil massage on growth in preterm infants: a randomized controlled trial

A CONSORT-compliant article

Yen-Chi Liao, RN, MSN, Yu-Hsuan Wan, RN, BS, Pi-Hui Chen, RN, MBA, Ling-Yu Hsieh, RN, MSN*

Abstract

Background: Medium-chain triglyceride (MCT) oil consists of 8–12 carbons with higher absorption and provides better calories than long-chain triglyceride oil. This study was to explore the effect of MCT oil massage on growth in preterm infants.

Methods: A prospective, single-blind, randomized (two treatments and one control) study was conducted. Preterm infants weighing between 1500 and 2000 g were recruited and randomly assigned to three groups: the MCT oil massage, massage alone and no massage groups. The standardized massage intervention consisted of two 5-min phases, including tactile and kinesthetic stimulation, which were given three times a day for 7 consecutive days. Premature infants in the oil massage group received massage with 10 mL/kg/day of MCT oil divided equally into three applications. Weight, length and head circumference were measured in the three groups at birth and on study days 1 to 7.

Results: Forty-eight neonates were evaluated with 16 in each of three groups. The linear mixed effect model was adjusted for other factors, and results showed that weight gain on the 4th day in the oil massage group was greater than that in the no massage group ($P < .05$). From the 5th to 7th day, weight gain in the oil massage group was greater than that in the other two groups ($P < .05$). Regarding head circumference and height, this study found that the MCT oil massage group did not have better results than the other two groups. No adverse events were noted in the massage groups.

Conclusion: The results indicate that preterm infant daily massage with MCT oil is an effective intervention for weight gain that should be recognized as part of low-birth-weight infant developmental care.

Trial registration: clinicaltrials.gov identifier NCT04281563, Registered on 24 February 2020.

Abbreviation: MCT = medium-chain triglyceride.

Keywords: growth, massage, medium-chain triglyceride oil, preterm infants, weight

1. Introduction

Tactile stimulation is important to promote the growth and development of premature infants, and massage therapy provides systematic and purposeful tactile stimulation through human hands.[1] Numerous studies have been performed on the effects of massage in premature infants and have demonstrated that massage activates the vagal nervous system, thereby increasing gastric activity, serum insulin levels, and weight gain; improving neuronal and brain development; and reducing pain, risk of neonatal sepsis and neonatal stress.[2–4] However, preterm infants are at risk of increased transepidermal water loss and infections due to epidermal immaturity. A systematic review found that the emollient and anti-infective properties of coconut oil applied topically may reduce the risk of infection and improve weight gain and the skin condition in preterm infants.[5] Based on the benefits of massage and the application of oil to the skin for premature infants, previous studies have suggested that massage with oil could enhance skin barrier function,[6] promote body temperature regulation,[7] and absorb some fats.[8] Arora, Kumar and Ramji[9] also consider oil to be an agent that acts as a source of energy and nutrition and improves overall growth.

Therefore, there have been studies that chosen low-irritation and more natural oils, including olive oil,[7] coconut oil,[8] sunflower oil,[10] sesame oil,[11] and medium-chain triglyceride (MCT) oil,[12] as massage oils, and most of these studies support the finding of better weight gain in premature infants treated by massage with oil. In a study by Hosseinzadeh et al,[11] massage with sesame oil not only increased weight but also improved height among low-weight neonates. MCT oil is different from

Editor: Qinhong Zhang.

The authors have no funding to disclose.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the present study are available from the corresponding author on reasonable request.

Department of Nursing, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi, Taiwan.

** Correspondence: Ling-Yu Hsieh, Department of Nursing, Ditmanson Medical Foundation Chia-Yi Christian Hospital, No. 539 Chung-Shau Road, Chia-Yi City 60002, Taiwan (R.O.C.) (e-mail: 10023@cych.org.tw).*

How to cite this article: Liao YC, Wan YH, Chen PH, Hsieh LY. Efficacy of medium-chain triglyceride oil massage on growth in preterm infants: a randomized controlled trial: A CONSORT-compliant article. Medicine 2021;100:30(e26794).

Received: 11 May 2020 / Received in final form: 24 May 2021 / Accepted: 10 July 2021

http://dx.doi.org/10.1097/MD.0000000000026794

long-chain fatty oils that were applied in previous studies. Saeadi et al[12] first used MCT oil as a medium-chain fatty oil, which consists of 8–12 carbons with higher absorption and provides better calories than long-chain triglyceride oil. However, Saeadi et al[12] included preterm infants from 28 to 37 weeks of age, and the wide age range of cases resulted in different nutrition support plans that could become confounding factors impacting growth indicators. Therefore, our study focused on premature infants who were 1500–2000 g in weight and further explored the growth effect of massage with oil on height and head circumference. In addition, in the first 10-day massage study by Scafidi et al[13] suggested that the weight gain advantage was emerging on day 6 of the massage period. Hence, this study was designed to test the hypothesis that preterm infants weighing 1500–2000 g exhibit better growth after 7 days of massage with MCT oil compared to the massage alone and control groups.

2. Methods

2.1. Research design and participants

A prospective, single-blind, randomized (two treatments and one control) study was conducted in the newborn center of the Ditmanson Medical Foundation Chia-Yi Christian Hospital (DMF-CYCH) between July 7, 2017 and July 6, 2019. Inclusion criteria were as follows: gestational age between 28 and 37 weeks, weight between 1500 and 2000 g after enrollment, medically stable condition, and ≥120 cc per day feeding. Exclusion criteria were as follows: congenital anomalies, skin disease, requirement for mechanical ventilation, requirement for O_2 therapy, and presence of fracture.

This study was approved by the Institutional Review Board (CYCH IRB No: 106041). Written informed consent was obtained from the parents of preterm infants prior to enrollment. The right to withdraw from this study at any time was explained to each parent.

2.2. Randomization and masking

The researcher used the SPSS software (version 21.0; IBM Corporation, Somers, NY) to generate the random allocation sequence using block randomization with six blocks. Eligible premature infants were randomly assigned to three groups: group 1 (massage with MCT oil), group 2 (massage alone), and group 3 (no intervention) according the random number sequences placed in sealed opaque envelopes. The standardized massage techniques was performed three times a day for 7 consecutive days in group 1 and group 2. Two trained nurse took turns performing standardized massage techniques that could not be masked after allocation given the nature of the intervention. However, the data analyst was blinded to the meaning of the group assignment code.

2.3. Sample size

The sample size was calculated on the basis of a previous study[12] with a statistical power of 80%, an effect size of 0.4, an pooled standard deviation of 1.059 and an alpha level of .05 (two-tailed). According to the repeated measured ANOVA, the number of groups was 3, and the number of measurements was 7. A total of thirty-nine subjects was calculated for inclusion. A post hoc power analysis indicated that the number of preterm infants allocated to each group (n = 16) possessed 89% power.

2.4. Outcome measures

Data collection instruments included demographic characteristics and growth parameters, such as weight, height and head circumference. Demographic information included gestational age, gender, type of milk feeding, Apgar scores at 1 min and 5 min and feeding amount. Weight, length and head circumference were measured in the three groups at birth and on study days 1 to 7. The weight of the infants was obtained without clothes on a digital weighing scale with a sensitivity of 5 grams at 8 o'clock every morning. The weighing scale was calibrated at regular intervals. Head circumference was measured from the supraorbital ridge to the occiput using a non-stretchable tape. The height was measured from the supine crown-heel length using an infantometer. All measurements were performed by two trained senior nurses, and the intraclass correlation coefficient was 0.96.

2.5. Interventions

Two trained nurse took turns performing standardized massage techniques in group 1 (massage with MCT oil) and group 2 (massage alone). The standardized massage intervention consisted of two 5-min phases: tactile and kinesthetic stimulation.[14] The massage force was approximately 300 g, and the massager practiced applying the pressure using a food scale. The massage was given in the prone and supine positions, and the actions included gentle touching of the head, back and limbs for five 1-min periods, six passive flexion/extension movements lasting 10 s each for each arm followed by each leg, and finally both legs together for a total of five 1-min periods. Premature infants in the oil massage group received massage with 10 mL/kg/day of MCT oil divided equally into three applications.

2.6. Statistical analysis

The analysis was included all premature infants in their randomized group. Categorical data were evaluated via the chi-square test or Fisher's exact test and are presented as n (%), as appropriate. Continuous data with a normal distribution were analyzed by one-way analysis of variance and are presented as the mean ± SD. Continuous data without a normal distribution are presented as the median (interquartile range) and were analyzed using the Kruskal–Wallis test. In the multivariate analysis, the linear mixed effect model was used to investigate potential differences in case and control groups for changes in weight, height, and head circumference (compared to the first day) adjusted for gender, type of milk feeding, Apgar score at the 5th minute, feeding amount, and gestational age at study day 1. Restricted maximum likelihood (REML) estimation was used along with an unstructured covariance because of the smallest Bayesian information criterion (BIC) compared with autoregressive and compound symmetry covariance. The changes in weight, height and head circumference were analyzed as repeated observations at 2–7 days.

All statistical analyses were analyzed with SAS 9.4 (SAS Institute, Cary, NC, USA). A two-sided *P* value of .05 was considered significant.

3. Results

A total of 214 preterm infants were hospitalized in the newborn center during the study period. In total, 163 infants did not meet

the inclusion criteria and 3 parents declined to participate in the study. Finally, 48 subjects were enrolled and analyzed in the study with 16 in each of three groups. In both group 1 and group 2, 15 infants (93.8%) completed the study, and only 1 infant did not complete the 7-day data collection due to discharge. In group 3, 14 infants (87.5%) completed the study, and 2 infants did not complete the 7-day data collection due to discharge (Fig. 1). The birth weight of the infants was 1756.4 ± 288.0 g in group 1, 1659.6 ± 368.8 g in group 2 and 1704.8 ± 256.5 g in group 3. Table 1 shows that the baseline characteristics of preterm infants were not significantly different among the intervention and control groups.

Table 2 shows the estimate of groups and time for the change in weight, height, and head circumference from study day 1. After adjusting for related factors, the model showed that the weight change in the preterm infants in group 1 was 39.17 g, which was significantly greater than that of group 3 (SE: 15.66, $P = .02$). The weight change had an increasing trend with time and a significant increase starting at study day 3 (estimate: 25.54, SE: 6.37, $P < .001$). The height and head circumference of premature infants all slightly increased with time, but there were no significant differences among the three groups.

The observation time was further fixed. After adjusting the correlation factors, we tested whether there was a significant difference in the growth of the neonates at each time point. Figure 2 shows the least squares means of the change in weight, height, and head circumference at study days 2 to 7 compared with day 1 with a mixed-effects model. The increase in weight change in group 1 was increased compared with that in groups 2 and 3. From day 4, the weight gain in group 1 was significantly greater than that in group 3 (71.30 vs 29.39 g). From the 5th day to the 7th day, the weight gain of group 1 was significantly greater

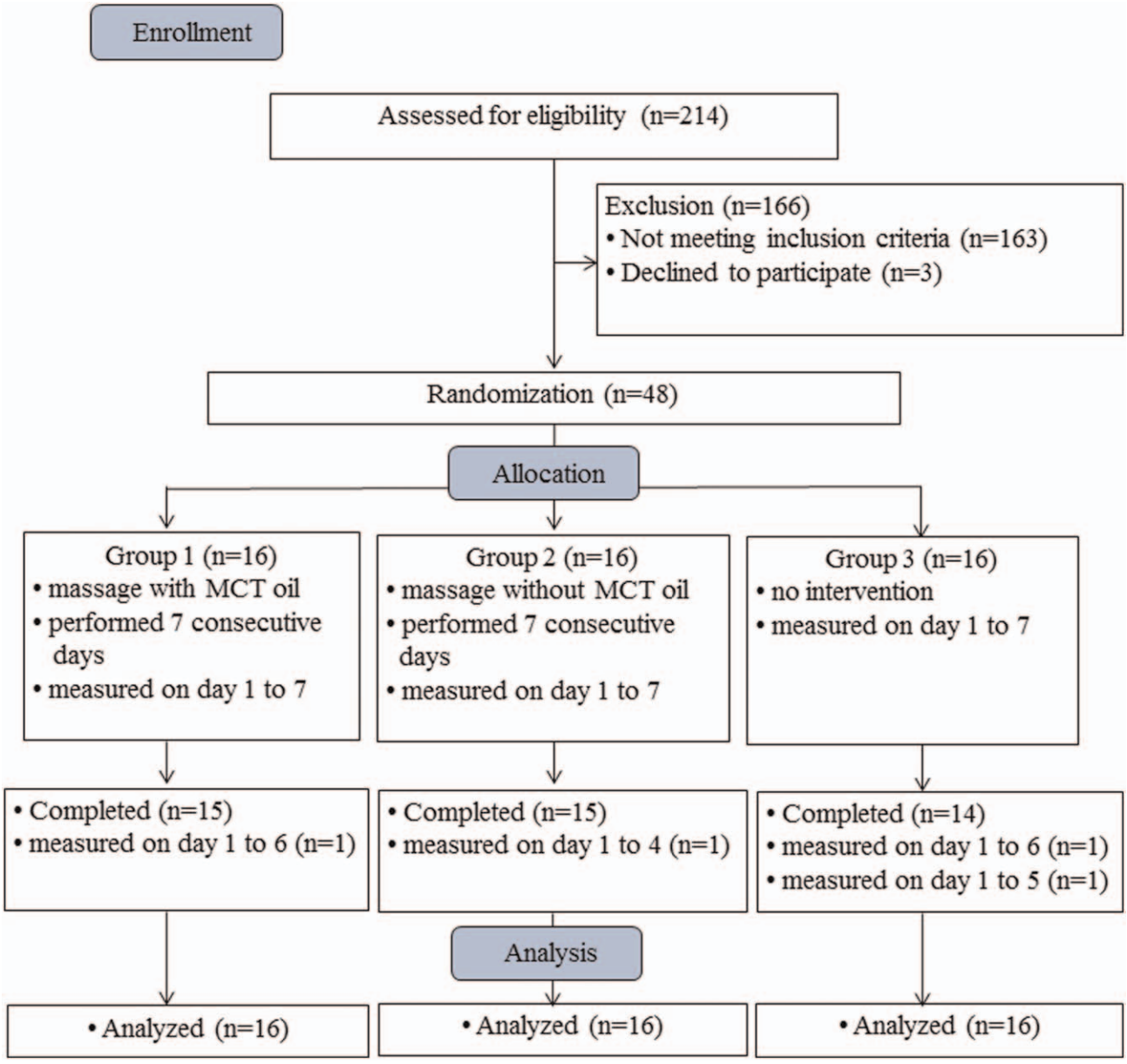

Figure 1. The flowchart of preterm infants through this study. MCT = Medium-chain triglyceride.

Table 1

Baseline characteristics of the preterm infants.

Variable	Group 1 (n = 16)		Group 2 (n = 16)		Group 3 (n = 16)		
	n (%) or mean ± SD or median (IQR)	*Min-Max*	n (%) or mean ± SD or median (IQR)	*Min-Max*	n (%) or mean ± SD or median (IQR)	*Min-Max*	*P*
Gender							.56*
Boy	6 (37.5)		8 (50.0)		9 (56.3)		
Girl	10 (62.5)		8 (50.0)		7 (43.8)		
Type of milk feeding							.63†
Breastmilk	7 (43.8)		6 (37.5)		10 (62.5)		
Formula	7 (43.8)		6 (37.5)		4 (25.0)		
Mixed	2 (12.5)		4 (25.0)		2 (12.5)		
Birth gestational age (wk)	33.4 ± 2.3	28.0–36.29	33.0 ± 2.4	26.9–35.6	34.0 ± 1.5	30.6–35.9	.37‡
Birth weight (g)	1756.4 ± 288.0	878 – 2066	1659.6 ± 368.8	986–2078	1704.8 ± 256.5	1148–2090	.72‡
Apgar score at 1 min	7.9 ± 0.9	6 – 9	7.9 ± 1.2	6–9	8.0 ± 1.5	3–9	.73‡
Apgar score at 5 min	8.9 ± 0.7	8 – 10	8.9 ± 0.9	7–10	9.1 ± 1.3	5–10	.51‡
Gestational age at study day 1(wk)	35.1 (34.4–35.9)	32.6–36.9	35.1 (34.3–35.6)	32.1–36.6	35.9 (34.7–36.6)	33.7–36.9	.18§
Feeding amount at study day 1 (ml)	201.5 ± 45.0	120 – 280	212.0 ± 42.9	160–280	237.0 ± 60.5	120–360	.27‡
Weight at study day 1 (g)	1828.3 ± 97.3	1600 – 1990	1810.9 ± 155.9	1525–1990	1793.8 ± 151.9	1500–1970	.78‡
Height at study day 1 (cm)	44.6 ± 1.9	41 – 47	44.3 ± 2	40.5–47	43.9 ± 1.6	41–47	.57‡
Head circumference at study day 1 (cm)	30.2 ± 0.9	29–31.5	30.1 ± 0.9	29–32	30.3 ± 1	28–32	.89‡

SD = standard deviation, IQR = interquartile range.
* chi-square test.
† Fisher's exact test.
‡ Kruskal–Wallis test.
§ ANOVA test.

than that of group 2 and group 3 (day 5: 93.80 vs 46.92 vs 52.82 g; day 6: 133.80 vs 70.25 vs 78.43 g; day 7: 164.39 vs 91.99 vs 94.96 g) (Fig. 2A). There was no significant difference in height between the three groups at any time during the observation period (Fig. 2B). In terms of head circumference growth, on day 7, a significant difference was noted between group 2 and group 3 (the least squares means of the change in head circumference: group 2 vs group 3: 0.13 cm vs 0.03 cm) (Fig. 2C). During the intervention periods, neither the preterm infants in group 1 nor those in group 2 experienced any adverse events.

Table 2

Estimate of groups and time for the change of weight, height and head circumference with a mixed-effects model.

Variable	Weight				Height				Head circumference			
	Estimate	SE	95% CI	*P*	Estimate	SE	95% CI	*P*	Estimate	SE	95% CI	*P*
Intercept	−195.27	215.20	(−630.19, 239.66)	.37	0.10	0.26	(−0.42, 0.61)	.71	−0.23	0.46	(−1.15, 0.7)	.62
Group												
1	39.17	15.66	(7.53, 70.82)	.02	0.02	0.02	(−0.02, 0.06)	.30	0.01	0.03	(−0.06, 0.08)	.75
2	2.92	15.73	(−28.88, 34.72)	.85	0.01	0.02	(−0.02, 0.05)	.46	0.05	0.03	(−0.01, 0.12)	.12
3	0				0				0			
Time (day)												
1	0				0				0			
2	12.46	6.37	(−0.08, 24.99)	.051	<0.001	0.01	(−0.02, 0.02)	1.00	0.01	0.01	(−0.01, 0.04)	.32
3	24.54	6.37	(12.01, 37.08)	<.001	0.004	0.01	(−0.02, 0.026)	.71	0.03	0.01	(0.0004, 0.06)	.047
4	45.27	6.37	(32.74, 57.81)	<.001	0.02	0.01	(−0.003, 0.04)	.10	0.03	0.01	(0.003, 0.06)	.03
5	64.15	6.41	(51.53, 76.76)	<.001	0.02	0.01	(0.0009, 0.05)	.04	0.04	0.01	(0.01, 0.07)	.01
6	94.01	6.45	(81.31, 106.71)	<.001	0.04	0.01	(0.01, 0.06)	.002	0.04	0.01	(0.012, 0.07)	.006
7	116.79	6.54	(103.92, 129.65)	<.001	0.06	0.01	(0.04, 0.09)	<.001	0.07	0.01	(0.04, 0.1)	<.001
Gender												
Boy	14.20	12.33	(−10.71, 39.12)	.26	0.01	0.01	(−0.02, 0.04)	.53	0.01	0.03	(−0.05, 0.06)	.78
Girl	0				0				0			
Type of milk feeding												
Formula + Mixed	−17.48	13.72	(−45.21, 10.25)	.21	0.02	0.02	(−0.01, 0.05)	.25	0.03	0.03	(−0.03, 0.09)	.30
Breastmilk	0				0				0			
Apgar score at 5 min	−6.05	6.39	(−18.97, 6.86)	.35	−0.005	0.01	(−0.02, 0.011)	.53	−0.02	0.01	(−0.04, 0.01)	.21
Feeding amount at study day 1(ml)	0.22	0.12	(−0.03, 0.47)	.09	<0.001	<0.001	(0.0001, 0.001)	.02	<0.001	<0.001	(−0.0002, 0.001)	.15
Gestational age at study day 1(wk)	5.42	5.71	(−6.12, 16.96)	.35	−0.004	0.01	(−0.02, 0.009)	.52	0.01	0.01	(−0.02, 0.03)	.54

CI = confidence interval, SE = standard error.

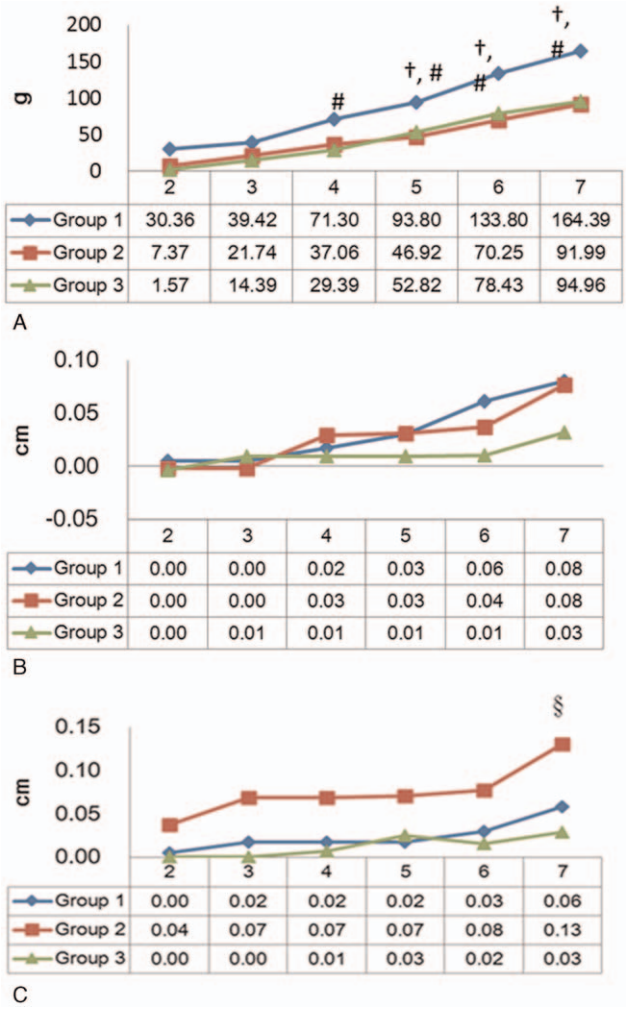

Figure 2. Least squares means of the change of (A) weight, (B) height and (C) head circumference at days 2 to 7 compared with day 1 with a mixed-effects model. #: group 1 compared with group 3: $P < .05$. †: group 1 compared with group 2: $P < .05$. §: group 2 compared with group 3: $P < .05$.

4. Discussion

In this study, we evaluated the effect of massage with MCT oil on growth in preterm newborns weighing between 1500 and 2000 g. The results showed that after 7 consecutive days of massage, compared with the first day, the increased weight of preterm infants who received the MCT massage was significantly better than the other two groups. The weight change exhibited an increasing trend with time and a significant increase starting at study day 3. This result indicates that the effect of massage with MCT oil on weight gain occurred in a short time. Our findings are the same as those of other studies. Saeadi et al[12] reported significant weight gain on the 7th day in the MCT oil massage group and in the massage group, whereas weight loss was observed in the control group. Kumar et al[15] recruited neonates with birth weights <1800 g who were divided into an oil massage group and a standard care group and found that weight gain in the sunflower oil massage group was higher than that in the control group at 28 d. Jabraeile et al[7] indicated that preterm infants under massage with olive oil had greater weight gain than infants who received massage without oil. In another study, Hosseinzadeh et al[11] trained mothers to massage their neonates with sesame oil for four weeks, and the findings showed that the mean weight gain in low-weight neonates in the intervention group was 217 grams greater than that in the control group. Fallah et al[10] showed that the mean weight at ages 1 month and 2 months was significantly greater in premature neonates with 1500–1999 g weight after the application of sunflower oil massage for 14 consecutive days compared with that of the massage alone group. In a study by Sankaranarayanan et al,[8] newborn newborns weighing 1500–2000 g also showed that coconut oil massage resulted in a significantly greater weight gain velocity in 31 days compared with that obtained with mineral oil and placebo in the preterm baby group. The author explained that oil application could potentially benefit skin barrier function, therefore reducing transepidermal water loss and helping thermoregulation; however, better temperature regulation may promote better weight gain. In contrast, Arora et al[9] recruited neonates with birth weights < 1500 g and found that weight gain was not significantly greater in the sunflower oil massage group compared with the other groups. However, when the author excluded infants who had > 20% interruption of massage, the standardized weight gain was significantly greater in the oil massage group compared with the massage only group and the no massage group. The author hypothesized that dermally applied oil may be stored in fat cells as a source of energy without altering the body's lipid metabolism, which is why it can promote growth.

Regarding head circumference and height, this study found that the MCT oil massage group was not better than the other two groups in terms of height growth, and the head circumference of the massage alone group was significantly better than that of the control group only on the 7th day. This result is the same as those of previous investigations. Two studies by Arora et al[9] and Fallah et al[10] demonstrated that the height and head circumference of premature infants treated with sunflower oil were not significantly better than those of premature infants treated with massage alone or no massage. However, different results have been found in two other studies. Sankaranarayanan et al[8] found that the length gain velocity was significantly increased in the coconut oil group than in the powder group. Hosseinzadeh et al[11] also showed that the mean significant increase in the height in the group receiving massage with sesame oil was 0.7 centimeters greater than that in the control group during a 4-week period. Therefore, the current research evidence shows that massage with oil is not effective in promoting head circumference growth, and there is no consistent conclusion about improving height. Another reason may be that the development of bones and head circumference requires more time to be observed.

The shorter chain length of the MCT oil used in this study allowed them to be more rapidly hydrolyzed and absorbed into the body than long-chain triglycerides. This enabled the MCT to provide energy faster to promote weight gain and resulted in the occurrence of no side effects in this study.

Regarding limitations of this study, most premature babies who lived in the newborn center were stable, and the short hospital stays made it infeasible to perform longer interventions and long-term follow-ups. Therefore, we taught and encouraged parents continue providing massages with MCT oil in preterm babies after returning home to maintain benefits.

5. Conclusion

The results of this study suggested that MCT oil massage has beneficial effects on weight gain in preterm neonates weighing between 1500 and 2000 g. In clinical practice, weight gain is the main indicator to judge whether premature babies mature enough and can be discharged. Therefore, accelerating weight gain through massage with oil in preterm infants not only decreases the length of the hospital stay but also reduces medical costs.

Preterm infant daily massage with MCT oil is a simple, effective and safe intervention for weight gain that should be recognized as part of low birth weight infant developmental care and an option for nutritional supplementation.

Acknowledgment

The authors would like to thank all the participants in the newborn center in this study.

Author contributions

Conceptualization: Yen-Chi Liao.
Data curation: Yu-Hsuan Wan, Pi-Hui Chen.
Investigation: Yen-Chi Liao, Yu-Hsuan Wan.
Methodology: Yen-Chi Liao, Yu-Hsuan Wan, Pi-Hui Chen, Ling-Yu Hsieh.
Writing – original draft: Yen-Chi Liao, Pi-Hui Chen, Ling-Yu Hsieh.
Writing – review & editing: Ling-Yu Hsieh.

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