

ABSORPTION OF MEDIUM CHAIN TRIGLYCERIDE IN THE
LOW BIRTH WEIGHT INFANT AND EVALUATION OF MCT
MILK FORMULA FOR LOW BIRTH WEIGHT INFANT NUTRI-
TION USEING OF THE LATIN SQUARE TECHNIQUE

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It is well recognized that MCT (Medium Chain Triglyceride) has a favorable effect on growth of infants with malabsorption syndrome due to impaired fat digestion or absorption¹.

The Low Birth Weight Infants (LBWI) have temporal malabsorption, because of poor butter fat absorption. This is especially true within first 30 days of the infants life. Although absorption of fat is improved using half skimmed milk or milk fortified with vegetable fat, it is still insufficient.

The excellent absorption of MCT in the LBWI has been confirmed and the application of MCT substituted milk for the LBWI nutrition was reported with better weight gains (Yamashita, F. et al., 1967)^{2) 3) 4)}.

The purpose of this study is to confirm the above data utilizing the Latin square technique in order to contribite both accuracy and impartiality to the results.

MATERIALS AND METHODS

Eight LBWI (Table 1) were fed with 4 milk formulas (A, B, C and D in Table 2) using the Latin square technique.

Infants were divided in two Latins quare groups (#1-4, #1*-4*) as shown in Table 3. Infants in the Latin square groups were fed a different milk formula every week for 4 weeks in order of the listed Latin square groups.

TABLE 1
Infants (Low Birth Weight)

#	Name	Sex	Weight at Birth	Birth date	Age (days)*	Weight**
1	T. K.	m	1620(SFD) +	'69-6-29	19	1590
1*	M. T.	f	1940	7-3	15	1721
2	K. K.	m	1790	7-4	14	1695
2*	A. T.	f	1500(SFD)	7-6	12	1450
3	H. T.	"	2000	7-13	19	1839
3*	Y. M.	"	1650	7-11	21	1585
4	A. M.	"	1950	7-15	17	1740
4*	A. K.	"	1700	7-13	18	1541

total 8 cases +SFD : Small-For-Dates-Baby **onset of exp.

TABLE 2
Composition of Formula (per 100 ml prepared)

	A (L-LCT)	B (L-MCT)	C (P-MCT)	D (P-LCT)
Concentration (g/dl)	15	15	17	17
Calories (Ca/dl)	74	74	76	76
Fat*(g/dl)	3.3	3.3	2.2	2.2
Protein (g/dl)	2	2	2.8	2.8
Na (mg/dl)	38.6	38.6	73	73
Sugar (g/dl)	Lactose : Dex. -M. : Sucrose :	8.1 0.5 0.5	8.1 0.5 0	7.7 3.6 0

* Type of fat (g/100 g)

milk

MCT :	0	78.8	79.1	0
Veg. fat :	21.2	21.2	20.9	20.9

* Composition of Fatty Acid

	C ₈	C ₁₀	C ₁₆	C ₁₈	C ₁₈ ⁼¹	C ₁₈ ⁼²
Formula : B	54.6	24.2	1.1	0.3	2.7	17.1
" C	54.8	24.3	1.1	0.3	2.7	16.8

TABLE 3
Latin Squares
Infants

Period	#1	2	3	4	#1*	2*	3*	4*
I	A	B	C	D	A	B	C	D
II	B	D	A	C	B	D	A	C
III	C	A	D	B	C	A	D	B
IV	D	C	B	A	D	C	B	A

Period : 1 week each

The composition and the concentration of 4 milk formulas are shown in Table 2. All prepared formulas are isocaloric, but high in protein, low in fat (C, D), and low in sodium (A, B), and MCT is substituted only in formulas B and C. In formulas A and D, the fat consist of 79% butter fat and 21% vegetable oil. The vegetable fat consists of corn oil in formula A, D and consist of safflower oil in formula B, C.

The prepared formulas are given in amount of 160 ml/Kg Body Weight/day, and 120 Cal/Kg wt./day by indwelling polyethylene feeding tube until complete of the study (Table 4). The feedings with trial formulas were started after the establishment of a sufficient caloric intake by the infants.

TABLE 4
Nutritional Intake (per Kg. Body Weight)

	A	B	C	D
Formula (ml)	160	160	160	160
Calories (Ca)	118	118	122	122
Protein (g)	3.2	3.2	4.5	4.5
Fat (g)	5.3	5.3	3.5	3.5
Sugar (g)	14.6	14.6	18	18
Na (mg)	62	62	117	117

The infants under trial feeding were kept in air conditioned nusery isolated from other LBWI. Clinical sign and symptom, stool frequency and consistency as well as incidence of vomiting were carefully recorded by nurses and doctors.

Infant weights were checked daily. Fecal weight were measured in the balance study period. The balance studies were performed for 3 consecutive days at the end of each week. The fat content in the formulas and in the feces were analyzed by the method of Friedner, et al. (1967)⁵.

TABLE 5
Data by Formulas (A, B, C, D) and Age Periods (I, II, III, IV)
(T : Total ; Av. : Average values)

(1) Fat Absorption Rate (%)

	A	B	C	D	T.
I	80.2	95.3	97.7	66.6	339.8
II	69.8	89.5	92.0	76.6	327.9
III	94.8	91.4	95.0	57.7	338.9
IV	75.4	99.9	97.6	68.6	341.5
T.	320.2	376.1	302.3	269.5	1348.1
Av.	80.1	94.0	95.6	67.4	

(1*)

	A	B	C	D	T.
I	79.6	91.0	95.3	59.9	325.8
II	73.8	97.6	93.4	81.0	362.3
III	90.3	97.9	93.9	57.7	323.3
IV	73.7	98.5	92.0	92.1	356.3
T.	317.4	385.0	374.6	290.7	1367.7
Av.	79.4	96.3	93.7	72.7	

(2) Gain in Weight (g/day)

	A	B	C	D	T.
I	23.3	38.2	57.7	60.5	179.7
II	12.3	40.0	46.5	35.8	140.3
III	18.0	17.2	57.5	42.8	129.8
IV	1.5	26.3	83.3	37.3	148.4
T.	55.1	121.7	245.0	176.3	598.2
Av.	13.8	30.4	61.3	44.1	

(— : edema case included)

(3) Fecal Weight

	A	B	C	D	T.
I	9.2	3.0	1.4	12.0	25.6
II	11.9	3.8	4.0	7.7	27.4
III	5.6	5.9	2.4	11.9	25.8
IV	14.4	0.8	1.5	11.4	28.1
T.	41.1	13.5	9.3	43.0	106.9
Av.	10.3	3.4	2.4	10.8	

(4) Stools of Frequency

	A	B	C	D	T.
I	2.1	3.0	2.6	1.9	9.6
II	3.1	2.0	1.0	2.4	8.5
III	2.1	2.7	2.3	2.1	9.2
IV	1.6	3.1	2.9	3.0	10.6
T.	8.9	10.8	8.8	9.4	37.9
Av.	2.2	2.7	2.2	2.4	

(5) Incidence of loose stools

	A	B	C	D	T.
I	0	2	4	0	6
II	0	2	2	2	6
III	0	4	6	0	10
IV	1	3	4	1	9
T.	1	11	16	3	31
Av.	0.3	2.8	4.0	0.8	

(6) Incidence of vomiting

	A	B	C	D	T.
I	0	0	0	0	0
II	0	0	0	1	1
III	0	0	0	0	0
IV	0	0	1	0	1
T.	0	0	1	1	2
Av.	0	0	0.3	0.3	0.3

(2*)

	A	B	C	D	T.	Av.
	36.1	61.0	45.8	44.8	187.7	47.
	3.3	46.2	44.3	38.3	166.1	41.5
	37.3	28.3	44.5	30.8	106.9	36.7
	13.3	31.7	54.2	35.0	134.2	33.6
	90.1	167.2	188.8	148.9	594.9	
	22.5	41.8	47.2	37.4		

(3*)

	A	B	C	D	T.	
	11.5	4.5	3.9	11.3	31.2	
	8.5	1.1	3.0	10.5	23.1	
	5.7	1.3	3.9	10.7	21.6	
	11.6	0.8	2.4	6.7	21.5	
	37.3	7.7	13.2	39.2	97.4	
	9.3	1.9	3.5	9.8		

(4*)

	A	B	C	D	T.	
	3.0	1.9	2.3	2.4	9.6	
	4.0	2.4	1.9	1.0	9.3	
	2.7	1.7	2.1	3.6	10.1	
	1.8	1.9	1.6	2.9	8.2	
	11.5	7.9	7.9	9.9	37.2	
	2.9	2.0	2.0	2.5		

(5*)

	A	B	C	D	T.	
	0	0	3	0	3	
	0	3	0	0	3	
	0	3	6	0	9	
	0	3	1	2	6	
	0	9	10	2	21	
	0	2.3	2.5	0.5		

(6*)

	A	B	C	D	T.	
	4	2	0	0	6	
	1	1	0	1	3	
	0	0	1	1	2	
	0	0	0	0	0	
	5	3	1	2	11	
	1.3	0.8	0.3	0.5		

The rate of fat absorption was calculated as follows : $100\% - (\text{fat content in feces in 3 days} / \text{fat content in formula in 3 days}) \times 100\%$. All infants studied exhibited favorable growth and good acceptance without marked diseases except for 2 "late edema" ¹⁴⁾ cases occurring at 39-43 days (Table 11).

Results for the milk formulas (A, B, C, D) and trial periods (I, II, III, IV) shown in Table 5. The variables in this study were infants, formulas and trial periods.

Statistically several significant differences were confirmed in these variables when 4 milk formulas were used (Table 6).

1) Fat absorption, 2) weight gain expressed as g/day calculated from the formula : (Body Wt. at 7 the day - that of 1st day)/(7-1), 3) fecal weights ; 5) Stool consistency (incidence of loose stools) was different but only in the 2nd square.

TABLE 6
Differences in Variables

Variables	1. Periods	2. Infants	3. Formulas
1. Fat Absorption	() ()	() ()	(**) (*)
2. Weight Gain	() (**)	() (*)	(*) (**)
3. Weight of Feces	() (**)	() (**)	(**) (**)
4. Stool Frequency	() ()	() ()	() ()
5. Loose Stools	() ()	() ()	(*) ()
6. Vomiting	() ()	() ()	() ()

() : () = square 1:2

* : significant difference at $F_6^3(0.05)$

** : highly significant at $F_6^3(0.01)$

TABLE 7
Differences in 4 Formulas

Formulas	A (L-LCT)	B (L-MCT)	C (P-MCT)	D (P-LCT)	Significance (F_6^3)
1. Fat Absorption (%)	80.1 79.4	94.0 96.3	95.6 93.7	67.4 72.7	** *
2. Gain in Weight (g/day)	13.5 22.5	30.4 41.8	61.3 § 41.8	44.1 § 37.4 §	* **
3. Weight of Feces (g/day)	10.3 9.3	3.4 1.9	2.4 3.5	10.8 9.8	** **
4. Frequency of Stool (number/day)	2.2 2.9	2.7 2.0	2.2 2.0	2.4 2.5	
5. Loose Stool (days of loose stools per week)	0.3 0	2.8 2.3	4.0 2.5	0.8 0.5	*
6. Vomiting : (number per week)	0 1.3	0 0.8	0.3 0.3	0.3 0.5	

* : significant ($p=0.05$), ** : highly significant ($p=0.01$)

§ : including "late edema" cases (# 1, 1*, 2)

The effects of the 4 formulas were analyzed statistically as shown in Table 7, 8. The following conclusions were made. 1) Absorption rate of fat is better MCT (B, C) milk formula group. 2) the weight gains were better in the MCT milk formula groups (B) than in the LCT milk formula group (A)(Comparison between C and D formula is omitted, because of these groups include the "late edema" cases. 3) Infants of MCT milk formula excret smaller amount of feces than that of LCT milk formulas. 4) Incidence of loose stool is higher in the MCT formula group than LCT group when the incidence is expressed as the number of days with loose stool per week. 5) No differences were found in stool frequency and/or incidence of vomiting.

TABLE 8

*Differences in 4 Formulas ----**Statistical Analysis (*: significant at p=0.05)**(Formulas ----- A : LCT, B : MCT, C : MCT, D : LCT)*

(1) Fat Absorption

in Square 1 :	A (80.1) : D (67.4) *
	B (94.0) : A (80.1) *
	C (95.6) : D (67.4) *
	B (94.0) : C (95.6) -
in Square 1* :	A (79.4) : D (72.7) -
	B (96.3) : A (79.4) *
	C (93.7) : D (72.7) *
	B (96.3) : C (93.7) -

conclusion : better fat absorption in MCT Milk (B, C)

(2) Gain in Weight

in Square 1 : and 2 :	B (30.4) : A (13.8) *
	B (41.8) : A (22.5) *

A, B : C, D or C : D : not comparable because C, D group include the data of edema cases. (underlined in table 5).

conclusion : better weight gain in MCT (A) milk than in LCT-Milk

(3) Weight of Feces

in Square 1, 2 :	A (10.3) : B (3.4) *
	A (9.3) : B (1.9) *
	D (10.8) : C (2.4) *
	D (9.8) : C (3.5) *
	A : D, B : C,

conclusion : smaller amount of feces in MCT (A, D) Milk

(in Square 2, the weight of feces is greater in the 1 st experimental week period than other weeks : the weight of feces in case 4* is greater than other cases)

(4) Incidence of loose stool

only in square 1 :	A (0.3) : B (2.8) *
	C (4.0) : D (0.8) *

conclusion : stool consistency is more loose in MCT (A, D) Milk feeding period.

Fat absorption study : It was found to be very important to perform fat absorption studies during the early days of the infants life in LBWI. This is true because fat absorption improve daily in these cases. Furthermore difficulties were encountered when attempting to evaluate nutritional studies of LBWI. The physiological loss of the body weight or insufficient intake of the formula due to small volume of the stomach and also the gradual increase of feeding volume make the evaluation difficult. In our study, therefore, feeding studies were started after establishment of sufficient caloric intake by infants.

Latin square technique : This technique was first applied for infant nutrition in 1960 (Brown, G. W. et al.⁶⁾). This is very convinient for small numbers of samples with many variables. Significant differences between MCT milk formula feeding and LCT Milk formula feeding were confirmed in several instances using this technique.

Determination of Fecal Fat : Unmodified Van de Kamer's method was found to be unsatisfactory for the MCT fat determination^{5) 7) - 10)}.

Therefore, Friedner's method⁵⁾ was used in this study, although there were no significant differences between the modified Van de Kamer's method (Yamagata, K.¹¹⁾) and Friedner's mehod in a previous study (Table 9)³⁾. This may be attributed to "fortunate saving grace of nearly compensating errors" as suggested by Senior, J. R. (1668).

Evaluation of Growth by Weight Gain : Evaluation of the milk formula for LBW Inutrition was difficult in this study, because the trial period for each formula is only 7 days. However, it was speculated that a more pronounced weight gain would be obtainable in MCT milk formula feeding in LBWI.

Average weight gain in these studies for formula MCT (B) vs LCT (A) was 30.4 vs 13.8 in the Latin saure #1, and 41.8 vs 22.5 in Latin square #2. In a previous study, the long term feeding study showed avarege weight gains for MCTf ormula group vs LCT formula group to be 40 (13 cases) vs 22.5 (13 cases) with highly significant difference^{3) 4)} (Table 10).

Metabolism of MCT in the Infants : MCT tend to burn quickly and is converted to energy without a remarkable deposit of fat in the adipose tissue of the rat^{1) 2)}. Weight gain is smaller in the MCT feeding group than that obtained for the LCT feeding group in rats¹²⁾. It is very interesting that the weight gains of the LBWI fed MCT substituted milk formula is better than that of MCT formula group. There might be some difference in metabolism of MCT fat between LBWI and adult (or rats).

Stool Consistency : Loose stools offer more frequent in the MCT milk formula group than that of LCT milk formula group. The possible cause of this loose stools may be due to the high osmolarity of MCT. Osmolarity of the MCT substituted milk (B, C) vs LCT milk (A, D) is 403, 423 vs 375, 410 mOsm/l.

These 4 formulas contain lactose in high concentrations as shown in Table 2. This phenomena may not necessarily correlate with the cause of the loose stools, since all formulas have nearly same concentration of lactose. Although the mechanism of the loose stools is still unknown, infants showing loose stools usually have no weight loss, nor signs of dehydration and usually showed better weight gains.

TABLE 9
Rate of Fat Absorption Measured by Van de Kamer-Yamagata's Method and Friedner et al's Method

Feeding by Mehods	LCT Milk				MCT Milk			
	Kamer	Friender	Diff.*	%diff.**	Kamer	Friender	Diff.*	%diff.**
# Infants***								
1	77.5	76.5	+1	1	93.6	93.8	-0.2	0
2	93.6	92.1	+1.5	1	94.1	96.2	-2.1	2
3	72.7	80.5	-7.8	11	91.8	96.8	-5	5
4	69.2	63.8	+5.4	8	94.1	94.1	0	0
5	56.3	64.2	-7.9	14	88.2	90.2	-2	2
6	70.3	70.5	+0.2	0	96.6	96.6	0	0

* Diff. =Absorption Rate by Kamer's method - Friendner's Method

** %diff. =absolute values of $(Kamer \times 100 / Friender - 100) \%$

*** These infants are of different group than that of infants employed for Latin square evaluation (TABLE 1-9)

TABLE 10
Comparison of gain in weight between MCT milk formula and LCT milk formula group fed for long term period (Yamashita, F. et al.^{3) 4)})

Milk formula	MCT	LCT
Infants #		
1	50.0	17.9
2	38.3	20.0
3	38.9	30.0
4	45.9	35.0
5	32.1	12.1
6	32.7	21.2
7	35.0	24.7
8	38.2	14.7
9	50.0	20.9
10	34.4	25.0
11	42.3	20.0
12	40.9	24.4
13	41.8	26.4
Average	40.0	22.5**

(N=13)

** (highly significant by t-test, p<0.01)

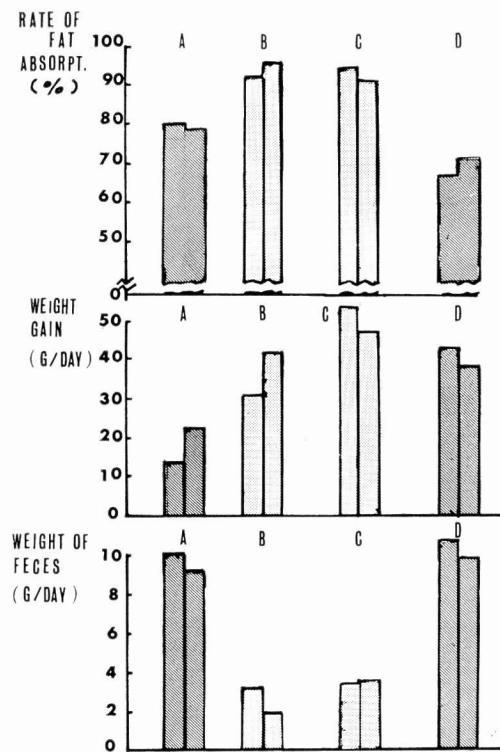


Fig. 1 Rate of Fat Absorption, Gain in Weight and Weight of feces using 4 Different Milk Formulas

TABLE 11
Cases of "Late Edema"

#, Name, Sex	day (age) of onset	Formulas at 3rd week / 4th week	Alubumin (plasma, g/dl)	Total protein	days (age) of exam.
1. M. K., M	43 (+ facial)	C (P-MCT)/D (P)	3.7	4.4	45
1*. M. T., F	40 (+ facial)	C (P-MCT)/D (P)	3.0	4.5	41
2. K. K., M	39 (# face, bodies)	A (L-LCT)/C (P-MCT)	2.9	4.4	40

No edema cases

2*. A. T., F	A (L-LCT)/C (P-MCT)	2.8	4.1	38
3. H. T., F	D (P-LCT)/B (L-MCT)	3.5	5.2	31
3*. Y. M., F	" / "	3.2	4.8	33
4. A. M., F	A (L-MCT)/A (L-LCT)	3.1	4.7	29
4*. A. K., F	B (L*-MCT)/A (L-MCT)	3.2	5.0	30

Underlined: data in 3rd week

Late Edema : "Late edema"¹⁴⁾ was observed in 3 cases given C (MCT) and D (LCT) formulas (Table 11). These formulas contain more sodium, higher protein and lower fat than A (LCT) or B (MCT) milk formula. Because the amount of the milk (water) given was identical in all infants, there might be some correlation between edema and high sodium content in C, D milk. No definite statement can be made at this time in refered to a correlation between edema and constituents in the MCT milk formula.

SUMMARY

Absorption rate of the MCT fat and the MCT substituted milk used for Low Birth Weight Infant Nutrition was evaluated, using the Latin square technique in 8 infants.

Excellent MCT fat absorption, and improved weight gain, higher incidence of loose stools, and lower amount of fecal excretion in MCT substituted milk fed Low Birth Weight Infants was confirmed.

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