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The elimination of free fatty acids, free glycerol and triglycerides from the plasma of low-birth-weight infants receiving intravenous fat emulsion and glucose

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The disappearance rate of plasma free glycerol, free fatty acids and triglycerides following the termination of short-term (6-hr) infusion of fat emulsion (Intralipid®) was studied in 12 low-birth-weight infants. The mean K values for each lipid component were found to be higher in infants receiving 10% glucose. Owing to the wide individual variation of responses and the small number of infants studied, only the disappearance rate of free fatty acids reached the level of significance. It is concluded that increased amounts of glucose given simultaneously with fat emulsion could diminish hyperlipidaemia by increasing the clearance of lipids from the plasma.

The role of glucose administration in intravenous feeding is not merely to provide calories to maintain an adequate energy balance; its availability for creating specific metabolic and hormonal conditions is also essential to ensure an optimal ratio of anabolic and catabolic substrate utilization. Thus, e.g. adequate protein synthesis from amino acids and hence a positive nitrogen balance could hardly be achieved without the hormonal effects of glucose infusion.

In view of the well-known relationship between carbohydrate and fat metabolism [1, 2, 9, 10, 19, 22, 23] it is logical to assume that fat utilization is more efficient if glucose is administered simultaneously. Studies performed in adults [17] have shown that while the elimination of free fatty acids increased, the rate of clearance of triglycerides remained unaffected when greater amounts of glucose were given. Likewise, the disappearance rate of triglycerides from the blood following repeated intravenous bolus injections of fat emulsion into low-birth-weight infants did not increase when a 10% glucose-fructose solution was given between the injections [13].

Our studies dealing with the metabolic responses to fat emulsion infused over a 6-hrs period [18] gave an opportunity to study the clearance of free glycerol, free fatty acids and triglycerides from the plasma of low-birth-weight infants receiving a baseline parenteral calorie supply either as 5% or 10% glucose. The present paper reports on results pointing

toward the need and importance of the concomitant use of carbohydrate and fat emulsion in complete parenteral nutrition.

Methods

The examinations were performed on 12 premature infants within the first two days of extrauterine life. Birth weight ranged between 1350 g and 2150 g (mean, 1736 g), and gestational age between 30 and 37 weeks (mean, 33.4 weeks). The weight of nine infants was appropriate for gestational age and that of three below the 10th percentile. The infants were selected on the basis of their inability to tolerate oral or tube feeding without inducing apnoeic spells and causing aspiration.

The technique and design of intravenous alimentation were as follows. Six infants received 5% glucose at a rate of 2.8 mg/kg/min, and 6 infants 10% glucose at a rate of 4.8 mg/kg/min infused into a scalp vein. After the first 12 hours of intravenous glucose alimentation, in addition to glucose a fat emulsion (Intralipid®) was infused over a 6-hrs period at a rate of 5.6 mg/kg/min. Following the termination of Intralipid administration again only glucose was given over the next 24 hr.

An umbilical venous catheter was inserted to withdraw blood samples for following the changes in the concentration of free glycerol, free fatty acids and triglycerides in the fasting state, before, at the end, as well as at 30, 60, 90, 120 minutes, 12 hrs and 24 hrs after Intralipid supplementation. Free fatty acids were determined according to Dalton and Kowalski [7], and Laurell and Tibbling [16]; free glycerol and total glycerol by the UV method using the Boehringer Biochemica Test Combination; neutral fat was obtained from the equation (total glycerol—free glycerol) $\times$ 9.62 = mg neutral fat/100 ml. The kinetic characteristics of the three lipid components were defined by following the fall of their concentration at 30 minute intervals over the first two hours after termination of the infusion of fat emulsion. The three consecutive points from 30 to 90 minutes of the semilogarithmic concentration plot were used for calculating half time:

$$T^{1}/_{2} = \frac{t \times \log 2}{\log E_1 - \log E_2}$$

and utilization constant:

$$K\,(\%/\text{min}) = \frac{\ln Y_1 - \ln Y_2}{t_2 - t_1} \times 100$$

For statistical analysis, the means and standard errors were calculated; when it seemed necessary, significance was estimated by Student's t test.

Results

The plasma concentration of free glycerol, free fatty acids and triglycerides obtained in two groups of low-birth-weight infants at different times during the observation period are shown in Fig. 1. It is seen that the concentration of each lipid parameter by the end of the first 12 hrs glucose period was found to be lower than in the fasting state. This fall, however, was not significant. The markedly increased concentration of these factors in response to infusion of fat emulsion over six hours fell gradually approaching or reaching the pre-Intralipid levels over two hours following termination of fat supplementation. Thereafter, while glucose infusion was being continued at a constant rate for the next 24 hours, the plasma content of free glycerol, free fatty acids and triglyc-

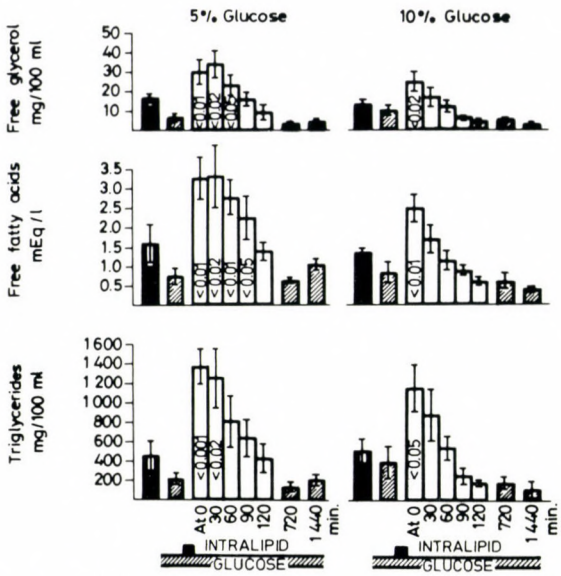

FIG. 1. Responses to Intralipid infusion of blood glucose, plasma FFA and triglycerides in low-birth-weight infants receiving 5% or 10% glucose as a base-line calorie supply. ■ Fasting values; ▤ values obtained before Intralipid infusion while the infants were receiving glucose only; □ values obtained at 30-minute intervals over a two-hour period, at 720 and 1440 minutes after the termination of Intralipid infusion

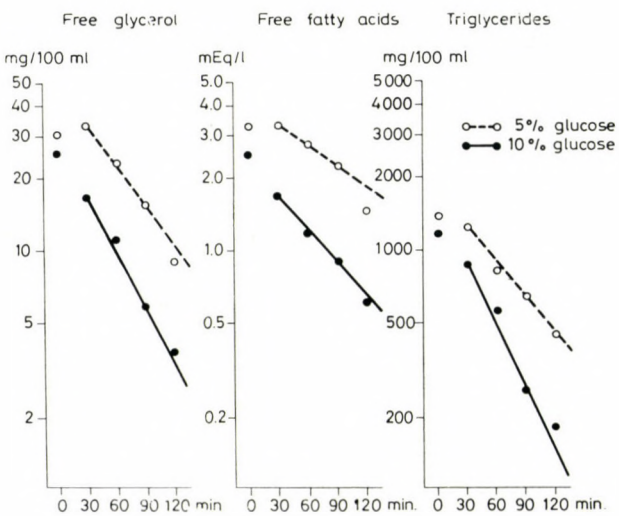

FIG. 2. Disappearance of free glycerol, free fatty acids and triglycerides from the plasma after a six-hour period of Intralipid infusion into low-birth-weight infants receiving 5% or 10% glucose

TABLE I

Individual and mean utilization constants and half times in the two groups of infants

Number	Free glycerol		Free fatty acids		Triglycerides	
	Utilization constant	Half time, min	Utilization constant	Half time, min	Utilization constant	Half time, min
5% glucose						
1	1.00	69.0	0.36	189.9	0.39	177.7
2	0.95	72.4	0.93	74.5	1.26	54.6
3	2.22	31.0	0.62	111.0	0.75	91.5
4	1.07	64.4	0.61	113.2	1.77	39.0
5	1.71	40.3	0.59	115.9	0.76	91.1
6	1.26	54.8	0.80	86.1	1.26	54.8
Mean	1.37	55.3	0.65	115.4	1.03	84.8
± SE	0.20	6.7	0.07	16.4	0.20	20.5
10% glucose						
7	1.67	41.3	1.71	40.3	1.70	40.6
8	4.35	15.9	2.51	27.5	4.03	17.1
9	2.08	33.2	1.47	47.0	1.19	58.0
10	2.54	27.1	0.95	72.6	1.29	53.4
11	1.57	44.0	0.98	70.6	1.13	61.2
12	1.38	50.2	1.03	67.2	1.54	44.9
Mean	2.26	35.3	1.44	54.2	1.81	45.9
±SE	0.45	5.1	0.24	7.5	0.45	6.5
p	0.1–0.05	<0.05	<0.02	<0.01	0.2–0.1	0.2–0.1

erides was diminished in relation to that observed prior to intravenous fat emulsion.

The mean semilogarithmic plot of the post-Intralipid concentration of free glycerol, free fatty acids and triglycerides obtained in the two groups (5 and 10% group) is demonstrated in Fig. 2; it shows that emulsified fat was rapidly cleared from the plasma of low-birth-weight infants receiving intravenous glucose.

Table I summarizes the calculated individual and mean half time and K value (utilization constant) of disappearance for each parameter in the two groups of infants. It can be seen that each lipid component was more rapidly eliminated from the blood of infants in the 10% glucose-group, but only the disappearance constant of free fatty acids was significantly higher than in infants receiving 5% glucose. The decrease in

half time of free glycerol also reached the level of significance.

Discussion

There is a complex and mutual relationship and interaction between carbohydrate and fat metabolism [1, 2, 9, 10, 19, 22, 23]. A markedly raised plasma triglyceride or free fatty acid level may be associated with a decreased glucose tolerance and, in turn, oral or parenteral glucose administration may increase the removal of triglyceride and free fatty acids from the plasma. This interrelationship between the two nutrients, mediated probably by metabolic and hormonal factors [4, 6, 9, 11, 27], appears to be of great practical importance in total parenteral nutrition, when glucose and fat emulsion are simultaneously given for an adequate supply of nutrients and calories. Under such conditions, profound alterations in the metabolic and hormonal milieu are to be expected, whose exploration is essential to get a deeper insight into the interaction and metabolic fate of the two important sources of energy.

Experimental and clinical studies [3, 5, 8, 14, 15, 17, 27] dealing with kinetic principles of the elimination and utilization of parenterally administered fat emulsion have shown that infused lipids, even at high concentrations, are partly stored, oxidized, or metabolized by the neonatal organism. In intravenous alimentation of the newborn, it is of great importance that the maximum disappearance rate of triglycerides intravenously injected as Intralipid in preterm infants was found to be within the normal adult range [12, 13, 24, 25, 26]. This observation suggests that low-birth-weight infants are capable of removing triglycerides from the blood by various mechanisms and organs.

In a previous study [21] we have shown that a certain proportion of the lipids administered is completely oxidized, resulting in a fall of the respiratory quotient and an increased contribution of fat combustion to energy metabolism. Furthermore, in studies [18] related to the changes in plasma nutrients and metabolites provoked by exogenous triglycerides (Intralipid) we observed some correlative alterations suggestive of interaction in hepatic metabolism and substrate utilization leading to stimulation of gluconeogenesis. All these findings in low-birth-weight infants prove a reasonably sufficient elimination and utilization capacity of intravenously administered fat emulsion and indicate metabolic effects that necessitate further research and clinical studies to clarify various aspects of complete intravenous nutrition in the newborn.

The present study has confirmed the observations of Gustafson et al. [12, 13] concerning the ability to clear the plasma from exogenous fat. In addition to the difference with regard to elimination of free glycerol, fatty acids and triglycerides, the observations outlined above also show that increasing amounts of simulta-

neously administered glucose increase the removal rate of lipid. Hence, glucose, the most important source of calories, can be regarded as a useful tool to increase the eliminating capacity of premature infants. Although only the increase in K value for free acids had reached the level of significance, the elimination of free glycerol and triglycerides also showed a tendency to increase in response to 10% glucose. Contrary to this finding, in adults receiving complete parenteral nutrition MacFadyen et al. [17] observed no difference in triglyceride clearance when the amount of glucose was increased; the disappearance rate of free fatty acids, however, was found to be considerably elevated.

The individual K values for the different lipid components (free glycerol, free fatty acids, triglycerides) obtained in the present study showed a wide variation. Obviously, several factors, exogenous and endogenous, influence serum fat clearance in the early period of extrauterine life. Thus, low-birth-weight due to intrauterine malnutrition has been shown to be associated with a low utilization rate of exogenous lipid as compared with that in well-nourished preterm infants [13]. It is conceivable that in such instances a concurrent hypertonic (10%) glucose infusion would not only correct the glycopenia but might also be useful in preventing the accumulation of plasma lipids. The metabolic and hormonal state associated with glucose deficiency in intrauterine malnourished infants could well be one of the factors responsible for the low tolerance to intravenous fat emulsion.

To clarify the exact mechanism of the increased removal rate of lipid components caused by 10% glucose infusion, further investigations are necessary. Hyperinsulinism which has been shown to occur in response to hypertonic glucose administration in low-birth-weight infants [20] might be one of the hormonal and metabolic factors contributing to the increased elimination from the blood. But, whatever the mechanism, glucose can be regarded as a component of the nutritive mixtures capable of controlling lipid blood levels during complete intravenous feeding. Administration of adequate quantities of glucose simultaneously with Intralipid prevents hyperlipidaemia, and allows to take maximum benefit of the use of fat emulsion as part of a well-balanced intravenous nutrition.

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