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Metabolic changes in newborn infants following surgical operations

I. Blood levels of glucose, plasma free fatty acids, α-amino nitrogen, plasma amino acid ratio and urea nitrogen

By

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In 29 newborn infants subjected to surgery for congenital anomalies, the blood glucose, free fatty acid (FFA), amino acid, α-amino nitrogen and blood urea levels were observed from the first to the seventh postoperative days.

The blood glucose level showed moderate changes in the postoperative period, while FFA decreased significantly.

The combined concentration of non-essential amino acids (glycine + glutamine + serine + taurine) and that of essential amino acids (leucine + isoleucine + valine + methionine), their quotient (Whitehead's ratio), as well as the α-amino nitrogen level indicated dynamic changes in the postoperative period.

The gradual return of blood urea to the preoperative level is explained by the diminished breakdown and the improved excretory function of the kidney following surgical procedures.

It has been shown earlier that the changes occurring in the concentrations of the main plasma nutrients and in the acid–base status during anaesthesia and surgery, and in the first 24 postoperative hours, were different in the neonate and the older child and even more so in the adult. The metabolic changes taking place during surgery diminished or even disappeared shortly after surgery or within the first postoperative day [16, 17]. It seemed promising to study the metabolic characteristics on the 2nd to 7th postoperative days, and the changes in blood sugar and plasma free fatty acid (FFA), lactate, α-amino nitrogen, and plasma amino acids occurring in response to a gradual increase of the caloric intake.

Materials and Methods

Observations were made on twenty-nine newborn infants undergoing surgical procedures for congenital anomalies. Only infants were considered in whom the duration of surgery had reached at least 70 minutes. Data for the neonates studied are presented in Table I.

In the case of blood sugar and FFA the patients were divided into two groups according to whether developmental anomalies did or did not directly affect the alimentary tract. The former group (oesophageal, small intestinal or rectal atresia) will be referred to as "alimentary" and the latter (meningomyelocele, diaphragmatic hernia) as "non-alimentary". Blood sugar concentration was measured with the o-toluidine method of Pryce [18], while the levels of plasma free fatty acids were estimated by the colorimetric method of Laurell and Tibbling [12].

TABLE I

Relevant clinical data of patients subjected to emergency surgery

Number and sex of patients		Diagnosis	Gest. age, week	Weight at birth, g	Weight, percentile	Age at surgery, hours	Died, day	Delivery	Concomitant, additional malformation or complication
1	F	Oesophageal atresia	36	2080	<10	36		Premature rupture of membrane	—
2	M	Gastroschisis	35	1800	<10	12		—	Tetralogy of Fallot; tricuspidal stenosis; bilateral hydroureter
3	F	Jejunal atresia	38	3200	50—75	12	5	Adhering placenta	Bilateral hydroureter
4	F	Lumbal meningomyelocele	38	2640	10—25	168		—	—
5	M	Intestinal obstruction	37	2900	25—50	36		Breech presentation	Cerebral and spinal haemorrhage
6	F	Thoraco-lumbar meningomyelocele	37	2770	25—50	2		—	—
7	M	Anorectal agenesis	?	2350	?	26	6	Twin pregnancy	—
8	M	Oesophageal atresia	39	3150	25—50	10		Premature rupture of membrane	Atrial septal defect
9	F	Thoraco-lumbar meningomyelocele	?	3000	?	72		—	Severe deformation of vertebrae
10	F	Thoraco-lumbar meningomyelocele	38	2950	25—50	12		Caesarean section	—
11	M	Anorectal agenesis	37	2400	10—25	30	4	?	Multiple malformation
12	F	Lumbar meningomyelocele	38	2700	10—25	5		Breech presentation	Arthrogryposis
13	M	Diaphragmatic hernia	38	2340	<10	72		Premature rupture of membranes	—
14	M	Lumbar meningomyelocele	37	1650	<10	14		Resuscitation at birth	Severe intrauterine dystrophy
15	M	Lumbar meningomyelocele	38	3600	75—90	96		Preoperative shock due to blood loss	—

16	F	Lumbar meningomyelocele	38	3200	50—75	10		—	—
17	F	Omphalocele	38	3650	75—90	11		—	Rotational malformation of midgut
18	M	Anorectal agenesis	?	2400	?	5		—	Hydronephrosis
19	M	Intrauterine perforation of colon	35	3200	90	60		—	Peritonitis
20	F	Sacral teratoma	39	3500	25—50	120		—	—
21	F	Lumbar meningomyelocele	38	3110	25—50	48		?	Multiple malformation
22	M	Anorectal agenesis	36	2850	25—50	7		—	—
23	M	Omphalocele	?	2350	?	20		—	Rotational malformation of midgut
24	M	Lumbo-sacral meningo-myelocele	?	2800	?	18		?	—
25	F	Lumbar meningomyelocele	39	3950	90	30		?	—
26	F	Anorectal agenesis	37	2150	<10	27		—	—
27	M	Persistent omphalomesen-teric duct	38	3110	25—50	79		—	—
28	M	Intestinal atresia	35	2950	75—90	37		Premature rupture of membrane	—
29	M	Oesophageal atresia	?	1950	?	36	5	?	Bronchopneumonia

The plasma amino acid ratio, i.e. the ratio of the concentrations of glycine + serine + glutamine + taurine to those of leucine + isoleucine + valine + methionine, was determined by WHITEHEAD's method [24], as modified by MESTYÁN et al. [13]. For estimation of the plasma α-amino nitrogen and blood urea levels, the ninhydrin method of BAILEY [2], and the diacetylmonoxime method of SIEST [22] were used. In the postoperative period, the newborn babies were nursed in incubators at an ambient temperature of 32—34 °C. Daily fluid requirement was estimated at 100—150 ml/kg/24 hours according to the patient's age. The daily electrolyte requirement in the case of parenteral administration of fluid was given in 5% or 10% glucose. Correction of the blood acid–base status with sodium bicarbonate was carried out when the base excess (BE) exceeded —10 mEq/l. In addition, in a few cases a blood transfusion was also necessary in the postoperative period. An effort was made to offer the caloric and fluid requirement orally. In some cases, mostly in infants with anomalies of the intestinal tract or of the abdominal wall, parenteral feeding was necessary [4]. Our policy in parenteral feeding was flexible; usually, we administered 60—90 cal/kg/24 hours. This regime meant a volume of 120—150 ml/kg/24 hours, with 10—15 g/kg/24 hours glucose, and 3 g/kg/24 hours protein. From time to time also 1—2 g fat/kg/24 hours was administered. Thus, only the maintenance demand was met by the parenteral feeding regime.

In order to ensure near-standard conditions for the examination, the blood samples collected on the 1st, 2nd, 3rd, 5th and 7th postoperative days were obtained after 6—8 hours of fasting. When a continuous drip infusion was necessary, the drip of 5% glucose + 0.45% sodium chloride was changed to one of 0.45% saline for a 6—8-hour period. Owing to some deaths resulting from congenital anomalies or associated defects and to the difficulty of collecting blood, we were not able to follow-up all the newborn infants.

The results were analyzed by Student's *t*-test, accepting $p < 0.05$ as the level of significance. The values obtained in each postoperative period were compared with those found at the end of the first 24 postoperative hours.

RESULTS

Figure 1 shows a slight decrease in the mean blood sugar level on the 2nd and 3rd postoperative days. However, 5 days after surgery it returned to its initial value of 70 mg/100 ml measured at the end of the first postoperative day. This figure shows that the fall in the blood glucose concentration during the first days of observation was due to a fall in blood concentration of the patients in whom the developmental anomalies did not directly affect the alimentary tract. The individual reactions varied, however, considerably. In a few cases the values for blood glucose, which at the beginning were higher or lower than the average, gradually decreased or increased.

The mean plasma FFA level is shown in Fig. 2. The relatively constant values (985—952 μEq/l) during the first 3 postoperative days were followed by a decrease to a mean level of 614 μEq/l ($p < 0.05$) by the end of the 5th postoperative day. By the 7th day of observation the mean FFA level had fallen to 500 μEq/l ($p < 0.01$). It decreased consistently in the babies in whom the alimentary tract was directly affect-

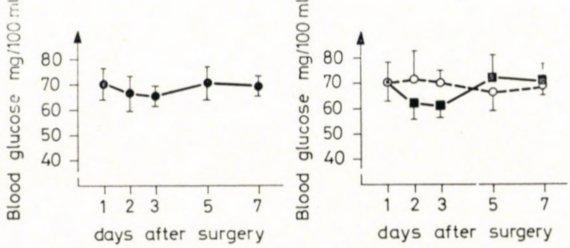

FIG. 1. Blood glucose level in newborn infants during the postoperative period. Mean values ± standard error. ● All cases; ■ "alimentary"; ○ "non-alimentary"

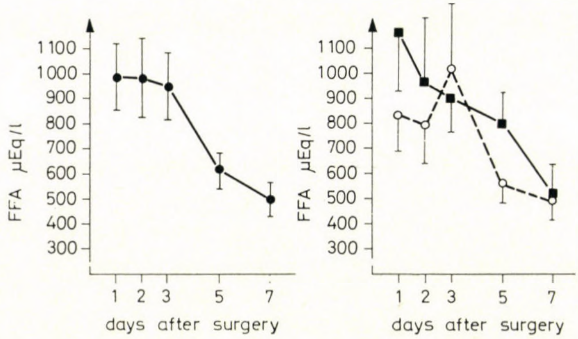

FIG. 2. Plasma FFA level in newborn infants during the postoperative period. Mean values ± standard error. ● All cases; ■ "alimentary"; ○ "non-alimentary"

ed. In the other group of patients there was a transient rise on the 3rd postoperative day. In both groups the mean FFA level had fallen to less than the initial value by the 7th postoperative day.

Figure 3 shows the concentrations of the four non-essential and the four essential amino acids. After a moderate rise, the concentration of glycine + serine + glutamine + taurine fell below the initial level. In contrast, the concentration of essential amino acids (leucine + isoleucine + valine + methionine) after an initial depression, exceeded the mean value at the end of the first postoperative day. From the 3rd day on these changes resulted in a decrease of Whitehead's ratio. Neither the decrease of Whitehead's ratio nor the changes of the two amino acid groups were significant statistically.

In Fig. 4 it is seen that the mean concentration of plasma α-amino nitrogen decreased in the first postoperative days, followed by a rise at the end of the observation period. Neither change was significant statistically.

Figure 5 shows that the values for blood urea did not change significantly during the first 3 postoperative days. Five days after surgery a significant fall of nearly 10 mg/100 ml

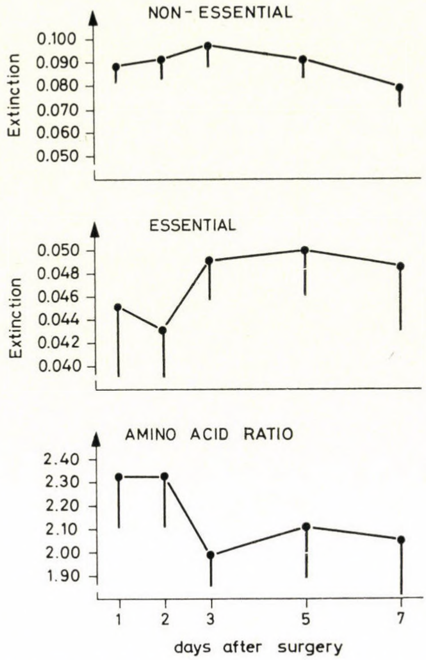

FIG. 3. Extinction values for the two groups of amino acids, and the plasma amino acid ratio in newborn infants during the postoperative period. Mean values ± standard error

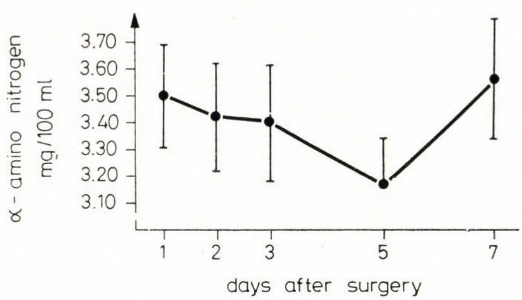

FIG. 4. Plasma α-amino nitrogen level in newborn infants during the postoperative period. Mean values ± standard error

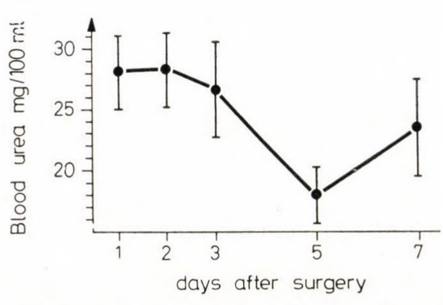

FIG. 5. Blood urea level in newborn infants during the postoperative period. Mean values ± standard error

was noticed ($p < 0.01$). By the end of the observation period, the blood urea level was returning to its original value.

Discussion

The 33-hour mean age of the newborn babies at surgery was of great importance in caloric supply. In ten babies the birth weight was less than 2500 g, and in five patients signs pointing to intrauterine malnutrition were noticed. Thus, the foetal glucogen stores had probably diminished or were depleted by the time of surgery. The fat depots were partly or totally exhausted. It may be assumed that the metabolic and hormonal effects of the surgical trauma, anaesthesia, hypoxia and hypothermia, together with the effect of partial or total starvation can, at least temporarily, cause a critical metabolic condition for the operated newborn infant. Besides the diminished endogenous glucose production due to the depleted carbohydrate reserves, the disturbances in the utilization of glucose must also be taken into account. Howard [11] called attention to the impaired peripheral glucose utilization following surgical interventions in adults; this was closely connected with the diminution of glucose tolerance.

The concept of "diabetes of injury" is based on the diminished utilization of glucose caused by the absolute or relative lack of insulin in the phase of convalescence after some injury [15]. This theory may explain the increase of pyruvate and lactate levels during infusion of glucose [6]. Akamatsu et al. [1] observed that after surgery glucose utilization diminished for a few days only. In order to explain the postoperative disorders of carbohydrate metabolism, some other hormonal effects and interactions must be taken into account in addition to the decreased secretion and diminished activity of insulin. Adrenaline, by its glucogenolytic effect, enhances the passage of glucose into the blood circulation. On the other hand, the vasoconstriction reduces the oxygen and glucose supply of the cells. Furthermore, adrenaline has an inhibitory effect on the secretion of insulin. Glick et al. [9], and Ross et al. [21] found an increased secretion of growth hormone in the postoperative period.

Few papers have dealt with the changes and disorders of carbohydrate metabolism following a surgical intervention in newly born babies. In newborn rabbits, Elphick [7] supposed a relationship between the reduced utilization of glucose and the mobilization of fat, and the enhanced secretion of adrenaline and noradrenaline. Elphick's assumption was explained by the fact that the glycogen stores of newborn animals are meagre and so the enhancement of glycogenolysis is not followed by a considerable increase in blood glucose concentration. Cornblath and Schwartz [3] regard the low utilization of glucose in the neonatal period as favourable for the glucose supply to the brain, as in starving newborns more glucose of endogenous or exogenous origin will be available for the brain to cover its energy supply. The average concentration of blood glucose between the 2nd and 7th postoperative days was fairly stable compared with the levels observed during surgery and on the first postoperative day [15].

Apart from a few newborn infants operated upon for meningomyelocele, our patients received a low caloric intake. In the great majority of the babies, a mechanic or paralytic intestinal obstruction occurred in the postoperative period. In such cases part or the whole of the caloric supply had to be administered parenterally. Accordingly, the 70 mg/100 ml concentration of blood glucose should be regarded as high. However, oral and parenteral feeding was stopped 6 hours before the blood samples were collected and therefore did not play an important role in the slight elevation of the blood glucose level. The increase was probably caused by a diminished utilization of glucose due to the surgical trauma. Enhanced metabolism of fat following surgery has been observed by a number of authors. Moore et al. [14] indicated that in adults its rate varies according to the clinical situation after surgery and may exceed 2000 calories per day. Wadström [23] found an increased FFA level after surgery.

In our investigations a decreased FFA level was observed between the 2nd and 7th days, while during the operation, as well as on the first postoperative day a well-defined increase of the FFA level took place [15] which might have been caused by the traumatic effect of anaesthesia and surgery (increased release of catecholamines and steroids, metabolic effects of anaesthetics, hypoxia, hypothermia, acidosis, etc.). In the postoperative period, however, the FFA level showed a tendency to decrease, but it was still higher than normally. This behaviour of fat metabolism can be explained by the fact that in the postoperative period the complex hormonal and metabolic changes evoked by surgery are returning to the preoperative level and the state of hypoalimentation. These combined hormonal and metabolic processes typical of the adaptation to extrauterine life explain why we have failed to find a reciprocal relationship between glucose and FFA metabolism [4, 19]. Elphick [8] also failed in demonstrating a relation between the above-mentioned parameters in newborn infants following surgery.

Since we could not determine the plasma concentration of the individual amino acids, we estimated the combined concentration of the non-essential glycine + glutamine + serine + taurine and that of the essential leucine + isoleucine + valine + methionine, which are included in Whitehead's plasma amino acid quotient [24]. The results indicated that the free plasma amino acid pool changed dynamically during and after surgery. Our observations have substantiated the findings of Mestyán et al. [13] in that the combined effect of anaesthesia and surgery did not significantly modify the sequence of Whitehead's ratio in the first few days of life.

The α-amino nitrogen level also revealed some alterations which, in all probability, had resulted from a redistribution of the intra- and extracellular amino acid pools. The changes had probably been induced by endogenous metabolic and hormonal reactions, although the exogenous factor, like oral or parenteral feeding, could not be neglected.

The gradual return of blood urea to its preoperative level in the postoperative period was due to the diminished oxidation of amino acids and the restoration of circulation and respiration. The blood urea level in children under the age of two years was found to return to the preoperative level by the fourth to sixth postoperative day [10]. According to Rickham [20], the gradual decrease of blood carbamide in newborn infants following surgery can be explained by the diminished breakdown of protein and the improved excretory function of the kidneys.

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