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Metabolic Effects of Anaesthesia and Surgery in the Newborn: Blood Glucose, Plasma Free Fatty Acid, Free Amino Acid and Blood Lactate Level in Newborn Puppies

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To approach the problem of how far anaesthesia and surgery might be responsible for the metabolic changes in newborn infants undergoing surgery for congenital malformation, investigations were carried out on a total of 37 puppies of an average age of 3 days. One group of puppies was subjected to anaesthesia for 60 min, and the other to anaesthesia + a standard surgical procedure also of 60 min duration. The changes in blood glucose, plasma FFA, blood lactate, plasma amino-acid ratio and α-amino-nitrogen level were measured.

(i) Anaesthesia largely contributed to the metabolic changes observed during surgical procedures in newborn puppies.

(ii) Surgical stress exerted an additional increasing effect on blood glucose caused by anaesthesia.

(iii) In plasma FFA of both groups of animals a definite but statistically non-significant fall was observed.

(iv) The increase in lactate level was more pronounced in the anaesthetized and operated animals than in those subjected to anaesthesia alone.

(v) The increase in α-amino-nitrogen level in both groups of animals was associated with changes in the circulating free amino acid pool, as indicated by Whitehead's plasma amino-acid ratio.

(vi) The mechanisms of the metabolic responses to anaesthesia or anaesthesia + surgery are not quite clear. In all probability, they can be accounted for by the various hormonal reactions and their interactions.

In newborn infants considerable changes in the plasma concentration of various plasma nutrients occur during and after surgery [12]. Actually, two factors, anaesthesia and surgical trauma, should be considered in explaining the metabolic responses to surgical procedures. It appears reasonable to assume that these two factors may exert both quantitatively and qualitatively different effects on the metabolism of newborn infants. Since it is not possible to examine these factors separately in human neonates, we undertook a comparative investigation of the effects of anaesthesia and surgery in newborn puppies.

Material and Methods

The examinations were carried out on a total of 37 newborn puppies of an average age of 3 days (range 1 to 5 days) and weighing between 350 and 540 g. A fasting period of ten hours preceded the experiment. Seventeen animals were subjected to anaesthesia lasting 60 minutes and 20 puppies to anaesthesia and to a standard surgical procedure.

Anaesthesia was carried out without premedication. Halothane was given by means of a miniature mask, with the puppies expiring into the outside air. As a standard surgical procedure, laparotomy and resection of a 10 cm long segment of the small intestine followed by end to end anastomosis was performed. Anaesthesia + surgery did not last longer than 60 minutes.

Blood glucose concentration was estimated with Pryce's o-toluidine method [13] after deproteinization. The plasma free fatty acids (FFA) and lactate concentrations were determined with the method described by Laurell and Tibbling [7] and Barker and Summerson [2], respectively. The ratio of the combined plasma levels of non-essential glycine + glutamine + taurine + serine to those of essential leucine + isoleucine + valine + methionine was determined according to Whitehead [16]. The α-amino-nitrogen concentration was measured according to the ninhydrine method of Bailey [1]. In both groups of puppies blood samples were drawn immediately after the induction of anaesthesia and at the end of the experimental period (60 min). Since it is difficult to puncture the femoral artery in unanaesthetized animals, and preliminary examinations had shown that the concentration of metabolites in blood withdrawn before and immediately after induction of anaesthesia were practically the same, blood obtained under the latter conditions was used for comparison. Statistical analysis of the results was performed according to Student's t-test. For evaluation of the relative changes, the one-sample t-test was used, $p < 0.05$ being accepted as the level of significance.

Results

Fig. 1 shows that anaesthesia itself produced a considerable increase ($p < 0.01$) in the blood glucose level of the infantile puppies. An even more pronounced response ($p < 0.001$) was observed during anaesthesia + surgery. In both groups there was a definite but not significant fall in mean plasma FFA concentration.

It should be noted that not every animal responded with a fall in the plasma FFA level, in some no response or even an increase was observed. Because of the wide scatter of the initial values, the relative changes in plasma FFA level were also calculated (Table I). In contrast to the absolute changes, the percentage fall of FFA in the anaesthetized and operated group proved to be significant ($p < 0.05$).

In the anaesthetized group the mean lactate level rose from 21.4 mg per 100 ml to 26 mg per 100 ml ($p < 0.05$). At the same time the elevation of 11.8 mg per 100 ml in the anaesthetized + operated group was statistically significant ($p < 0.01$) (Fig. 1). For the same reason as in the case of FFA, the relative changes in lactate level were also calculated and evaluated statistically.

As it can be seen in Fig. 2, the mean increase in the plasma α-amino-nitrogen level was similar but insignificant in both groups of puppies. However, the mean relative rise (Table I)

TABLE I

Relative changes in blood glucose, plasma FFA, blood lactate and amino-nitrogen levels during anaesthesia (60 min), and anaesthesia + surgery (60 min) in puppies (mean + SE)

		Number of cases	Percentage change	p	SE
Blood glucose mg%	Anaesthesia	17	+49	=0.001	± 6.1
	Anaesthesia + surgery	20	+64	<0.001	± 3.1
FFA μEq/l	Anaesthesia	16	−32	>0.05	±23.5
	Anaesthesia + surgery	19	−35	<0.05	±14.2
Blood lactate mg%	Anaesthesia	16	+36.2	<0.001	± 4.7
	Anaesthesia + surgery	20	+66	<0.001	± 3.6
α-amino-nitrogen mg%	Anaesthesia	17	+24	<0.05	± 5.7
	Anaesthesia + surgery	20	+22	<0.05	± 3.9

both in the anaesthetized and in the anaesthetized + operated group turned out to be significant ($p < 0.05$).

In Fig. 2 it can also be seen that the mean ratio of the extinction values of the essential amino acids to those of the non-essential ones included in Whitehead's quotient showed a definite but not significant fall in the anaesthetized puppies ($p < 0.05$). The fall in the ratio resulted from the disproportionate increase of the extinction values of the essential ($p < 0.05$) and non-essential groups ($p < 0.05$) of amino acids. In the anaesthetized + operated group the changes in the extinction values and their ratio were minimal.

Fig. 3 demonstrates the relationship between blood lactate and H^+ concentration immediately after induction and after 60 minutes of anaesthesia. In both groups a highly significant correlation developed between the two parameters during the experimental procedures.

DISCUSSION

As regards the changes in blood glucose concentration, it can be concluded that anaesthesia itself may cause hyperglycaemia. The additional response to the standard surgical procedure shows that both factors contribute to the rise in blood glucose occurring during the operation of anaesthetized newborns.

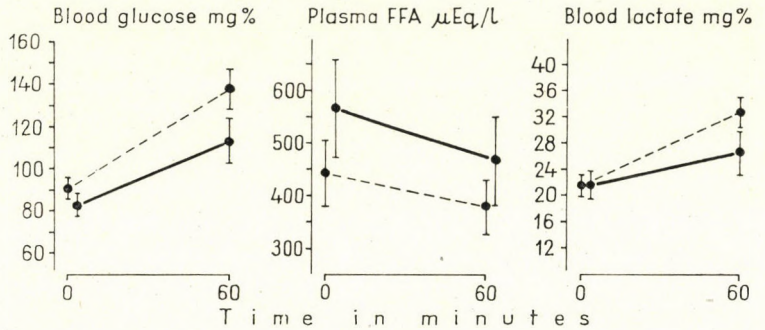

FIG. 1. Changes in blood glucose, plasma FFA and blood lactate level during anaesthesia (60 min) and anaesthesia + surgery (60 min) in puppies (mean + SE)

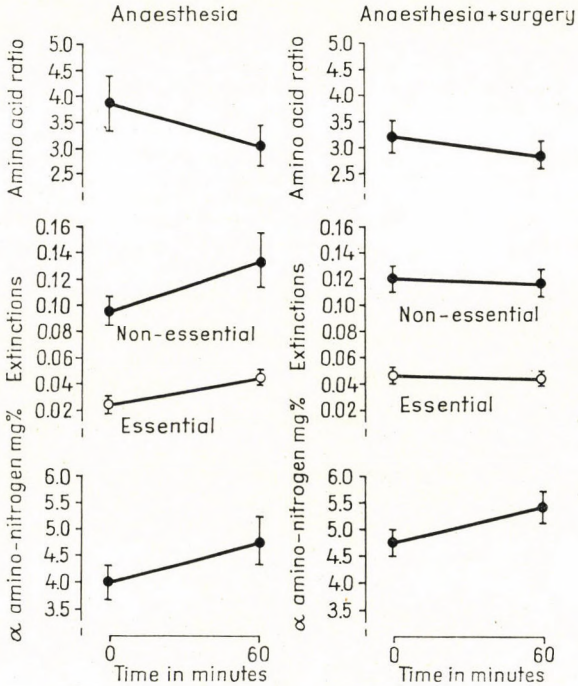

FIG. 2. Plasma amino acid ratio; extinction values indicating the combined concentration of the essential leucine + isoleucine + valine + methionine and that of the non-essential glycine + serine + glutamine + taurine ; and amino-nitrogen level in both groups of puppies

The changes in FFA were the same in the two groups of animals: a slight fall was obtained at the end of the experimental period. This and to some extent our findings in newborn infants fit into the concept of reciprocal relationship between plasma FFA and glucose level [5, 14]. In contrast to the present results, in adults a considerable increase in plasma FFA during surgery has been reported [3, 4, 11]. This difference in the re-

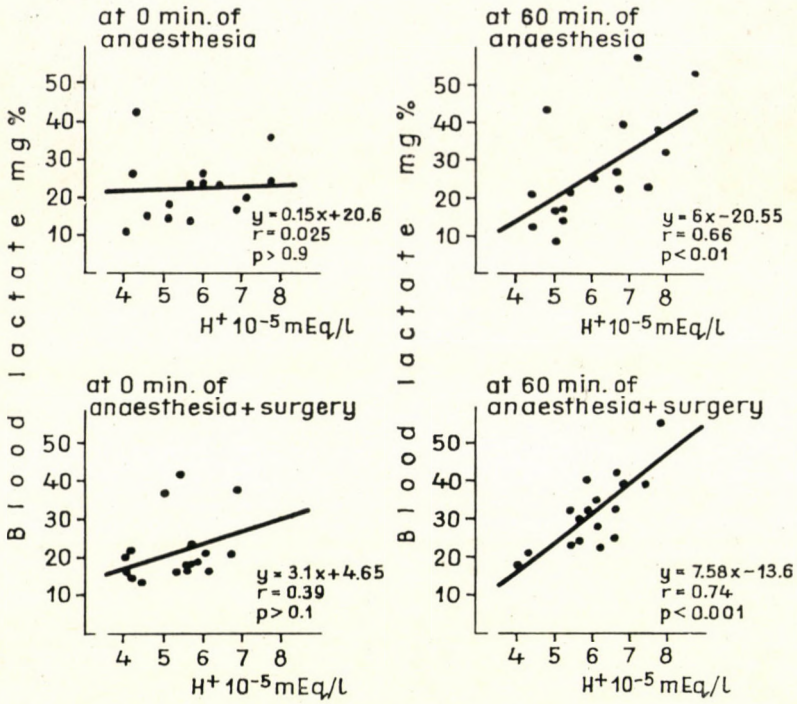

FIG. 3. Correlation between H^+ concentration and blood lactate level during anaesthesia (60 min) and anaesthesia + surgery (60 min) in puppies

sponse of FFA to anaesthesia + surgical intervention is difficult to explain without the knowledge of hormonal reactions playing an essential role in the regulation of fat and carbohydrate metabolism.

It is the surgical stress which seems to be mainly responsible for the increase in blood lactate level (hypotension, accumulation of catecholamines, opening of the arterio-venous shunts and the resulting tissue hypoxia). ROKKANEN et al. [15] regard the increase in lactate level as a more reliable sign of tissue hypoxia than the O_2-tension measured in the peripheral veins. The relative constancy of the lactate level during anaesthesia indicates that anaesthesia in itself does not cause considerable tissue hypoxia.

Similarly as we have observed in newborn infants [12], the intraoperative metabolic acidosis found in the puppies must have also been caused by an accumulation of blood lactate.

As regards the changes in Whitehead's plasma amino acid ratio, it can be concluded that the anaesthesia caused a definite fall comparable to that observed in newborn infants. The disproportionately larger increase in the extinction value representing the combined concentration of the essential leucine + isoleucine + valine + methionine was responsible for the fall in the ratio. In the anaesthetized and operated group of pup-

pies only a slight decrease of the ratio was observed. In all probability, the hormonal reactions influencing the distribution of amino acids between the extracellular and intracellular pool play an important role in the changes of the plasma amino acid pattern.

As in newborn infants, the increase in α-amino-nitrogen level is in accordance with the elevation in plasma concentration of the two groups of amino acids included in Whitehead's quotient. It is well-known that in adults glucose loading decreases the α-amino-nitrogen contents of the plasma and the concentration of essential amino acids, which is probably due to the effect of enhanced insulin secretion on protein synthesis [6, 8, 9, 10]. As an explanation for the difference it seems reasonable to assume that the hormonal and metabolic reactions associated with hyperglycaemia due to endogenous glucose mobilization caused by anaesthesia and surgery, differ substantially from the response to exogenous glucose loading.

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