NON-GLUCONEOGENIC FATE OF LACTATE DURING THE EARLY NEONATAL PERIOD IN THE RAT

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1. Introduction

Owing to the low carbohydrate content of milk, the newborn has to stimulate the gluconeogenic mechanism to supply glucose to those tissues using it as a compulsory metabolic fuel. The main liver gluconeogenic enzymes are induced after delivery, their activities remaining high throughout the suckling period [1,2]. This agrees with the high gluconeogenic capacity of suckling rat liver reported in vivo [2,4] and in vitro [5]. Consequently, it has been generally assumed that the lactate which accumulated in fetal rat blood during the last stages of gestation is consumed after delivery through the gluconeogenic pathway [6]. However, plasma lactate is depleted before the induction of gluconeogenic enzymes has taken place [7]. Thus, the utilization of plasma lactate occurs within the first 2 h after delivery (i.e., the 'presuckling' period) when liver phosphoenolpyruvate carboxykinase, fructose bisphosphatase and glucose 6-phosphatase activities are too low to account for active gluconeogenesis [7].

These results prompted us to investigate the fate of lactate during the first 2 h after delivery. The study was extended to the pre-term newborn as a model of transient impairment of lactate consumption. We found [7] that pre-term rats show a resistance to plasma lactate utilization during the first hour after delivery but full capacity for lactate removal is accomplished during the second hour. This fact provides a system for checking the fate of lactate in our experimental conditions. The results reported here suggest that plasma lactate is consumed immediately after delivery as a consequence of its oxidation through the tricarboxylic acid cycle. In addition, our results seem to support the idea that gluconeogenesis from lactate is insignificant during the brief pre-suckling period.

2. Materials and methods

Albino Wistar rats of known gestational age were used for the experiments. Pregnant rats on day 21 or 22 were killed by cervical dislocation and the fetuses were delivered by rapid hysterectomy. The newborns were weighed and those presenting lower weight than the average of the litter discarded. Neonates weighing 4.3 ± 0.1 g or 5.5 ± 0.1 g (mean ± SEM) were considered as 'pre-term' and 'term' rats, respectively. Newborns were immediately injected with 4 μCi [U-^{14}C]-lactate and maintained in 50 ml stopped flasks at 37°C in a continous stream of water-saturated air. The radioactive CO_2 evolved was trapped in 2 × 5 ml of 20% (w/v) KOH. After 0, 1 or 2 h animals were killed by decapitation, exsanguinated and the livers removed. Plasmas were used to determine lactate concentrations [8] and radioactive lactate and glucose [9]. Livers were used to determine radioactive glycogen [10]. Initial specific radioactivities of plasma lactate and body pool sizes were calculated according to [6,11,12]. Lactate respired was calculated from values of radioactive CO_2 evolved and the mean of the specific radioactivity of plasma lactate during the observational periods. Lactate produced was calculated from the changes of body pool sizes and the values of lactate respired.

3. Results and discussion

Table 1 shows the fate of radioactive lactate injected to term and pre-term newborn rats during the first 2 h after delivery. About 43% of the total radioactivity injected was respired as CO_2 by term newborns during the first 2 h after delivery (23% and

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Table 1
The fate of lactate in term and preterm newborn rats during the early neonatal period

Time elapsed from delivery (h)		Radioactive CO_2 evolved (dpm × 10^{-3}/h)	Spec. radioact. plasma lactate (dpm × 10^{-3}/μmol)	Lactate body pool size (bps) (μmol)	Lactate respired (μmol)/h)	(% initial bps)	Lactate produced (μmol/h)	(% initial bps)
0	Term	–	190	46.7	–	–	–	–
1		2096 ± 27	126 ± 4	48.0	13.3	28.4	+14.6	31.3
2		1758 ± 50	82 ± 4	27.9	16.9	36.2	− 3.2	–
0	Pre-term	–	400	22.2	–	–	–	–
1		423 ± 26	245 ± 30	27.1	1.3	5.9	+ 6.2	27.9
2		1118 ± 44	148 ± 8	26.1	5.7	25.6	+ 4.7	21.2

Results are means ± SEM (n = 7–10). Data without SEM are calculated

19% during the first and the second hour, respectively). However, the amount of radioactive CO_2 respired by pre-term rats during the same period was substantially smaller, being 17% of the total radioactivity injected (4% and 13% during the first and the second hour, respectively).

The specific radioactivity of plasma lactate decreased in both groups of newborns during the observation period (table 1), suggesting that lactate was produced by neonatal tissues during this period. The mean of the specific radioactivity of plasma lactate throughout each observation period may be used to convert values for radioactive CO_2 evolved to values of lactate respired (table 1). According to these calculations 30 μmol of lactate underwent oxidation in term newborns during the first 2 h of extrauterine life. The lactate respired by preterm newborns during the same period was much lower (~7 μmol). However, the lactate respired depends on the lactate body pool size which might vary considerably between the two groups of newborns owing to their different weights. The lactate body pool sizes were greater in term than pre-term newborns specially during the first hour after delivery (table 1). Despite this fact, term newborns respired ~65% of their initial lactate body pool size during the first 2 h after delivery while pre-term newborns respired only ~31% of their initial body pool size during the same period. These results clearly suggest that the capacity for lactate oxidation is lower in pre-term than term rats. It is noteworthy that no significant differences were found between the capacity of lactate oxidation shown by the term rats during the first hour and the capacity of lactate oxidation observed in pre-term rats during the second hour. These results closely agree with the suggestion [7] that pre-term rats showed a transient resistance to lactate utilization at delivery which was overcome after the first hour of extrauterine life.

The lactate produced by neonatal tissues within the observation periods may be calculated from the changes of lactate body pool size and the values of lactate respired. According to these calculations (table 1), a substantial amount of lactate was produced in term newborns during the first hour after delivery. However, no lactate was produced in the same group during the second hour. In pre-term newborns lactate production was similar during the first and the second hour but lower than those observed in term newborns during the first hour. However, when these data were related to initial body pool size, the capacity of lactate production was seen to be similar in each group, except in term rats during the second hour when lactate production was hardly observed. This result seems to suggest that anaerobic glycolysis was inhibited in term newborns 1 h after delivery. Whether this inhibition was caused by increased oxygen availability or by the maturation of the mitochondrial oxidative machinery remains to be established. It is noteworthy that lactate production is concurrent with lactate respiration (table 1), suggesting that both processes occur in different tissues. In addition, lactate respired during the pre-suckling period comes not only from lactate accumulated in fetal blood but also from lactate produced after delivery.

Finally, no significant amounts of radioactivity (<0.1% total injected) were found in plasma glucose and liver glycogen 1 and 2 h after radioactive lactate administration, suggesting that gluconeogenesis from lactate was insignificant during the first 2 h.

In conclusion, our results suggest that lactate is utilized during the pre-suckling period presumably through the tricarboxylic acid cycle. The latter pro-

vides a system for the complete utilization of glucose already transformed into lactate by anaerobic glycolisis. The minimal incorporation of radioactive lactate into glucose and glycogen indicates that gluconeogenesis from lactate may be irrelevant during this period. Consequently, it may be concluded that adaptation to extrauterine life includes the immediate utilization of oxygen in order to increase energy production. The defective utilization of such oxygen may be a shortcoming for the pre-term newborn.

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