Relationships between plasma concentrations of Epidermal Growth Factor, insulin and iodated thyroid hormones in early and normal weaned rabbits

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SUMMARY

As the iodated thyroid hormones, insulin as well as the somatotropin-IGF axis and EGF are the main regulators of growth and development in neonate, the purpose of this study was to investigate the relationships between EGF, insulin and thyroid hormones in early and normal weaning rabbits and their effects on body mass accumulation. A total of fifty clinically healthy New Zealand white rabbit puppies were divided into 2 equal groups depending on the weaning age: in the group A, puppies were weaned when they were 21 days old, whereas rabbits of the group B were weaned at 35 days of life. Body weights and plasma hormone (insulin, TT3 and TT4) and EGF concentrations were measured in 5 animals per group on the weaning day (day 0), 7, 14 and 21 days after weaning and when animals were 95 days old. The body weights for the experimental period and at the final time point were significantly lower in the early weaned rabbits compared to controls. Furthermore, while the body weight gains were maximal during the first week after weaning, then decreased and remained constant in controls, the growth was delayed in early weaned rabbits, the highest body weight gains being obtained between the 14th and the 21st days post weaning. The mean growth was delayed in early weaned rabbits, the highest body weight gains were significantly lowered in the early weaned rabbits compared to controls. By contrast, the plasma T4 concentrations were significantly increased in the group A. These results clearly indicated that EGF acts also as an endocrine factor and that the early weaning negatively affects growth in rabbits by interfering with endocrine secretion, and particularly with the thyroid function.

Keywords: Rabbits, Weaning, EGF, Insulin, iodated thyroid hormones, Growth.

RÉSUMÉ

Relations entre les concentrations plasmatiques de l’EGF (Epidermal Growth Factor), de l’insuline et des hormones thyroïdiennes iodées chez les lapins normalement sevrés ou sevrés précocement

Comme les hormones thyroïdiennes iodées, l’insuline ainsi que l’axe somatotrope et l’EGF sont principalement impliqués dans la croissance et le développement du nouveau-né, cette étude a eu pour objectif d’établir les relations existantes entre l’EGF, l’insuline et les hormones thyroïdiennes chez des lapins sevrés précocement ou normalement sevrés ainsi que leurs effets sur la croissance pondérale. Au total, 50 lapereaux blancs de Nouvelle Zélande, cliniquement sains ont été aléatoirement répartis en 2 groupes égaux en fonction de l’âge au sevrage : les lapins ont été respectivement sevrés à 21 jours dans le groupe A et à 35 jours dans le groupe B. Les poids vifs et les concentrations plasmatiques hormonales en insuline, TT3 / TT4 et en EGF ont été mesurés sur 5 animaux par groupe pour chaque échéance (le jour du sevrage, 7, 14 et 21 jours après et lorsque les lapins étaient âgés de 95 jours). Les poids vifs pendant et à la fin de la période expérimentale ont été significativement plus faibles chez les lapins sevrés précocement que chez les contrôles. De plus, alors que les gains de poids ont été maximaux 1 semaine après le sevrage, puis ont diminué pour rester constants chez les contrôles, un retard de croissance a été observé chez les lapereaux sevrés précocement, les gains de poids maximaux étant obtenus entre le 14ème et le 21ème jour après le sevrage. Les concentrations plasmatiques hormonales moyennes, excepté celles de TT4, ont été significativement plus faibles chez les lapins sevrés précocement (groupe A) que chez les lapins sevrés normalement (groupe B) : alors que les concentrations en insuline et en TT3 ont progressivement augmenté chez les contrôles, elles sont restées stables, voire basses, dans le groupe A, bien que les concentrations en insuline fussent significativement augmentées par rapport aux valeurs initiales et proches des valeurs contrôles lorsque les animaux étaient âgés de 95 jours. Les variations des concentrations en EGF en fonction du temps ont été similaires dans les 2 groupes mais des diminutions significatives de ce paramètre ont été observées chez les lapins sevrés précocement par rapport aux contrôles le jour du sevrage, 21 jours après et à la fin de la période expérimentale. Les poids vifs, les concentrations en insuline et en EGF ont été significativement corrélées dans les 2 groupes ; de plus, le poids vif et la TT4 ont été positivement associés dans le groupe A. En revanche, les concentrations plasmatiques en TT4 étaient considérablement élevées à 30 chez les lapins sevrés précocement puis ont progressivement diminué alors qu’elles sont restées constantes chez les contrôles. Par conséquent, les concentrations plasmatiques en TT3 et en TT4 ont été fortement corrélées seule- lement chez les contrôles et une corrélation significative et négative a été mise en évidence entre le poids vif et la TT4 dans le groupe A. Ces résultats indi- quent clairement que l’EGF agit aussi comme un facteur endocrine et qu’un sevrage précoce affecte négativement la croissance chez le lapin en interférant avec les sécrétions endocrines et en particulier avec la fonction thyroïdienne.

Mots clés : Lapins, Sevrage, EGF, Insuline, hormones thyroïdiennes iodées, Croissance.
Introduction

The early weaning of rabbits could decrease energy needs and increase reproductive performance of dams, without affecting puppy growth and development [36, 41, 42]. There are available data showing that early weaning does not affect body mass and meat quality in fattening period [15, 44].

It is well known that thyroid hormones [8] and insulin as well as EGF-like ligands [40] and the somatotropin - insulin like growth factor axis [23] are the main endocrine and/or auto-paracrine regulators of neonatal animal growth and development. However, the precise mechanisms by which these hormones and growth factors are involved in control of body mass accumulation in rabbits during the post-weaning period are not well elucidated.

EGF has been isolated from various tissues and body fluids, the highest concentration being established in amnion fluid, saliva, colostrum, milk, urine, but it could be also identified in secretions of respiratory and gastrointestinal tracts [4, 11, 21]. The major sources of EGF for newborn animals are colostrum and milk. EGF has been isolated from milk in mice, sows, rats, sheep, humans and cows but the recorded quantities varied according to the animal species [10, 16, 18, 20, 29, 30]. In addition, the effects of EGF on body mass accumulation after weaning are not fully understood. There are contradictory data about the presence of EGF in blood plasma. The existing of EGF ligand in milk and its lack in blood plasma suggest a paracrine action [11, 12, 39]. In rats, mice and humans the plasma level of EGF is about 1 ng/L [4, 17, 32].

During the suckling period, the T3 and T4 secretion in newborns is mainly stimulated by the milk TSH [33, 37]. However, the circulating EGF in physiological concentrations was reported to affect the function and growth of transplanted thyroid gland in newborn rats [27]. The thyroid hormone synthesis and their peripheral metabolism could be depressed by EGF [27, 38]. In the same way, a marked decrease of T3 and T4 plasma concentrations has been reported in sheep after EGF application [9]. On the other hand, a significant increase of TSH plasma concentration was detected ten minutes after intravenous infusion of EGF in rats [1]. The inhibitory effect of EGF on thyroid function is probably due to a negative feed-back control mechanism balancing ligand secretion by the thyroid gland itself [5]. According to Morisset [24], thyroxin is one of the key modulator of pancreas functional maturation, suggesting a functional link between thyroid hormones and insulin.

The detection of EGF in plasma raises the question of its endocrine effects although in the literature, evidences for autocrine and paracrine actions predominate. Therefore, it is necessary to investigate the functional relationships between EGF and the other endocrine glands (thyroid and pancreas) involved in the regulation of the growth and development of neonate in the post-weaning period. That is the reason why the propose of this study was to measure plasma concentrations of EGF, insulin and thyroid hormones in neonate rabbits and to compare them after an early or a normal weaning.

Materials and Methods

ANIMALS AND PROTOCOL DESIGN

The experimental procedure was approved by the Commission of ethics at the Faculty of Veterinary Medicine of Trakia University. Fifty clinically healthy New Zealand white rabbits (provided by the Agricultural Institute, Stara Zagora) were used in the study. The puppies were divided in two groups depending on the weaning age as follow: half of them (n = 25) were early weaned at 21 days old (group A) whereas the others were weaned on day 35 (group B) according an experimental 7 days long procedure. The rabbits were housed in metal cages (80 x 60 x 40 cm) in temperature-controlled room (18 - 20ºC) and the light/dark regime corresponded to the circadian cycle. The animals were fed ad libitum with granulated forage.

Thereafter, body weights were recorded and blood samples were collected by the puncture of the v. jugularis using sterile tubes with heparin as anticoagulant at the days 0 (weaning day), 7, 14, 21 and 74 for the group A or 60 for the group B, on 5 rabbits in each group, thereafter the rabbits were slaughtered (according to the recommendations of Commission of ethics). The last time point has differed between the 2 groups since the weaning day but it corresponded to the same age for rabbits (95 days old). Blood samples were centrifuged (2000 g, at room temperature for 15 minutes) and plasmas were stored at -20°C until used.

BIOCHEMICAL ANALYSIS

The blood plasma EGF concentrations were determined with a heterologous Enzyme-Linked Immuno-Sorbent Assay (ELISA) (human EGF kit, catalogue number EIA 3969, DRG Instruments GmbH, Germany) according to the manufacturer’s instructions. The given technical performances were the following: intra-assay variation coefficient: 4.4%; inter-assay variation coefficient: 5.3%; sensitivity < 1 ng/L; range: 5 - 811 ng/L.

The plasma insulin, total T3 and total T4 concentrations were determined with commercial radioimmunoassay kits (Immunotech, Prague, Czech Republic): Insulin IRMA kit (catalogue number IM 3210, intra-assay variation coefficient: 3.4%; sensitivity: 0.5 mU/L; range: 0.3 – 300 mU/L) - Total T3 (TT3) RIA kit (catalogue number IM 1699, intra-assay variation coefficient: 3.3%; inter-assay variation coefficient: 8.6%; sensitivity: 0.1 nmol/L; range: 0.75 – 12.00 nmol/L) - Total T4 (TT4) RIA kit (catalogue number IM 1447, intra-assay variation coefficient: 5.1%; inter-assay variation coefficient: 8.6%; sensitivity: 13 nmol/L; range: 25 - 400 nmol/L).

STATISTICAL ANALYSIS

The statistical processing of the data was performed by ANOVA (Statistica v. 6.1, StatSoft Inc., USA, 2002). All data were presented as mean values ± standard deviation (mean ± SD) and tested for normality by the Kolmogorov-
Smirnov test. The statistical significance of differences between groups was determined by LSD-test of the PostHot comparison of ANOVA. Tree levels of significance were considered: $P < 0.05$: $P < 0.01$ and $P < 0.001$. Pearson test was used for the determination of correlation coefficients between parameters.

## Results

### WEIGHT GROWTH

After early (when rabbits were 21 days old, group A) or normal weaning (when rabbits were 35 days old, group B), the body weights of rabbits gradually increased (Table I); in the both 2 groups, the body weights were significantly and markedly increased compared to the initial weight (recorded the weaning day) at the 14th and the 21st days post weaning and when rabbits were 95 days old (74 days post weaning for the group A and 60 days post weaning for the group B) ($P < 0.001$). However, contrary to the early weaned rabbits, this parameter was also significantly enhanced in rabbits of the group B since the 7th day post weaning ($P < 0.01$). Besides, the body weights measured in normal weaned rabbits were significantly higher than those recorded in the early weaned rabbits for all the time points considered ($P < 0.001$) even when animals had the same age; at 95 days old, the mean body weight in the group B was 1.17 higher than in the group A ($P < 0.001$). Moreover, the growth profiles reflected by the transient body weight gains (calculated for a given period) and the cumulated body weight gains (calculated since the weaning day) deeply differed between the 2 groups: whereas the growth rate was maximal between the weaning day and the 7th day post weaning then decreased and remained constant for the other periods in normal weaned rabbits, the body weight gains of the early weaned rabbits remained low until the 14th day post weaning then dramatically increased between the 14th and the 21st days post weaning and finally decreased again for reaching a growth rate similar to normal weaned rabbits (Table I).

### INSULIN PROFILE

As shown in Table II, the plasma insulin concentrations remained unchanged in the group A until the 21st day post weaning then they markedly and significantly increased at the end of the experimental period compared to the initial values ($P < 0.01$). In group B, the hormone concentrations slowly increased but not significantly until the 14th day post weaning, but they became significantly higher than the basal values on day 7 (14th day post weaning) and on day 60 ($P < 0.001$). Despite these weak variations of the insulin profile between the 2 groups, no significant variation of the plasma insulin concentrations was evidenced between early or normal weaned rabbits.

### IODATED THYROID HORMONE PROFILE

In the group B (rabbits normally weaned), no significant effect of time post weaning was noticed on plasma TT3 and TT4 concentrations (Table II). In the group A, the plasma TT3 concentrations more greatly fluctuated and a significant decrease of the hormone concentrations was noticed at the 7th day post weaning compared to the initial values ($P < 0.05$). In addition, the plasma TT3 concentrations were generally lower in early weaned rabbits than in normal weaned animals (TT3 means (calculated for all time points): 3.12 ± 0.65 for the group A vs. 3.82 ± 1.01 for the group B: $P < 0.01$). As far as plasma TT4 concentrations were concerned, they abruptly ($P < 0.001$) decreased on day 7 after weaning in the

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**Table I**: Body weights and growth rates (body weight gains in g/d) observed in early weaned rabbits (rabbits were 21 days old, group A) and in normal weaned rabbits (rabbits were 35 days old, group B) according to time after weaning. Results are expressed as means ± standard deviations.

<table>
<thead>
<tr>
<th>Days after weaning</th>
<th>Early weaning (group A)</th>
<th>Normal weaning (group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>Body weight (g)</td>
<td>329 ± 52A,a</td>
</tr>
<tr>
<td></td>
<td>BWG 0-7 (g/d)</td>
<td>20.4 ± 5.4A,a</td>
</tr>
<tr>
<td>Day 7</td>
<td>Body weight (g)</td>
<td>472 ± 37A,a</td>
</tr>
<tr>
<td></td>
<td>BWG 7-14 (g/d)</td>
<td>16.9 ± 9.3a</td>
</tr>
<tr>
<td>Day 14</td>
<td>Body weight (g)</td>
<td>590 ± 40A,b</td>
</tr>
<tr>
<td></td>
<td>BWG 0-14 (g/d)</td>
<td>18.6 ± 6.2A,a</td>
</tr>
<tr>
<td>Day 21</td>
<td>Body weight (g)</td>
<td>986 ± 80A,c</td>
</tr>
<tr>
<td></td>
<td>BWG 14-21 (g/d)</td>
<td>56.6 ± 8.2B,c</td>
</tr>
<tr>
<td></td>
<td>BWG 0-21 (g/d)</td>
<td>31.3 ± 6.0b</td>
</tr>
<tr>
<td>Day 74 / 60*</td>
<td>Body weight (g)</td>
<td>2660 ± 72A,d</td>
</tr>
<tr>
<td></td>
<td>BWG 21-74/60 (g/d)</td>
<td>31.6 ± 1.4b</td>
</tr>
<tr>
<td></td>
<td>BWG 0-74/60 (g/d)</td>
<td>31.5 ± 1.6A,b</td>
</tr>
</tbody>
</table>

* BWG: Body weight gain; * this time point corresponds to 74 days post weaning for the group A and to 60 days post weaning for the group B.

**Different superscripts A, B in the same row indicate significant differences ($P < 0.01$ or $P < 0.001$) between the 2 groups.**

**Different superscripts a,b,c,d in the same column indicate significant differences ($P < 0.01$ or $P < 0.001$) according to time for a given parameter.**
group A, then gradually declined and remained significantly \((P < 0.001)\) lower until the end of the experimental period (Table II). Globally, the plasma TT4 concentrations appeared more elevated in the group A than in the group B (TT4 means calculated for all time points): 56.96 ± 3.18 for the group A vs. 41.14 ± 1.85 for the group B: \(P < 0.05\), particularly during the first 2 weeks after weaning; remarkably high plasma TT4 concentrations were recorded at the weaning day in early weaned rabbits compared to normal weaned rabbits \((P < 0.001)\).

**PLASMA EGF CONCENTRATIONS**

Whereas the plasma EGF concentrations remained relatively stable in the group A, a gradual decrease of this parameter was observed in the group B until the 14th day post weaning \((14\text{th} \text{ day vs. weaning day: } P < 0.01)\) and thereafter values increased again for being closely related to the initial EGF concentrations (Table II). During the whole experimental period, plasma EGF concentrations in the group B were markedly higher compared to the group A, the differences being statistically significant on day 0 \((P < 0.05)\), day 21 \((P < 0.001)\) and when animals were 95 days old \((P < 0.05)\). In addition, the mean EGF concentration in normally weaned rabbits was also significantly higher than in early weaned animals (EGF means (calculated for all time points): 11.28 ± 1.86 ng/L for the group A vs. 13.56 ± 2.38 ng/L for the group B: \(P < 0.001\)).

**CORRELATIONS**

The body weights significantly and positively correlated in the group A and in the group B with the plasma concentrations of insulin \((r = 0.72, P < 0.001)\) and \(r = 0.60, P < 0.01\), respectively) and EGF \((r = 0.47 \text{ and } r = 0.41 \text{ respectively, } P < 0.05)\) (Table III). However, it was also positively associated with the plasma TT3 concentrations \((r = 0.49, P < 0.05)\) and negatively with the plasma TT4 concentrations \((r = -0.46, P < 0.05)\) in the early weaned rabbits but not in animals normally weaned.

It was only in the group A that significant and positive correlations were obtained between the concentrations of insulin in one hand and EGF \((r = 0.44, P < 0.05)\) or TT3 \((r = 0.62, P < 0.01)\) in the other hand. By contrast, EGF and thyroid hormones did not correlate together in either group. Finally, a highly significant and positive association between TT3 and TT4 concentrations was evidenced only in the normal weaned rabbits \((r = 0.80, P < 0.001)\).
Early weaning (group A) & Normal weaning (group B) \\
<table>
<thead>
<tr>
<th></th>
<th>Insulin</th>
<th>EGF</th>
<th>TT₃</th>
<th>TT₄</th>
<th>Insulin</th>
<th>EGF</th>
<th>TT₃</th>
<th>TT₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW</td>
<td>r = 0.72</td>
<td>r = 0.47</td>
<td>r = 0.49</td>
<td>r = -0.46</td>
<td>r = 0.60</td>
<td>r = 0.41</td>
<td>r = 0.39</td>
<td>r = 0.10</td>
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<tr>
<td></td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.01</td>
<td>P &lt; 0.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Insulin</td>
<td>r = 0.44</td>
<td>r = 0.62</td>
<td>r = -0.26</td>
<td></td>
<td>r = 0.39</td>
<td>r = 0.23</td>
<td>r = 0.16</td>
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</tr>
<tr>
<td></td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.01</td>
<td>NS</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>EGF</td>
<td>r = 0.23</td>
<td>r = -0.11</td>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td></td>
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</tr>
<tr>
<td>TT₃</td>
<td>r = 0.24</td>
<td></td>
<td></td>
<td></td>
<td>r = 0.80</td>
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<td></td>
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<tr>
<td></td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
<td>P &lt; 0.001</td>
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</tbody>
</table>

BW: Body weight; NS: Not significant.

### Table III: Correlation coefficients between body weights and plasma hormone (insulin, TT₃ and TT₄, EGF) concentrations in early weaned rabbits (rabbits were 21 days old, group A) and in normal weaned rabbits (rabbits were 35 days old, group B).

### Discussion

Early weaning without adapted diet is possible but results in a serious stress because during the first days the young rabbits did not gain weight. According to PIATTONI et al. [28] early weaned rabbits adapt very quickly to rough forage feeding. However, our results demonstrate that there is a marked difference in body mass between early and normal weaned animals at the end of the experimental period: rabbits of group B are 1.17 heavier than those of group A. In addition, the growth rates remained significantly lower in early weaned rabbits compared to the normal controls during the first 14 days after weaning and despite a growth acceleration within the third week (the body weight gain reached 56.6 g/d at this time), the body weight gains measured until the end of the experimental period were also depressed compared to the normally weaned rabbits. These results confirm the negative effect of early weaning on the weight growth in rabbits as shown by FERGUSON et al. [13] and GALLOIS et al. [14], and this delayed growth could also compromise growth rates during the fattening period [35].

As there were no available usual values for plasma EGF concentrations in rabbits, it was assumed that the EGF concentrations measured in normally weaned rabbits in the present study could be considered as physiological values in the post-weaning period. By comparing with these values, it was observed an overall decline of plasma EGF concentrations in early weaned rabbits, particularly at the weaning day, on day 21 and at the end of the experiment. This difference in plasma EGF concentrations between the 2 groups would be related to the higher capacity of EGF endogenous synthesis in normal weaned rabbits which were 2 weeks older than early weaned rabbits and which consequently presented functionally more developed structures as salivary glands and kidneys [4, 11, 21]. Positive and significant correlations were observed in both 2 groups between body weights and EGF concentrations (P < 0.05) suggesting that EGF can partially control the body mass accumulation: indeed, the plasma EGF concentrations gradually declined during the first 2 weeks and were minimal at the 14th day post weaning when the body weight gain between the 7th and the 14th day was also notably depressed in normal weaned rabbits; growth was globally delayed like plasma EGF concentrations in early weaned rabbits. BERSETH [2] has previously shown that normally weaned rat pups exhibited a greater body weight than early weaned pups on the same age. Nevertheless, plasma EGF concentrations dramatically increased over the physiological ranges leads to disproportional and retardant growth because of an exacerbated development of epithelial tissues at the expense of muscles, adipose and bone mass [40].

In the present study, the plasma insulin concentrations remained relatively constant in the 21 days long post weaning period in the early weaned rabbits and were significantly increased compared to initial values only when animals were 95 days old whereas, in the normally weaned controls, the hormone concentrations gradually increased earlier and became significantly increased compared to the initial values since the 21st day. By contrast, a precocious decrease of the plasma insulin concentrations was observed in early weaned rats (the weaning was performed when they were 18 days old) [22]. Consequently the weaning timing appeared to poorly influence the plasma insulin concentrations in rabbits contrary to rats. In addition, insulin concentrations significantly and positively correlated with body weight in early weaned rabbits and in controls. The essential role of insulin in modulating body growth after birth is a consequence of direct effects transmitting via its homologous receptor and post-receptor signalling pathways and indirect effects on other modulators of growth, such as the growth hormone-IGF axis [23]. On the other hand, a significant and positive association between plasma concentrations of insulin and EGF was found in the early weaned rabbits suggesting additive actions of the 2 ligands on growth. Agonistic metabolic actions of insulin and EGF [6, 25] have been found to be due to the similarity of protein-kinase activity in their intracellular receptor region [19, 43] which results in an identical effect on the stimulated cells [7]. However, the interactions between insulin and EGF appeared very transient in normal controls (no positive correlation between the 2 parameters was found) probably because of a simultaneous increase of the endogenous
synthesis of the both 2 hormones, leading to divergent biological actions with the age.

The thyroid hormones are known to promote growth, development and adaptation of animals after birth [8, 34]. The 3, 5, 3’-tri-iodo-thyronine (T3) is the more active thyroid hormone and is mainly produced by extra-thyroidal tissues via deiodination of the outer ring of the 3, 5, 3’, 5’-tetra-iodothyronine (T4) also named thyroxin [3]. Significantly lower mean TT3 concentration was evidenced in early weaned rabbits than in normally weaned controls, indicating that the early weaning has negatively influenced the extra-thyroidal deiodination of the outer ring of the 3, 5, 3’, 5’-tetra-iodothyronine and is mainly produced by extra-thyroidal tissues via 5, 3’-tri-iodothyronine (T3) is the more active thyroid hormone and is mainly produced by extra-thyroidal tissues via 5, 3’-tri-iodothyronine. In agreement with that, a significant negative correlation between TT3 and body weight in early weaned rabbits proves the marked effect of thyroid hormones on body mass accumulation. The strong positive correlation between TT3 and TT4 concentrations only observed in normal weaned rabbits indicates a functional maturation of thyroid gland which is very important for postnatal growth and development. Probably the weaning in an earlier stage of life is a stress factor for rabbits, leading to a massive T4 thyroidal secretion coupled to an inefficient thyroxin conversion into rT3 (3, 3’, 5’-tri-iodo-thyronine). In agreement with that, a significant negative correlation between TT4 and body weight was found in the group A. Consequently, the early weaning of rabbits has negatively influenced the thyroid gland function. Nevertheless, the thyroid activity also depends on other factors such as the concentrations of TRH, TSH and iodine in dam’s colostrum and milk and the lack of these substances in earlier stage of life could partially explain the observed changes.

It was established that the administration of EGF in rabbits had no effect on serum tri-iodo-thyronine (T3) and total and free thyroxin (TT4 and FT4) concentrations [26]. However, in sheep a dual inhibitory effect of EGF on both thyroid hormone secretion and peripheral metabolism was found [9]. In the present study no correlation between EGF and thyroid hormones was found in early and normal weaned rabbits, confirming in this way the lack of interaction between plasma EGF and thyroid hormone concentrations [26]. In addition, we found that this relationship is independent of weaning age of rabbits. Probably, the relationship between iodoated thyroid hormones and EGF would be species specific and this fact might explain the results observed in sheep. Surprisingly, insulin and TT3 concentrations significantly correlated positively in the group A but not the in group B. In rats, the effects of the thyroid hormones on IGF-I secretion has been found to be age-dependent and mainly mediated by insulin during the neonatal period and by GH in adult [31]. The occurrence of the interaction between insulin and TT3 in early weaned rabbits could be a stress induced compensatory mechanism.

In conclusion, the results indicate that the early weaning negatively affects the rabbit’s growth because of the immaturity of the compensatory mechanisms, leading to depressed body mass in early weaned animals. The detection of EGF in plasma and its variable associations with iodoated thyroid hormones, insulin and body mass in early and normal weaned rabbits shows that in addition to its paracrine and autocrine effects, this growth promoting factor also exhibits some endocrine actions which the intensity is depending on the age of weaning.

References