Amyline Hormone, Leptin and Other Metabolic Hormones in Preterm Babies

1Adham Hegazy, 1Maha Awadalla, 2Salwa El-Batrawy, 3Abeer Abdel-Mageed and 1Ahmed Eleswed

1Pediatric Dept. and 1Clinical Pathology Dept, Ain Shams University and 2Biologic Anthropology Dept, National Research Center in Cairo

Abstract: Prematurity is a growing problem, advances in life supporting techniques have resulted in increased survival of more preterm neonates whom we expected to die before. Those preterm babies have several problems and on the top of these problems comes metabolism. Amylin is a recently discovered neuropeptide hormone from the calcitonin gene-related peptide. It is co-secreted with insulin by direct activation of the prestema area where the

INTRODUCTION

Prematurity is defined as gestational age less than 37 weeks. Estimated incidence of prematurity is 10% of which 4% are less than 32 weeks of gestation[4].

Leptin hormone is an adipocyte derived hormone. It is involved in body weight regulation. A dramatic increase in serum leptin after 34 weeks of gestation associates the rapid accumulation of fetal fat mass during this period. It was noticed that there is decline in the level of leptin in full term neonates after delivery and this allows preservation of energy expenditure in these neonates; however, in preterm neonates, leptin level remains high[2].

Insulin is secreted by beta cells of pancreatic islands of Langerhans. It increases fat deposition and decreases lipolysis, glycogenolysis and gluconeogenesis[5]. Insulin has an indirect effect on leptin by exerting a negative feedback on cortisol secretion[5].

Cortisol hormone is secreted from Zona Fasciculata of the adrenal cortex. It stimulates gluconeogenesis by decreasing glucose utilization, increasing protein catabolism and lipolysis[5]. It has a positive feedback on the secretion of leptin[3].

Amylin is a recent hormone derived from the calcitonin gene related peptide. It is co-secreted with insulin from pancreatic beta cells in response to nutrient intake[4]. Amylin is a potent inhibitor of gastric motility and plays a role in controlling carbohydrate absorption by regulating the efflux from the stomach to the small bowel. In addition to this local effect, there is evidence that amylin has neuroendocrine effect influencing glycemic control, satiety and long-term energy homeostasis[5]. Amylin plays its satiating effect by direct activation of the prestema area where the
nucleus of the solitary tract relays its effect to the higher brain structures controlling the appetite and inducing satiety. Hence the name; neuropeptide hormone [6].

**Aim of the Work:** The aim of this work is to determine the levels of Amylin, leptin and other metabolic hormones namely cortisol and insulin in preterm neonates to establish the relationship of these hormones with both adipo-insular axis and hypothalamic-adrenal axis compared to full-term neonates.

**Materials and Methods**

This study is a case-control cross-sectional which was conducted in Neonatal intensive care unit at Ain Shams University Hospital, Cairo in the period June 2006 to August 2006. Newborn babies were divided into two groups. Patient group (Group 1) comprised 30 preterm neonates (gestational age 32-36 wk). Second group was the control group (Group 2) comprised 15 full term newborn babies (gestational age 37-41 wk).

All babies were subjected to full history taking including prenatal, natal, and postnatal histories with thorough clinical examination. Routine lab tests e.g. CBC, C-reactive protein, electrolytes, random sugar, and blood culture were done to all participant newborns.

Both groups of newborns were subjected to simultaneous assessment of blood glucose level, amylin, cortisol, insulin, and leptin in cord blood; while the premature group ONLY (Group 1) were subjected to another simultaneous assessment of blood glucose level, cortisol, insulin and leptin on DAY 5 of life. Collection of blood in day 1 was done through the umbilical cord while a venipuncture under complete aseptic technique was used in day 5 to collect blood. Hormonal levels were determined using immunoassay techniques.

Statistical analysis of obtained data was carried out using SPSS version 11.5 to determine mean values with standard deviation and correlation coefficient.

**Results and Discussions**

**Results:** There was no statistical difference between both groups regarding sex distribution (in preterm group 1 there was 16 M and 14 F while in full term group 2, there was 7 M and 8 F).

As shown in Table 1, the amylin level in day 1 was statistically lower in preterm babies GROUP 1 (1.721 ± 1.41 Pmol/l) when compared to full term newborns GROUP 2 (3.517 ± 2.245 Pmol/l) with p value of <0.001. We found also significant correlation between amylin level in day 1 for the preterm GROUP 1 and serum glucose level being the higher the glucose level the higher the amylin level (r = 0.417 and p = 0.043) as seen in Figure 1.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Pre-terms (cases)</th>
<th>Full term (controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylin</td>
<td>-1.721(Pmol/l)</td>
<td>3.517(Pmol/l)</td>
</tr>
<tr>
<td>Level</td>
<td>±1.410</td>
<td>±2.245</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td></td>
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</tbody>
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The insulin level of preterm babies “GROUP 1” in both days 1 (9.346 ± 4.996 µU) and day 5 (7.833 ± 2.717 µU) was higher than in full term babies “GROUP 2” (6.571 ± 1.869 µU) in day 1 but this difference was not statistically significant (Table 2). Also the difference between the two levels in days 1 and 5 among the premature GROUP 1 was not statistically significant.

The mean level of serum leptin in the premature newborns “GROUP 1” in day 1 (5.937 ± 4.15 ng/ml) was statistically higher than the mean serum leptin level in the full term newborns “GROUP 2” in day 1 (3.78 ± 3.338 ng/ml) with p value of < 0.044 as shown in Table 3. Although the serum leptin level in day 5 for the premature newborns “GROUP 1” (4.753 ± 3.776 ng/ml) is still higher than that of full term newborns “GROUP 2” mentioned above but this difference was not statistically significant with p value of < 0.448. The decrease in serum leptin level from day 1 to day 5 in the preterm GROUP 1 was not statistically significant (p = 0.102).

The study also showed that the higher the leptin level the lower the glucose level in both days 1 and 5 in the premature GROUP 1 and in day 1 for the full term GROUP 2 but this correlation was not statistically significant.

Our study also showed that the higher the body weight among the full term newborns “GROUP 2” the lower is the serum leptin level and this correlation was statistically significant (r = -0.2 and p = 0.026) as seen in Table 4 and Figure 2. The same correlation was found in the premature GROUP 1 when correlating leptin level in day 1 to the birth weight of these babies (Figure 3).

The mean level of cortisol of the premature newborns “GROUP 1” in day 1 (5.366 ± 3.24 µg/dl) was lower than that of the full term GROUP 2 in day 1 (15.3 ± 9.096 µg/dl) and this difference was highly...
Fig. 1: Scattered curve showing the correlation between amylin hormone level and glucose level in Preterm neonates.

Fig. 2: Scattered chart showing the correlation between gestational weight and leptin hormone level in full term neonates (r=0.208, P=0.026).

Fig. 3: Scattered chart showing the correlation between gestational weight and leptin hormone level in preterm neonates.
Blood glucose is the major energy source for all tissues, and maintaining a normal glucose homeostasis is critical for efficient energy metabolism. Glucose homeostasis depends on interplay of endocrine and metabolic or enzymatic processes that control glucose uptake and utilization, as well as glucose production during periods of fasting and feeding to ensure a continuous supply. Premature infants and low birth weight babies have slightly lower glucose levels than full term infants\(^{[9]}\).

Amylin and insulin are produced by $\beta$ cells of Langerhans in response to hyperglycemia and through two complete different mechanisms. On the other hand, counter-regulatory hormones like cortisol and glucagon aim to elevate blood glucose when it declines below normal levels. Amylin lowers glucose level through different mechanisms; first by acting centrally to induce satiety, also it diminishes glucagon and digestive enzymes secretion and finally by restraining rate of gastric emptying and thus control nutrient appearance and postprandial glucose concentration\(^{[9]}\).

We found statistically higher level of amylin in full term GROUP 2 babies when compared to premature GROUP 1 and we found also the higher the glucose level the higher the amylin level in both groups. We postulate that this statistically significant difference in amylin level between both groups is attributed to the difference in blood glucose level between the two groups being higher in full term babies. Kariamkonda\(^{[9]}\) found similar results when serum amylin level was higher among a group of infants of diabetic mothers when compared to healthy newborns and they assumed that the higher level of blood glucose to which IDM babies were exposed stimulated release of amylin hormone. In the same way, Fineman\(^{[9]}\) studied amylin level in a group of IDM babies and found a higher level of amylin hormone in babies born to mothers with poorly controlled diabetes and assumed that this might be caused by high level of glucose which again agrees with the fact that amylin hormone is secreted in response to hyperglycemia\(^{[9]}\).

Although not statistically significant, insulin level was higher among the premature GROUP 1 in both days 1 and 5 when compared to full term GROUP 2.
due to increase need of insulin in premature babies to enhance glycogen and protein storage and spares fat stores in these smaller babies.

Leptin is a hormone which has been the focus of many researches over the last two decades. It plays a role in metabolism and energy expenditure. Higher levels of leptin reduces food intake, increases energy expenditure and hence weight loss, It is now clear that leptin is involved in glucose metabolism and functions as a metabolic and neuroendocrine hormone[10].

The present study showed that serum leptin level was higher among preterm GROUP 1 when compared to full term GROUP 2 in day 1 and this difference was statistically significant. This is in agreement with Schubring who found higher level of leptin among preterm infants than in full term ones and then a decline of its level in preterm infants with improvement in feeding and weight gain[11]. The lower level in full term infants coincides with preservation of energy expenditure and increase in body weight while the higher level in preterm neonates might contributes to their poor feeding and poor weight gain and this coincides with the role of leptin in energy expenditure and weight gain[10].

In our study, there was no statistically significant difference in correlating serum leptin with glucose level. Most probably, it seems that the role of leptin in controlling blood glucose level is indirect. The role of leptin is more evident in affecting satiety and energy expenditure and this mechanism may in turn affects blood glucose level.

In our study, cortisol level was highly statistically significant to be lower in premature GROUP 1 when compared to full term GROUP 2. The level of cortisol in preterm infants shows ascending pattern and got higher by day 5 but still lower than full term day 1 level but no statistically significant difference at this time. Jonetz et al[12] detected the same finding of increase in cortisol level with age and this was attributed to maturation of adrenal cortex and probably better response to stress as the age advances[12]. Another study showed that premature babies had lower basal cortisol level in response to stress when compared to full term newborns exposed to the same stress[13].

We can conclude that there is a highly complex process involving the interaction of metabolic hormones and their roles in the regulation of glucose homeostasis, weight gain and growth of newborns whether preterm or full term babies. Further studies are needed to assess the maturation of these hormones with age in relation to body metabolism and growth and probably discovery of new hormones interacting with these recent hormones.

REFERENCES
