CLINICAL STUDY

Growth and obesity and its association with plasma level of steroid hormones and insulin-like growth factor-I (IGF-I) in Slovak female students

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Abstract: The aim of the present study was to examine the possible role of steroid hormones and insulin-like growth factor 1 (IGF-I) in the control of human growth and obesity. We measured plasma level of progesterone, testosterone, estradiol and IGF-I in 301 young women at different stages of their ovarian cycle, and compared them to the standard morphometric indexes of their growth and obesity - body height, body weight, abdomen circumstance and waist to hip ratio (WHR). The ovarian cycle-dependent changes in plasma progesterone and estradiol, but not in testosterone and IGF-I level were found. Young women with higher body height had significantly higher plasma level of estradiol, testosterone and IGF-I, but not of progesterone, compared to subjects with lower body height in both follicular and luteal phases of the ovarian cycle. Subjects with a higher body weight had significantly higher plasma estradiol and progesterone, but not testosterone and IGF-I than subjects with lower body weight in both follicular and luteal phases of ovarian cycle. Women with a higher abdomen circumference had significantly lower plasma estradiol, but not the other hormones than the subjects with lower abdomen circumference. Women with higher WHR index had significantly higher plasma level of estradiol, but not other hormones than subjects with lower WHR index in both follicular and luteal phases of ovarian cycle. The present observations suggests: (1) that luteal phase of the women ovarian cycle is characterised by a dramatically increase in both progesterone and estradiol, but not in testosterone and IGF-I release, (2) that in human females growth can be up-regulated by testosterone, estradiol and IGF-I, but not by progesterone, (3) that body mass can be up-regulated by progesterone and estradiol, but not by testosterone or IGF-I, and (4) that women obesity (high WHR, but not abdomen circumference) can be promoted by estradiol, but not by other steroid hormones or IGF-I (Tab. 1, Fig. 4, Ref. 45). Full Text in PDF www.elis.sk. Key words: growth, obesity, estradiol, testosterone, progesterone, IGF-I.

Growth and development of the individuals is a dynamic phenomenon, which is regulated by a complex of internal (genes, hormones) factors. The second decade of human life is characterized by many significant changes (morphological, psychological, social and economic). Physiological changes include rapid physical growth, endocrine (hormonal) changes, termination of

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Growth of organism is under control of growth hormone, which stimulates insulin-like growth factor I (IGF-I) and under the control of gonadal steroids – estrogens and androgens, whose promote growth hormone release and the local production of IGF-I (Pescovitz et al, 1985).

Estradiol is the main female steroid hormone, which belongs to estrogen family (Mathews et al, 1999). Estradiol targets mainly reproductive organs, but also stimulates bone growth during the "pubertal jump" (Creager, 1992). There are publications demonstrating a positive association of a higher estradiol level with a higher body height and body weight in premenopausal (Dorgan, 1995, Finstad, 2009) and fertile (De Pergola, 2006) woman, as well as an association of a higher estradiol level with lower WHR (Waist to hip ratio) value in premenopausal woman (Jasienska, 2004). WHR is an appropriate indicator of body fat content (Park et al, 2002; Suh et al.; 2002), which is widely used as a convenient index of abdominal obesity (Pouliot et al, 1994; Ross et al, 1992) and related metabolic syndrome (Hollmann et al, 1997).

Testosterone is a steroid hormone, which belongs to androgen family (Mathews et al, 1999). Testosterone plays a fundamental role in development and maintenance of reproductive tissues and

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growth in both men and women (Mooradian et al, 1987). There are reports on the association of a higher testosterone level with higher body weight and high WHR value in premenopausal women (Sowers, 2001, Pasquali et al, 1991, Van Anders and Hampson, 2005) and obese women (Kirschner, 1990).

Progesterone is a female sex hormone, which belongs to the group of progestagens (Stanczyk, 2002). There are publications demonstrating the association of a higher estradiol level with higher body height and body weight in both premenopausal and premenopausal women (Vitzthum, 2002, Lager and Ellison, 2005), as well as the negative association of a higher progesterone level with lower WHR level in premenopausal women (Jasienska, 2004).

IGF-I is a peptide hormone, an important extracellular mediator of growth hormone and gonadotropins effects (Schams et al, 1999, Werner and LeRoith, 2000). There are publication demonstrating stimulatory effect of IGF-I on growth in rats (Liu et al, 1993) and people (Melmed and Cohn, 2005).

The examination of the association between hormone level with their possible target processes, such as growth and obesity is a popular approach to understand hormonal mechanisms regulating these processes. There are only few published data suggesting the association of steroid hormones and IGF-I with growth and obesity. Furthermore, the results of these studies are not always consistent and inconclusive. There are practically no data concerning the involvement of hormones in the control of growth and metabolism in the most important, adolescent period. Some data concerning the association of hormone levels and indicators of growth and obesity in young people are completely missing. The associations of estradiol level with obesity indicators, such as abdomen circumference, associations of testosterone level with body height and abdomen circumference, associations of progesterone level with abdomen circumference and associations IGF-I level with abdomen circumference and index of WHR has not been studied yet. This suggests the importance of further studies, whose could provide the missing information concerning the associations between steroid and peptide hormone release and individual indices of growth and obesity in youth.

The aims of this work was to determine the plasma levels of steroid hormone and IGF-I in Slovak students girls in different stages of ovarian cycle, as well as to examine a possible association between plasma levels of these hormones and common morphological indices of growth and obesity (body height, body weight, abdomen circumference, index of WHR) in these women.

Materials and methods

The subjects, morphological measurements and blood collection

The subjects of our studies were 301 young Slovak women aged 19–20, students of the Faculty of Natural Sciences, Constantine the Philosopher University in Nitra, originating from different regions of Slovakia. All participants gave their informed consent for participation in the study, which was carried out in accordance with the Helsinki Declaration of 1975. The morfometric methods for determining body proportion used in our studies were consistent with common methods of standard anthropometry (Martin, Saller, 1966;

Tab. 1. Categories of women WHR index and their relation to health risk (Svačina, 2000; Komárek, 2007).

Index of central obesity (Waist hip ratio, WHR)	
Waist circumference (cm)	x 100 / gluteal hip circumference (cm)
Category of WHR	Type of fat distribution
<0.85	more peripheral, ideal, no risk
0.85-0.90	sedately, low risk
0.90-0.95	more central, moderate risk
>0.95	central, high risk

Fetter et al, 1967). Somatometric characteristic were measured using the following instruments: digital scale, anthropometer and tape measure. Body height, body height, abdomen circumference and index of central obesity (Waist to hip ratio, WHR) were measurement with 0.1 cm accuracy, the accuracy of body weight measurement was 0.1 kg. At the basis of the measured morphological parameters and type of fat distribution, we calculated the WHR index (Komárek, 2007) and resulted health risk (Svačina, 2000) (Tab. 1).

We divided the studied individuals into the two groups (a group of young women with above-average and below-average) according to value of each morfometric index and WHR. In addition, in each person, we determined the levels of steroid hormones and IGF-I in blood plasma (see below).

Before collection of blood, each person completed the questionnaire, where she indicated the date of the last menstruation to determine the actual phase of the ovarian cycle. On the basis of the phase of ovarian cycle, the studied subjects were divided into two groups (women in the follicular and luteal phase of ovarian cycle). Subjects in ovulation phase of ovarian cycle were excluded from the studies.

A blood sample was collected from all the fasting probands in the morning hours (8–10 a.m.), in sterile tubes with heparin, under the supervision of qualified medical personnel, in accordance with ethical regulations of the SR on biomedical research, and written informed consent of all the participants. All procedures were approved by the Ethics Committee of Hospital in Nitra (Slovak republic). After collecting, the blood was centrifuged x300g, and obtained plasma was frozen at -70°C until the analysis was performed.

Determination of hormones in blood plasma

Blood samples were subsequently transferred to the Animal Production Research Centre, Nitra, where they were analysed. After thawing, we determined the steroid hormones and IGF-I hormone levels in blood samples by using commercial RIA or IRMA kits as described below. All analytical kits were designed to determine the corresponding molecules in human blood. They contained the reference plasma samples for validation of the measured values and calibration curves. All the samples were analysed in duplicates.

Determination of estradiol

Concentration of estradiol in blood plasma was determined by RIA using the commercial kits from Imunotech (Marseille, France) according to the instruction of manufacturer. Sensitivity of the assay was 6.0 pg/ml. The intra- and inter-assay coefficients of variation were 12.1 % and 11.2 % respectively.

Determination of testosterone

The concentration of testosterone was determined by RIA using the commercial kits from Imunotech according to the guidelines of manufacturer. Sensitivity of the assay was 0.025 ng/ml. The intra- and inter-assay coefficients of variation were 14.8 % and 15.0 % respectively.

Determination of progesterone

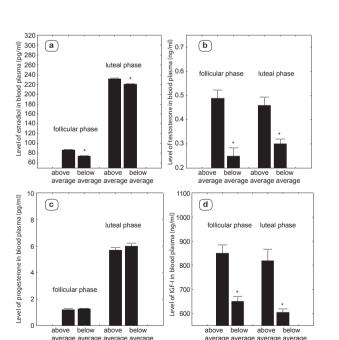
Concentration of progesterone in blood plasma was determined by RIA using the commercial kits from Imunotech according to the instruction of manufacturer. Sensitivity of the assay was 0.05 ng/ml. The intra- and inter-assay coefficients of variation were 5.8 % and 9.0 % respectively.

Determination of IGF-I

Concentration of IGF-I in blood plasma was determined with acid-ethanol extraction by using IRMA kits from DSL (Webster, TX, USA) according to the instruction of manufacturer. Sensitivity of the assay was 0.3 ng/ml. The intra- and inter-assau coefficients of variation were 3.4% and 8.2% respectively.

Statistical analysis

As mentioned above, morphological indexes enabled us to divide all the studied subjects into the two groups, with aboveaverage and below-average values of indexes of growth and obesity. In all groups, we evaluated the plasma level of hormones and calculated the average \pm S.E.M in each group. Due to ovarian cycle-dependent changes in hormone level, subjects at follicular



and luteal phases of cycle were analysed separately. Differences in hormone level between the groups were determined by using the computer software Statistica 7 (Statsoft, Prague, Czech Republic). Differences at levels * $p \le 0.05$, ** $p \le 0.01$ or *** $p \le 0.001$ were considered as significant.

Results

The association between phases of ovarian cycle and plasma hormone levels

In the follicular phase of ovarian cycle were 47.12 % (n=49) of studied women. In the luteal phase of ovarian cycle were 52.88 % (n=55) of subjects. The level of estradiol in the follicular phase of ovarian cycle (80.10 ± 2.55 pg/ml) in young women was significant lower (p<0.001) than in the luteal phase (226.05 ± 3.31 pg/ml). No significant differences between the level of testosterone in the follicular (0.37 ± 0.07 ng/ml) and luteal (0.37 ± 0.06 ng/ml) phase of ovarian cycle were found. The level of progesterone in the follicular phase of ovarian cycle (1.23 ± 0.27 pg/ml) in young women was significantly lower (p<0.001) than in the luteal phase of the cycle (5.97 ± 0.67 pg/ml). No significant differences between the follicular (850.39 ± 19.20 ng/ml) and luteal (848.55 ± 18.03 ng/ml) phase of ovarian cycle in plasma IGF-I level were found.

The association between plasma hormones level and body height

Levels of hormones during both follicular and luteal phase of ovarian cycle in subjects with above-average and below-average body height are shown on the Figure 1.

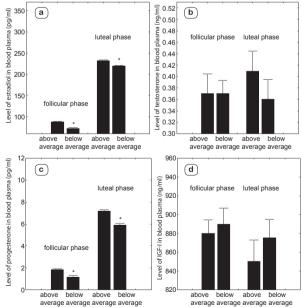


Fig. 1. Level of a) estradiol, b) testosterone, c) progesterone and d) IGF-I hormone in blood plasma of young women with above-average and below-average body height, respectively. Values are the mean \pm S.E.M. * significant difference between groups of subjects with above-average and below- average body height in the same phase of ovarian cycle.

Fig. 2. Level of a) estradiol, b) testosterone, c) progesterone and d) IGF-I hormone in blood plasma of young women with above-average and below-average body weight, respectively. Values are the mean \pm S.E.M. * significant difference between groups with above-average and below- average body weight in the same phase of ovarian cycle.

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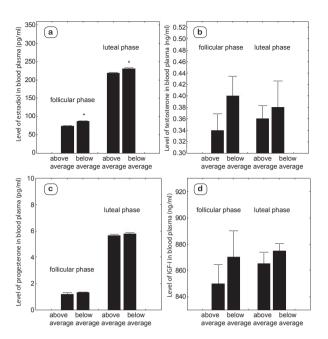


Fig. 3. Level of a) estradiol, b) testosterone, c) progesterone and d) IGF-I hormone in blood plasma of young women with above-average and below-average abdomen circumference, respectively. Values are the mean \pm S.E.M. * significant difference between the groups in the same phase of ovarian cycle.

The level of estradiol (Fig. 1a), testosterone (Fig. 1b) and IGF-I (Fig. 1d) was significantly higher in women with above-average body height (n=165; 54.81 %) than in women with below-average body height (n=136; 54.18 %). These differences occurred in both follicular phase (p<0.05) and luteal phase (p<0.05) of ovarian cycle.

No significant differences between women in above-average body height and below-average body height in both phases of ovarian cycle in plasma progesterone level (Fig. 1c) were found.

The association between plasma hormones level and body weight

The levels of hormones during the follicular and luteal phase of ovarian cycle in subjects with above-average and below-average body weight are shown on Figure 2.

The level of estradiol (Fig. 2a) and progesterone (Fig. 2c) was significantly higher in women with above-average (n=143; 47.51 %) than in subjects with below-average (n=158; 52.49 %) body weight. These differences occurred in both follicular phase (p<0.05) and luteal phase (p<0.05) of ovarian cycle.

No significant differences between the groups in both phases of ovarian cycle in plasma testosterone level (Fig. 2c) and IGF-I level (Fig. 2d) were found.

The association between plasma hormones level and abdomen circumference

The levels of hormones during the follicular and luteal phase of ovarian cycle in subjects with above-average and below-average abdomen circumference are shown on Figure 3.

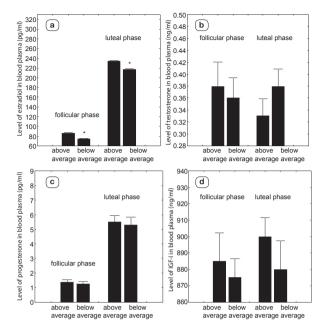


Fig. 4. Level of a) estradiol, b) testosterone, c) progesterone and d) IGF-I hormone in blood plasma of young women with above-average and below-average WHR index, respectively. Values are the mean \pm S.E.M. * significant difference between the groups in the same phase of ovarian cycle.

The level of estradiol (Fig. 3a) was significantly higher in women with below-average abdomen circumference (n=158; 52.49 %) than in women with above-average abdomen circumference (n=143; 47.51 %). These differences occurred in both follicular phase (p<0.05) and luteal phase (p<0.05) of ovarian cycle.

No significant differences between the above-average and below-average abdomen circumference groups in both phases of ovarian cycle in plasma testosterone level (Fig. 3b), progesterone (Fig. 3c) and IGF-I level (Fig. 3d) were found.

The association between plasma hormones level and WHR index

The levels of hormones during the follicular and luteal phase of ovarian cycle in subjects with above-average and below-average WHR index are shown on Figure 4.

The level of estradiol (Fig. 4a) was significantly higher in women with above-average WHR index (n=151; 50.17 %) than in women with below-average WHR (n=150; 49.83 %). These differences occurred in both follicular phase (p<0.05) and luteal phase (p<0.05) of ovarian cycle. No significant differences between the groups with above-average and below-average WHR in both phases of ovarian cycle in plasma testosterone level (Fig. 4b), progesterone (Fig. 4c) and IGF-I level (Fig. 4d) were found.

Discussion

Are there any relations between hormone levels and phases of ovarian cycle?

The values of plasma hormones levels in human plasma were

within standard values reported by the manufacturer RIA kits and the previous investigators of hormones in women plasma (Neal, 2000; Pospíšil, 2002; Skalba, 2003; Silbernagl and Despopoulus, 2004).

In our experiments, a dramatic rise in both progesterone and estradiol, but not in testosterone and IGF-I level occurred in women after a transition from follicular to luteal phase. This observation corresponds the previous reports on an increase in plasma the level of progesterone and estradiol (Neal, 2000; Silbernagl and Despopoulus, 2004), but not of testosterone (Skalba, 2003) in the luteal phase of human ovarian cycle, when formation of corpus luteum is associated with an increase in ovarian steroidogenesis. We are probably the first, who studied the ovarian cycle-associated changes in plasma IGF-I.

Are there any relations between body height and hormone levels in blood plasma?

The association between higher levels of estradiol and higher body height in premenopausal women (20–40 years old) (Dorgan et al, 1995, Finstad et al, 2009) and in pubertal women (Pescovitz et al, 1985) was reported previously. In our studies, young women with above average body height had a higher estradiol level then women with below average body height. Our results correspond the observations on pre- and pubertal women published; previously. Moreover, is the first demonstration of a similar association between the estradiol level and body height in young women. Our results together with previous observations suggest that estrogen can promote growth in women in different ages.

Study Pescovitz et al (1994) demonstrated the association of higher testosterone level with higher body height in pubertal boys. In our work, we found significantly higher testosterone level in young women with high body height. We are probably the first who demonstrated the association of plasma testosterone level with growth, and, therefore, the possible stimulatory action of androgen on women growth.

Study Vitzthum et al (2002) demonstrated the association between higher progesterone level with higher body height in premenopausal woman (average age: 28 years) from Bolivia. On the contrary, in our work, we didn't find the association of progesterone level with body height in Slovak young women. Therefore, our results didn't demonstrate the involvement of progestagen in control of women growth, however it is not to be excluded, and that the role of this hormone can depends on age and ethnic of observed women.

Studies Liu et al (1993), Melmed and Conn (2005) demonstrated the stimulation effect of IGF-I on the growth of rats and of small children, respectively. However, to our knowledge, our work is the first demonstration of the association between plasma IGF-I level and growth in mature people. We found significantly higher IGF-I level in women with higher body height. Our results confirmd the role of IGF-I in up-regulation of human growth.

Overall, our results confirm and expand the data obtained previously suggesting that estradiol is involved in growth control in pubertal, young and premenopausal woman, testosterone is involved in growth control in boys and young women, IGF-I is involved in growth control in rats, small children and young woman. Furthermore, this is the first demonstration that testosterone and IGF-I are involved in growth control in young woman.

Are there any relations between body weight and hormone levels in blood plasma?

According to the results reported by De Pergola et al (2006), these lower levels of estradiol could be associated with higher body weight in obese premenopausal women (average age: 30 years). On the contrary, in our study estradiol level was significantly higher in young healthy women with above average body weight. Our observations, as well as the observations of De Pergola et al (2006), indicated the interrelationships between plasma estrogen and body weight, and, therefore, involvement of this hormone in control of body mass. On the other hand, the pattern of this interrelationships observed by us and De Pergola et al (2006) are opposite. These differences might be explained by various estrogen functions in body weight regulation in normal and obese women and/or in women in different ages.

The results reported by Sowers et al (2001) demonstrated an association between higher testosterone levels and higher body weight in premenopausal women (25–50 years old). In our study on younger girls, we didn't find a relation between testosterone levels and body weight. They suggested that in young women, in contrast to older ones, testosterone might not be involved in body weight regulation.

The results published by Lager and Ellison (1990) demonstrated the association between lower progesterone levels and lower body weight in premenopausal women (average age: 29 years). In our study, we observed significantly increased progesterone levels in younger women with an above average body weight. Therefore, our results confirmed the observations of Lager and Ellison (1990). Our and previous results suggested that progesterone can be a promoter of body weight not only in older, but also in young women.

There is no published data concerning the relation between IGF-I levels and body weight. Such relations were not been found in our studies, too. These results suggest that IGF-I is probably not involved in body weight regulation.

Overall, our main results confirm and expand the observations of our predecessors suggesting that estradiol and progesterone are involved in body weight regulation in both young and premenopausal women. Furthermore, our observations provide the first evidence that testosterone and IGF-I aren't involved in growth regulation in young women.

Are there any relations between abdomen circumference and hormone levels in blood plasma?

Mayes and Watson (2004) demonstrated an association between higher estradiol levels and higher abdomen circumference in postmenopausal women. In our study, we found that plasma estradiol level was significantly higher in subjects with low abdomen circumference values. Therefore, results of both our studies and of Mayes and Watson (2004), indicated the association between estrogens and abdominal circumference. On the other hand, these two studies demonstrated different interrelations between estradiol

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levels and abdominal circumference. This differences could be due to different age of the studied subjects. It is not to be excluded that stradiol can decrease abdominal circumference in young subjects and increase it in postmenopausal women.

In the available literature we did not find data on the relation between testosterone, progesterone and IGF-I and abdomen circumference. In our study, we didn't find any significant difference in the testosterone, progesterone and IGF-I levels between the subjects with low and high abdomen, which indicated that these hormones weren't involved in the regulation of abdominal circumference.

Overall, our results, together with few relevant published data, suggest that estradiol is involved in the regulation of abdomen circumference in young and premenopausal women. Furthermore, it is the first evidence that testosterone, progesterone and IGF-I aren't involved in the regulation of abdominal circumference in young women.

The relation between WHR index and hormone levels

Jasienska et al (2004) demonstrated a negative relation between plasma estradiol levels and WHR index in premenopausal women (age average: 29 years). On the contrary, in our study, we found that estradiol levels were significantly higher in the group of subjects with above average WHR index. The available differences could be due to age-dependent changes in the role of estradiol in obesity regulation during individual development.

The results of several previous studies demonstrated the positive relation between higher testosterone levels and higher WHR index values in morbidly obese women (Kirschner et al, 1990) and premenopausal women (Pasquali et al, 1991; Van Anders and Hampson, 2005). In our study, we didn't find a relation between testosterone levels and WHR index, i.e. we did not confirm the previous data on involvement of androgen in control of obesity. The discrepancy between the obtained results can be due to differences in metabolic state (our study group was represented mainly by non-obese types with more peripherally distributed fat with low or without health risks) and age of studied women. Our observations suggested that in young women, unlike in older and obese women, testosterone presumably wasn't involved in obesity regulation.

The results obtained by Jasienska et al (2004) demonstrated also an association between higher progesterone levels and low WHR index values in premenopausal women. In our study, we didn't find any interrelationships between these parameters, and therefore we did not demonstrate the involvement of progesterone in control of obesity in young women. The differences between our observations and observations of Jasienska et al (2004) could be due to different ages women observed in different studies.

In the available literature we didn't find any publications concerned relation between IGF-I levels and WHR. In our study, no such association was found too suggesting that IGF-I is not directly involved in control of obesity in young women.

Altogether, the available observations suggest that estradiol, but probably not testosterone, progesterone or IGF-I can be involved in control of women obesity.

Possible interactions between several observed indexes and their practical impact

The association between growth rate and plasma levels of the estrogen, progestogen, and IGF-I may be explained by the ability of steroid hormones to stimulate release of growth hormone which in turn stimulates the local production of IGF-I, promoter of cartilage growth (Pescovitz et al, 1985, Martel-Pelletier et al, 1998, Goldenberg and Barkan, 2007). Our observations suggest that IGF-I may mediate growth-promoting affect not only of androgens but also of estrogens and progestagens. Moreover, growth regulation via mutual functional interrelationships between estrogens, androgens and progestagens (as precursors, metabolites and object of feedback regulation) (Silbernagl and Despopoulos, 2004) could not be excluded. Anyway, our observations confirm and expand existing data concerning interaction between steroid hormones, peptide hormones (GH/IGF-I), growth, stature development and obesity in young women.

Better development of adipose tissue and more frequent occurrence of obesity in women versus men could be associated with sexual dimorphism in production of steroid hormones. Adipose tissue is involved in conversion of androgens to estrogens. This role of adipose tissue may explain the association between higher body weight, higher levels of estradiol but lover of testosterone in the blood plasma (Price et al, 1998, Powder et al, 2006). On the other hand, the association of higher estradiol level with below-average abdomen circumference observed in our studies suggests that estradiol in young women participate in formation the female stature. Thus, the association of body weight and abdomen circumference with serum estradiol should be considered separately, but not as a comprehensive indicator of a single process.

An explanation the interrelationships between morphological indexes and hormones could be complicated by several different factors affecting these indexes. For example, WHR rate depends on growth, body mass and obesity, whose can be develop independently under control of different regulators. For example, Zambarano and Singh (1997) demonstrated, that androgenicity in women is associated with a higher WHR, independently of body weight. Similarly, in our studies, the increased levels of estradiol was associated with an increased WHR value, but also with increased body weight and body height, factors whose have an opposite action on WHR value.

The association between growth, body mass, obesity and hormones provides evidence for hormonal regulators of these processes. Our observations suggest (1) that in young women growth can be up-regulated by testosterone, estradiol and IGF-I, but not by progesterone, (2) that body mass can be up-regulated by progesterone and estradiol, but not by testosterone or IGF-I, and (3) that obesity (high WHR, but not abdomen circumference) can be promoted by estradiol, but not by other steroid hormones or IGF-I. These data could help in search for hormonal regulators of growth, development and metabolism, as well as for hormonal treatment of growth disorders and obesity.

An other potential area of application of the obtained data could be characterisation and prediction of growth, development and obesity on the basis of blood analysis. The present observations suggest that plasma level of estradiol could be a marker of young women growth, body weight, female stature and obesity. Additional hormonal indicators could be useful to characterize and to predict only growth (testosterone, IGF-I) and body weight/obesity (progesterone). These additional hormones could be either functional independent from estradiol or they could be its precursors, regulators or mediators of action on some parameters (Pescovitz et al, 1985; Silbernagl and Despopoulos, 2004). On the other hand, we cannot exclude, that the observed statistical association reflects not the direct functional link between hormonal and morphological parameters, but the existence of hypothetical third factor affecting both hormonal and morphological parameter. For example, malnutrition can reduce IGF-I level, which results impaired growth (Matera and Rapaport, 2002). Poor social environment and related alcohol consumption can both induce retardation in body growth and development (Ornoy and Ergaz, 2010), increased estradiol and reduce testosterone level in blood (Gavaler and Van Thiel, 1992).

Taken together, our observations and observations of our predecessors demonstrate statistical and, possiblyy, functional link between some hormonal and morphometric indices. These findings may be useful for development of hormonal markers for diagnostics or prediction of growth and metabolic disorders. Furthermore, they could help in search for hormonal regulators of growth, development and metabolism, as well as for treatment of growth disorders and obesity. It is not to be excluded that screening and application of these hormones can help to identify, to prevent and to treat these disorders.

References

1. Creager JG. Human Anatomy and Physiology. USA: Wm. C. Brown Publishers, 1992, 835 pp.

2. De Pergola G, Maldera S, Tartagni M, Pannacciulli N, Loverro G, Giorgino R. Inhibitory Effect of Obesity on Gonadotropin– Estradiol– and Inhibin B Levels in Fertile Women. Obesity 2006; 14: 1954–1960.

3. Dorgan JF, Reichman ME, Judd JT, Brown C, Longcope C, Schatzkin A, Albanes D, Campbell WS, Franz C, Kahle L et al. The relation of body size to plasma levels of estrogens and androgens in premenopausal women (Maryland– United States). Cancer Causes Control 1995; 6: 3–8.

4. Evans DJ, Hoffmann RG, Kalkhoff RK, Kissebah AH. Relationship of Androgenic Activity to Body Fat Topography– Fat Cell Morphology – and Metabolic Aberrations in Premenopausal Women. J Clin Endocrinol Metab 1983; 57 (2): 304–310.

5. Fetter V, Prokopec M, Suchý J, Titlbachová S et al. Antropologie. Prague, Czech republik: G. Fischer Verlag, 1967, 704 pp.

6. Goldenberg N, Barkan A. Factors regulating growth hormone secretion in humans. Endocrinol Metab Clin N Amer 2007; 36: 37–55.

7. Finstad SE, Emaus A, Tretli S, Jasienska G, Ellison PT, Furberg AS, Wist EA, Thune I. Adult Height–Insulin– and 17β–Estradiol in Young Women. Cancer Epidemiol Biomarkers Prev 2009; 18: 1477–1483.

8. Frank GR. The role of estrogen in pubertal skeletal physiology: epiphyseal maturation and mineralization of skeleton. Acta Paediatr 1995; 84: 628 – 630.

9. Gavaler JS, Van Thiel DH. Hormonal status of postmenopausal women with alcohol-induced cirrhosis: further findings and a review of the literature. Hepatology 1992; 16: 312–319.

10. Goldenberg N, Barkan A. Factors regulating growth hormone secretion in humans. Endocrinol Metab Clin N Amer 2007; 36: 37–55.

11. Hollmann M, Runnebaum B, Gerhard I. Impact of waist–hip–ratio and body–mass–index on hormonal and metabolic parameters in young–obese women. Intern J Obesity 1997; 21: 476–483.

12. Jasienska G, Ziomkiewicz A, Ellison PT, Lipson SF, Thune I. Large breasts and narrow waists indicate high reproductive potential in women. Proceedings of the Royal Society London Series B 2004; 271 (1545): 1213–1217.

13. Kipke MD. Adolescent development and the biology of puberty: summary of a workshop on new research. Washington, USA: National Academies Press, 1999, 44 pp.

14. Kirschner MA, Samojlik ES, Drejka M, Szmal E, Schneider G, Ertel N. Androgen–estrogen metabolism in women with upper body versus lower body obesity. J Clin Endocrinol Metab 1990; 70: 473–479.

15. Lager C, Ellison PT. Effect of moderate weight loss on ovarian function assessed by salivary progesterone measurements. Am J Hum Biol 1990; 2: 303–312.

16. Liu JP, Baker J, Perkins AS, Robertson EJ, Efstratiadis A. Mice carrying null mutation of genes encoding insulin-like growth factor 1 (IGF-1) and type 1 IGF receptor (IGF-1r). Cell 1993; 75: 59–72.

17. Martel-Pelletier J, Di Battista JA, Lajeunesse D, Pelletier JP. IGF/ IGFBP axis in cartilage and bone in osteoarthritis pathogenesis. Inflamm Res 1998; 47: 90–100.

18. Martin R, Saller K. Lehrbuch der Anthropologie. Stuttgart, Germany: G. Fischer Verlag, 1966, 661 pp.

19. Matera L, Rapaport R. Growth and Lactogenic Hormones: Neuroimmune Biology, Volume 2. Elsevier Science: Oxford, UK, 2002, 308 pp.

20. Mathews CK, van Holde KE, Ahern KG. Biochemistry. San Francisco, USA: Addison Wesley Longman, 1999, 1186 pp.

21. Mayes JS, Watson GH. Direct effects of sex steroid hormones on adipose tissues and obesity. Obesity Rev 2004; 5: 197–216.

22. Melmed S, Conn PM. Endocrinology: basic and clinical principles 2nd ed. Totowa, New Jersey, USA: Humana Press, 2005, 440 pp.

23. Mooradian AD, Morley JE, Korenman SG. Biological Actions of Androgens. Endocrine Rev 1987; 8: 1–28.

24. Neal MJ. Basic Endocrinology: An Interactive Approach. Malden, Mass: Blackwell Science, 2000, 282 pp.

25. Ornoy A, Ergaz Z. Alcohol abuse in pregnant women: effects on the fetus and newborn, mode of action and maternal treatment. Int J Environ Res Public Health 2010; 7: 364–379.

26. Park YW, Heymsfield SB, Gallagher D. Are dual–energy x–ray absorptiometry regional estimates associated with visceral adipose tissue mass? Intern J Obesity 2002; 26: 978–983.

27. Pasquali R, Casimirri F, Balestra V, Flamia R, Melchionda N, Fabbri R, Barbara L. The relative contribution of androgens and insulin in determining abdominal body fat distribution in premenopausal women. J Endocrinol Invest 1991; 14 (10): 839–846.

28. Pescovitz OH, Rosenfeld RG, Hintz RL, Barnes K, Hench K, Comite F, Loriaux DL, Cutler GB. Jr. Somatomedin–C in accelerated growth of children with precocious puberty. J Pediatr 1985; 107: 20–25.

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29. Pospíšil MF, Drobná N, Neščáková E, Siváková D, Thurzo M. Biológia človeka II. Bratislava, Slovak republic: Univerzita Komenského Bratislava, 2002, 264 pp.

30. Pouliot MC, Destpres JP, Lemieux S, Moorjani S, Bouchače C, Tremblay A, Naderu A, Lupien PJ. Waist circumference and abdominal sagittal diameter: Best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Amer J Cardiol 1994; 73: 460–468.

31. Price TM, O'Brien SN, Welter BH, George R, Anandjiwala J, Kilgore M. Estrogen regulation of adipose tissue lipoprotein lipase--possible mechanism of body fat distribution. Am J Obstet Gynecol 1998; 178: 101–107.

32. Puder JJ, Monaco SE, Gupta SS, Wang J, Mayer L, Ferin M, Warren MP. Estrogen and exercise may be related to body fat distribution and leptin in young women. Fertility Sterility 2006; 86 (3): 694–699.

33. Ross R, Leger L, Morris D, de Guise J, Guardo R. Quantification of adipose tissue by MRI: Relationship with anthropometric variables. J Appl Physiol 1992; 72: 787–795.

34. Schams D, Berisha B, Kosmann M, Eispanier R, Amselgruber WM. Possible role of growth hormone, IGFs, and IGF-binding proteins in the regulation of ovarian function in large farm animals. Domestic Animal Endocrinol 1999; 17: 279–285.

35. Silbernagl S, Despopoulos A. Atlas fyziologie člověka. Grada publishing: Praha, 2004, 448 p.

36. Singh D, Zambarano RJ. Offspring sex ratio in women with android body fat distribution. Human Biology 1997; 69: 555–566.

37. Skalba P. Endokrynologia ginekologiczna. Warsawa, Poland: PZWL, 2008, 346 pp.

38. Sowers MF, Beebe JL, McConnell D, Randolph J, Jannausch M. Testosterone Concentrations in Women Aged 25–50 Years: Associations with Lifestyle– Body Composition– and Ovarian Status. Amer J Epidemiol 2001; 153: 256–264.

39. Stanczyk FZ. Pharmacokinetics and potency of progestins used for hormone replacement therapy and contraception. Rev Endocr Metab Disord 2002; 3: 211–224.

40. Steinberg L. Adolescence. McGraw-Hill College, 1998, 519 pp.

41. Suh YS, Kim DH, Lee IK. Usefulness of lumbar AP Spine DXA for measuring the percentage of perilumbar regional fat and predicting visceral fat in obese postmenopausal women. Nutrition 2002; 18: 84–85.

42. Svačina S. Obezita a diabetes. Praha, Czech republic: Maxdorf, 2000, 307 pp.

43. Van Anders SM, Hampson E. Waist-to-Hip Ratio Is Positively Associated With Bioavailable Testosterone but Negatively Associated With Sexual Desire in Healthy Premenopausal Women. Psychosomatic Med 2005; 67: 246–250.

44. Vitzthum VJ, Bentley GR, Spielvogel H, Caceres E, Thornburg J, Jones L, Shore S, Hodges KR, Chatterton RT. Salivary progesterone levels and rate of ovulation are significantly lower in poorer than in better–off urban–dwelling Bolivian women. Hum Reprod 2002; 17: 1906–1913.

45. Werner H, Leroith D. New concepts in regulation and function of insulin-like growth factors: implications for understanding normal growth and neoplasia. Cell Mol Life Sci 2000; 57: 932–942.

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