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Study of the Precocious Puberty and Related-hormone Concentration

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Abstract

This study is conducted to study distribution of DHEAs value and IGFBP3 value of children with precocious puberty in comparison with normal children and analyze correlation of their influence in precocious puberty. Study subjects were children who had visited pediatrics department of a University hospital from Jan. 2011, to Dec. 2011. Total count of the subjects was 94, with 45 male and 49 female. 54 were subjects with precocious puberty and the other 40, normal. Furthermore, gathered data were analyzed in frequency, T-test, ANOVA, and correlation test, using SPSS 19.0. In correlation analysis of DHEAs and IGFBP3 value in child with precocious puberty, correlation value of DHEAs was .442 and IGFBP-3, .464 ($p < .01$). Correlation coefficients were distributed comparatively low. In conclusion, when diagnosing precocious puberty, tests on sexual hormones and pituitary hormones such as LH, FSH, and ACTH besides DHEA-S and IGFBP3 tests should be performed and as such study has a small group of subjects, it should be further expanded with more cases as subjects.

Keywords: Children, Dehydroepiandrosterone, Luteinizing Hormone, Precocious Puberty

1. Introduction

As the number of children visits hospitals for precocious puberty increases, it is becoming a social issue, recently[1]. This is related to socio-economical growth[2]. Usually, increase in testicular volume in boys and development of breasts in girls are the signs of puberty[3]. However, earlier presentation of beginning of puberty becomes prominent with rapid economical growth[3]. With this interest in the background, researches on obesity and early puberty are actively being studied, but only a few studies represent metabolic index for normal weighted children and diet control element[1]. Precocious puberty means secondary sex character shown prior to 8 years old in female and 9 years old in male[4]. The types of symptom in 80~95% of female have no specific etiology, but organic factors are seen in 20% of male[1]. Precocious puberty is classified to true precocious puberty with activation of HPA axis and pseudo precocious puberty with activation of HPA axis[5]. However, increased growth speed and body type due to increased gonadal steroid hormones accelerates body growth[6]. In recent years, adult height is increasing, beginning of puberty is earlier, and the period of initiation is thought to be familial trait or genetic factors[3]. Especially, genetic factors may be controlled by pollution, nutrition status, frequent infection, and chronic disorders[7]. Therefore, tracing etiologic factors and observing them thoroughly are important[6]. Furthermore, the worldwide trend for beginning period of puberty (girls) is getting earlier than the past[8]. The study result from Pediatric Research in Office Setting (PROS) in America with 17,000 children aged between 3-12 shows accelerated period of developing pubic hair and breasts.[9] However, the reasons for this study result are possibility of obesity[10] and the risk of congenital etiologic disease [11]. Up to this point, we follow previous diagnostic standard[12]. According to the statistics, 40% of boys and 80~90% of girls have no significant reasons for idiopathic true precocious puberty. Also, average menarche time is twelve, which suggest 2years of acceleration over past 80 years[13].

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Above all, children with precocious puberty need early diagnosis and treatment since it brings early epiphyseal fusion and decrease in height in adulthood[3]. GnRHa, the treatment for precocious puberty, delays early sexual growth by inhibiting secretion of sexual hormone, and it may cause increase in height when they become adults by regressing sexual hormone to extend the duration of puberty[4,14,15]. However, tumor or ovary tumor may be the causes for the precocious puberty, and early diagnosis and treatment are very important in this case[6]. Thus, there are many factors relative to precocious puberty and confirmation of those various factors described above are necessary[3]. Therefore, this study was confirmed to analyze the correlation effects by comparing the pediatric patients suffering from precocious puberty to normal children and investigating the DHEAs values and IGFBP3 values. Investigating the meaning of DHEA-S test and IGF-BP3 test among those hormone tests performed during the time when the precocious puberty patients visit to diagnose precocious puberty and see the differences with other normal children to study the correlation with precocious puberty.

2. Subject of Study and Methods

2.1 Subject of Study

We tested with pediatric clinical specimen treated at a university hospital from January 2012 to December 2013 by classifying pediatric specimen with precocious puberty and normal pediatric specimen. Total numbers of specimen are 94, which are 45 males and 49 females, and 54 precocious puberty specimens and 40 normal specimens.

2.2 Study Methods

We analyzed ages, body ages, average concentration and differences of DHEA-S values, correlation of precocious puberty to DHEA-S and IGFBP-3 by classifying the subject specimens into diagnostic specimen for precocious puberty and normal specimen. Test method for DHEA-S is immune radiometric assay. We put a 50ul of specimen into an antibody coated tube and then put 100ul of radioisotope and cleansed them after 1 hour of reaction, then measured with r-countor. Also, we put a 50ul of specimen into an antibody coated tube and then put 400ul of radioisotope and cleansed them after 3 hour of reaction, then measured with r-countor with immune radiometric assay for IGFBP-3.

2.3 Data Analysis

The result performed in this study is generally suggested as mean ±SD and %. We used T-test, ANOVA, and Correlation exam for each test subject by using SPSS version 19.0 program for statistics, and the level of significance is $p<0.05$.

3. Results

3.1 Distribution by Age

The distribution of age is between 3 to 13, and 7 years olds are the biggest portion of the group Table 1.

3.2 Distribution by Bone Age

Use Bone ages when the patients were diagnosed as precocious puberty were between 3 to 13, and 8 years olds are the biggest portion of the group Table 2.

3.3 Size Distribution of Uterus by Precocious Puberty

The numbers of female precocious puberty patients were 28, average uterus diameter was 1.68cm, average uterus width was 2.20cm, average uterus length was 3.49cm, the right Fallopian tube was 2.07cc, and the left Fallopian tube was 1.89cc Table 3.

3.4 Distribution of Measured Values of DHEAs and IGFBP3

Distribution of measure DHEAs values was average 30.92 in normal group, and 77.06 in precocious puberty group.

Table 1. Distribution by age (n=94)

Year	N	%
3	1	1.1
4	2	2.1
5	9	9.6
6	14	14.9
7	22	23.4
8	21	22.3
9	9	9.6
10	7	7.4
11	7	7.4
12	1	1.1
13	1	1.1
sum	94	100.0

Table 2. Distribution by bone age (n=94)

Year	N	%
3	2	2.1
4	2	2.1
5	2	2.1
6	5	5.3
7	8	8.5
8	11	11.7
9	9	9.6
10	10	10.6
11	3	3.2
13	2	2.1
sum	54	100

Table 3. Size distribution of uterus by precocious puberty

uterus	N	Min	Max	Mean	SD
D(cm)[1)]	28	1.22	2.45	1.68	.39
W(cm)[2)]	28	1.59	2.92	2.20	.39
L(cm)[3)]	28	2.0	4.9	3.49	.70
RF(cc)[4)]	28	1.2	4.0	2.07	.90
LF(cc)[5)]	28	0.9	2.8	1.89	.71

[1)]Diameter, [2)]Width, [3)]Length,
[4)]Right fallopian tube, [5)]Left Fallopian tubes

Distribution of measure IGFBP3 values was average 2788 in normal group, and 3330 in precocious puberty group Table 4.

3.5 Significant Elements for Precocious Puberty

Significant elements for pediatric precocious puberty are IGFBP3, DHEAs, and significant probability was p<.01 Table 5.

3.6 Correlations of DHEAs and IGFBP3 in Precocious Puberty

Correlation distribution of precocious puberty children and the values of DHEA-S, DHEA-S shows 0.442 of correlation coefficient, and GFBP3 shows 0.464 of correlation coefficient with significant probability p<.01. Correlation coefficient was relatively low Table 6.

Table 4. Data of DHEAs and IGFBP3

		N	*1)* Mean	*2)* SD	95% confidence interval of average	
					Low	*High*
IGF-BP3	Nor*	40	2788	366	2671	2905
	P.P**	54	3330	604	3165	3495
	Total	94	3099	580	2980	3218
DHEAs	Nor*	40	30.92	4.69	29.42	32.43
	P.P**	54	77.06	61.5	60.26	93.86
	Total	94	57.43	51.9	46.80	68.06

* Normal , ** precocious puberty

Table 5. Significant for precocious puberty

Variable	F	p
Year	18.45	.000
IGFBP3	25.17	.000
DHEAs	22.30	.000

Table 6. Correlations of DHEAs and IGFBP3 in precocious puberty

		P[1)]	D[2)]	I[3)]
P[1)]	*Pearson*	1	.442**	.464**
	p		.01	.01
D[2)]	*Pearson*	.442**	1	.675**
	p	.01	.01	.01
I[3)]	*Pearson*	.464**	.675**	1
	p	.01	.01	

** $P < .01$
[1)]precocious puberty, [2)]DHEAS, [3)]IGFBP3

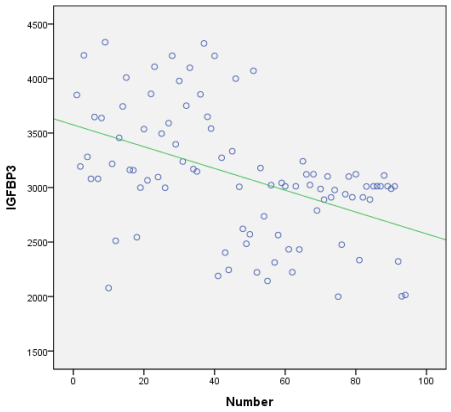

Figure 1. Scatter plot of IGFBP3.

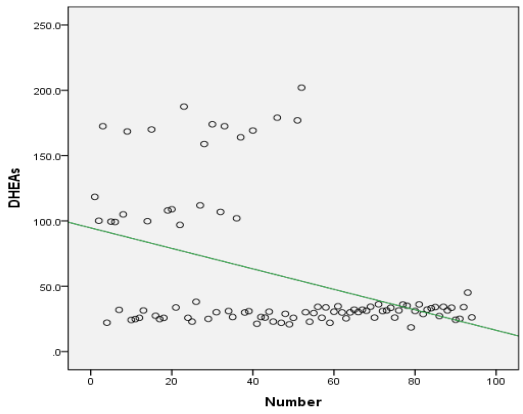

Figure 2. Scatter plot of DHEAs.

3.7 Satter Plot of DHEAs and IGFBP3 Value

Scatter plot shows value distribution of DHEA-S and IGFBP3 Figure 1 and 2.

4. Discussions and Conclusion

A conclusion According to the results, age range of pediatric patients is between 3 to 13, and 7 years old is the most common. Bone age of pediatric precocious puberty is between 3 to 13, and 8 years old was the most common. The number of female precocious puberty was 28, average diameter of the uterus was 1.68cm, average width of the uterus was 2.20cm, average length of the uterus was 3.49cm, the volume of right Fallopian tube was 2.07cc, and the volume of left Fallopian tube was 1.89cc. Also, distribution of measure DHEAs values was average 30.92 in normal group, and 77.06 in precocious puberty group. Correlation distribution of precocious puberty children and the values of DHEA-S, DHEA-S shows .442 of correlation coefficient, and GFBP3 shows .464 of correlation coefficient with significant probability p<.01. Correlation coefficient was relatively low. It is known that 10~20% of DHEA are initiated from the testicles or ovary. Clinically, if it is high concentration, it may be the causes for idiopathic precocious puberty or polycystic ovary. If it is low concentration, it may be the causes for delayed puberty or hypopituitarism. IGFBP3, as a growth factor, is tested for growth hormone with IGF1 and IGF2. If it is clinically high concentration, it may be correlated with acromegaly, and if it is low concentration, it may be correlated with GH defect. Therefore, we statistically analyzed pediatric patients' blood with precocious puberty by comparing it to normal children's blood.

According to the results, measured values of DHEA-S and IGFBP3 with precocious puberty are correlated, but the correlation coefficient was low. Thus, when diagnosing precocious puberty with blood test, DHEA-S and IGFBP3 test are significant, but co-testing with other sex hormones such as LH and FSH may make it more helpful. Same results can be seen from the studies performed by Lee [5] and Hong [16]. Therefore, we'd like to make a following suggestion for effective diagnosis for hematologic exam of precocious puberty.

First, perform DHEA-S and IGFBP3 hematologic exam. Secondly, confirmation with sexual hormonal test and hypothalamic test such as LH, FSH, and ACTH is necessary. Since this study has small number of study object, representative nature may seem to be lacking. As a result, we suggest further studies with more cases.

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