Journal of Pediatric Endocrinology

Open Access

Austin Publishing Group

Research Article

Correlation of Gonadotropins and Estradiol Level 1 Hour after Depot Triptorelin with Clinical Criteria of Adequate Pubertal Suppression in Girls with Central Precocious Puberty

Kobra SA*

Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Iran

***Corresponding author:** Kobra SA, Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, IR Iran

Received: January 27, 2017; **Accepted:** April 21, 2017; **Published:** May 01, 2017

Abstract

Background: GnRH analogues such as Triptorelin are main stay for treatment of Central Precocious Puberty (CPP). We evaluated correlation of gonadotropins and Estradiol level one hour after administration of depot Triptorelin with other evidences of pubertal suppression.

Materials and Methods: Twenty seven girls were considered for this study after written informed consent. All patients had rapidly progressive CPP according to clinical and laboratory criteria and were under treatment with depot Triptorelin. After 3-24 dose of depot Triptorelin, blood sample was collected 1 hour after drug injection for LH, FSH and Estradiol levels. The growth velocity determined and the left hand graph obtained to determine bone age and skeletal maturation rate. Correlation of gonadotropins and Estradiol level with other evidences of pubertal suppression determined.

Results: In a period of 2 years (from 2014 to 2015), 28 patients enrolled. The mean age was 9.27 ± 1.49 years. Four patients (12.1%) recognized as inadequate pubertal suppression. Mean growth velocity was 6.21 ± 1.81 cm/year. The mean LH ± SD was 1.34 ± 1.16 IU/l (range 0.1-5.7 IU/l). Bone maturity index was at or above one in 6 (23.1%) of 26 patients. Mean LH/FSH ratio was 0.77 ± 0.7 and 23 subjects (71.9%) has LH/FSH ratio less than one. LH, FSH and Estradiol level did not correlate with growth velocity, bone maturation rate, or with interval of Triptorelin administration. Serum LH level had significant correlation only with FSH (R= 0.383, P= 0.030) and bone age (R = -0.421, P = 0.032). Estradiol level had significant correlation with bone age (R = -0.798, P < 0.0001).

Conclusion: Diagnosis of inadequate pubertal suppression in girls with CPP is dependent on clinical, laboratory and radiological findings. LH levels one hour after injection of depot Triptorelin alone is not sufficient for finding of inadequate suppression. Serum Estradiol levels can also help to find the inadequacy of treatment.

Keywords: Gonadotropin-releasing hormone; Triptorelin; Central precocious puberty

Introduction

Precocious puberty is defined with onset of early signs of puberty at an age less than two standard deviations below the mean age of onset of puberty in normal individuals. Precocious puberty is defined in girls with the appearance of secondary sexual characteristics before the age of 8 years [1-3]. Treatment of precocious puberty noticed hypothalamic-pituitary-gonadal-axis. Gonadotropin-releasing hormone agonists (GnRHa) are standard treatment of true precocious puberty [4]. GnRH agonists can prevent many complications of precocious puberty [5]. Early diagnosis and treatment of premature sexual development during can delay puberty, reverse secondary sexual characters, reduce emotional disorders and their families concerns, reduce the risk of sexual abuse the risk of breast cancer, delay menarche in girls and eventually improve final height [6]. Biochemical methods (the level of LH, FSH, Estradiol) or the clinical score (pubertal tanner stage, skeletal maturity rate, growth rate) can be used to assess the appropriate response to treatment with GnRH analogue and adequate suppression of puberty. Intravenous gonadotropin stimulation test is the gold standard test in the evaluation of sufficient suppression of central precocious puberty but it is not pleasant for time and economy [7,8]. Therefore, the measurement of LH levels before or after injection of gonadotropin analog is used as a standard test in patients, to ensure the accuracy of the test in the evaluation of sufficient suppression of puberty; it can be compared with the clinical scores. Clues to enough suppression of puberty include the following: 1) regression or lack of progress in maturity tanner stage [2] skeletal maturity index of 1 or less (bone age

Kobra. © All rights are reserved

Citation: Kobra SA. Correlation of Gonadotropins and Estradiol Level 1 Hour after Depot Triptorelin with Clinical Criteria of Adequate Pubertal Suppression in Girls with Central Precocious Puberty. J Pediatri Endocrinol. 2017; 2(1): 1016.

Table 1: General characteristics and comparison of two groups.

Variable	Total	Group A	Group B	P value
Number	28	24	4	-
Age	9.28 ± 1.54	9.47±1.36	8.1±2.24	.189
Weight	37.8 ± 8.4	38.17±8.33	35.5±9.62	.693
Height	138 ± 7.4	139±6.57	133±10.8	.167
BMI	19.73 ± 3.89	19.73±3.98	19.76±3.17	.694
Pubertal stage suppression	28	26	2	<.0001
Growth velocity (cm/yr)	6.21 ±1.67	6.2±1.78	6.3±.92	.490
Bone age	11.13 ± 1.46	11.44±.93	8.83±2.75	.042
Bone maturity rate (mo. /mo.)	9.94 ± 4.5	9.73±4.33	11.46±6.51	.737
LH	1.2 ±.88	1.18±.73	1.38±1.27	.998
FSH	2.25 ± 1.47	2.08±1.52	3.23±.4	.065
Estradiol	26.46 ± 60.45	12.16±12.75	112.2±142	.070

LH: Luteinizing Hormone; BMI: Body Mass Index; FSH: Follicle-Stimulating Hormone

changes / chronological age changes) 3) growth rate less than 2SDS for chronological age [9]. The most previous studies regarding the evaluation of sufficient suppression of puberty after GnRH agonist injection had focus on the LH level and less focused on clinical evidence of maturation inhibition. Also most of these studies have been paid to the assessment of LH after injection of leuprolide and there is only two studies have been done on Triptorelin Depot [3,10]. Therefore, this study aimed to investigate the correlation between hormone levels of LH, FSH and Estradiol an hour after administration of depot Triptorelin with clinical criteria of pubertal regression in girls with central precocious puberty.

Materials and Methods

In a longitudinal study during a period of 2 years (from 2014 to 2015) 28 girls with CPP who were under treatment with depot triptorelin considered for this research. The study conducted in the pediatric endocrinology clinic of Kashan University of Medical Sciences. The diagnosis of precocious puberty made if onset of secondary sexual characteristics was before 8 years or menarche before 9 years of age. The hormonal criteria for the diagnosis of CPP have been used on the basis of international recommendations [11-13]. Patients were included in the study if 1) CPP has been proved with clinical and laboratory criteria and 2) good compliance for treatment and hormonal and radiologic studies. Exclusion criteria: irregular follow up visits, irregular use of depot triptorelin, no cooperation for hormonal and radiologic investigations, growth hormone deficiency, thyroid dysfunction, chronic diseases and developmental disorders. The weight, height, BMI and pubertal stage were determined at first and at 3 month intervals. Sexual maturation staging determined by Marshall-Tanner method [14]. Growth rate expressed as centimeters per year. Bone age determination performed by Bayley-Pinneau method and adult height prediction by Greulich-Pyle method [15,16]. Our treatment protocol is to treat all patients at first by depot Triptorelin 3.75 mg IM every once 28 days and in the absence of sufficient suppression of puberty, injection intervals will be reduced to 25 and then to 21 days. Within 3-24 months after starting treatment, blood sample was drawn for LH and FSH and Estradiol level one hour after depot Triptorelin injection. Serum levels of LH and FSH and estradiol were measured by immunoassay. Patients according to the clinical, laboratory and radiological findings divided into two groups:

Group A: adequate suppression of puberty,

Group B: inadequate suppression of puberty. The study design approved by ethical committees of Kashan University of Medical Sciences and written consent obtained from the parents of patients.

Statistical analysis was performed with SPSS, version 16.0 (SPSS software Inc, Chicago, IL, USA). Values were presented as mean ± standard deviation. P values lesser than 0.05(two-sided) considered as statistically significant.

Results

We have 32 girls with central precocious puberty under treatment with Triptorelin, 4 cases were excluded because of the simultaneous growth hormone therapy. In a period of 24 months, 28 patients enrolled. The mean age at the diagnosis of precocious puberty was 7.41 ± 1.51 years. The mean age at study time was 9.28 ± 1.54 years. Age had positive correlation with bone age (R: 0.821, P< 0.001). At the time of study Triptorelin 3.75 mg has been used for 14 children (50%) every 28 days, 8 children (28.6%) every 25 days and 6 (21.4%) children every 21 days. Drug interval did negative correlation with age (R: -0.456, P: 0.008) and bone age (R: -0.533, P: 0.005). A total of 4(14.3%) patients recognized as the inadequate pubertal inhibition based on the clinical, laboratory and radiologic criteria (group B), others diagnosed as adequate inhibition of puberty (group A). General characteristics and comparison of two groups showed in (Table 1). Two groups were not different in respect of age, weight, height, BMI, Bone Maturity Rate (BMR) and growth velocity. Clinical and laboratory characteristics of children with insufficient pubertal suppression showed in (Table 2). Adequate suppression of physical signs of puberty was seen in 26 (92.9%) subjects, but no in 2 (7.1%), these two patients were obese and both had Estradiol level of over 100 pg/ml. Ten subjects (35.7%) were obese. Obesity did negative correlation with age (R: -0.361, P: 0.039) and negative correlation with adequate suppression of breast tanner staging (R: -0.359, P: 0.042). Pubertal stage suppression had negative correlation with bone age (R: -0.492, P: 0.012).

All cases had serum LH concentration below 3.5 IU/L. Three cases had LH concentration above 2.5 IU/L, which all had clinically suppressed puberty. The serum concentrations of FSH was less than or equal to 5.7 IU/L in all subjects. Mean LH/FSH ratio was 0.67 ± 0.53 and 20 subjects (74.1%) has LH/FSH ratio less than one. The serum concentrations of LH had positive correlation with serum concentrations of FSH (R: 0.383, P: 0.030) and negative correlation with bone age (R: -0.435, P: 0.036). LH, FSH and Estradiol level did not correlate with growth velocity, bone maturation rate, or with duration of Triptorelin administration. LH/FSH ratio only did correlate with age (R:-0.351, P: 0.048).

Serum Estradiol concentration was less than10 pg/L in 16 cases (57.1%), between 10-20 pg/ml in five cases (17.9%), between 20-50 pg/ml in five cases (17.9%), and 2 cases (7.1%) had Estradiol level of over 100 pg/ml. Estradiol level did negative correlation with bone age (R: -0.798, P <0.0001) and positive correlation with need to dose adjustment (R: 0.354, P: 0.065).

Table 2: Clinical and laboratory characteristics of children with insufficient pubertal suppression.

Dose interval	Estradiol	FSH	LH	BMR	Growth velocity	Obesity	Pubertal suppression	Age	Case number
28	111	3.66	3.2	18.84	7.2	Yes	yes	5.25	1
25	19.1	3.38	0.81	9	6.5	No	No	7.75	2
28	5.04	3.20	1.20	6.55	5.02	No	No	10.58	3
28	313.69	2.7	0.3	-	6.5	Yes	yes	8.83	4

LH: Luteinizing Hormone; FSH: Follicular Stimulating Hormone; BMR: Bone Maturity Rate

Bone maturity index was at or above one in six (23.1%) of 26 patients. Mean growth velocity was 6.21 ± 1.67 cm/year. Growth velocity did negative correlation with age (R: -0.527, P: 0.004) and bone age (R: -0.408, P: 0.043). From a total of 25 patients, 19 cases (76%) had Bone Maturity Rate (BMR) of less than one year for each year and 6 patients (24%) with BMR of more than one year per year.

Discussion

We examined the correlation between Estradiol, LH and FSH levels one hour after administration of triptorelin (Diphereline) with clinical and radiological criteria of adequate pubertal suppression in girls with central precocious puberty. Previous studies have shown that treatment with triptorelin every 28 days has a positive impact to improve final height in children with CCP [17-19]. The clinical scores (tanner stage, growth rate) or paraclinical methods (the level of LH, FSH and Estradiol, bone maturity rate) can be used to assess the appropriate response to treatment with GnRH analogue. Intravenous gonadotropin stimulation test is the gold standard test for the evaluation of sufficient suppression of central precocious puberty [5,7,8]. However, this test is uncomfortable (because it requires multiple blood samples (time-consuming and high cost for patients. Therefore, the levels of LH before or after injection of gonadotropin analog is used as a standard test in these patients [3,19-23]. The rational for this research was two: 1-Previous studies had less focus on correlation of gonadotropins and Estradiol level with clinical criteria of adequate pubertal suppression. 2- Similar studies have been paid to the assessment of LH level after injection of leuprolide and only two studies have been done on triptorelin [10,24]. At first Salerno, et al. suggest a single blood sample for LH, FSH and Estradiol levels 12 hour after the therapeutic dose injection of GnRH agonist (triptorelin) is useful to assess suppression of the puberty in girls treated for CPP. The response compared with conventional GnRH stimulation test (2 days before the therapeutic triptorelin injection). LH and FSH peaks observed 12 hour postinjection whereas peak Estradiol level occurred after 24 hour. 15 fully suppressed patients who treated with the GnRHa, had a peak values of LH (2.1 ± 1.6 IU/l), FSH (4.4 ± 2.4 IU/l) and Estradiol (72.6 ± 1.5 pmol/l) during GnRH stimulation test in comparison with LH (1.6 ± 1.3 IU/l), FSH (3.9 ± 2.2 IU/l) and Estradiol levels (72.5 ± 1.9 pmol/l) 12 h after the GnRHa administration. In seven girls with clinical evidence of incomplete pubertal suppression, the Estradiol level was higher 12 hr after the GnRHa administration than GnRH stimulation test (136.3 ± 44.4 pmol/l and 73.0 ± 0.0 pmol/l respectively). Also they had higher levels of LH (2.8 ± 0.9 IU/l) and FSH (9.7 ± 4.7 IU/l), than 15 fully suppressed patients [10]. Lawson and Cohen (1999) report a sensitivity of 75% and a specificity of 100% for single LH measurement 40 min after sc LHRH test in comparison with iv LHRH test (100% sensitivity, 95% specificity). They developed a clinical score for pubertal suppression include growth velocity, Tanner stage and bone age progression. Biochemical suppression defined as peak LH level less than 2 IU/L during IV LHRH test [9]. Lewis et al. (2013) showed random LH in children treated with histrelin implant for CPP does not revert to a prepubertal range in more than one-half of patients in contrast to complete suppression of hypothalamic-pituitary-gonadal documented by GnRHa stimulation test [18]. Briton, et al. (2004) compared the peak LH level after classic GnRH test with the LH level two hour after depot leuprolide acetate administration. In well-controlled girls according to the clinical criteria, the mean LH 2 hour after depot leuprolide was 2.7 ± 1.9 IU/L (0.7-6.6 IU/ l) in comparison with LH peak after a classical GnRH test [1.4 ± 0.6 IU/L (<0.6 to 2.3 IU/L)]. They defined an LH level below 6.6 IU/L 2 hour after depot leuprolide as the LH cut-off values for adequate therapy. Two from 18 girls had not adequate clinical pubertal suppression. The LH level 2 hour after depot leuprolide was 11 and 7.5 IU/L respectively [19]. The mean LH level was lower in our work but in our study no significant difference found in mean LH 1 hour after depot triptorelin in two groups. Also in a study the peak concentration of LH level after GnRH stimulation test in six patients treated with monthly leuprolide had not significant differences between patients with well suppressed puberty and incompletely suppressed patients. This study has a low sample size [25]. Estradiol is the key hormone that accelerates breast development, growth rate and bone maturation in girls with CPP. In our experience Estradiol level did not correlate with growth velocity, bone maturation rate, or with duration of triptorelin administration. Similar to our results, Estradiol levels were below the detection limit in 75% of the thirty girls with CPP during treatment with depot leuprolide acetate and did not correlate with skeletal maturation rate or growth velocity [22]. Freire et al. reported Estradiol level 24 hour after therapeutic dose of depot triptorelin (3.75 mg) from 82 follow up visits, in 78, Estradiol level was <14 pg/ml. The 99th percentiles of LH and FSH three hour after therapeutic dose of triptorelin were 4.0 and 6.3 IU/l, respectively [26]. A significant dose-response relationship was observed in twenty girls with central precocious puberty treated with deslolerin [27]. For 14 children with central precocious puberty treated with depot leuprolide every 4 weeks FSH and LH levels measured in a period of 30 to 60 minutes after the fourth dose of drug injection. The mean serum level of LH was 0.83 mIU/ml, similar to the peak values after intravenous injection of GnRH (0.6) or subcutaneous GnRH test (0.54). 13 out of 14 children had clinical signs of suppress puberty, but not in one person, this patient had FSH: 7mIU / ml, LH: 5.1mIU/ml and Estradiol: 1.1 pg/ml. These researchers suggested the LH levels higher than 3mIU/ml 30 to 60 minutes after the drug injection as an indicator of insufficient inhibition of the pituitary [19]. Demirbilek et. al. (2012) evaluated 142 girls with central precocious puberty, they found the LH levels equal to or less than 2.5mIU/ml, 90 minutes after administration of the third dose of leuprolide acetate has 88%

sensitivity and 100% specificity for pubertal suppression, compared with IV GnRH stimulation test. In this study, 16 of 25 children with LH levels of higher than 2.5mIU/ml had enough inhibition of puberty based on IV GnRH stimulation test [8]. In our study four patients had LH levels higher than 2.5 mIU/ml and three of them had enough pubertal suppression. In another research, data of 584 IV GnRH stimulation test (314 tests for diagnosis of CPP and 270 to evaluate suppression of puberty) as the gold standard in the diagnosis and treatment of precocious puberty were analyzed and concluded that the level of LH in 40th minutes can be used for diagnosis of CPP (cut-off value of 5 IU/L) with 98% sensitivity and 100% specificity, and in the 20th minute (cut-off value of 2 IU/L) for sufficient suppression of puberty can be used with 100% sensitivity and specificity [7]. In a study LH level 3 hours after injection of depot leuprolide acetate (11.25 mg, every 3 months) was 2.58 ± o.54 IU/L (1.3-4.3), all children studied (n = 7) had clinically sufficient control of maturity [17]. In our study, only 2 patients had LH levels of above 3.3 IU / L, which of course were at clinically controlled puberty.

Conclusion

Our study showed the diagnosis of inadequacy of drug and decide to adjust the dose for the treatment of central precocious puberty in girls is still dependent on many factors (clinical, laboratory and radiological findings) and LH levels one hour after injection depot Triptorelin alone is not enough to find the inadequacy of treatment. The serum estradiol level can more help to find the inadequacy of drug. Further research is necessary to determine indicators of sufficient suppression of puberty as well as the effect of different doses in inhibiting puberty, especially about Triptorelin drug, because most studies are about leuprolide.

References

1. Kim D, Cho SY, Maeng SH, Yi ES, Jung YJ, Park SW, et al. Diagnosis and constitutional and laboratory features of Korean girls referred for precocious puberty. Korean Journal of Pediatrics. 2012; 55: 481-486.
2. Alessandri SB, Pereira Fde A, Villela RA, Antonini SR, Elias PC, Martinelli CE Jr, et al. Bone mineral density and body composition in girls with idiopathic central precocious puberty before and after treatment with a gonadotropin-releasing hormone agonist. Clinics. 2012; 67: 591-596.
3. Strich D, Kvatinsky N, Hirsch HJ, Gillis D. Triptorelin depot stimulation test for central precocious puberty. Journal of Pediatric Endocrinology and Metabolism. 2013; 26: 631-634.
4. Seminara S, Nanni L, Generoso M, Mirri S, Leonardi V, Slabadzianiuk T, et al. Effect of treatment with cyproterone acetate on uterine bleeding at the beginning of GnRH analogue therapy in girls with idiopathic central precocious puberty. Hormone Research in Paediatrics. 2010; 73: 386-389.
5. Nabhan ZM, Walvoord EC. Treatment of Gonadotropin-Dependent precocious puberty. 2010; 345-362.
6. Fuqua JS. Treatment and outcomes of precocious puberty: An update. Journal of Clinical Endocrinology and Metabolism. 2013; 98: 2198-2207.
7. Kandemir N, Demirbilek H, Özön ZA, Gönç N, Alikaşifoğlu A. GnRH stimulation Test in precocious puberty: Single sample is adequate for diagnosis and dose adjustment. JCRPE Journal of Clinical Research in Pediatric Endocrinology. 2011; 3: 12-17.
8. Demirbilek H, Alikasifoglu A, Gonc NE, Ozon A, Kandemir N. Assessment of gonadotrophin suppression in girls treated with GnRH analogue for central precocious puberty; Validity of single luteinizing hormone measurement after leuprolide acetate injection. Clinical Endocrinology. 2012; 76: 126-130.
9. Lawson ML, Cohen N. A single sample subcutaneous luteinizing hormone (LH)-releasing hormone (LHRH) stimulation test for monitoring LH suppression in children with central precocious puberty receiving LHRH agonists. The Journal of clinical endocrinology and metabolism. 1999; 84: 4536-4540.
10. Salerno M, Di Maio S, Gasparini N, Mariano A, Macchia V, Tenore A. Central precocious puberty: A single blood sample after gonadotropin-releasing hormone agonist administration in monitoring treatment. Hormone Research. 1998; 50: 205-211.
11. Wang ZF, Li GJ. Value evaluation of follicle stimulating hormone and luteinizing hormone in the diagnosis of precocious puberty in girls by ROC curve analysis. Chinese Journal of Contemporary Pediatrics. 2012; 14: 441-444.
12. Soriano-Guillen L, Argente J. [Central precocious puberty: epidemiology, etiology, diagnosis and treatment]. Anales de pediatria (Barcelona, Spain: 2003). 2011; 74: 336 e1-336 e13.
13. Chung EM, Biko DM, Schroeder JW, Cube R, Conran RM. From the radiologic pathology Archives: Precocious puberty: Radiologic-pathologic correlation. Radiographics. 2012; 32: 2071-2099.
14. Allali S, Lemaire P, Couto-Silva AC, Prété G, Trivin C, Brauner R. Predicting the adult height of girls with central precocious puberty. Medical Science Monitor. 2011; 17: PH41-PH48.
15. Paxton ML, Lamont AC, Stillwell AP. The reliability of the Greulich-Pyle method in bone age determination among Australian children. Journal of Medical Imaging and Radiation Oncology. 2013; 57: 21-24.
16. Bar A, Linder B, Sobel EH, Saenger P, DiMartino-Nardi J. Bayley-Pinneau method of height prediction in girls with central precocious puberty: Correlation with adult height. Journal of Pediatrics. 1995; 126: 955-958.
17. Acharya SV, Gopal RA, George J, Bandgar TR, Menon PS, Shah NS. Utility of single luteinizing hormone determination 3 h after depot leuprolide in monitoring therapy of gonadotropin-dependent precocious puberty. Pituitary. 2009; 12: 335-338.
18. Lewis KA, Eugster EA. Random luteinizing hormone often remains pubertal in children treated with the histrelin implant for central precocious puberty. The Journal of pediatrics. 2013; 162: 562-565.
19. Brito VN, Latronico AC, Arnhold IJ, Mendonca BB. A single luteinizing hormone determination 2 hours after depot leuprolide is useful for therapy monitoring of gonadotropin-dependent precocious puberty in girls. The Journal of clinical endocrinology and metabolism. 2004; 89: 4338-4342.
20. Benetti-Pinto CL, Camargo LB, Magna LA, Garmes HM, Petta CA. [Predictive factors for height gain in idiopathic central precocious puberty treated with GnRH analogues]. Revista brasileira de ginecologia e obstetricia: revista da Federacao Brasileira das Sociedades de Ginecologia e Obstetricia. 2008; 30: 609-613.
21. Prasad HK, Khadilkar VV, Jahagirdar R, Khadilkar AV, Lalwani SK. Evaluation of GnRH analogue testing in diagnosis and management of children with pubertal disorders. Indian journal of endocrinology and metabolism. 2012; 16: 400-405.
22. Kunz GJ, Sherman TI, Klein KO. Luteinizing hormone (LH) and estradiol suppression and growth in girls with central precocious puberty: is more suppression better? Are pre-injection LH levels useful in monitoring treatment? Journal of pediatric endocrinology & metabolism: JPEM. 2007; 20: 1189-1198.
23. Bhatia S, Neely EK, Wilson DM. Serum luteinizing hormone rises within minutes after depot leuprolide injection: implications for monitoring therapy. Pediatrics. 2002; 109: E30.
24. Ostojic SM. Prediction of adult height by Tanner-Whitehouse method in young Caucasian male athletes. QJM: monthly journal of the Association of Physicians. 2013; 106: 341-345.
25. Cook JS, Doty KL, Conn PM, Hansen JR. Assessment of depot leuprolide acetate dose-adequacy for central precocious puberty. The Journal of clinical endocrinology and metabolism. 1992; 74: 1206-1209.
26. Freire AV, Gryngarten MG, Ballerini MG, Arcari AJ, Escobar ME, Bergada I, et

al. Assessment of Estradiol Response after Depot Triptorelin Administration in Girls with Central Precocious Puberty. Horm Res Paediatr. 2016; 85: 58-64.

27. Klein KO, Baron J, Barnes KM, Pescovitz OH, Cutler GB, Jr. Use of an ultrasensitive recombinant cell bioassay to determine estrogen levels in girls with precocious puberty treated with a luteinizing hormone-releasing hormone agonist. The Journal of clinical endocrinology and metabolism. 1998; 83: 2387-2389.

Kobra. © All rights are reserved

Citation: Kobra SA. Correlation of Gonadotropins and Estradiol Level 1 Hour after Depot Triptorelin with Clinical Criteria of Adequate Pubertal Suppression in Girls with Central Precocious Puberty. J Pediatri Endocrinol. 2017; 2(1): 1016.