

Comparison of Serum Progesterone in Non-Viable Pregnancy and Ectopic Pregnancy

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Abstract- Ectopic pregnancy (EP) and miscarriage are important differential diagnosis of first trimester vaginal bleeding. In first trimester, serum progesterone value can be 5-20 ng/ml in EP and miscarriage. Since delay in diagnosis of EP could have high mortality and morbidity, the aim of this study was comparison of serum progesterone value in EP and miscarriage in order to differentiate these conditions. A total of 60 patients (30 EP and 30 miscarriages) with gestational age of 5-7 weeks by LMP were enrolled in this study. The titer of progesterone and β hCG of serum were measured. The mean of progesterone and β hCG titers were compared in two groups by Student's t-test. The mean progesterone titer for all patients was 6.36 ± 5.62 ng/ml, with a minimum value of 0.44 and maximum value of 21.50 ng/ml. Serum progesterone level in 33 patients was lower than 5 ng/ml and in 27 patients was between 5-25 ng/ml. Mean serum progesterone for miscarriage was 6.803 ± 5.72 and for EP was 5.915 ± 5.45 ng/ml. Difference between two values was not significant statistically ($P=0.067$). Mean β hCG for miscarriage was 1313.04 IU/l and for EP 1805.56 IU/l. Mean patients age were 27.2 totally that for miscarriage was 25.8 and for EP 28.5 years. This study indicated, the mean value of progesterone could not differentiate EP from miscarriage.

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Introduction

Vaginal bleeding in first trimester occurs in the 25% of pregnancies (1). Two main differential diagnoses for the causes of bleeding in the first trimester of pregnancies are abortion and ectopic pregnancy (EP). Both conditions are diagnosed with retardation of menstruation and vaginal bleeding. Doubling time of β hCG at the beginning of pregnancies is regular and almost two-fold each 48 hours. However, increase rate is low in non-viable pregnancies. When rising of β hCG is abnormal, differentiation between EP and abortion are needed. Two methods for accurate diagnosis are including trans-vaginal ultrasonography and determining progesterone level.

Considerable increase were observed in prevalence of EPs at the recent decades that majority of those are in patients with 35-55 years old (2). Ectopic pregnancy within Africo-Americans and other ethnic minorities is 1.6 fold higher than Caucasians. The risk of EP following previous EP is 7-13 folds. Some risk factors

have been suggested for increase prevalence of EP. These risk factors include sexually transmitted diseases (STD), contraceptive methods such as IUD, failure of tubal ligation, induced abortion, assisted reproductive technologies (ART), and tubal reconstructive surgeries (3).

Early fetal loss is estimated to be about 40%, but women rarely seek medical attention for it, so there is no medical record, and it is not reported in retrospective studies due to recall bias; therefore, 3/4 of all early fetal loss is never recognized (4). On the other hand, EP is a condition that necessitates diagnoses of a normal pregnancy and miscarriage. One of valuable items for differentiation normal pregnancy from abnormal pregnancy is serum progesterone but it is abnormal in abortion and EP. When β hCG titer is lower than 1500 IU/l the accurate diagnosis between EP and intrauterine pregnancy (IUP) is detection of progesterone serum level. Serum progesterone level in EP and abortion are low but it might have a diagnostic potential for differentiation of EP and abortion. The purpose of this

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study was to evaluate progesterone level in EP and abortion for accurate diagnosis of these conditions.

Materials and Methods

This study was conducted at the University Hospital of Fatemeh from March 2008 through November 2009. In this comparative study, 30 patients with definitive diagnosis of EP and a cohort of 30 patients with abortion were enrolled. The patients were women with pregnancy more than 5 weeks and less than 7 weeks and the patients with habitual abortion exclude of the study. Diagnosis for EP was based on β hCG higher than 1500 IU/l and transvaginal ultrasound study. Biochemical pregnancies were those with transient elevations in β hCG concentration but without implantation sites. The tubal pregnancy explored by surgery. Spontaneous abortions were characterized by an implantation site with the eventual arrest of development and definitive diagnosis for abortion was on the basis of: detecting intra uterine pregnancy sac, or bleeding and dilated cervix. Two ml blood sample were taken from each patient and progesterone and β hCG were measured by a diagnostic kit from DRG Company according to manufacturer’s instruction.

The mean value of progesterone and β hCG were compared between two groups of patients using Student’s t-test.

Results

The mean age of the patients was 27.2. In the EP group, this mean was 28.57 and in the abortion group was 25.87 years old. The most cases of EP were happened in the 31 years and the most of abortions happened in the 23 years old.

The range of progesterone value were 0.44 to 21.50 ng/ml and mean of progesterone in the EP group was 5.91 ± 5.45 ng/ml and in the abortion group was 6.80 ± 5.72 ng/ml. The difference in progesterone level was not statistically significant between groups. The mean of β hCG in the EP group was 1805.56 ± 2254.7 IU/l and in the abortion group was 1313.04 ± 1188.16 IU/l. This difference was not also statistically significant. The value of progesterone in the EP and abortion groups in terms of lower or higher than 5 ng/ml is shown in table 1. Frequency of progesterone in terms of gestational age in the EP and abortion groups is demonstrated in table 2.

Table 1. The value of progesterone in the EP and abortion groups in terms of lower or higher than 5 ng/ml.

Groups	Progesterone < 5 ng		Progesterone >5 ng (5-25 ng)		Total	
	No.	%	No.	%	No.	%
EP	20	66.7	10	33.3	30	100
Abortion	13	43.3	17	56.7	30	100
Total	33	55	27	45	60	100

Table 2. The value of progesterone in terms of gestational age in the EP and abortion groups.

Gestational age	Progesterone < 5 ng		Progesterone >5 ng (5-25 ng)		Total	
	No.	%	No.	%	No.	%
5 weeks						
EP	5	16.66	2	6.66	7	23.33
Abortion	3	10	1	3.33	4	13.3
6 weeks						
EP	5	16.66	3	10	8	26.66
Abortion	3	10	9	30	12	40
7 weeks						
EP	5	16.66	10	33.33	15	50
Abortion	7	23.33	7	23.33	14	46.66
Total	33	55	27	45	60	100
EP	15	50	15	50	30	100
Abortion	13	43.3	17	56.7	30	100

Discussion

This study indicated no differences observed between the value of progesterone in the EP and abortion. In order to differentiate early fetal loss from EP more accurately, one must first develop a simple method to identify early pregnancy. EP is common complication in women but remains difficult to diagnose and differentiate from miscarriage accurately. When β hCG titer is lower than 1500 IU/l and gestational sac is not observed in sonography, one approach to differentiate EP from viable pregnancy is determining serum progesterone titer. Progesterone level is low in EP and abortion. However, it is not clear what level of progesterone is diagnostic for EP. Horne *et al.* reported that, inhibin/activin beta-B expression was lower in decidualized endometrium from EP when compared with that of ongoing pregnancies or miscarriages (5). Similar concentrations of progesterone have been reported in two groups that indicate, this factor could not consider as a valid marker for differentiation of these two conditions.

The study of El Bishry and Ganta showed that a protocol combining single serum progesterone measurement and β hCG is helpful in managing women with suspected EP, when the ultrasound examination is inconclusive (6). High levels of progesterone are reassuring as regards ongoing viable pregnancies and low levels allow a definitive differentiation between viable and non-viable pregnancies. However, low progesterone concentration could not efficiently differentiate between miscarriage and ectopic pregnancy. They suggested that, the use of β hCG levels in conjunction with serum progesterone is helpful, particularly with serum progesterone levels between 16-80 nmol/l (6). In another study by measuring CA-125 and progesterone, women with EP had significantly low progesterone concentrations, compared to both women with intrauterine (IU) abortive pregnancy and controls. Women with abortion had significantly higher CA-125 levels, compared to the other two groups (7). When using progesterone concentration of less than 10.75 ng/ml as cut-point for the diagnosis of EP, sensitivity, specificity, positive and negative predictive values were 85%. When using CA-125 concentration of more than 41.9 U/ml as a threshold for the diagnosis of IU abortive pregnancy, sensitivity, specificity, positive predictive value and negative predictive value were 80%, 87%, 66% and 93% respectively (7).

In a controlled trial, the sensitivity, specificity, and predictive value of serum progesterone <45 nmol/l in

identifying nonviable pregnancies were determined for each of the groups of pregnant and non-viable pregnancies. Sensitivity and specificity of serum progesterone in predicting non-viable pregnancies were 88.6% and 87.5%, respectively in spontaneously pregnant patients who presented to the emergency department with pain or bleeding. These values were 58.8% and 100% in infertile patients who had undergone controlled ovarian hyper-stimulation for *in vitro* fertilization or intrauterine insemination (8).

On the other hand Valley *et al.* reported that serum progesterone cannot reliably discriminate ectopic pregnancy *versus* spontaneous abortion in pregnant patients with no definite IUP on endo-vaginal ultrasonography; however, a low serum progesterone (<11 ng/ml) in this sonographic category suggests an abnormal pregnancy (9).

Even though many studies were done on the measuring serum progesterone (10-12) or single serum activin A for evaluating this condition (13,14), but controversies results get open doors for investigations in this field. Our findings also indicated on the basis of a single serum progesterone measurement cannot differentiate an EP from an aborted gestation.

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References

1. Cunningham FG, Leveno RJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics, 23th ed, New York: McGraw-Hill Medical 2011: 259-61.
2. Berek JS. Berek & Novak's Gynecology, 14th ed. Philadelphia: Lippincott Williams & Wilkins 2012;450-60.
3. Speroff LM, Fritz A. Clinical Gynecology, Endocrinology, & Infertility, 17th ed. Philadelphia: Lippincott Williams & Wilkins 2005: 922-30.
4. Gibbs RS, Karlan BY, Haney AF, Nygaard I. Danforth's Obstetrics & Gynecology. 10th ed. 2008, Philadelphia: Lippincott Williams & Wilkins 2008: 747-50.
5. Horne AW, van den Driesche S, King AE, Burgess S, Myers M, Ludlow H, Lourenco P, Ghazal P, Williams AR, Critchley HO, Duncan WC. Endometrial inhibin/activin beta-B subunit expression is related to decidualization and is reduced in tubal ectopic pregnancy. J Clin Endocrinol Metab 2008; 93(6): 2375-82.

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6. El Bishry G, Ganta S. The role of single serum progesterone measurement in conjunction with beta hCG in the management of suspected ectopic pregnancy. *J Obstet Gynaecol* 2008; 28(4):413-7.
7. Katsikis I, Rousso D, Farmakiotis D, Kourtis A, Diamanti-Kandarakis E, Panidis D. Receiver operator characteristics and diagnostic value of progesterone and CA-125 in the prediction of ectopic and abortive intrauterine gestations. *Eur J Obstet Gynecol Reprod Biol* 2006; 125(2):226-32.
8. Perkins SL, Al-Ramahi M, Claman P. Comparison of serum progesterone as an indicator of pregnancy nonviability in spontaneously pregnant emergency room and infertility clinic patient populations. *Fertil Steril* 2000; 73(3):499-504.
9. Valley VT, Mateer JR, Aiman EJ, Thoma ME, Phelan MB. Serum progesterone and endovaginal sonography by emergency physicians in the evaluation of ectopic pregnancy. *Acad Emerg Med* 1998; 5(4):309-13.
10. al-Sebai MA, Kingsland CR, Diver M, Hipkin L, McFadyen IR. The role of a single progesterone measurement in the diagnosis of early pregnancy failure and the prognosis of fetal viability. *Br J Obstet Gynaecol* 1995;102(5):364-9.
11. McCord ML, Muram D, Buster JE, Arheart KL, Stovall TG, Carson SA. Single serum progesterone as a screen for ectopic pregnancy: exchanging specificity and sensitivity to obtain optimal test performance. *Fertil Steril* 1996; 66(4):513-6.
12. Ugurlu EN, Ozaksit G, Karaer A, Zulfikaroglu E, Atalay A, Ugur M. The value of vascular endothelial growth factor, pregnancy-associated plasma protein-A, and progesterone for early differentiation of ectopic pregnancies, normal intrauterine pregnancies, and spontaneous miscarriages. *Fertil Steril* 2009; 91(5):1657-61.
13. Florio P, Severi FM, Bocchi C, Luisi S, Mazzini M, Danero S, Torricelli M, Petraglia F. Single serum activin a testing to predict ectopic pregnancy. *J Clin Endocrinol Metab*. 2007; 95(5): 1748-53
14. Florio P, Gabbanini M, Borges LE, Bonaccorsi L, Pinzauti S, Reis FM, Boy Torres P, Rago G, Litta P, Petraglia F. Activins and related proteins in the establishment of pregnancy. *Reprod Sci*. 2010;17(4):320-30.