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Six-Month Follow-Up After Mole Evacuation

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Abstract

Background: Most gestational trophoblastic neoplasias (GTN) develop following hydatidiform mole; but may occur after abortion, normal pregnancy or even ectopic pregnancy.
Objectives: The aim of this study was to assess the importance of six-month follow-up of uncomplicated molar pregnancy after achieving undetectable β-human chorionic gonadotropin (β-hCG) levels.
Patients and Methods: In this retrospective study, molar pregnancies with negative β-hCG were compared with those with positive β-hCG during a six-month follow-up.
Results: A total of 279 women with molar pregnancy, treated at two referral university hospitals in Tehran were analyzed and 86 patients (31%) who had completed their follow-up period were included. Of the evaluated patients (n = 86), the pathology report indicated complete mole for 66 patients (77%) and partial mole for 20 patients (23%). All 86 patients had achieved at least one undetectable β-hCG level during their follow up, and none showed evidence of relapse.
Conclusions: We found that in patients with uncomplicated molar pregnancy, relapse is unlikely after achieving undetectable serum β-hCG levels. Further investigations with larger sample sizes and preferably prospective design are needed to make a definite conclusion.

Keywords: Gestational Trophoblastic Disease, Hydatidiform Moles, HCG Beta

1. Background

Gestational trophoblastic disease (GTD) includes complete or partial hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor (1). Previous studies have reported different incidences of GTD in different parts of the world. It is 5 - 15 times more prevalent in Far East and South East Asia compared to Western industrial countries (2). The hydatidiform mole (complete or partial) occurs in approximately 1 per 500 to 2000 pregnancies in the Unites States. An Iranian study performed by Shahverdi et al. between years 2004 and 2009 in a university hospital in Tehran, reported the prevalence of GTD as 13.3 per 1000 deliveries (3). In another study by Javey et al. in southern parts of Iran in 1978, the prevalence of hydatidiform mole was reported as one in 314 pregnancies (4). In another Iranian study conducted between years 1998 and 2007, the frequency of hydatidiform mole was reported as 3.1 per 1000 live births (5).

In fact, gestational trophoblastic neoplasia (GTN), which histologically includes invasive mole, choriocarcinoma and placental site trophoblastic tumor is a subgroup of GTD, and is characterized by aggressive myometrial invasion of trophoblastic tissues with metastatic ability. Most GTNs develop following a hydatidiform mole, yet may occur after abortion, normal pregnancy or even ectopic pregnancy (1). The probability of progression to GTN is 1 - 5% and 15 - 20% for partial and complete moles, respectively (6). After treatment of GTD, including molar evacuation, serial measurements of β-human chorionic gonadotropin (β-hCG) levels are the most efficient and useful assessment for GTN diagnosis and follow-up in women with molar pregnancy. In most previous reports, it is recommended that patients with molar pregnancies should be followed by serial measurements of β-hCG for six-month. This follow-up period is not only time-consuming, which reduces patients' compliance for taking part in follow-up visits, but may not be cost effective. Furthermore, unintended pregnancies that may occur in this period interfere with this long-term supervision. Recently, several studies have shown that minimization of the follow-up period is safe (7). In this study, which to the best of our knowledge was performed for the first time

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in Iran, we analyzed the data of patients with molar pregnancy, who were diagnosed and treated at two referral hospitals in Tehran since ten years ago.

2. Objectives

The aim of this study was to evaluate the importance of serial measurement of β-hCG in detecting GTN after achieving undetectable β-hCG levels during six-month follow-up of patients treated for uncomplicated moles.

3. Patients and Methods

This descriptive retrospective study was performed at two referral hospitals of Tehran. During a ten-year period of evaluating patients' records (April 2005 to March 2015) at a pathology department, all women with a diagnosis of complete or partial mole following suction evacuation and endometrial curettages were selected. The patients' records were evaluated after receiving their informed consent. The data including age, gestational age at the time of evacuation, number of pregnancies, number of previous abortions, family history of molar pregnancy, and β-hCG level before surgery were collected. The follow-up protocol was as follows: measurement of serum β-hCG level, weekly until three negative β-hCG results, followed by reassessment on a monthly basis for six-month if β-hCG results remained negative continuously. The inclusion criterion was the pathologic diagnosis of complete or partial mole. The exclusion criterion was incomplete documents as well as incomplete follow-up. Meanwhile, based on patient records, the time between the date of treatment (curettage) and the date that the serum level of β-hCG was normal for the first time during the aforementioned follow-up period was calculated and recorded (in weeks).

The results are given as mean and standard deviation for quantitative variables as well as frequency and percentages for qualitative data. For bivariate analyses, to compare between patients with complete and partial molar pregnancy, categorical variables were compared by the Pearson chi-square or Fisher's exact test, and continuous variables were compared by Student's t or Mann-Whitney U test. Statistical evaluation was performed by the SPSS software, version 20 (SPSS, Inc., Chicago, IL, USA) and a P value of less than 0.05 was defined for level of significance.

4. Results

Out of 279 patients included in this study based on their records and consent form, only 86 (31%) completed the six-month follow-up. Based on the inclusion and exclusion criteria of this research, for the rest of the candidates (193 patients) there were no reliable, documented follow-up data and thus they were excluded from the study. Of the evaluated patients (n = 86), the pathology report indicated complete moles for 66 patients (77%) and partial moles for 20 patients (23%). The patients' age ranged from 15 to 50 years with a mean of 26.8 years and there was no significant difference between the two groups of complete and partial mole (mean age was 27.2 and 25.5 years in patients with complete and partial mole, respectively) (Table 1). Demographic variables are shown in Table 1. All 86 patients had been treated by evacuation curettage. Gestational age at time of curettage ranged from 5 to 24 weeks with mean of 12.4 weeks, with no significant difference between the two groups (13 and 12 weeks for complete and partial mole, respectively). Overall, 40% of the patients were experiencing their first pregnancy. Nearly 70% of patients had no history of abortion (Table 1). In this study, after the six-month follow-up, no patient had increased level of β-hCG after achieving negative results in the pregnancy test following molar evacuation. The average post treatment time to have a normal pregnancy test was 7.2 weeks, again with no significant difference between the two groups [7.2 (range: 1-32) vs. 7 (range: 2 - 20) weeks in complete and partial mole, respectively; $P < 0.75$]. The mean β-hCG level (IU/L) before curettage was 163,092 among all patients, 187,453 (range: 186 - 3,170,000) in the complete mole group and 73,767 (range: 200 - 674,000) in the partial mole group. Although, the mean β-hCG level before curettage in patients with complete mole was 2.5 times more than the partial mole group, this difference was not statistically significant (P = 0.40).

In patients who attained a negative pregnancy test in seven or less weeks after curettage, mean β-hCG level before curettage was 44,816 (range: 200 - 470,000) IU/L while it was 458,783 (range: 186 - 3,170,000) IU/L in patients who reached a negative pregnancy test in more than seven weeks after curettage, and there was a significant difference between these two groups (P = 0.022). On the other hand, when the level of β-hCG was compared on this basis, in patients who obtained a negative β-hCG in equal, less than seven weeks after evacuation, mean β-hCG level was significantly less than the other group. In this regard, although there was no statistically significant difference between complete versus partial mole group, the outcome was more notable in the complete mole than the partial mole group (P=0.062 and P=0.209 for complete and partial mole, respectively) (Table 2).

Table 1. Comparison of Variables in Patients with Complete or Partial Moles

Parameter	Total	Mole		P value
		Complete	Partial	
Age (years)				0.66[a]
Mean ± SD	26.8 ± 8.3	27.2 ± 8.7	25.5 ± 6.8	
Median (Range)	24.5 (15 - 50)	25.5 (15 - 50)	24 (16 - 44)	
95% CI	25 to 29	25 to 29	23 to 28	
Gestational age (weeks)				0.583[a]
Mean ± SD	12 ± 4	13 ± 4	12 ± 4	
Median (Range)	12 (5 - 24)	11 (5 - 24)	12 (6 - 20)	
95% CI	12 to 12	11 to 15	10 to 14	
β-hCG before evacuation (IU/L)				0.402[a]
Mean ± SD	163093 ± 468582	187454 ± 518300	73768 ± 191444	
Median (Range)	12355 (186 - 317)	13320 (186 - 317)	8540 (200 - 674)	
95% CI	40364 to 285822	34305 to 340603	-34551 to 182087	
Time of negative β-hCG after curettage (weeks)				0.758[a]
Mean ± SD	7.1 ± 4.4	7.2 ± 4.5	7 ± 4.2	
Median (Range)	6 (1 - 32)	6 (1 - 32)	6 (2 - 20)	
95% CI	6 to 8	6 to 8	5 to 9	
Gravida, No. (%)				
1	36 (42.9)	28 (43.8)	8 (40.0)	0.973[a]
2	23 (27.4)	16 (25.0)	7 (35.0)	
3	9 (10.7)	8 (12.5)	1 (5.0)	
4	7 (8.3)	5 (7.8)	2 (10.0)	
5	5 (6.0)	4 (6.2)	1 (5.0)	
6	1 (1.2)	1 (1.6)	0 (0.0)	
7	3 (3.6)	2 (3.1)	1 (5.0)	
History of abortion				
No	58 (69.0)	43 (67.2)	15 (75.0)	0.438[a]
1	22 (26.2)	17 (26.6)	5 (25.0)	
2	3 (3.6)	3 (4.7)	0 (0.0)	
4	1 (1.2)	1 (1.6)	0 (0.0)	
Family history of mole				
No	81 (94.2)	62 (93.9)	19 (95.0)	> 0.99[b]
Yes	5 (5.8)	4 (6.1)	1 (5.0)	

Abbreviation: β-hCG: beta-human chorionic gonadotropin; CI, confidence interval; SD, standard deviation.
[a] Based on Mann-Whitney test.
[b] Based on Chi-square test.

5. Discussion

It is known that after molar evacuation, the probability of conversion to GTN for complete mole is 15 - 20% and for partial mole is about 1 - 5% (8-11). Therefore, after molar evacuation, serial measurement of β-hCG is the most important part of follow-up, assessing the response to the treatment as well as early detection of GTN. For this reason, six-month follow-up after achieving negative β-hCG level is

Table 2. Serum Level of β-hCG Before and After Evacuation[a]

	Type of Mole	Duration Between Evacuation ond Normal β -Hcg				P Value
		≤ 7 Weeks		>7 Weeks		
		Mean ± SD	Median (range)	Mean ± SD	Median (range)	
β -hCG before evacuation (IU/L)	Total	44816 ± 89194	7813 (200 - 470000)	458783 ± 808602	90000 (186 - 3170000)	0.022
	Complete	51814 ± 98928	8200 (200 - 470000)	510904 ± 8816312	110000 (186 - 3170000)	0.062
	Partial	20714 ± 3 5212	2800 (200 - 103100)	32927 ± 382041	19200 (5580 - 674000)	0.209

[a]Based on Mann-Whitney test.

recommended for all patients with molar pregnancy. Recently, several studies have shown that when β-hCG level becomes undetectable after molar evacuation (complete or partial), the probability of relapse is too low to be followed for six-month. They suggested that there is no need to check monthly β-hCG level for six-month and that the patients can be allowed to become pregnant after passing three months of follow-up, especially older patients, who desire to become pregnant sooner (12-14).

In a study by Feltmate et al. in 2003, 320 patients with uncomplicated molar pregnancy who had been randomly selected, were evaluated. After achieving negative β-hCG, no patient developed GTN (14). Based on the results of our study on 86 Iranian women with molar pregnancy, there was no case of GTN after attaining a normal serum level of β-hCG following evacuation. Based on our findings, the probability of conversion of uncomplicated molar pregnancy to GTN after evacuation and achieving negative β-hCG is near zero. Although, follow-up is necessary after molar evacuation, long-term monitoring of β-hCG, initially weekly and then monthly, up to six-month, is associated with increased anxiety and also imposes a financial load on the family and also bears great economic burden for governmental health systems. Therefore, based on the findings of our research and other studies, it might be suggested that there is no need for follow-up after a normal β-hCG test; however, as the sample size of this study was small more extensive studies with larger sample sizes are required for this protocol.

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