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Human chorionic gonadotrophin as an indicator of persistent gestational trophoblastic neoplasia

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Abstract

Background: Gestational trophoblastic neoplasia (GTN) disease is excessive and inappropriate proliferation of trophoblast after termination of the pregnancy. Many attempts have been made to improve follow-up procedures, but no studies have evaluated Human Chorionic Gonadotrophin (HCG) as a post treatment indicator. Thus we aimed to know β-HCG variability in post treatment pregnancies.

Methods: 40 Molar affected pregnancies were followed post-surgical treatment by serum β-HCG level in a tertiary level hospital. All subjects were treated by evacuation and followed by β-HCG every week for three weeks, then every month for six months.

Results: 30 women were normal (group I) and 10 (group II) diagnosed as GTN cases. Serum β-HCG which obtained serially shown significant differences between two groups (p=0.001). The quantity of β-HCG/week had significantly higher level than normal females (p<0.001)

Conclusion: Our results suggested that β-HCG serum level could be used as a strong indicator for identifying affected patients at early stage.

Keywords: Gestational trophoblastic neoplasia, Molar pregnancy, β-HCG, Chemotherapy.

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Introduction

Gestational trophoblastic neoplasia (GTN) is an excessive and inappropriate proliferation of trophoblast after the end of pregnancy that comprised a spectrum of pregnancy-related disorders. Initial treatment involves uterine evacuation, with a histopathological diagnosis (1). There are significant regional and racial differences in the incidence of GTN worldwide. It is a rare but important pregnancy-related disorder with an incidence of 1 in 400 in Asia and Latin America with higher rate in western countries (1, 2). The GTN is one of the most curable malignancies. The intrinsic sensitivity of the tumor to certain antineoplastic agents, in particular sensitive assays for human chorionic gonadotropin, has made it detectable and capable of being efficiently followed-up (2). The GTN requires chemotherapy, surgery or a combined treatment modality (3). Chemotherapy is the main modality of treatment for patients with GTN.

The cure rate in patients with low-risk GTN is approximately 100% and is estimated to exceed 80% in patients at high-risk (4,5). Surgical treatment such as a hysterectomy is rarely needed. However, in some countries, the incidence of hysterec-

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tomy has been estimated to be up to 35% in all cases of GTN (6). Post-surgical treatment follow up of patients is a main goal of new medicine. Many attempts have been made to improve follow-up procedures, but there are no studies that have evaluated Human Chorionic Gonadotrophin (HCG) as a post treatment indicator. Therefor we aimed to know β-HCG variability in post treatment pregnancies.

Method

Subjects

In this Cross-sectional study, all patients with molar affected pregnancies during year 2012, referred to Firoozgar Hospital obstetrics and gynecology. We followed consecutive 40 molar affected pregnancies post-surgical treatment by serum β-HCG level in patients. All patients with invasive molar, a history of prophylactic chemotherapy and also metastatic case were excluded. All subjects were treated by utrine evacuation and followed by β-HCG every week for three weeks, then every month for six months. In addition demographic data, gestational and abortion past history were used in this study.

The women were divided into two groups based on GTN involvement after three weeks based on HCG levels. All data included serial β-HCG which compared together. That was aimed to know GTN effects on variation of serum β-HCG differences at exact times in post treatment period. The β-hCG was measured by a solid-phase, twosite immunoradiometric assay (ELSA F-βHCG; CIS Ltd., Gif-sur-yvette Cedex, France) maximum of 2 hours post antecubital phlebotomy.

Statistical Analysis

Mean, median, range, standard deviation (SD), frequency and frequency percentage were determined using statistical software SPSS (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, Illinois, USA), and using descriptive analyses. For comparison of the averages between study groups, independent T test was used after the normal distribution of data tested to determine whether it followed by 1-sample KS; and Chi square statistical test used for the comparison of qualitative ratios. Generalized linear Model (GLM) was utilized to appear significant differences in time-HCG between two groups. In all tests, significance level was considered as two tails with p value less than 0.05.

Results

30 women were normal (group I) and 10 other (group II) were detected as GTN cases.

The mean age of patients was 28.4 ± 4.6 years in group I (with no evidences of GTN), and 30.2 ± 4.7 years in group II (affected by GTN), with no significant difference ($p = 0.32$).

There were infertility problems among 3 and 1 patients in Group I and II, respectively ($p = 0.34$), with the Follow-up time of 25 to 27 weeks.

Abortion history was found in one, from GTN group, which did not differed significantly with the other group.

Gravity with a mean of 2.1±0.6 and 2.2±0.6 in Group I and II, respectively, also without significance difference ($p=0.35$).

The Serum β-HCG obtained serially shown significant differences between two groups ($p=0.001$), but its amounts had decreasing pattern in normal group rather than the GTN affected cases. However toward the end of study this pattern was reversed, particularly between 25-27th weeks.

The GLM model demonstrated that the amount of β-HCG/week had significantly higher level than normal females ($p<0.001$).

Combined diagrams are also shown in the results.

Discussion

There is no single test currently available that exactly differentiates continuing non-complicated from GTN in post molar treated cases. Ultrasound scanning and β-HCG are probably the best single diagnostic and prognostic tests available in threatened

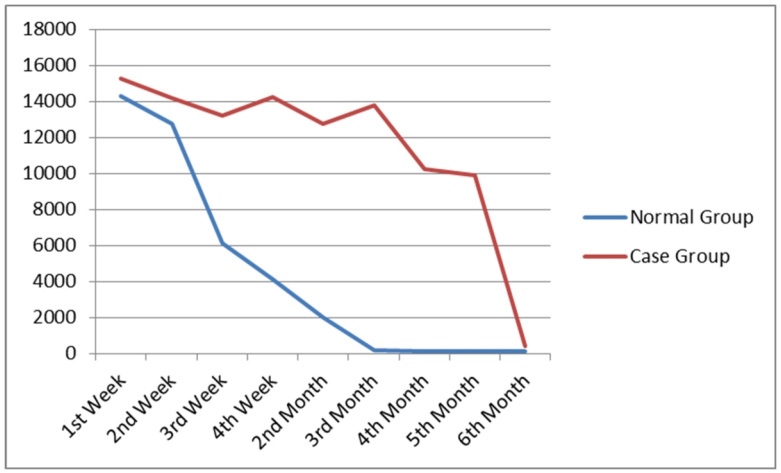

Fig. 1. The β-HCG/week results for the normal and case group.

uterine evacuation. Despite of importance of β-HCG level in follow up there was no attempt to evaluate post op amounts of serum β-HCG in these patients.

The normal range of free β-HCG has been debated (7-13). Kang et aL (8) suggested that the range of free β-HCG is narrow and constant throughout pregnancy. McGrath et al. (10) suggested high early concentrations which declined prior to the HCG peak.

Rangwala et aL (12) and Thomas et al. (14) suggested that free β-HCG concentrations increase rapidly, reaching maximum values at 8-9 weeks of gestation and then declining gradually during the following 11-12 weeks; however, the values remained very low in comparison with those of HCG. Alazzam et aL (13) found a significant free J-HCG peak in the third month of gestation.

Nevertheless, the same studies exhibited considerably more agreement on the concentrations of HCG, which show wide variations at different stages of pregnancy in the same individuals and also among women with pregnancies of the same gestational age. The HCG concentrations also show considerable overlap with abnormally low and high values, which makes the interpretation of any results difficult, especially at the time of the HCG peak at 1-12 weeks of gestation. In addition, the half-life of HCG is probably long. It has been reported to be between 12 h (11-15).

Gestational trophoblastic neoplasia is highly responsive to chemotherapy and prognosis is excellent following treatment, especially in low-risk patients. Some previous studies have examined the link between hCG levels and the likelihood of complete treatment of molar pregnancy without significant difference in the median hCG values when comparing the group that completed low-risk treatment with those that required a change of treatment.

There was no evidence to clarify role of β-HCG in diagnosis of post molar complications. We found that β-HCG decreased more rapidly in non-affected women, however at fewer amounts this fluctuated reversely. Indeed β-HCG/week ratio differed significantly between the groups, reflects that normal patient's hormone fell more rapid than affected people.

Based on our data we resulted that there was a significant differences of β-HCG amount between two groups of post molar women, one which treated completely and other who switched to the GTN. In both groups post molar β-HCG curve decreased however this rate was significantly faster in cured women. It means that post molar β-HCG curve could acts as a suitable guide to show GTN and differed it from healthy cases, and also useful for post molar follow up.

Our study had weak points and lack some dimensions. Hyperglycosilated HCG is an-

other isomer of β-HCG that could appear brightly as a guide factor to detect post molar situation in complicated pregnancies. This type of β-HCG may appear some differences and plays an axis role to differentiated treated post molar pregnancies from GTN.

Conclusions

For first time in this profile we tried to understand variability of β-HCG concentrations based on post molar complications. Our results suggested that β-HCG serum level could be used as a meaningful indicator to distinguish affected patients at early stage of the treatment.

In summary, our data suggests that it is reasonable to rely on post treatment β-HCG to distinguish complicated molar pregnancy from completely treated one.

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