Assessing the return Potential of Foetal Trophoblastic Neoplasia Following This process of Plasma Beta-HCG.

Elham Moghaddam

Department of Obstetrics and Gynecology, Ahvaz Jondishapour University of Medical Sciences, Ahvaz, Iran

*Corresponding Author : Elham Moghaddam, Department of Obstetrics and Gynecology, Ahvaz Jondishapour University of Medical Sciences, Ahvaz, Iran

Abstract

Background : While chemotherapy is a viable treatment option for many GTN patients, a tiny percentage of these patients will experience a relapse following full recovery. To the best of our knowledge, our region does not have any information regarding GTN instances that have relapsed. The objective of this study is to assess the probability of recurrence of gestational trophoblastic neoplasia (GTN) following normalisation of serum βhCG levels.

Methods : Between 2011 and 2017, patients with confirmed GTN diagnosis who were admitted to the gynaecology ward of Imam Khomeini Hospital after molar pregnancy were the subject of this descriptive-analytical study using registered hospital data. Included were patients who have been diagnosed with postmolar GTN using at least five bhcg readings.

Information about the patient was assessed, including the initial serum BhcG level, the duration till BhcG resolution, the forms of molar pregnancy, the treatment regimens, the necessity of recuretage relapse, and, lastly, the interval between BhcG resolution and relapse.

Results : A total of 239 patients with GTN were assessed in this study, comprising 180 whole and 59 partial moles. The patients ranged in age from 16 to 47 years old, with a mean age of 28.8 years. A mean concentration of 170,000 IU/ml was found for βhCG. Within the range of 4 to 12 months, the average time for βhCG resolution was 8.19 months. Three percent, or nine patients, experienced recurrence. The average duration from βhCG resolution to recurrence was 20.94 months. Patients who experienced a recurrence had a considerably lower mean initial level of βhCG (p <0.0001).

The patients undergoing treatment with numerous drugs had the highest rate of recurrence. Additionally, there was a strong correlation between the disease stage and the rate of recurrence.

Conclusion : Despite the fact that GTN recurrences are uncommon, the poor prognosis of these patients suggests that ongoing monitoring of bHCG levels for a minimum of two years is necessary to stop the disease from getting worse.

Keywords : *Gestational Trophoblastic Neoplasia, Molar Pregnancy, Recurrence*

Introduction

A collection of illnesses known collectively as gestational trophoblastic disease (GTD) are distinguished by aberrant trophoblastic tissue proliferation. Invasive moles, choriocarcinomas, placental trophoblastic tumours, and epithelioid trophoblastic tumours are among the malignant forms of GTD known as gestational trophoblastic neoplasia (GTN). Molar pregnancies are most frequently followed by these malignancies, even though they can occur weeks or years after any kind of pregnancy (Heller, 2015; Barroilhet, 2018; Shaaban, Rezvani, Haroun, Kennedy, Elsayes, Olpin, Salama, Foster, & Menias, 2017; Reva Tripathi, 2017; Biscaro, Braga, & Berkowitz, 2015). The four criteria for diagnosing GTN are as follows: no decline in hCG-β levels after four weeks, elevated hCG-β serum level for three consecutive weeks, hCG-β detection nine months after mole removal, and histological diagnosis of choriocarcinoma. These guidelines are recommended by the International Federation of Obstetrics and Gynaecology (FIGO).

After having their moles removed, some of the patients with molar pregnancies did not fully recover and went on to develop malignancies. Thus, it has been very crucial to identify a suitable marker for the early prediction of neoplasia (Seckl, Sebire, & Berkowitz, 2010). Vaginal bleeding during the first trimester

Review Article

or abnormal ultrasound findings between weeks 12 and 18 of pregnancy are typical symptoms of GTN in women. When a tumour invades the uterus, it may cause severe vaginal bleeding in certain instances or rupture the myometrium, which might result in intraperitoneal haemorrhage in other instances. Furthermore, according to Mangaglia, Garavaglia, Cavoretto, Gentile, Scarfone, and Rabaiotti (2008), an intrauterine necrotizing tumour may serve as an infection focus.

In recent years, a great deal of research has been done to identify the right markers for the early detection of GTN. A number of studies, for instance, recommended the ratio of hCG-α and hCG-β or the ratio of B-HCG before and one week after mole excision as suitable early predictors of GTN (Kang, Choi, & Kim, 2012). If the hCG value is normal for three weeks in a row (less than five mIU/mL) and remains normal for up to nine months, GTD is said to be treated. Only half of patients attend planned medical visits during molar pregnancy, and the primary issue in poor nations is the cessation of follow-up after hCG normalisation (Schmitt, Doret, Massardier, Hajri, Schott, Raudrant, & Golfier, 2013).

The probability of a GTN recurrence following hCG normalisation was suggested by the accounts of relapsed patients. It was demonstrated by Bagshawe et al. that GTN may spontaneously reappear following the normalisation of serum hCG levels. Therefore, once hCG levels have stabilised, a standard follow-up regimen is implemented. In a recent publication, the authors Jankilevich, Uberti, Braga, Bianconi, Maesta, Viggiano, Sun, Cortes Charry, Salazar, Grillo, & Moreira de Andrade recommended monitoring hCG levels for at least nine months following normalisation. Our goal in this study is to find out how often GTN relapses once serum hCG levels have stabilised.

Material and Methods

Research Framework

This descriptive-analytical study collected hospital data from patients admitted to the gynaecology ward of Imam Khomeini Hospital between 2011 and 2017 who had a confirmed diagnosis of GTN after a molar pregnancy. Individuals who were diagnosed with postmolar GTN and had at least five bhcg measurements were included; those whose records were incomplete were not. During the study years, patient data such as baseline serum BhcG, time to BhcG resolution, forms of molar pregnancy, treatment regimens, necessity to prevent relapse, and lastly, the interval between relapse and BhcG resolution was assessed.

Explanations

Postmolar GTN was characterised by the presence of one of the following FIGO standards: when the hCG plateau persists for four measures across a minimum of three weeks, i.e., days 1, 7, 14, and 21. when there is an increase in hCG on days 1, 7, and 14 for three consecutive weekly measurements for a minimum of two weeks. if choriocarcinoma has been diagnosed histologically.

Examining Data Statistically

The mean, median, standard deviation, frequency, and percentage were used to characterise the data. The Mann-Whitney or independent student t-test was used to perform the mean comparison. To compare the proportions, the chi-square test was used. The relapse period was described using the Kaplan-Meier plot. Using SPSS version 20, every statistical analysis was completed.

Results

239 GTN patients, comprising 180 whole and 59 partial moles, were assessed in the current investigation. The patients ranged in age from 16 to 47 years old, with a mean age of 28.8 years. The βhCG concentration ranged from 760 to 850,000 IU/ml, with a mean value of 170,000. Within the range of 4 to 12 months, the average time for βhCG resolution was 8.19 months. The majority of patients (157 patients) had treatment with a single medication, such as actinomycin (131 patients) and MTX (26 patients). Additionally, 16 patients (6.7%) had recurettage treatment, while 66 patients (27.6%) received multi-drug chemotherapy. Three percent, or nine patients, experienced recurrence. The average duration from βhCG resolution to recurrence was 20.94 months. Two groups of our patients—one with a recurrence and the other without—were created. In neither group was the mean age of the patients statistically significant. Patients who experienced a recurrence had a considerably lower mean initial level of βhCG (p <0.0001). Between the two groups, there was no discernible difference in gestational age. Furthermore, there was no significant difference in the mean period duration of βhCG normalisation between the two groups (0.66). The patients undergoing treatment with numerous drugs had the highest rate of recurrence. Additionally, there was a strong

correlation between the disease stage and the rate of recurrence. Two patients were in stage 1, two in stage 2, three in stage 3, and two in stage 4 in the relapsed group.

Discussion

Chemotherapy can cure a large number of GTN patients, but a tiny percentage of them will relapse even after they fully recover. Because it occurs infrequently, previous research has used small sample sizes. To the best of our knowledge, our region does not have any information regarding GTN instances that have relapsed. Consequently, the patients with and without relapsed GTN were compared in this retrospective cohort analysis. In this study, the recurrence rate was 3.7%. It was comparable to earlier research. Yang and others. Similar outcomes to the ones found in this investigation were reported by 314 participants (3.4%) in a study involving 1130 people.

The same group did, however, identify a 6.5% recurrent GTN rate between, which was much higher than the results of our investigation (Kong, Zong, Cheng, Jiang, Wan, Feng, Ren, Zhao, Yang, & Xiang, 2020). Moreover, a study on GTN that was conducted after molar pregnancy by Barga et al. revealed that 10 out of 2284 GTN patients will relapse (Braga, Maestá, Matos, Elias, Rizzo, & Viggiano, 2015).

Furthermore, our findings indicated that the time interval between βhCG resolution and relapse was 20.1 months. Ten months was the shortest recurrence time, although some individuals experienced recurrences up to 47 months later. In line with the current investigation in a Barga et al. Nine months following βhCG resolution, all diagnoses were made, with a mean interval of 18 months between diagnosis and recurrence (Braga, Maestá, Matos, Elias, Rizzo, & Viggiano, 2015). Nevertheless, Yang and his colleagues' investigation found that this period was three months, which was less than our findings. While the meantime was recorded in our study, the median length of recurrence was published in the Yang study, which is different from the current study. Furthermore, the Yang study demonstrated, in line with the current investigation, that 10% of patients experienced recurrence after two years and that over 78% of patients experienced recurrence within a year following therapy (Kong, Zong, Cheng, Jiang, Wan, Feng, Ren, Zhao, Yang, & Xiang, 2020).

These results suggest that upon full recovery, bHcg levels should be continuously monitored. In a study including 4,000 GTN patients, Balchandran and colleagues recommended that following full recovery, the level of Bhcg be tracked for a minimum of a year (Balachandran et al., 2019).

Additionally, our results demonstrated that patients with recurrence had considerably lower baseline B-hcg levels. These results were consistent with the Powles et al. study. The cause is not fully known, though. However, the tumour in these patients would probably be made up of low-maturity cells and altered cells that are unable to make Bhcg. There have been cases of this tumour kind before.

Conclusion

The results of this investigation show that, despite the comparatively low rate of GTN recurrence, ongoing monitoring of bHCG levels for a minimum of two years is necessary to halt the advancement of the disease in these patients. Our study's strength was the initial evaluation of Khuzestan's GTN patients, which we conducted in this study. The study's drawback was that we did not examine the patient survival rate.

References

1. Balachandran et al. (2019). When to stop human chorionic gonadotrophin (hCG) surveillance after treatment with chemotherapy for gestational trophoblastic neoplasia (GTN): A national analysis on over 4,000 patients. Gynecol Oncol, 155, 8-12.

2. Barroilhet, L. M. (2018). Gestational Trophoblastic Disease. Gynecologic Care, 360.

3. Biscaro, A., Braga, A., & Berkowitz, R. S. (2015). Diagnosis, classification and treatment of gestational trophoblastic neoplasia. Revista Brasileira de Ginecologia e Obstetrícia, 37(1), 42-51.

4. Bolze, P. A., Riedl, C., Massardier, J., Lotz, J. P., You, B., Schott, A. M., Hajri, T., & Golfier, F. (2016). Mortality rate of gestational trophoblastic neoplasia with a FIGO score of ≥ 13. American Journal of Obstetrics and Gynecology, 214(3), 390-e1.28.

5. Braga, A., Maestá, I., Matos, M., Elias, K. M., Rizzo, J., & Viggiano, M. G. (2015). Gestational trophoblastic neoplasia after spontaneous human chorionic gonadotropin nor-

malization following molar pregnancy evacuation. Gynecologic Oncology, 139(2), 283-7.

6. Couder, F., Massardier, J., You, B., Abbas, F., Hajri, T., Lotz, J. P., Schott, A. M., & Golfier, F. (2016). Predictive factors of relapse in low-risk gestational trophoblastic neoplasia patients successfully treated with methotrexate alone. American Journal of Obstetrics and Gynecology, 215(1), 80-e1.

7. Eysbouts, Y. K., Ottevanger, P. B., Massuger, L. F., IntHout, J., Short, D., Harvey, R., Kaur, B., Sebire, N. J., Sarwar, N., Sweep, F. C., & Seckl, M. J. (2017). Can the FIGO 2000 scoring system for gestational trophoblastic neoplasia (GTN) be simplified A new retrospective analysis from a nationwide data-set. Annals of Oncology.

8. Fosså, S. D., Waehre, H., & Paus, E. (1992). The prognostic significance of prostate specific antigen in metastatic hormone-resistant prostate cancer. British Journal of Cancer, 66(1), 181-4.

9. Heller, D. S. (2015). Gestational Trophoblastic Neoplasia. In OB-GYN Pathology for the Clinician 2015 (pp.215-227).

10. Jankilevich, G., Uberti, E., Braga, A., Bianconi, M. I., Maesta, I., Viggiano, M., Sun, S., Cortes Charry, R., Salazar, A., Grillo, B. M., & Moreira de Andrade, J. (n. d.). Treatment of patients with gestational trophoblastic neoplasia (GTN) in 12 South America referral centers: Results after 10 years since international FIGO consensus.

11. Kang, W. D., Choi, H. S., & Kim, S. M. (2012). Prediction of persistent gestational trophobalstic neoplasia: The role of hCG level and ratio in 2weeks after evacuation of complete mole. Gynecologic Oncology, 124(2), 250-3.

12. Kong, Y., Zong, L., Cheng, H., Jiang, F., Wan, X., Feng, F., Ren, T., Zhao, J., Yang, J., & Xiang, Y. (2020). Management and risk factors of recurrent gestational trophoblastic neoplasia: An update from 2004 to 2017. Cancer Medicine.

13. Mangili, G., Garavaglia, E., Cavoretto, P., Gentile, C., Scarfone, G., & Rabaiotti, E. (2008). Clinical presentation of hydatidiform mole in northern Italy: has it changed in the last 20 years. American Journal of Obstetrics and Gynecology, 198(3), 302-e1.

14. Reva Tripathi, M. S. (2017). Gestational Trophoblastic Neoplasia. Evidence Based Clinical Gynecology.

15. Schmitt, C., Doret, M., Massardier, J., Hajri, T., Schott, A. M., Raudrant, D., & Golfier, F. (2013). Risk of gestational trophoblastic neoplasia after hCG normalisation according to hydatidiform mole type. Gynecologic Oncology, 130(1), 86-9

16. Seckl, M. J., Sebire, N. J., & Berkowitz, R. S. (2010). Gestational trophoblastic disease. The Lancet, 376(9742), 717-29.

17. Shaaban, A. M., Rezvani, M., Haroun, R. R., Kennedy, A. M., Elsayes, K. M., Olpin, J. D., Salama, M. E., Foster, B. R., & Menias, C. O. (2017). Gestational Trophoblastic Disease: Clinical and Imaging Features. Radio Graphics, 37(2), 681-700.

18. Yang, J., Xiang, Y., Wan, X., & Yang, X. (2006). Recurrent gestational trophoblastic tumor: Management and risk factors for recurrence. Gynecologic Oncology, 103(2), 587-90.