دراسة تراجع إيجابية قيم B – HCG المصلي عقب الرحى العدارية في عينة من مريضات مستشفى دار التوليد الجامعي بدمشق في المدة بين (2007 – 2009)

إعداد طالب الدكتوراه
محمـــد بشابشـــة*

إشراف الأستاذ الدكتور
بشار الكردي**

الملخص

خلفية البحث وهدفه: أمراض الأرومة الغاذية الحملية هي عبارة عن شذوذات تتصف بارتفاع مستوى HCG في المصل ومجموعة من الأعراض السريرية، وتصنف أمراض الأرومة الغاذية الحملية إلى أمراض سليمة وأمراض خبيثة. تقويم منحنى التراجع لمستوى B-HCG عند مريضات الرحى العدارية التامة والجزئية في عينة من مريضات مستشفى دار التوليد بدمشق.

مواد البحث وطرائقه: في هذه الدراسة (دراسة مستقبلية) أخذت عينات دموية من جميع المريضات المحولات والمراجعات إلى شعبة أمراض الأرومة الغاذية في مستشفى التوليد وأمراض النساء الجامعي بدمشق بين المدة (2007 - 2009)؛ وذلك لقياس مستوى B-HCG في المصل بعد الإفراغ بطريقة Enzyme Linked Fluorescent Assay (ELFA).

النتائج: جرى التراجع العفوي لمستوى B-HCG المصلي في تسعٍ وأربعين حالة من مريضات الرحى العدارية (81.7%) بعد التجريف، وهناك إحدى عشرة حالة من الرحى العدارية (18.3%) شخصت على أساس مستوى B-HCG المتتابع بأمراض الأرومة الغاذية المستمرة.

الاستنتاج:لا يوجد اختلاف في زمن المتابعة بين الرحى العدارية التامة والرحى العدارية الجزئية، كما أن سلبية واحدة لمستوى B-HCG بعد التجريف كافية لتأكيد متابعة التراجع في مريضات الرحى العدارية.

كلمات مفتاحية: أمراض الأرومة الغاذية الحملية، الحاثه النخامية المشيمية الإنسانية، الرحى العدارية التامة، الرحى العدارية الجزئية.

* قسم التوليد وأمراض النساء - كلية الطب البشري- جامعة دمشق.
** أستاذ- قسم التوليد وأمراض النساء - كلية الطب البشري- جامعة دمشق.

Study of Serum B-HCG Positivity Regression after Hydatidiform Mole in a Sample from the Department of Obstetrics & Gynecology at Damascus University Hospital

Mohammad A. Bashabsheh* **Bashar Al-Kurdi****

Abstract

Background & Objective: Gestational trophoblastic disease is a group of disorders characterized by elevated HCG, a constellation of clinical symptoms, and may be classified into benign and malignant conditions .

To evaluate spontaneous regression curves of B-HCG in patients with complete mole and partial mole.

Materials & Methods: This prospective study conducted between the period 2007-2009 at the Obstetrics and Gynecology hospital at Damascus University.

Blood samples were obtained from all patients referring or presenting to Obstetrics and Gynecology hospital at Damascus University to measure the levels of serum B-HCG by Enzyme linked Fluorescent Assay (ELFA).

Results: 49 hydatidiform moles (81.7%) presented spontaneous remission of the disease.

There are 11 cases of hydatidiform mole (18.3%) diagnosed as persistent trophoblastic disease based on serial levels of B-HCG.

Conclusion: In this study there is no different follow up time for complete mole and partial mole, and a single undetectable HCG level post evacuation is sufficient follow up to ensure remission in patients with Hydatidiform mole.

Key words :Gestational trophoblastic disease, Human chorionic gonadotropin, complete mole and Partial mole.

* Department of Oncology at Damascus University hospital of obstetric and Gynecological /Faculty of Medicine.
** Prof. Department of Oncology at Damascus University hospital of obstetric and Gynecological /Faculty of Medicine

Introduction & Literature review

The hydatidiform mole is classified into two types based upon gross morphology, histopathology and chromosomal pattern [1].

Complete mole is characterized by diffused swelling of the chorionic villi with diffused trophoblastic hyperplasia, and is not associated with fetal tissues. The most karyotype of complete mole is 46XX and about 10 % have a 46 XY [2, 3]. Partial mole is characterized by focal swelling of the chorionic villi with focal trophoblastic hyperplasia, and is associated with fetal tissues [4].

Since the reports by Delfs [5] and Brewer et al [6], the importance of human chorionic gonadotropin (HCG) determinations following evacuation of a hydatidiform mole to detect trophoblastic disease has been universally recognized. The recent development of serum radioimmunoassay specific for the B subunit of HCG provides a sensitive, specific and economic means of performing follow up [7].

This marker (HCG) can be used effectively to diagnosed post molar gestational trophoblastic neoplasia (GTN), assess treatment response, and detect recurrent disease.

After evacuation, HCG levels are monitored at least every two weeks until they are undetectable.

The American College of Obstetrician and Gynecologists currently recommends HCG follow up evaluations at monthly intervals for 6 months thereafter [8]. It was found that the risk of GTN for patients whose HCG level declined below 50 mIU/ml during third to seventh week following molar evacuation was < 3.4%. An HCG level >2.000 mIU/ml at any point during week 3-8 after molar evacuation conferred at least a 50% risk of GTN and an HCG level >200 mIU /ml during the same period conferred at least a 35% risk. An HCG level >50 mIU/ml after the fourth week following molar evacuation conferred a GTN risk of at least 25% [9].

The duration of human chorionic gonadotropin surveillance for partial hydatidiform moles had been studied and the results support the suggestion that a single undetectable human chorionic gonadotropin level after evacuation is sufficient follow up to ensure remission in patients with partial hydatidiform moles [10].

It was found that women whose HCG level declined below 50 mIU/ml during their follow up were found to be at no more than 1.1% risk for developing persistent gestational trophoblastic neoplasia, irrespective when this level was reached, women whose HCG levels were below 200 mIU/ml in the fourth week after evacuation (59.8% of all women), or below 100 mIU/ml in the sixth week after evacuation (65.8 % of all women), had a risk of persistence below 9% HCG levels below 2,000 mIU/ml in the fourth week after evacuation (13.3% of women) were associated with a 63.8% risk of developing persistent disease.

It was concluded that these data may allow clinicians to evaluate the risk of persistence disease of their patients with complete molar pregnancy have based on early HCG results after molar evacuation; in the fourth week after evacuation 59.8% of women may be counseled that their risk of developing persistent GTN is substantially reduced form their base line. Whereas 13.3% of women may be warned that their risk of developing persistent GTN is greater than 50% [11].

It was reported that spontaneous regression in (HCG) positivity in serum is more rapid in patients with partial hydatidiform mole and slower in complete hydatidiform mole and invasive mole. There is no significant change in malignant potential regarding early detection and treatment [12].

Materials and Methods

Between the period 2007 - 2009 at the Obstetrics and Gynecology Department of Damascus University Hospital, 60 cases of hydatidiform mole were followed histological specimens and analysis for all cases.

Hydatidiform mole was classified as complete mole or partial mole according to gross and microscopic criteria table 1 [13, 14].

Table 1: Hydatidiform mole (2007-2009)

Total patients observed	N = 60	%
Complete mole	24	40%
Partial mole	36	60%
Persistent gestational trophoblastic disease	11	18.3%
Post complete mole	7	29.2%
Post partial mole	4	11.1%

After evacuation of the mole, all patients were followed by serial B-HCG with Enzyme Linked Fluorescent assay (ELFA), monitoring of B-HCG started every two weeks after evacuation of the mole until B-HCG was undetectable three times running, then monthly for 6 months, then every two months for

the remaining period (which is 6 months) if remission was spontaneous.

All patients, who were evacuated by suction curettage and sharp curettage, must use barrier or natural contraceptive methods until B-HCG is no longer detectable.

After that, those who wish to use contraceptive methods prescribed the bill or IUD. When the B-HCG is no longer detectable for a year, pregnancy is allowed again.

Results

49 hydatidiform moles (81.7%) presented spontaneous remission of the disease.

The B-HCG levels fell below the sensitivity of the assay method in 36 patients (73.5%) within 60 days of evacuation, and in 6 patients (12.2%) between 61 – 90 days and in 7 cases (21.9%) between 91 – 120 days.

Table 2: Time intervals until B-HCG titers returned to normal levels in 49 cases with spontaneous remission (2007 – 2009)

Interval	Complete mole remission %		Partial mole remission %	
30 – 60 days	17	70.8%	22	88.8%
61 – 90 days	3	17.6%	3	9.4%
91 – 120 days	0	%	7	21.9%

In 11 (21.9%) cases a diagnosis of persistent gestational trophoblastic disease based on the B-HCG profile table 3.

Table 3: Indications of chemotherapy treatment during follow up period

Indication	Complete mole N = 7%		Partial mole N = 4%	
Raised B-HCG	2	28.6%	-----	
B-HCG plateau	5	71.4%	4	100%
Total	7		4	

All cases of persistent gestational trophoblastic disease received chemotherapy, 9 cases received methotrexate and folinic acid, 4 (low risk) cases of partial mole and 5 (low risk) cases of complete mole [14]. Two patients of complete mole (high risk) received EMA - CO regimen [15] because their B-HCG showed increase or plateau in the HCG levels during the follow up period.

Discussion

The findings of this study confirm that Hydatidiform mole patient which has a limited number of patients 11 (18.3%) need to be given chemotherapy according to the follow up of serum B-HCG.

In contrast, no treatment was given to patients with detectable B-HCG but constantly diminishing levels of B-HCG.

After evacuation of complete mole, 15 – 20 % has been reported to develop persistent tumor [16, 17] in contrast, post molar tumor occurs after partial mole in 4 – 9 % [18, 19].

After evacuation of a complete mole, HCG levels may predict the risk of persistent disease; levels of HCG after evacuation may be employed by clinicians to either reassure patients that they are low risk of persistence,

Or to identify patients at high risk of persistent disease. If patients are at high risk of developing persistent disease and are at high risk of in complete follow up, they may benefit from empiric chemotherapy [11].

Deaths from this disease are very rare today among patients included in a program of post molar biochemical surveillance and are encountered almost exclusively in countries where no such organization exists [20, 21].

Conclusion

In this study there is no different follow up time for complete mole and partial mole, and a single undetectable HCG level post evacuation is sufficient follow up to ensure remission in patients with Hydatidiform mole.

References

1. Szulman AE. Syndromes of Hydatidiform moles- partial vs. complete.J repord Med 1984; 29:788 – 91.
2. Kajii T, Ohama K. Androgenetic origin of Hydatidiform mole. Nature 1977; 268: 633 – 4.
3. Pattillo R A sasakis, katayama KP, Roesler M, Mattingly RF.Genesis of 46 XY Hydatidiform mole. Am J Obstet Gynecol 1981; 141: 104 -5.
4. Szulman A.E. and Surti U. The syndromes of hydatidiform mole II. morphologic evaluation of complete and partial mole. Am J Obstet Gynecol, 1978;132 :20-7.
5. Delfs E: chorionic gonadotropin determinations with hydatidiform mole and chorionic .Ann NY Academy sci 8: 125, 1959.
6. Brewer JI,Torok EE, Webster A, et al : hydatidiform mole. Am J Obstet Gynecol 101:557, 1968.
7. Vaitukaitis JL, Braunstein GD, Ross GT: A radio immune assay which specifically measures human chorionic gonadotropin in the presence of
human luteinizing hormone. Am J Obstet Gynecol 113: 751, 1972.
8. American College of Obstetrics and Gynecologists. Diagnosis and treatment of gestational trophoblastic disease: ACOG practice bulletin no.:53. Obstet and Gynecol 2004; 103: 1365 – 177.
9. Whitfield B. Growdon , M.D et al: post evacuation HCG levels and risk of gestational trophoblastic neoplasia among women with partial molar pregnancies.J repord Med 2006; 51 : 871- 874.
10. Isaac lavie, MD et al: Duration of human chorionic gonadotropin surveillance for partial hydatidiform moles. Am J Obstet Gynecol 2005 May; 192(5): 1362-4.
11. Wolfberg AJ, et al: post evacuation HCG levels and risk of gestational trophoblastic neoplasia in women with complete molar pregnancy. Obstet and Gynecol 2005 September; (106) (3): 548-52.
12. Rob.L., Robova H. et al: serum HCG positivity regression in different molar pregnancies: clinical Trends and prognosis Gynek 66, 2001, 4,5.230-235.
13. Szulman A.E. and Surti U. The syndromes of hydatidiform mole I. Cytogenetic and morphologic correlations. Am J Obstet Gynecol, 131, 665 – 668, 1978.
14. Vassilakos P., Riotton G. and Kajii T. Hydatidiform mole: two entities. A morphologic and cytogenetic study with some clinical consideration. Am J Obstet Gynecol, 127, 167–170, 1977.
15. Berkowitz R.S., Goldstein D.P. Bernstein M.R. Methotrexate with citrovorum factor rescue as primary therapy for gestational trophoblastic disease .Cancer, 50: 2024-2027, 1982.
16. Newlands E.S., Bagshawe K.D., Begent R.H.J, Rustin .G.J.S., Holden L.,Dent J.: Developments in chemotherapy for medium and high risk patients with gestational trophoblastic tumors (1979- 1984).BJOG ,93:63-69,1986.
17. Berkowitz R.S., Goldstein D.P. Bernstein M.R. Management of molar pregnancy. J repord Med 1981; 26:208-12.
18. Lurain JR, Brewer JI, Torok EE,Halpern B. Natural history of hydatidiform mole after primary evacuation . Am J Obstet Gynecol, 1983; 145: 591-5.
19. Szulman A.E.and Surti U. The clinico pathologic profile of the partial hydatidiform mole. Obstet and Gynecol 1982; 59: 597-602.
20. Berkowitz RS,Goldstein DP, Bernstein MR.Natural history of partial molar
pregnancy. Obstet and Gynecol 1985; 66: 677-81.
21. Bagshawe K.D.: UK registration scheme for hydatidiform mole 1973- 1983. BJOG, 93:529-531, 1986.

تاريخ ورود البحث إلى مجلة جامعة دمشق 2010/10/7.
تاريخ قبوله للنشر 2011/4/25.