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The impact of uterine re-curettage, pre-evacuation and week-one level of hCG on the number of chemotherapy courses in treatment of post molar GTN

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Background: Post molar GTN was reported to occur in 7.5-20% of patients following evacuation of complete hydatidiform moles and in 2.5-7.5% following evacuation of partial moles. The role of uterine re-curettage in post molar GTN is not clear.

Objectives: Study of the correlation of pre-evacuation and week- one level of hCG, and uterine re-curettage to the number of chemotherapy courses in treatment of post molar GTN.

Patients and methods: This retrospective study included 29 cases of post molar GTN through reviewing their medical records.

Results: There were 25 cases (86.21) of low risk, and 4 cases of high risk score (13.79%). The 3 year survival was 96.6%. There were non-significant correlation of age, parity, pre-evacuation level and hCG in week-1 to number of chemotherapy courses, while uterine re-curettage was significantly correlated to number of chemotherapy courses (p=0.04).

Conclusion: Uterine re-curettage was significantly correlated to less number of chemotherapy courses in patients with post molar GTN (p=0.04). Pre-evacuation and week-1 hCG were not correlated to number of chemotherapy cycles. A large prospective randomized trial to clarify the beneficial effect of uterine re-curettage is recommended.

Key words: Gestational trophoblastic neoplasia; hCG; re-curettage

INTRODUCTION

Gestational trophoblastic neoplasia (GTN), is the term now commonly applied to persistent or invasive gestational trophoblastic disease. GTN is typically diagnosed in asymptomatic women undergoing routine hCG monitoring after evacuation of a complete molar pregnancy. It is recognized today as the most curable gynaecologic malignancy (1). The reported incidence of GTN is 2/1000 pregnancies in Japan and 0.6-1.1/1000 pregnancies in Europe (2).

There are many classifications of GTN, in 1973, Hammond and colleagues classified GTN into non metastatic and metastatic diseases, the later is further subdivided into good prognosis metastatic disease and poor prognosis metastatic disease. In 1976, Bagshawe suggested the use of a prognostic scoring system. The WHO has adopted a modification of Bagshawe's scoring system (1).

At present, most low-risk GTN patients are initially treated with single-agent methotrexate due to its known activity, low toxicity, and low cost (3). However, between 10% to 31% of patients treated with single-agent methotrexate for low-risk disease (World Health Organization score 0–6) will require second line treatment due to tumour resistance (4).

Many cases of post molar GTN are identified early at a presymptomatic stage based on plateuing or rising hCG concentrations and subsequently treated successfully with chemotherapy. In such cases, histopathological confirmation of the precise nature of the post molar GTN usually is not available (5). Second uter-

ine evacuation can be a useful therapeutic option for patients with presumed persistent trophoblastic disease not mandating immediate chemotherapy, particularly where the hCG level is <1500 IU/L. Patients with documented persistent trophoblastic disease on histological examination of the second evacuation sample are more likely to require chemotherapy (6). Women with persisting disease are only considered for repeat uterine evacuation in the UK when the hCG is less than 5000 IU/ l and ultrasound imaging suggests that the disease is confined to the uterine cavity (7). However, Growdon and colleagues (8), concluded that dilatation and curettage within 1 week after the diagnosis of persistence did not affect future chemotherapy requirements.

The current retrospective study aimed at evaluation of the impact of uterine re-curettage, pre-evacuation and week-one level of hCG on the number of chemotherapy courses in treatment of post molar GTN.

PATIENTS AND METHODS

The study was performed through reviewing the records of 29 patients who were diagnosed as post molar gestational trophoblastic neoplasia during the period from 1/1/2008 to 31/12/2010 in Mansoura University Hospital, Egypt.

The cases were diagnosed as GTN after persistent positive hCG more than 6 months, plateuing, or rising serum level of hCG after evacuation of molar pregnancy or after histological diagnosis of choriocarcinoma, invasive mole, or placental site trophoblastic tumour (PSTT).

The patients were evaluated with respect to age, parity, type of vesicular mole, clinical presentation, and presence of metastasis. The level of serum B-subunit of hCG before molar evacuation, one week later, and its level on follow up visits were studied.

Uterine re-curettage and pathological findings were evaluated. The chemotherapy treatment for these cases was studied regarding its type (single or multiple agent), number of courses till complete response (hCG is below the pregnant level).

All women were classified as low-risk or high-risk disease using FIGO and WHO scoring systems.

The correlation between uterine re-curettage, pre-evacuation hCG, and week-one hCG to number of the needed chemotherapy courses was studied.

Statistical analyses were carried out using the statistical package SPSS 15.0 for Windows (SPSS, Chicago, IL, USA). The means and standard deviations (SD) were calculated for continuous variables. An independent sample *t*-test was used to evaluate the associations between continuous variables. Two-sided p-values were considered statistically significant at $p < 0.05$.

RESULTS

The study included 29 cases of post molar GTN, they were managed in departments of Gynaecology and Clinical Oncology, Mansoura University Hospital, Egypt during the period from 1/1/2008 to 31/12/2010. There were 25 cases (86.21) of low risk (WHO score less than 7), and 4 cases of high risk score (13.79%). The survival of low-risk cases was 100%. One case of mortality from high-risk cases (3.4%), the 3 year survival was 96.6%. There were 3 cases of metastatic GTN (10.35%); 2 of these cases developed lung metastasis and one case developed lung and brain metastasis.

Table (1), shows the descriptive data of the cases regarding age, parity, pre-evacuation hCG, week-one hCG, and number of chemotherapy courses.

Regarding the type of antecedent vesicular mole, 22 of 29 cases (75.9%) developed after complete moles while 7 of 29 (24.1%), developed after partial moles. Twenty-one Cases (72.41%), presented by post molar bleeding and eight cases (27.59%), referred due to persistent hCG beyond 6 months after

Table 1. Mean and median age, parity, pre-evacuation level, and week-one level of hCG

	Age	Parity	Pre-hCG*	W1- hCG**	courses
Number	29	29	29	29	29
Mean	27.90	1.31	152610.69	37765.62	3.69
Median	28.00	1.00	60000.00	10000.00	3.00
Standard Deviation	7.47	1.33	2.97	65463.56	3.04
Minimum	17.00	.00	2000.00	60.00	.00
Maximum	44.00	4.00	1000000.00	230000.00	15.00

*: pre-evacuation level of hCG

**: week-one level of hCG

molar evacuation, plateuing hCG, or rising hCG after being negative.

The cases were diagnosed as post molar GTN after admission by serial serum hCG detection; 18 cases (62.1%) had raised hCG after being negative, 4 cases (13.8%) had plateuing hCG, and 7 cases (24.1%), had persistent hCG beyond 6 months after molar evacuation.

Re-curettage was done within one week of diagnosing GTN for 14 cases (48.3%), according to the clinician opinion. The histopathology of the curettage specimens is shown in table (2).

Twenty-three of the low risk cases received methotrexate as first-line therapy in a dose 1 mg/kg (day 1,3,5,7), alternating with folinic acid 0.1 mg/kg (day 2,4,6,8). The 3 high risk cases received methotrexate, adriamycin, cisplatinum combination (MAC) protocol. Three cases (10.3%), did not receive chemotherapy due to decline of hCG after re-curettage.

Three cases in our study failed to respond to methotrexate monotherapy (3/23; 10.35%). One case received etoposide as second line therapy for 4 cycles. The second case received etoposide-vincristine combination for 3 cycles. The third case failed to respond to MAC combination and received etoposide-cisplatinum as third line but failed to respond and hysterectomy was performed.

Table (3), shows the correlation between uterine re-curettage and number of chemotherapy courses. As can be noticed from the table, the correlation was significant (P value 0.04).

Table (4), shows the correlation of age, parity, pre-evacuation level of hCG and hCG in week-1 to number of chemotherapy courses; as can be seen from the table, there were non significant correlation.

Table 2. Histopathology of the cases with uterine re-curettage

	Count	%
Choriocarcinoma	7	50%
Benign molar tissues	5	35.71%
Invasive mole	1	7.14%
PSTT*	1	7.14%
Total	14	100%

PSTT*: Placental site trophoblastic tumour

Table 3. Relationship between uterine re-curettage and number of chemotherapy courses

		Chemotherapy courses			
Re-curettage	**N***	**Mean**	**Standard Deviation**	**Std. Error Mean**	**P value**
YES	14	2.50	1.55662	.41603	0.040
NO	15	4.80	3.68782	.95219	

N*: number

Table 4. Correlation of age, parity, pre-evacuation hCG, and week-1 hCG to number of chemotherapy courses

	P value	Pearson Correlation
Age	0.746	.063
Parity	0.581	-.107-
Pre-hCG*	0.937	-.015-
W1- hCG**	0.700	-.075-

Pre-hCG*: pre-evacuation hCG

W1-hCG**: week -1 hCG

DISCUSSION

Post molar GTN was reported to occur in 7.5-20% of patients following evacuation of complete hydatidiform moles and in 2.5-7.5% following evacuation of partial moles. The vast majority of cases occur during the first 6 months after molar evacuation (1).

The role of uterine re-curettage in post molar GTN is not clear. Women with persisting disease are only considered for repeat uterine evacuation in the UK when the hCG is less than 5000 IU/ l and ultrasound imaging suggests that the disease is confined to the uterine cavity (7). However, Growdon et al (8), concluded that dilatation and curettage within 1 week after the diagnosis of GTN did not affect future chemotherapy requirements.

This retrospective study included 29 cases of post molar GTN, they were managed in departments of Gynaecology and Clinical Oncology, Mansoura University Hospital, Egypt, during the period from 1/1/2008 to 31/12/2010.

Table (1), shows the socio-demographic criteria of our cases. The mean age was 27.9 years which agreed with data published by Kaye (9), from Uganda. The mean parity was 1.3 which did not agree with Kaye as 68% of his patients had 5 or more deliveries. This may be explained different community criteria.

The mean pre-evacuation hCG level was 152610.7 mu/ml, the mean hCG level one week after evacuation was 37765.6 mu/ml, and the mean number of chemotherapy cycles was 3.7 (range 0-15).

Gestational trophoblastic neoplasia has a good prognosis and considered as the most curable gynaecologic

malignancy (1), The 3-year survival of low –risk cases was 100% and was 96.6% for low and high risk cases, this was supported by other authors (8,10,11).

Table (2) shows the histopathology of post molar GTN after uterine re-curettage. Seven of fourteen cases (50%), were choriocarcinoma this finding was agreed with Pongsaranantakul and Kietpeerakool (12).

Re-curettage was done for 14 cases (48.3%). Table (3), showed that there was a significant negative correlation between uterine re-curettage and number of chemotherapy cycles (p = 0.04). So, performing uterine re-evacuation in cases of post molar GTN was associated with lower number of chemotherapy cycles. This finding was in agree with Pezeshki et al (6) and McGrath et al (7). However, this concept did not agree with Growdon (28), who concluded from his study that dilatation and curettage within 1 week after the diagnosis of persistence of GTN did not affect future chemotherapy requirements. The possible therapeutic benefit of uterine re-curettage may be due to removal of some of the active trophoblstic tissues from endometrium and superficial myometrium.This may explain spontaneous regression of hCG after re-curettage without the need of chemotherapy in 3 cases (10.35%) of our study.

The pre-evacuation hCG and hCG in week-1 after uterine evacuation were not correlated to the number of chemotherapy cycles (p = 0.93 & 0.70 respectively), this finding did not agree with Deligdisch et al (13), who reported that patients requiring more intensive chemotherapy were more likely to present with high levels of hCG prior to treatment and to reach remission only after many courses of treatment this discrepancy may be due to a smaller sample size of our study.

CONCLUSION

Uterine re-curettage was significantly correlated to less number of chemotherapy courses in patients with post molar GTN (p = 0.04). Pre-evacuation and week-1 hCG were not correlated to number of chemotherapy cycles. A large prospective randomized trial to clarify the beneficial effect of uterine re-curettage is recommended.

Conflict of interest disclosure

Authors of this manuscript report that they have no conflict of interest of the contents of this work.

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