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The Curative Effect of a Second Curettage in Low-Risk Gestational Trophoblastic Neoplasia

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Abstract

Background: Gestational trophoblastic neoplasia (GTN), despite its widespread metastases, is a very common cancer in women that is curable. Although the GTN cases show a good response to chemotherapy, in an effort to reduce toxic drug exposure, the second curettage has been suggested for some patients. In the current study, we have aimed to compare the benefits of the second curettage in comparison with single-agent chemotherapy for low-risk GTN patients.

Methods: This retrospective observational study was carried out on GTN patients admitted to the gynecology department of Imam Khomeini Hospital in Ahvaz. The demographic profile of all participants was extracted. Patients' hospitalization records were also extracted from the files. Patients with an endometrial thickness above 10 mm were treated with re-curettage. The β hCG clearance time was estimated by the Kaplan Meier plot.

Results: In the present study, 148 patients with low-risk GTN stage 1 were studied. The time required for β-hCG clearance in patients undergoing re-curettage was significantly lower than the chemotherapy receiving group (7 months vs. 10 months, $p < 0.0001$). More than 50% of patients treated by re- curettage without needing chemotherapy. Moreover, the other 50% cases needed chemotherapy the number of courses was significantly lower than those received single-agent chemotherapy alone ($p < 0.0001$). The baseline β-hCG levels were significantly lower in those who did not need chemotherapy ($p = 0.012$). β-hCG resolution occurred more rapidly in patients undergoing re-curettage alone, while, those who received only chemotherapy had a longer duration for β-hCG clearance.

Conclusion: In general, the findings of this study showed that re-curettage could be used effectively in the treatment of GTN following molar pregnancy. This treatment reduces or eliminates the need for chemotherapy. Our findings also showed that the initial level of β-hCG could be considered as a predictive factor in response to curettage.

Keywords: GTN, Molar pregnancy, β-hCG; Second curettage

1. Introduction

Gestational trophoblastic diseases (GTD) include a variety of diseases during pregnancy that are commonly associated with abnormal trophoblastic proliferation and ranged from benign hydatidiform mole to malignant choriocarcinoma. Gestational trophoblastic neoplasia (GTN), despite its widespread metastases, is a very common cancers in women that is curable. GTN may be developed after molar, term, miscarriage, and even ectopic pregnancy. It is noteworthy that after the evacuation of molar pregnancy, persistent moles may remain in the uterus in more than in 15% of cases. Moreover, choriocarcinoma and also metastasis may develop in about 4% of cases (Khanlian, Smith, & Cole, 2003; Lurain, 2010; Seckl, Sebire, & Berkowitz, 2010).

Several staging and scoring systems have been developed for GTN. According to the Federation of Gynecology and Obstetrics (FIGO) system, GTNs are divided into low and high-risk groups. In the cases of low risk GTN the total scores obtained from the FIGO scoring system is less than 7. It is calculated based on the age of diagnosis-based, previous pregnancy outcome, interpregnancy interval, β-hCG serum level, the largest tumor size (uterus or metastasis, metastasis site, number of the identified metastases and number of drugs in previously failed chemotherapy) (Committee, 2002; van Trommel, Massuger, Verheijen, Sweep, & Thomas, 2005). The low-risk GTN patients treated with single-drug chemotherapy (Actinomycin - D or Methotrexate), while

high-risk GTNs are treated with multi-drug chemotherapy using Etoposide, Actinomycin-D, Cyclophosphamide, Vincristine, and Methotrexate) (Ng & Wong, 2003; R. Osborne & Gerulath, 2004).

When a molar pregnancy is diagnosed through routine pregnancy tests, the safest and standard way to empty the molar tissue is suction of curettage. After emptying the mole, some patients progress to a malignancy and needing chemotherapy (Kerkmeijer, Wielsma, Massuger, Sweep, & Thomas, 2007; Mangili et al., 2008). Although the GTN cases show a good response to chemotherapy, in an effort to reduce toxic drug exposure, the second curettage has been suggested for some patients (Pezeshki et al., 2004). Today, the gynecologists routinely use re-curettage for patients with persistent low-risk GTN in some medical centers. While, some other specialized centers believe that the risk of a second curettage is greater than its advantage, and therefore limit this procedure to patients with heavy bleeding (R. J. Osborne et al., 2016; van Trommel et al., 2005). In the current study, we aimed to compare the benefits of the second curettage in comparison with single-agent chemotherapy for low-risk GTN patients.

2. Material and methods

2.1 Study Design

This retrospective observational study was carried out on GTN patients admitted to the gynecology department of Imam Khomeini Hospital in Ahvaz. Women with low-risk GTN managed by second curettage or single-agent chemotherapy were included. Patients with incomplete hospital records were excluded from the study. The study has confirmed by the Ethical Committee of the Ahvaz Jundishapur University of Medical Sciences.

2.2 Measurements

The demographic profile of all participants was extracted. Patients' hospitalization records were also extracted from the files. GTN was defined as having one of the following criteria according to Table of Criteria for Diagnosis of Gestational Trophoblastic Neoplasia.

Table 1. Criteria for diagnosis of gestational trophoblastic neoplasia (Cunningham, Leveno, Bloom, Spong, & Dashe, 2014)

Criterion 1	Plateau of serum β-hCG level (± 10%) for four measurements during a period of three weeks or longer— days 1, 7, 14, 21
Criterion 2	Rise of serum β-hCG level > 10% during three weekly consecutive measurements or longer, during a period of two weeks or more—days 1, 7, 14
Criterion 3	Serum β-hCG level remains detectable for six months or more
Criterion 4	Histological criteria for choriocarcinoma

Patients with an endometrial thickness above 10 mm were treated with re-curettage, and there was no evidence in favor of uterine arteriovenous malformation (AVM) and the myometrial invasion to. Metastatic GTN patients were worked up by abdominal and pelvic sonography and Chest X-Ray.

2.3 Statistical Analysis

The data were described by descriptive statistics, including mean, median, standard deviation, frequency, and percentage. The means were compared by the independent t-test. The proportions were compared by the chi-square. The Kaplan Meyer analysis was used for determining the time for B-HCG resolution. All statistical analyses were performed using SPSS version 20. The *P-value* of less than 0,05 was considered significant.

3. Results

In the present study, 148 patients with low-risk GTN stage 1 were studied. Patients were divided into two groups as those receiving chemotherapy (group A) and re-curettage (group B). The mean age of the patients in groups A and B was 28.5 and 30 years, respectively ($p = 0.13$). Although most patients in group A were in the under-25 age group (69.1%), patients underwent second curettage were in the 25- to 35-year age group (64.8%). Endometrial thickness in all patients were above 10 mm. The initial β-hCG level did not show a significant difference in each group ($p = 0.53$). However, the time required for β-hCG clearance in patients undergoing re-curettage was significantly lower than the chemotherapy receiving group (7 months vs. 10 months, $p <0.0001$). More than 50% of patients in group B also needed chemotherapy. However, the number of chemotherapy courses was significantly lower than group A ($p <0.0001$) (Table 2).

Table 2. A comparison between patients receiving chemotherapy and patients undergoing recurettage

Characteristics	Second curettage N=74	Chemotherapy N=74	P-value
Age	30.01±5.4	28.5±6.26	0.13
<25	17 (30.9%)	38 (69.1%)	
25-35	46 (64.8%)	25 (35.2%)	
>35	11 (50%)	11 (50%)	
β-hCG Initial			
<500	1(100%)	0	P=0.53
500-5000	33(55%)	27(45%)	
5000-100000	39(45.9%)	46(54.1%)	
>100000	1(50%)	1(50%)	
B-hCG clearance	7(2-9)	10(6-12)	P<0.0001
Mol type			P=0.25
Complete Mole	59(53.2%)	52(46.8%)	
Partial Mole	15(40.5%)	22(59.5%)	
Chemo courses	4(1-7)	6(2-9)	P<0.0001

Furthermore, the patients, treated with re-curettage, were divided into two groups based on receiving or not receiving chemotherapy. The age distribution in both groups did not show any statistically significant difference ($p = 0.37$). However, baseline β-hCG levels were significantly lower in those which did not need chemotherapy ($p = 0.012$) (Table 3).

Table 3. A comparison between patients treated with second curettage and patients treated with second curettage plus chemotherapy

Characteristics	Second curettage	Second curettage+ chemotherapy	P-value
Age			P=0.37
<25	9(52.9%)	8(47.1%)	
25-35	22(47.8%)	24(52.2%)	
>35	3(27.3%)	8(72.7%)	
β-hCG Initial			
β-hCG Clearance	5(2-8)	8(4-10)	
<500	0(0%)	1(2.5%)	0.012
500-5000	22(64.7%)	11(27.5%)	
5000-100000	12(35.3%)	27(67.5%)	
>100000	0(2.5%)	1(2.5%)	
Mol type			P=0.38
Complete Mole	29(85.3%)	30(49.2%)	
Partial Mole	5(33.3%)	10(66.7%)	

β-hCG resolution occurred more rapidly in patients undergoing re-curettage alone, while, those who received only chemotherapy had a longer duration for β-hCG clearance (Figure 1).

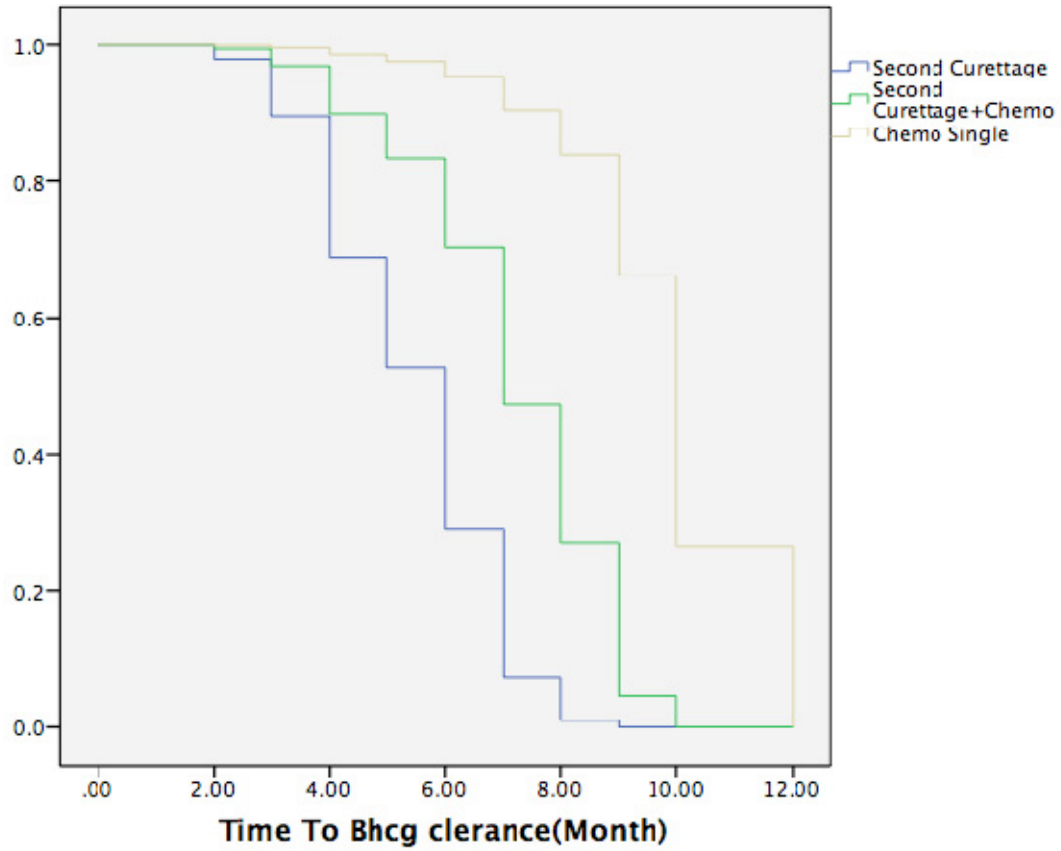

Figure 1. Comparison of β-hCG clearance duration in the studied patients.

In our study, there was not re-curettage complications such as perforation.

4. Discussion

In GTN following molar pregnancy, despite the removal of the hydatidiform mole, tumor activity persists and presented with no decrease or surging plasma B-hCG levels (van Trommel et al., 2005). Although chemotherapy is the first line treatment in these patients, re-curettage has been proposed as an alternative surgical treatment for them.

In the present study, it was shown that re-curettage caused non-chemotherapy treatment in about half of the patients and also a significant reduction with chemotherapy courses in the others. Previous findings have provided both positive and negative results. In a retrospective study, 37 GTN patients were evaluated and it was shown that only six patients recovered after curettage without the need for chemotherapy. The study also found that 8% of patients with curettage had uterine perforation. Therefore, the usefulness of curettage in this study was completely ruled out, the small sample size of this study has reduced the validity of its results (Schlaerth, Morrow, & Rodriguez, 1990). Moreover, in the study conducted by Van Trommel et al., the clinical efficacy of the second curettage was reported as 9.4%. Unlike the present study, they have examined patients with persistent trophoblastic disease (PTD) (van Trommel et al., 2005). However, in another study, Pezeshki et al. found that 60% of GTN patients recovered after re-curettage without the need for chemotherapy (Pezeshki et al., 2004). Also, in a phase II clinical trial, it was shown that re-curettage treated 40% of GTN patients without any side effects (R. J. Osborne et al., 2016). In addition, in another study, Ayatollahi et al. showed that 50% of patients were treated with re-curettage without the need for chemotherapy (Ayatollahi, Yekta, & Afsari, 2017).

Clinical centers for managing GTN patients have different approaches to the effectiveness of re-curettage. This treatment is mostly used to drain the remaining tumor tissue in the uterus or to control bleeding in newly

diagnosed patients. The risk of uterine bleeding, infection of the upper genital tract, or uterine perforation has always been cited as the main reason for discontinuation of curettage. However, the most complications have been managed by non-surgical treatments, and severe complication, including hysterectomy, had not been reported yet (Lorigan, Coleman, Ng, Coleman, & Hancock, 1996; Tidy et al., 2000). Of course, it should also be noted that delays in chemotherapy can lead to disease progression; as a result, some cases will need multi-drug chemotherapy. Hence, comprehensive multicenteric studies may help us to determine predictive factors for effectiveness of re-curettage therapy. In the present study, serum β-hCG levels were a factor in predicting the need for chemotherapy. Its level was significantly higher in patients requiring chemotherapy. These findings were consistent with the results of study conducted by Ayatollahi et al. (Ayatollahi et al., 2017), while, the study of Osbrone et al. did not show the predictive value of β-hCG in response to curettage therapy (R. J. Osborne et al., 2016). The studies are very limited to provide conclusive evidences; hence, more studies are needed to confirm the results.

5. Conclusion

In general, the findings of this study showed that re-curettage could be used effectively in the treatment of GTN follows molar pregnancy. This treatment reduces or eliminates the need for chemotherapy. Our findings also showed that the initial level of B-hCG could be considered as a predictive factor in response to curettage.

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Compliance with Ethics Guidelines

The Ethics Committee of Ahvaz Jundishapur University of Medical Sciences approved this study (IR.AJUMS.REC…..), and that the study is conformed with the Helsinki Declaration of 1964, as revised in 2013, concerning human and animal rights.

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