Retrospective Study On Management Of Gestational Trophoplastic Disease In Baghdad Teaching Hospital

Riyadh A. Al-Baldawi * FICOG Lecturer,

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Summary:

Background: *The Aim Of This Study Is To Determine The Modalities Of Treatment Of GTD In Baghdad Teaching Hospital And To Assess The Efficacy Of Our Management Protocols.*

Patients &Methods: *Department Of Obstetrics & Gynecology- Baghdad Teaching Hospital. Retrospective Analysis Of Case Records Between January 1999 To December2000. 41 Patients' Data Were Reviewed For Age, Gravidity, Parity, Blood Group, Antecedent Pregnancy And Clinical Presentation At The Time Of Diagnosis. Monitoring Of Hcg Level Before And After Chemotherapy, Other Investigations Were Reviewed, Looking For Number, Size And Site Of Metastasis. The Patient Were Classified According To WHO Scoring System. We Evaluate The Lines)f Management, Chemotherapeutic Protocols And The Number Of Chemotherapy Courses For 'atient's Remission.*

Results; *The Most Common Presenting Symptom Was Vaginal Bleeding 70.7%. Dilatation And iuction Curettage Was The First Line Of Treatment, Although 4 Patients (9.8%) Ended With hysterectomy For Persistent Bleeding. Based On WHO Scoring System, Initial Assessment Shows That 78.04 % In The Low Risk Group, And 19.5 %In The Medium Risk Group And One Patient In The High Risk Group. Complete Remission Was Achieved With Administration Of 2- 7 Courses Of Single Agent Chemotherapy In 84.3 % In The Low Risk Group, While 5 Patient (15.6%) Show Resistance To Single Agent Protocol And Shifted To Combined Chemotherapy. Nine Patients In The Medium And High Risk Groups Started With Combined Chemotherapy. The Cure Rate In The Low And Medium Risk Groups Were 100%.*

Conclusion; *Chemotherapy Is The Main Line Of Management For Persistent GTD In Baghdad Teaching Hospital, And For The Low Risk Group We Found That Parantral MTX And Folinic Acid Had A Very Good Remission Rate And Patients Whom Developed Resistance , And Those In The Medium Risk Group Can Achieve Excellent Remission Rate With Multiple Agents Chemotherapy.*

Key Wards; *Gestational Trophoblastic Disease, Chemotherapeutic protocols.*

Introduction:

Gestational Trophoblastic Diseases (GTD) are heterogamous group of conditions ranging from the benign hydatidiform mole to the malignant Choriocarcinoma. G.T.D arise from the human placenta, traditionally this group is divided histologically into three classification; H-mole (Partial mole, Complete mole), Invasive mole (chorioadenoma destruens) and Choriocarcinoma.(1)

Recently partial mole and placental site tumors (PSTs) have been histologically and clinically defined and are recognized as separate entities under the broad classification of G.T.D. Despite the apparent diversity of these entities they are all derived from the human placenta and derived from paternal genome with an occasional maternal contributionl and malignant form of G.T.D are among the most sensitive human solid malignancies respond to a wide variety of chemotherapeutic regimens, it is possible to achieve essentially 100% cure rate for patients with non metastatic G.T.D and for 65-90% for patient with metastatic G.T.D depending on distribution of patients within various risk categories("2).

Recent investigations into the treatment of nonmetastatic GTD concern regimens that are convenient, cost - effective , easily administered , minimally toxic,, and yet maintain the established, excellent cure ratep) .

This retrospective study details our modalities of treatment of GTD in Baghdad Teaching Hospital and to assess the efficacy of our management protocols.

** Department Obstetrics & Gynecology College Of Medicine / University Of Ba Ghdad*

Patiens & Methods:

This is a retrospective study for patients with GTD admitted to Gynecology and Obstetrics department of Baghdad teaching hospital, by which we reviewed all the patients Data from statistical department from January 1st 1999 to December 31st 2000.

47 patients were admitted as GTD, 6 patients had insufficient data for analysis were dropped from our study. 41 patients data were reviewed for Age, Gravidity, parity, Blood group for patients, antecedent pregnancy whither molar pregnancy, abortion, ectopic pregnancy or term pregnancy and clinical presentation at the time of diagnosis. Monitoring of HCG level before and after

chemotherapy. Investigations done before and during chemotherapy, Including chest X-Ray, pelvic and abdominal U/S, CBP, liver function test, renal function tests. Other investigation as CT scanning, MRI, or Doppler studies were done for selected patients, Looking for number size and site of metastasis to vagina, lung, spleen, kidneys, GIT, liver and brain. The patients were classified according to WHO scoring system into low, medium, and high risk group(2) . We evaluate the line of management whether surgical evacuation by dilatation and suction curettage or Hysterectomy. Chemotherapy protocols either single agent, combination or single agent followed by combination chemotherapy and the number of chemotherapy courses for patient remission, including number of patient missed to follow up or patient whom died.

Statistical analysis: Data were translated into codes using a specially designed coding sheet, and then interred into a computer system using DBASE III ' plus computer software. Statistical analyses were done using SPSS version 7.5 computer software (Statistical Package for Social Sciences). Frequency distributions for selected variables with proper graphical presentations were done.

Results:

During the period of 2 years, retrospective analyses of cases of persistent GTD were reviewed from demographic data and lines of management. As a tertiary center, our department receives patients from different hospitals. The total numbers of patients reviewed during this period were 47 patients, six patients were dropped from analysis for insufficient data. In our assessment of the scoring system , The age of the patients ranged from 17-50 years (mean 29.7+ - 8.8). 33 patents were below 39 years. And 8 patients > 39 years (table No 1).

In 31.7% of cases, molar pregnancy was their first pregnancy (table No 1).and in 90.2% of the patients, molar pregnancy was the antecedent pregnancy (table No 1),while 30 patients (78.9%) presents before 4 months since last pregnancy (table 1).19 patients (48.7%) there blood group were A which is not statistically significant (table 1).

The most common presenting symptom was vaginal bleeding 70.7%, although theca Lutein cyst were found in 17.1% of patients and neurological manifestations in one patient (table No 2).

Dilatation and suction curettage was the first line treatment, although re-evacuation was done in 68.2% for the 2nd time and 2 patients (5.7%) re-evacuated for the third time (table No 3), 4 patients (9.8%). Ended with Hysterectomy for persistent bleeding (table No 4).

Based on WHO scoring system classification, initial assessment show that 78 % in the low risk group and 19.5 % in the medium risk group and one patient 2.4% high risk group (table No 5).

Complete remission was achieved with administration of 2-7 courses of single agent chemotherapy in 27 cases (table No 6, and table No7). 5 patients (15.6 %) out of 32 patients in the low risk group show resistance to single agent protocols and shifted to combined chemotherapy ,this gives the single agent chemotherapy 84.3 cure rate, While 9 patients started with combined chemotherapy.

One patient in the high risk group died for neurological manifestation in spite of combined chemotherapy shown in table (5). The cure rate in cases of low and medium risk group were 100%.

Table 8 and figure 1 shows chemotherapeutic protocols used in our hospital, single agent (intramuscular methotrexate - folenic acid) was used in 65.8% of patient, modified EMA/Co were used in 9.8% of patients, Modified MAC III were used in 14.6% of patients, Modified Bagshaw were used in 2.4% of patient, and Modified POMB used in 7.9% of patient.

We use the modifications of these protocols because the embargo on our country limits our options in prescribing certain drugs.

Table 1: Frequency distribution of the study sample by age, blood group, parity, outcome of antecedent pregnancy, and period elapsing since last pregnancy (months).

	N	
Age in years (mean + SD= 29.7 + 8.8)	**33**	**80.5**
<40		
>39	**8**	**19.5**
Total	**41**	**100**
Parity	**13**	**31.7**
Primigravida		
Multipara	**28**	**68.3**
Total	**41**	**100**
Outcome of antecedent pregnancy	**37**	**90.2**
H. mole		
Full term	**4**	**9.8**

Others	**0**	**0**
Total	**41**	**100**
Period elapsing since last pregnancy (months)		
<4	**30**	**78.9**
4-6	**4**	**10.5**
7-12	**3**	**7.9**
>12	**1**	**2.6**
Total	**38**	**100**
Blood group of patients		
A	**19**	**48.7**
B	**6**	**15A**
0	**12**	**30.8**
AB	**2**	**5.1**
Total	**39**	**100**

Table 2: Frequency distribution of the study sample by presenting complaint.

Presenting complaint	N	%
Vaginal bleeding	29	70.7
Corpus lutium cyst	7	17.1
Vaginal mass	2	4.9
Neurological manifestations	1	2.4
Others	2	2.9
Total	41	100

Table 3: Frequency distribution of the study sample by HCG level-before treatment (iu/L), number of evacuations done, and presence of metastasis. N

HCG level-before treatment (iu/L) <1000 10,000 10,000-100,000	22127	53.7 29.3 17.1 1000-
Total	41	100
Number of evacuations done 1 23	11 28 2	26.8 68.3 4.9
Total	41	100
Metastasis Absent Present	338	80.519.5
Total	41	100

Table 4: Frequency distribution of the study sample by having hysterectomy. N

Hysterectomy Not done Done	374	90.2 9.8
Total	41	100

Table 5: Frequency distribution of the study sample by risk scoring system.

Risk scoring system	N	
Low risk Medium risk High risk	38	92.7 4.9 2.4
Total	41	100

Table 6: Frequency distribution of the study sample by type of chemotherapy.

	N	%
Type of chemotherapy Single agent	2796	65.9
Combination Single agent follow by combination chemotherapy		2212.2
Total	41	100

84.3 % of patients with low risk group cured by single agent protocol (intramuscular MTX and folinic acid).

Table 7: Frequency distribution of the study sample by number of chemotherapy courses received.

	N	ov$_a$
Number of chemotherapy courses		
2-3	**17**	**41.5 39.0 19.5**
4-5	**16**	
6-7	**8**	
Total	**41**	**100**

Table 8: Distribution of the study sample by chemotherapeutic protocol used.

chemotherapeutic protocol used	N	
1Single agent + Folinic acid	27	65.9
2Modified EMA/Co	4	9.8
3Modified MAC III	6	14.6
4Modified Bagshawe	1	2.4
5Modified POMB	3	7.3
Total	41	100

Note:
EMA/Co regimen: Etoposide + MTX + Actnnomycin D alternating with cyclophosphamide + Oncovein (vincristin)
MAC: Methotrexate +Actinomycin D + Cyclophosphamide or ChlorambuciL
Bagshawe: Hydroxyurea, Methotrexate, vincristin, cyclophosphamide, actinomycin and chlorambuciL
POMB: Cisplatinum + Oncovein + Methotrexate and Bleomycin

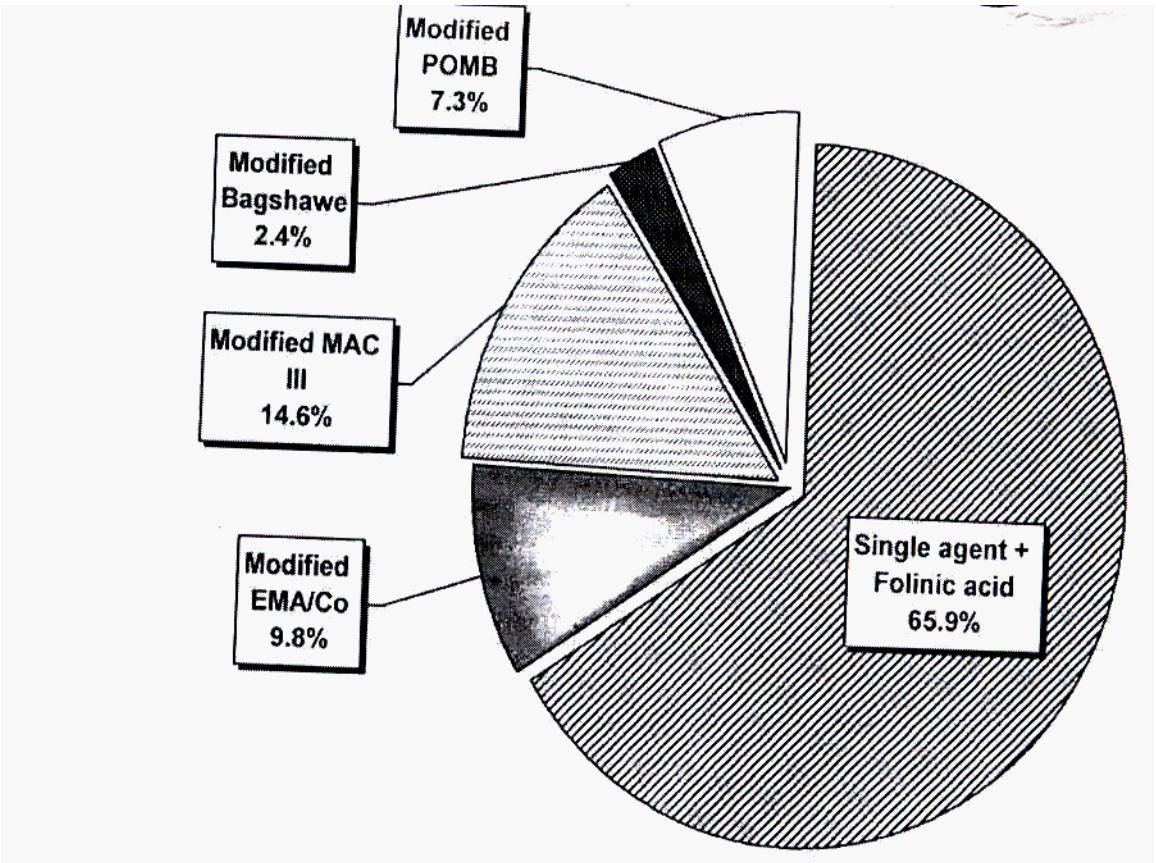

Figure 1: Pie chart showing the frequency distribution of the study sample by chemotherapeutic protocol used.

Discussion

The treatment of GTD has advanced significantly since the initial report of Li et al describing the efficacy of MTX. Today, patients with the non-metastatic form have remission rate of 100% and low relapse ratep).

Chemotherapy is the main line of treatment in the management of persistent GTD in our department. Our remission rate 84.3% with intramuscular MTX and folinic acid rescue for

patients in the low risk group. By using the same regimen Smith et al (4) achieved a remission rate of only 72.6% although Berkowitz et al. (3) showed an over all sustained remission rate of 89% using a similar regimen. Toxicity rarely necessitated a change of chemotherapy when using intramuscular MTX with folinic acid rescue(3), however, these patients are often hospitalized during the days of treatment.

While the treatment of low risk GTD with conventional methods has an excellent cure rate, yet efforts have been made to decrease toxicity and increase patient's convenience and cost effectiveness. Barter et al (3) treat low risk patients with oral MTX as only mean of their therapy, the standard dose 0.4 mg/kg with maximum dose 25mg/day for 5 consecutive days with a 9 days interval before the next course, achieving 87% remission rate. The toxicity associated with oral MTX are mild and have significant advantage of patient convenience and comfort, decreased cost and less interference with patient's daily work. The overall recurrence rate of 0% compares favorably with the 6.3% and 1.2% rate for intramuscular MTX, and MTX with folinic acid rescue, respectively(3,4). Alternative line of treatment as single agent include the prospective report by Petrilli et al (5) a biweekly out patient pulse of Actinomycin D showed 94% remission rate, nausea and vomiting and alopecia were the chief toxicities. Wong et al.(6) reported 100% remission rate with oral VP 16. but all patients show nausea and 92% had total alopecia.

We found five patients developed resistance to MTX and folinic acid rescue, and those in the medium risk group were treated with multiple agents chemotherapy. Different protocols were chosen (MAC, EMA/CO, POMB and Bagshaw) achieving 100% remission rate, 2-7 courses of treatment were needed to achieve remission, and 4 patients ended with hysterectomy for persistent vaginal bleeding and to decrease drug resistance. One patient in the high-risk group died because of brain metastasis and drug resistance. In our study we found that initial tumor response according to decreasing B hCG titer was good for all patients treated with any type of these protocols, yet drug toxicity and side effects cannot be assessed accurately due to insufficient data, and small sample size.

Kim SJ et al. (7)(in the study of independent risk factors in 165 cases of high risk GTD) proved that EMA/CO regimen were found to have low drug toxicity, early remission and a low failure rates, patients receiving the most effective chemotherapy for high risk GTD was EMA/CO than other regimens(7).

Paradinas FJ et al.. (8) suggest that patients with persistent GTD should receive EMA/CO regimen for high risk disease without loss of fertility. Most patients with relapsing or resistant disease can be treated effectively with surgery and/or cisplatin in EP/EMA (Etoposide, Platinum/Htoposide,MTX,Actinomycin D combination)(8). In patients who do not respond

to EMA/CO regimen, POMB regimen will achieve remission in around 40%, these are highly toxic treatment with high incidence of side effects(2). No role of radiotherapy or thoracatomy

in our patients management protocols. Ilancheran A et al. clam that judicious use of surgery and radiotherapy in the treatment of GTD will improve the survival rate. With appropriate treatment, the cure rates approach 100% in the low risk group and 80% in the high risk group(c)).

Although our management protocols gives an excellent remission rates, controlled prospective studies are needed to provide further information regarding patient's convenience, complications, and remission rates for each protocol, with special consideration to oral route of therapy(simple and convenient route).

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