Rescoring of Patients with Gestational Trophoblastic Neoplasia Using Modified Scoring System By Figo

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OBJECTIVE: The scoring system of GTN determines the treatment modalities. Scoring system was first improved by Bagshawe et al. in 1976. World Health Organisation (WHO) had modified this scoring system in 1983. FIGO reviewed and revised the WHO scoring system in 2000. In this study, the change in scores and risk groups of patients scored according to WHO, were analyzed when the patients were re-evaluated according to FIGO
STUDY DESIGN: The records of 71 patients with GTN were reviewed between 1994 and 2002. The first scoring system that determines the treatment modality was WHO scoring system in all patients. All patients were rescored by the FIGO's modified scoring system retrospectively.
RESULTS: In this study, 35.2% of 71 patients' score wasn't changed, while increased in 14.1% and decreased in 50.7%. In high-risk group (n=29) by the WHO scoring system the risk score was same in 31% of patients, increased in 27.6% and decreased in 41.4%. In the intermediate-risk group (n=15) risk score was same in 33.3% and decreased in 66.7%. In the low-risk group (n=27) the risk score was same in 40.7%, increased in 7.4% and decreased in 51.9% of patients.
CONCLUSION: Today the uncertainty of the scoring systems still remains. The univariant and the multivariant analyses of the studies about the effect of prognostic factors that are used in scoring systems on the treatment success declare different results. The new studies will show the validity of the last scoring system.
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Key Words: Gestational Trophoblastic Neoplasia, Scoring system

At present, it is possible to achieve almost 100% success for survival for low-risk gestational trophoblastic neoplasia (GTN) with single agent therapy.[1-5] However; agent resistance in 10-30% of cases and high rate of recurrence and metastases are observed at the high-risk GTN in spite of multiagent chemotherapy.[6-8]

In order to standardize the treatment, from 1960s to date, several studies have been conducted to determine the prognostic factors. Bagshawe et al. developed a scoring system including 13 risk factors in 1976.[9] World Health Organisation (WHO) modified Bagshawe's scoring system in 1983.[10] The International Federation of Gynecology and Obstetrics (FIGO) modified WHO scoring system at 25th annual meeting in 2000.[11]

FIGO recommended the new criteria which are cited below, in order to implement scoring system for the diagnosis of GTN and standardize the treatment.[12,13]

1. Criteria for the diagnosis of post hydatidiform mole trophoblastic neoplasia:

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a. 4 values or more plateau of hCG over at least 3 weeks (daysà 1,7,14,21),

b. A rise of hCG of 10% or greater for 3 values or longer over at least two weeks (daysà 1,7,14),

c. The presence of histologic choriocarcinoma,

d. Persistence of hCG 6 months after mole evacuation.

2. Criteria for methods used the diagnose metastases in GTN:

a. Chest X-ray is appropriate to diagnose lung metastasis. computerized tomography (CT) scan can be used,

b. Liver metastases may be diagnosed by CT scan or by ultrasound,

c. Brain metastases may be diagnosed by magnetic resonance imaging (MRI) and CT scan,

d. CT scan is preferred for the diagnose of intraabdominal metastases

WHO and FIGO propose common staging scoring system due to that these systems can't define prognostic factors actually and comparison can't be made, because of different systems in scientific studies. The goal that standard multiagent treatment is preferred for high-risk and single agent resistant patients. By this, intermediate-risk group is taken away from WHO scoring system.

In this study, the discrepancy in scores and risk groups of patients scored according to WHO, were analyzed when the patients were re-evaluated according to FIGO.

Table 1. WHO scoring system

Score	0	1	2	4
Age	≤39	>39	-	-
Antecedent Pregnancy	Hydatidiform mole	Abortion	Term pregnancy	-
Tumor age* (months)	<4	4-<7	7-<13	≥13
Pretreatment β-hCG (IU/l)	$<10^3$	10^3-<104	104-<105	≥105
Largest tumor size (with uterus) (cm)	-	3-<5	≥5	-
Site of metastasis	Lung	Spleen, Kidney	Gastrointestinal system, Liver,	Brain
The number of metastasis	-	1–4	5–8	>8
Previous failed chemotherapy	-	-	Single drug	2 or more drug
Blood group (woman X men)	-	O X A A X O	B AB	-

*The duration between former pregnancy and treatment

Table 2. FIGO scoring system (Modified WHO scoring system)

Score	0	1	2	4
Age	≤39	>39	-	-
Antecedent Pregnancy	Hydatidiform mole	Abortion	Term pregnancy	-
Tumor age* (months)	<4	4-<7	7-<13	≥13
Pretreatment β-hCG (IU/l)	$<10^3$	10^3-$<10^4$	10^4-$<10^5$	$\geq10^5$
Largest tumor size (with uterus) (cm)	-	3-<5	≥5	-
Site of metastasis	Lung	Spleen, Kidney	Gastrointestinal system	Liver, Brain
The number of metastasis	-	1–4	5–8	>8
Previous failed chemotherapy	-	-	Single drug	2 or more drug

*The duration between former pregnancy and treatment

Materials and Methods

Seventy-one patients with GTN were evaluated between 1994 and 2002. The scoring of patients was done by using the WHO scoring system until 2002. After that year, it was switched to FIGO scoring system.

The first scoring of patients was done by using the WHO scoring system[10] (Table 1). According to this scoring, GTN is divided into three groups as low-risk (score ≤5), intermediate-risk (score 6-7) and high-risk (score ≥8). Low-risk group received single agent methotrexate, intermediate-risk group received MAC III (methotrexate, actinomycin D, cyclophosphamide, folinic acid) and high-risk group received EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine). Also, unresponsive patients in low and intermediate-risk groups received EMA/CO.

FIGO modified WHO scoring system in 2000[11] (Table 2). GTN was divided into two groups as low-risk (≤6) and high-risk (≥7) in this new scoring system. Seventy-one patients were rescored through this system. According to this system, the following regimens of chemotherapy were accepted; single agent methotrexate for the patients in low-risk, and EMA/CO for the patients in high-risk.

If the patients' risk group was changed by new scoring system, it could be defined as down-staged or up-staged.

Results

The average age of the patients was 32.5 with a range of 17-57. When patients were rescored with new system which was described by FIGO, it was seen that there was no changing of risk score in 25 patients (35.2%), there was an increase in 10 patients (14.1%) and there was a decrease in 36 patients (50.7%) (Table 3). Risk group of four patients out of 71 (5.6%) were found to be changed.

According to the WHO scoring system, it was determined that there was no changing in scoring in 9 patients out of 29 (31%) who were accepted in high-risk GTN, there was an increase in eight patients (27.6%), and there was a decrease in 12 patients (41.4%). It was seen that

Table 3. The changing on the score

WHO scoring	FIGO scoring																
Score	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
0																	
1	1	2															
2		3	3														
3		1	3	2	1												
4			1	3	2		1										
5					2	2											
6					1	6	3										
7						2	1	2									
8							2	3	5	2	1						
9												1					
10								1			3		1				
11											2	1	1				
12											1	3					
13																1	
14																	1
15																	
16																	

The amounts in the table resemble the number of the patients

two patients who were accepted in high-risk in WHO scoring system were placed in low-risk group in the scoring system (down-staged) which FIGO had modified (Table 3).

According to the WHO scoring system, it was determined that there was no changing in scoring on five patients out of 15 (33.3%) who were in intermediate-risk GTN group, and there was a decrease (down-staged) on 10 patients (66.7%). It was seen that two patients from that 15 patients (13.3%) were placed in high-risk GTN group (up-staged) in the scoring system which FIGO had modified (Table 3).

According to the WHO scoring system, it was stated that there was no changing in scoring on 11 patients out of 27 (40.7%) who were accepted in low-risk GTN, there was an increase on two patients (7.4%), and there was a decrease on 14 patients (51.9%). The risk group of those 27 patients wasn't changed.

Discussion

The risk factors on GTN have been tried to be identified since 1960's. In 1976, Bagshawe et al. developed a scoring system by using prognostic factors[9] and then this scoring system was modified by WHO in 1983.[10] FIGO modified WHO scoring system in 2000. The changes have been accepted that differ from the 1983 WHO classification. The blood group risk factor was eliminated and risk factor for liver metastasis is upgraded from 2 to 4 in new scoring system.[11] Also the intermediate-risk group eliminated and GTN was divided into two groups as low-risk (score ≤6) and high-risk (score ≥7).

At present, the uncertainty of scoring system has still been continuing. Different results are obtained on univariant and multivariant analysis which was done about the effectiveness on the success of treatment of prognostic factors used in the scoring system. There are some reports about insufficiency of prognostic factors and the value of cut-off that are used for finding out the risk.[14,15]

Kim et al. evaluated the effects on the reply to EMA/CO of prognostic factors in high-risk GTN and stated that the age of tumor, the level of serum β-hCG before treatment, the number of metastatic organs, the chemotherapy given before, gravida and the type of surgery (with or without plan) affected the rate of therapy result.[14] Bower et al. showed that the metastasis of liver and brain, the age of tumor, and the type of ending of former pregnancy are characteristic on the reply to EMA/CO.[16] Escobar et al. determined the age of tumor, the site of metastasis and the system of scoring designated the result of treatment.[17]

The scoring system designates the options of treatment which is going to be given. At present, single agent chemotherapy (methotrexate, actinomycin-D, etoposide) in low-risk GTN and multiagent chemotherapy (EMA/CO) in high-risk GTN are used.

In this study, it is stated that there was no changing of scoring on 32.4% of 71 patients who were rescored with the

system of FIGO had modified. It was noticed that according to the WHO scoring system, the rate was 31% in the group of high-risk GTN, 26.3% in the group of intermediate-risk and 39.1% in the group in low-risk.

Two of 29 patients (6.9%) who were in high-risk group and had taken EMA/CO chemotherapy in WHO's scoring system were defined in low-risk group through FIGO's scoring system. Due to this, protecting patients from toxicity could be possible. At the same position, it was noticed that two of 42 patients (4.8%) (low and intermediate-risk) who were not in the group of high-risk in WHO's scoring system were in the high-risk group through the new system. The treatment in the new system with a single agent would be enough in 13 of 15 patients (86.7%) who were in the intermediate-risk group according to the former scoring system. Hancock et al. retrospectively evaluated the WHO scoring system and the other systems which is included FIGO system.[18] They noted that chemotherapy resistance and outcome were equivalent in all systems. They also reported that the use of only two prognostic grouping increased the proportion of patients in the low-risk group without compromising outcome.

The problems about the scoring of patients on GTN are not caused by only new developed scoring system. At the same time, there are problems in each parameter about scoring. Osborne et al. worked on the scoring of 200 women who had been scored with WHO's system until 2002.[19] They noted that the most mistakes, which were done during scoring, were in the measurement of β-hCG. Furthermore, they found out important rates of mistakes about the number of metastasis, the diameter of the biggest tumor and the style of ending of former pregnancy. The mistakes which will be done during scoring of patients are going to lead applying of wrong treatment and changing of statistical results.

Hepatic metastasis and blood grouping are main factors effecting scoring; FIGO scoring system has been used in our clinic since 2002. As a result, the lack of confidence on scoring system is still continuing. Sixty-five percent of scores and 5.6% of risk groups were found to be changed in this study. For that reason; in order to comment on new scoring system, it is necessary to observe treatment results of patients scored with it. The results which will be obtained are going to show the validity of the new scoring system.

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