Experimental
&
Clinical Article

EMA/CO Combination Chemotheraphy in Gestational Trophoblastic Neoplasia: Update of Our Results

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ABSTRACT

OBJECTIVE: In this study, we aimed updating our experience about the treatment success of EMA-CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine) chemotherapy in high-risk gestational trophoblastic neoplasia (GTN).

MATERIAL AND METHOD: Patients were scored according to FIGO's modified WHO system. Risk scoring of patients before 2000 was remade by using this system. Thirty-nine patients who were treated with EMA-CO between 1992 and 2013 because of high risk GTN or the resistance to single agent methotrexate and MAC III chemotherapy combinations were evaluated retrospectively. Adjuvant surgery and radiotherapy were used in selected patients. Response and effects of the prognostic factors to the response rate were analyzed.

RESULTS: Median follow-up time of the patients was 74.8 months (range, 1-203). Complete clinical response was obtained in 36 (92.3%) patients with only EMA-CO or EMA-CO and surgery. The response rate of treatment was 91.3% (n:21/23) in patients taking primary EMA-CO, 93.8% (n:15/16) in patients taking secondary EMA/CO chemotherapy. Resistance to the EMA-CO treatment developed in 6 (15.3%) patients and 3 of the patients with drug resistance died. During the follow-up time disease recurred in 3 (7.7%) patients. When the antecedent pregnancy was term pregnancy or the histopathological diagnosis was choriocarcinoma or when there was liver metastasis, the treatment success decreased. The effects of tumor dimension and the presence of metastasis tended to be statistically significant in determining the resistance to therapy.

CONCLUSION: EMA-CO regimen is highly effective for treatment of high-risk GTN. Because of the differences in many studies, risk factors for predicting the success of the treatment are not clear.

Keywords: EMA/CO, Gestational trophoblastic neoplasia, Prognostic factors

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Introduction

Gestational trophoblastic neoplasia (GTN) is a rarely seen interrelated trophoblastic malignity group which includes invasive mole, choriocarcinoma, placental trophoblastic tumor, epithelioid trophoblastic tumor. Several studies have been conducted to determine the prognostic factors and to standardize the treatment from 1960s to date. Bagshawe et al.[1] developed a scoring system including 13 risk factors in 1976. World Health Organization (WHO) modified Bagshawe's scoring system in 1983.[2] The International Federation of Gynecology and Obstetrics (FIGO) modified WHO scoring system at the 25th annual meeting in 2000.[3] The blood group risk factor was eliminated and risk factor for liver metastasis was upgraded from 2 to 4 in new scoring system. At present, FIGO's anatomic staging and FIGO modified WHO prognostic scoring are used (Table 1, Table 2). In order to determine the treatment, GTN have been defined as low risk (score ≤6) and high risk (score ≥7) in modified WHO prognostic scoring system.[4]

Even though the disease metastasizes commonly, high cure rates can be obtained in patients with GTN.[5] Multi-agent combined chemotherapy is suggested in patients with high risk GTN. Etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine (EMA-CO) is the most preferred combined chemotherapy regimen because it's associated with high survival rates and up to 80-90% of patients can complete the chemotherapy cycles.[6,7] At our previous report that was presented in 2006, this chemotherapy combination was shown to have 90.9% treatment success.[8]

In this study, we aimed to update our experience regarding the treatment success of EMA-CO chemotherapy Tablo 3.

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Table 1: FIGO stage

Stage 1	Disease confined to uterus
Stage 2	GTN† extending outside the uterus, but limited to genital structures (vagina, adnexa)
Stage 3	GTN extending to lungs with or without known genital tract involvement
Stage 4	All other metastatic sites (brain, liver etc.)

†GTN: Gestational trophoblastic neoplasia

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 (mIU/L)	$<10^3$	10^3-<104	104-<105	≥105
Largest tumor size (with uterus) (cm)	<3	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*

Table 3: EMA-CO Chemotherapy

EMA		
1. Day	Etoposide	100 mg/m², IV infusion in 200 ml %0.9 NaCl, over 30 minutes
	Actinomycin D	0.5 mg IV push
	Methotrexate	100 mg/m² IV push and 200 mg/m², IV infusion in 1000 cc %5 dextrose, over 12 hours
2. Day	Etoposide	100 mg/m², IV infusion in 200 mL %0.9 NaCl, over 30 minutes
	Actinomycin D	0.5 mg IV push
	Folinic Acid	15 mg , IM or orally every 12 hours for 4 doses beginning 24 hours after start of methotrexate
CO		
8. Day	Vincristine	1 mg/m² IV push
	Cyclophosphamide	600 mg/m², IV infusion

Intervals between courses of chemotherapy were 15 days

Material and Method

Forty patients who were treated with EMA-CO because of high risk GTN or because of the resistance to single agent methotrexate and MAC III (1st, 3rd, 5th and 7th days methotrexate 1mg/kg; 1st-5th days actinomycin D 12 ug/kg; 1st-5th days cyclophosphamide 3 ug/kg; 2nd, 4th, 6th and 8th days folinic acid) chemotherapy combinations between 1992 and 2013 were evaluated retrospectively. Patients with placental-site trophoblastic tumors were excluded because of the known chemotherapy resistance in these tumors.

Before 2000, patients were classified according to WHO scoring as low risk (score: ≤5), intermediate risk (score: 6 and 7) and high risk (score: ≥8). According to this classification, low risk patients received single agent methotrexate, intermediate risk patients received MAC III and high risk patients received EMA-CO. Patients who were in low or intermediate risk group and developed resistance to their first treatment were treated with EMA-CO.

In this study patients were scored according to FIGO's modified WHO system. Scoring of the patients diagnosed before 2000 was remade by using this system. According to modified WHO system, the patients in low risk (score <7) received single agent methotrexate treatment and the patients in high risk (score ≥7) received EMA-CO treatment. Patients who developed a resistance to single agent methotrexate received EMA-CO.

Before the treatment patients were evaluated with physical examination, chest x-ray, thorax and abdominal tomography, serum β-human chorionic gonadotropin (β-hCG) levels (studied by radioimmunoassay), complete blood count, serum biochemical analysis. Cranial computed tomography or MRI was performed only if necessary. The patients were assessed with pelvic examination, complete blood count, serum biochemical analysis, and serum β-hCG levels weekly for toxicity, response and ability to continue receiving chemotherapy. Renal, hepatic and bone marrow functions were tested before every

chemotherapy course (normal limits were accepted as; leukocyte ≥3000/mL, thrombocyte ≥100.000/mL, hemoglobin ≥10gr/dL, total bilirubin, SGOT, SGPT under two fold of the upper limit, glomerular filtration rate ≥60 ml/minute which is calculated according to Jellife formula). Dexamethasone 20 mg and H_2 receptor antagonists were given orally 7 and 14 hours before the chemotherapy, specifically for their antiemetic activity. H_1 receptor antagonists and 5HT3 receptor antagonists were given intravenously 1 hour before chemotherapy as premedication. Granulocyte-colony stimulating factor and erythropoietin were not given as routine prophylaxis. Patients with brain metastasis received 3000 cGy cranial radiotherapy immediately with chemotherapy.

The bioassay used for β-hCG assessment was IRMA CT β-hCG (REF KP14CT, Roma, Italy), RADIM (reference range 0-10 mIU/mL) until 2009. IRMA β-hCG Beckman Coulter (reference range 0-5 mIU/mL) kit and device have been used since 2009. The complete remission was defined as normal serum β-hCG levels in 3 consecutive values. If serum β-hCG levels didn't decrease after 2 courses of EMA/CO or if β-hCG levels drew a plateau for 4 consecutive values, it was considered as drug resistance. Increase in β-hCG levels except for pregnancy was assumed as recurrence in patients with remission. Four weeks of chemotherapy (2 courses of EMA/CO) were given to patients to impede recurrence when the β-hCG levels decreased below (until 2009 below 10 mIU/mL, after 2009 below 5 mIU/mL) the limit of normal range. All these criteria were also used to replace other chemotherapy protocols with EMA/CO.

Patients were followed with β-hCG levels every month and by pelvic examination and when necessary by chest x-ray every 3 months during the first year after remission. β-hCG levels, pelvic examination and chest x-ray were evaluated every 6 months during the second year and then yearly. Contraception was obtained with oral contraceptives for 1 year after remission.

The statistical analysis was made by using Chi-square test with SPSS 17.0 (Statistical Package for Social Sciences for Windows). The cut-off for statistical significance was set at $p < 0.05$.

Results

The mean age of the patients was 32.5 with a range of 17-57 years. Twenty-four patients received primarily EMA/CO treatment, 16 patients received secondary EMA/CO treatment because of resistance to single agent methotrexate (n=10) or to MAC III (n=6) chemotherapy. The risk score was ≥7 in 27 (67.5%) patients. Before the treatment, the average β-hCG level was 124.019 mIU/mL (range, 1656-789.139) and β-hCG level was >100.000 mIU/mL in 16 (40%) patients. In 8 (20%) patients histopathological diagnosis was choriocarcinoma. The previous pregnancy was term pregnancy in 12 (30%) patients. The age of tumor was over 13 months in 13 (32.5%) patients. The tumor size was ≥5 cm in 16 (40%) patients. Metastasis was detected in 21 (52.5%) patients. There was pulmonary metastasis in 18 (45%) patients, pelvic metastasis in 6 (15%) patients, liver metastasis in 5 (12.5%) patients, brain metastasis in 2 (5%) patients and renal metastasis in 1 (2.5%) patient. One of the patients who had pelvic metastasis also had metastasis in the vagina. In one of the patients who had liver metastasis, the tumor had also spread to the pancreas. In 9 (42.9%) patients, the number of metastasis was ≥8. Clinic-pathologic characteristics of the patients was given in detail at Table 4.

Table 4: Clinicopathologic risk factors

Factors		n	%
Score	≤6	13	32.5
	≥7	27	67.5
Age	≤39	28	70.0
	≥40	12	30.0
β-hCG (mIU/ml)	10^3-<10^4	10	25.0
	10^4-<10^5	14	35.0
	≥10^5	16	40.0
Histopathology	Choriocarcinoma	8	20.0
	Others	32	80.0
Tumor age* (month)	<4	15	37.5
	4-<7	7	17.5
	7-<13	5	12.5
	≥13	13	32.5
Antecedent pregnancy	Hydatidiform mole	19	47.5
	Abortion	9	22.5
	Term	12	30.0
Largest tumor size (cm)	<3	13	32.5
	3-<5	11	27.5
	≥5	16	40.0
Metastases	Absent	19	47.5
	Present	21	52.5
Pulmonary metastases	Absent	22	55.0
	Present	18	45.0
Pelvic metastases	Absent	34	85.0
	Present	6	15.0
Liver metastases	Absent	35	87.5
	Present	5	12.5
Cerebral metastases	Absent	38	95.0
	Present	2	5.0
Kidney metastases	Absent	39	97.5
	Present	1	2.5
Number of metastases	1-4	2	9.5
	4-8	10	47.6
	≥8	9	42.9
Previous chemotherapy	Primary	24	60
	Secondary	16	40

* *The period from previous pregnancy to treatment*

There was metastasis in 63% of the patients with a score ≥7, in 31% of the patients with a score ≤6. This difference had a tendency to be statistically significant (p=0.056). Liver and brain metastasis were only seen in patients with a score ≥7 (Table 5).

Hysterectomy was chosen as a part of the treatment in 7 of 17 patients to whom surgery was performed. Five patients who had been operated in other centers because of different reasons were referred to our hospital after a final diagnosis of GTN. Hysterectomy was performed to these 5 patients (4 patients during the chemotherapy and 1 patient before the chemotherapy) during the emergency operations done for the exploration of intraabdominal hemorrhage. During the surgery, appendectomy was performed in 2 patients and in 1 of these patients omentectomy was applied additionally. Since 2 patients had brain metastasis that could not be resected, targeted 3000 cGy radiotherapy was applied.

The average β-hCG level was 81.469 mlU/mL (range, 300-793.600 mIU/mL) for the 16 patients who were planned to take EMA/CO treatment because of resistance to single agent methotrexate and MAC III. One patient was lost to follow-up without completing the treatment after having 2 courses of chemotherapy. Resistance to the EMA/CO treatment developed in 6 patients (15.3%, n: 6/39). EMA/CO treatment was given to 3 of 6 patients primarily and other 3 patients took it secondarily. Four patients who had drug resistance underwent surgery as a part of the treatment and complete remission was obtained in 3 of these 4 patients. VIP (1^{st}-5^{th} days etoposide, VP-16; 75mg/m^2, 1^{st}-5^{th} days 1.2 g/m^2 ifosfamide; 1^{st}-5^{th} days 20 mg/m^2 cisplatin; 1^{st}-5^{th} days 1.2 g/m^2 mesna, 21 days interval) salvage therapy was given to fourth patient who had surgery but remission could not be achieved and the patient died. One of the 2 unresponsive patients treated nonsurgically received EMA/EP (1^{st} day etoposide 150 mg/m^2; 1^{st} day cisplatin 75 mg/m^2; 8^{th} and 9^{th} days etoposide 100 mg/m^2; 8^{th} day methotrexate 300 mg/m^2; 9^{th} and 10^{th} day folinic acid 30 mg/day; 8^{th} and 9^{th} days actinomycin D 0.5 mg/day; every 15 days) and then IMA (1^{st}-3^{rd} days ifosfamide 2.5 mg/m^2; 1^{st}-3^{rd} days mesna 2.5 mg/m^2; 1^{st} day adriamycin 60 mg/m^2; every 21 days) and the other patient received VBP (1^{st} and 2^{nd} days vinblastine 8 mg/m^2; 2^{nd}, 9^{th} and 16^{th} days bleomycine 30 mg; 1st-5^{th} days cisplatin 20 mg/m^2; every 21 days). These 2 patients died 3 and 5 months after the initiation of salvage chemotherapy, respectively.

Median follow-up time of the patients was 74.8 months (range, 1-203). During the follow-up time recurrence developed in 3 (7.7%) patients. Two of these 3 patients had pulmonary recurrence, the other one had a pelvic recurrence. In these patients the average recurrence time was 13 months (range, 9-18), histopathology was complete mole, the antecedent pregnancy was mole hydatidiform and the age of the tumor was ≥4 months. One of these patients had GTN score<6 and remaining 2 patients had GTN score≥7 (Table 6). After recurrence, 2 of them were treated with EMA/CO, 1 patient were treated with EMA/EP and complete remission was provided in these patients. The average follow-up time of these 3 patients were 54 months and 28 months from the first treatment and after recurrence treatment, respectively.

During the follow-up time 3 (7.7%) of 39 patients died. Time from primary treatment to the death was 3 months, 22 months and 66 months, respectively. In all these patients GTN score was ≥7, histopathology was choriocarcinoma, the antecedent pregnancy was term pregnancy and tumor dimension was ≥5 cm (Table 6).

Table 5: Presence and site of metastasis in relation to GTN score

Score	Present of metastases	Metastatic site				
		Pulmonary	Liver	Kidney	Cranial	Pelvic
Low risk (≤6)	4/13 (30.8%)	4/13 (30.8%)	-	-	-	1/13 (7.6%)
High risk (≥7)	17/27 (62.9%)	14/27 (51.8%)	5/27 (18.5%)	1/27(3.7%)	2/27 (7.4%)	5/27 (18.5%)

Table 6: Characteristics of patients who died and developed recurrence

Pt no	Sc	Age	Pathology	β-hCG (mIU/ml)	Tumor age(mt)	Tumor size(cm)	AP	Metastases site	Metastases number	Treat	Response	Process of disease	Recurrence site	DFS (mt)	Cure	Ex
1	≥7	24	CM	150.000	≥13	3-5	HM	Pulmonary +Liver	≥8	P	+	Recurrence	Pelvis	12	+	-
2	≥7	46	CM	48.645	≥13	3-5	HM	-	-	S	+	Recurrence	Pulmonary	18	+	-
3	≤6	33	CM	5000	4-7	<3	HM	-	-	S	+	Recurrence	Pulmonary	9	+	-
4	≥7	30	CC	11.273	<4	≥5	Term	Liver	≥8	S	-	Progression	-	-	-	+
5	≥7	30	CC	8800	4-7	≥5	Term	Liver	4-8	S	-	Progression	-	-	-	+
6	≥7	50	CC	317.419	≥13	≥5	Term	Pulmonary + Pelvis	<4	P	-	Progression	-	-	-	+

Pt: Patient, Sc: Score, β-hCG: β-human chorionic gonadotropin, mt: Month, AP: Antecedent pregnancy, Treat: Treatment, DFS: Disease free survival, CM: Complete mole, CC: Choriocarcinoma, HM: Hydatidiform mole, P: Primary, S: Secondary

Complete clinical response was obtained in 36 (92.3%) patients with only EMA/CO or EMA/CO and surgery. The rate of treatment response was 91.3% in primary EMA/CO and 93.8% in secondary EMA/CO therapy (p=0.77). When the antecedent pregnancy was term pregnancy or the histopathologic diagnosis was choriocarcinoma or when there was liver metastasis, the treatment success decreased (Table 7). The effects of tumor dimension and the presence of metastasis tend to be statistically significant in determining the resistance. However, there were no association between the success of treatment and the level of the risk score, age, type of previous chemotherapy, the place of metastasis except liver (lungs, pelvic and brain), the number of metastasis, the age of tumor and the level of β-hCG in diagnosis.

Table 7: Association between response rate and prognostic factors, univariate analysis

Factors		Response rate		p
		n	%	
Score	≤6	13/13	100	0.202
	≥7	23/26	88.5	
Age	≤39	26/28	92.9	0.837
	≥40	10/11	90.9	
Previous chemotherapy	Primary	21/23	91.3	0.778
	Secondary	15/16	93.8	
β-hCG (mIU/mL)	≤50.000	19/20	95	0.517
	>50.000	17/19	89.5	
Histopathology	Choriocarcinoma	4/7	57.1	0.001**
	Others	32/32	100	
Tumor age* (month)	<4 ay	14/15	93.3	0.832
	4-<7	6/7	85.7	
	7-<13	5/5	100	
	≥13	11/12	91.7	
Antecedent pregnancy	Hydatidiform mole	19/19	100	0.016**
	Abortion	9/9	100	
	Term	8/11	72.7	
Largest tumor size (cm)	<3	13/13	100	0.097
	3-<5	10/10	100	
	≥5	13/16	81.3	
Metastases	Absent	19/19	100	0.079
	Present	7/20	85	
Pulmonary metastases	Absent	20/22	90.9	0.709
	Present	16/17	94.1	
Pelvic metastases	Absent	32/34	94.1	0.269
	Present	4/5	80	
Liver metastases	Absent	33/34	97.1	0.004**
	Present	3/5	60	
Cerebral metastases	Absent	34/37	91.9	0.675
	Present	2/2	100	
Number of metastases	≤7	10/12	83.3	0.798
	≥8	7/8	87.5	

** The period from previous pregnancy to treatment*
*** Statistically significant (p<0.05)*

Discussion

The risk factors for GTN have been tried to be defined since 1960's. In 1976, Bagshawe et al. developed a scoring system by using prognostic factors.[1] Many scoring methods have been evaluated since 1976 in order to provide an effective treatment with lower toxic effects and to predict the success of treatment.[1,2] Bagshawe's scoring system was modified by WHO in 1983 and then FIGO modified WHO scoring system in 2000.[2,3] Modified WHO prognostic scoring system that is the most common scoring system is being used at present.[4]

The main treatment of GTN is chemotherapy.[9] Appropriate and timely treatment of high risk GTN prevents the life-threatening complications. Between 1970 and 1980 MAC III treatment was used efficiently but it had a very high hematologic toxicity. In 1991, EMA/CO regimen which has less hematologic toxicity and higher remission rates than MAC III, was developed by Newlands.[7]

EMA/CO is suggested as the first step combined chemotherapy at high risk GTN.[10] Remission rates were shown to be 86.2% and 91% by Bower et al.[11] and Kim et al.[12], respectively. However, remission rates that Lurain et al. demonstrated in 40 patients with high-risk GTN with primary and secondary EMA/CO treatment were very low (54% and 50%, respectively).[13] Escobar et al.[14] showed remission rates as 71% in all patients, 75% in primary treatment group and 65% in secondary treatment group in a study including 45 patients. In our study success rate was determined as 92.3% and it had a high success rate similar to the study of Bower et al. and Kim et al. This rate is determined as 91.3% in primary EMA/CO treatment and 93.8% in secondary EMA/CO treatment groups.

The drug resistance in our study was 15.3%. This rate has been shown to range between 14%-20%.[11,14,15] Lurain et al.[6] demonstrated drug resistance or relapse in 30% of the patients in the high-risk group who took EMA/CO. Recurrence rate is 19% in the study of Bollis et al.[15] In our study, recurrence is observed in 7.7% of the patients. The average time to recurrence was 13 months.

Risk factors are being used efficiently in determining GTN risk score. However, there are no determined factors for the prediction of the success of the treatment, since the factors determining the response to the treatment differed from one study to another.

In our study, term pregnancy as the antecedent pregnancy,

choriocarcinoma as the pathological diagnosis and liver metastasis reduced the success of the treatment. In addition, size of the tumor and presence of metastasis tended to be a determining factor for the treatment success. Ngan et al.[16] stated that the duration between treatment and previous pregnancy and the level of β-hCG in high-risk patients treated with EMA/CO were the two main factors affecting mortality. Escobar et al.[14] showed that tumor age, location of the metastasis and scoring system affected the complete treatment response. Lurain and Sciara[17] stated that choriocarcinoma as the histopathology, presence of metastasis except in the lung and vagina, previous term pregnancy and risk factor that was equal or greater than 3 reduced the treatment success. Lu et al.[18] stated that the site of the metastasis and the number of organs with metastasis had major role in the success of the treatment. Bover et al.[11] demonstrated that previous pregnancy, tumor age, liver and brain metastasis reduced treatment success significantly.

Conclusion

In the patients with high risk GTN taking EMA/CO combination chemotherapy, 92.3% complete success rate could be obtained. Besides, drug resistance and recurrence rates were 15% and 7.7%, respectively. Significant risk factors for the prediction of the success of treatment are not clear because of the differences in many studies. Further studies are needed in order to show the real importance of the scoring system and to define the factors for predicting the treatment success.

Gestasyonel Trofoblastik Neoplazide EMA/CO Kombinasyon Kemoterapisi: Sonuçlarımızın Güncellemesi

ÖZET

AMAÇ: Bu çalışmamızda yüksek riskli gestasyonel trofoblastik neoplazide (GTN) EMA-CO (etoposid, metotreksat, aktinomisin-D, siklofosfamid, vinkristin) kemoterapisi hakkındaki deneyimlerimizi güncellemeyi amaçladık.

GEREÇ VE YÖNTEM Hastalar FIGO'nun modifiye WHO sistemine göre skorlandı. 2000 yılından önceki hastaların skorlaması bu sisteme göre yeniden yapıldı. 1992-2013 yılları arasında yüksek riskli GTN tanısıyla veya tek ajan metotreksat ve MAC III kombinasyon tedavisine dirençten dolayı EMA-CO ile tedavi edilen 39 hasta retrospektif olarak değerlendirildi. Seçilmiş hastalara adjuvant cerrahi veya radyoterapi uygulandı. Tedavi cevabı ve prognostik faktörlerin cevap oranlarına etkisi analiz edildi.

BULGULAR: Hastaların ortanca takip süresi 74,8 aydı (aralık; 1-203). Sadece EMA-CO veya EMA-CO ve cerrah, ile tam klinik cevap 36 (%92,3) hastada elde edildi. Birincil tedavi olarak EMA-CO alan hastalarda başarı %91,3 (n:21/23) iken ikincil olarak EMA-CO alanlarda başarı %93.8 (n:15/16) idi. Altı (%15,3) hastada EMA-CO tedavisine direnç gelişti ve direnç gelişen 3 hasta öldü. Takipte 3 hastada (%7,7) nüks gelişti. Hastalığın term gebeliği takiben gelişmesi, histopatolojik tanının koryokarsinoma olması ve karaciğer metastazı tedavi başarısını azaltmaktaydı. Tümör boyutu ve metastaz varlığı ilaç direnciyle istatistiki olarak anlamlı olma eğilimindeydi.

SONUÇ: EMA-CO kemoterapisi yüksek riskli GTN'de etkin bir tedavidir. Birçok çalışmadaki farklılıklardan dolayı tedavi başarısını öngören faktörler net değildir.

Anahtar Kelimeler: EMA/CO, Gestasyonel trofoblastik neoplazi, Prognostik faktörler

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