Monotherapy for Low-Risk Gestational Trophoblastic Neoplasia with score 5-6

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Research Article

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Abstract

Objective

To investigate efficacy and safety of monotherapy in low-risk gestational trophoblastic neoplasia (GTN) patients with a high FIGO/WHO prognostic score of 5–6.

Methods

The low-risk GTN patients with a high FIGO/WHO prognostic score of 5–6 from January 2012 to December 2019 were enrolled. The study is a retrospective report. Real-world data were used to analyze the efficacy and safety of single-agent chemotherapy and combination chemotherapy in patients with a high FIGO/WHO prognostic score of 5–6.

Results

A total of 224 patients were enrolled, including 75 cases (33.5%) with a FIGO/WHO prognostic score of 5–6. Complete remission was in all patients. Among the 29 cases with a FIGO/WHO prognostic score of 5–6 taking single-agent chemotherapy, 22 cases (75.9%) developed drug resistance, the number of chemotherapy courses was 7.8 ± 2.1 , and the number of chemotherapy courses required for β -hCG to return to normal was 5.4 ± 1.8 . Among the 46 cases taking combination chemotherapy, 7 patients (15.2%) developed drug resistance, the number of chemotherapy courses was 7.4 ± 2.0 , and the number of chemotherapy courses required for β -hCG to return to normal was 4.8 ± 1.6 . There was a statistically significant difference in the drug resistance rate between these two subgroups ($P < 0.05$), but there was not statistically significant difference in the total number of chemotherapy courses or number of chemotherapy courses required for β -hCG to return to normal ($< 2 \text{ mIU/ml}$) ($P < 0.05$).

Conclusion

Monotherapy showed remarkable advantages in low-risk GTN patients with a FIGO/WHO prognostic score of 5–6.

Full Text

Gestational trophoblastic neoplasia (GTN) is the only gynecological malignant tumor related to pregnancy that can be cured by chemotherapy. Patients with metastatic disease, FIGO scores of 5-6, or histologic diagnosis of choriocarcinoma are more likely to require second-line therapy than Patients with nonmetastatic disease, FIGO risk scores lower than 4, and patients who do not have choriocarcinoma^[1,2]. Several controversies exist within the risk score with one of the current key challenges being whether low-risk patients scoring 5-6 should be still considered low risk and initially

treated with single-agent chemotherapy, given that these patients have a higher risk of resistance to single-agent chemotherapy^[3]. The rate of resistance to first-line single-agent chemotherapy in low-risk GTN patients with a high FIGO/WHO prognostic score of 5–6 has been shown to be 14 times higher than that in patients with a low FIGO/WHO prognostic score of 0–4^[4]. It is still controversial whether combination chemotherapy regimens work better.

The patients with low-risk GTN who were admitted to the West China Second University Hospital of Sichuan University from 2012 to 2019 were the subjects of the present study. The inclusion criteria was Stage I–III according to the 2000 FIGO GTN anatomical staging, with a FIGO/WHO prognostic score 5–6. The exclusion criteria were: (1) confirmed pathology of placental site trophoblastic tumor (PSTT), choriocarcinoma or epithelioid trophoblastic tumor (ETT); (2) receipt of non-standard treatment; (3) receipt of germicidal treatment such as MTX or traditional Chinese medicine; and (4) coexistence of other malignant tumors.

Patients were divided into a single-agent chemotherapy group and a combination chemotherapy group according to their regimen at the time of admission. The single-agent regimens include 5-day Methotrexate (MTX) or Actinomycin D, and the combination regimens include Methotrexate (MTX) + Actinomycin D or EMA-CO. The baseline of patients with FIGO/WHO prognostic score 5–6 is shown in table 1.

The efficacy evaluation of single-agent and combination chemotherapy is shown in table 2. A total of 224 low-risk GTN patients were enrolled. The follow-up time was 12–74 months, during which there were 3 (1.34%) cases of recurrence and no deaths. 75 patients (33.5%) had a FIGO/WHO prognostic score of 5–6, among which 46 (85.2%) developed drug resistance. The number of chemotherapy courses was 7.7 ± 1.8 , and the number of chemotherapy courses required for β -hCG to return to normal was 5.4 ± 1.8 . There were 29 patients who were undergoing single-agent chemotherapy, among which 22 (75.9%) developed drug resistance. The number of chemotherapy courses was 7.8 ± 2.1 , and the number of chemotherapy courses required for β -hCG to return to normal was 5.4 ± 1.8 . There were 46 patients who were undergoing combination chemotherapy, among which 7 (15.2%) developed drug resistance. The number of chemotherapy courses was 7.4 ± 2.0 , and the number of chemotherapy courses required for β -hCG to return to normal was 4.8 ± 1.6 . A statistically significant difference was found in the drug resistance rate between these two subgroups ($P < 0.05$); however, there was no significant difference between these two subgroups in terms of the number of chemotherapy courses or the number of chemotherapy courses required for β -hCG to return to normal ($P > 0.05$).

There were 12 FIGO stage III patients who were undergoing single-agent chemotherapy, among which 11 (91.7%) developed drug resistance. The number of chemotherapy courses was 8.4 ± 1.8 , and the number of chemotherapy courses required for β -hCG to return to normal was 5.7 ± 1.8 . There were 18 FIGO stage III patients who were undergoing combination chemotherapy, among which 3 (16.7%) developed drug resistance. The number of chemotherapy courses was 7.5 ± 2.0 , and the number of chemotherapy courses required for β -hCG to return to normal was 4.8 ± 1.8 . A statistically significant difference was found in the

drug resistance rate between the two subgroups ($P < 0.05$); however, there was no significant difference between these two subgroups in terms of the number of chemotherapy courses or the number of chemotherapy courses required for β -hCG to return to normal ($P > 0.05$). There was no discontinuation or abandonment of treatment due to intolerable adverse reactions or any serious adverse reactions leading to death.

A recent study in Canada on low-risk GTN investigated a total of 412 patients and reported a chemotherapy failure rate of 32% for patients with a FIGO/WHO prognostic score of 0–4, and a significantly increased failure rate of 59% for patients with a FIGO/WHO prognostic score of 5–6^[5]. Many scholars have debated whether the current staging and scoring system should be modified to a more precise model, so that some susceptible drug-resistant patients could adopt a more effective plan at the beginning of treatment. However, Braga A et al^[6] found approximately 60% of women with gestational trophoblastic neoplasia presenting with a FIGO risk score of 5–6 could achieve remission with single-agent therapy; almost all remaining patients have complete remission with subsequent multiagent chemotherapy. Primary multiagent chemotherapy should only be given to patients with metastatic disease and choriocarcinoma, regardless of pretreatment human chorionic gonadotropin concentration, or to those defined by our new predictors including metastatic disease, choriocarcinoma and pretreatment human chorionic gonadotropin concentration. Our results are consistent with Braga A et al' study^[6]. Monotherapy showed significant advantages in low-risk GTN patients with a FIGO/WHO score of 5–6 with or without lung metastases.

Declarations

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Conflict of interest: The authors declare no conflict of interest.

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Tables

Table 1. The baseline of patients with FIGO/WHO prognostic score 5-6

		single-agent	combination	total	P value
n		29 (38.7%)	46 (61.3%)	75	
age	Mean age	35.00±11.90	34.26±10.07	34.55±10.74	>0.05
	≥40 years	6 (20.7%)	9 (19.6%)	15	
FIGO stage	I-II	17 (58.6%)	28 (60.9%)	45	
	III	12 (41.4%)	18 (39.1%)	30	
pre-treatment HCG	<10 ³	3 (10.3%)	5 (10.9%)	8	
	10 ³ -10 ⁴	12 (41.4%)	19 (41.3%)	31	
	10 ⁴ -10 ⁵	9 (31.0%)	14 (30.4%)	33	
	>10 ⁵	5 (17.3%)	8 (17.4%)	13	
Pregnancy types	mole	20 (69.0%)	32 (69.6%)	52	
	abortion	7 (24.1%)	11 (13.9%)	18	
	term	2 (6.9%)	3 (6.5%)	5	
Interval	<4 m	15 (51.7%)	24 (52.2%)	39	
	4-6 m	8 (27.6%)	13 (28.3%)	21	
	7-12 m	6 (20.7%)	8 (17.4)	14	
	>12 m	0 (0)	1 (2.2%)	1	

Note: FIGO: International Federation of Gynecology and Obstetrics, WHO: World Health Organization.

Table 2. The efficacy evaluation of single-agent and combination chemotherapy

	n	drug resistance rate	P value	total number of chemotherapy courses	P value	number of chemotherapy courses required for β - hCG to return to normal ($<2\text{mIU/ml}$)	P value
FIGO/WHO prognostic score 5-6	75	46 85.2%		7.7 $\pm$ 1.8		5.4 $\pm$ 1.8	
FIGO/WHO prognostic score 5-6 and single- agent chemotherapy	29	22 75.9%	0.00001	7.8 $\pm$ 2.1	0.432	5.4 $\pm$ 1.8	0.092
FIGO/WHO prognostic score 5-6 and combination chemotherapy	46	7 15.2%		7.4 $\pm$ 2.0		4.8 $\pm$ 1.6	
FIGO/WHO prognostic score 5-6 and FIGO III stage single- agent chemotherapy	12	11 91.7%	0.00002	8.4 $\pm$ 1.8	0.145	5.7 $\pm$ 1.8	0.15
FIGO/WHO prognostic score 5-6 and FIGO III stage combination chemotherapy	18	3 16.7%		7.5 $\pm$ 2.0		4.8 $\pm$ 1.8	

Note: FIGO: International Federation of Gynecology and Obstetrics, WHO: World Health Organization.