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RESEARCH ARTICLE

Efficacy of EMCO therapy on serum β-hcg levels in GTN at Dr. M. Djamil Padang Hospital

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Abstract

Introduction: *Etoposide, Methotrexate, Cyclophosphamide, and Vincristine (EMCO) Chemotherapy is used as an alternative therapy for patients with a diagnosis of Gestational Trophoblastic Neoplasm (GTN) at Dr. M. Djamil Hospital Padang because Actinomycin D has not been included in the National Formulation (FORNAS).*
Purpose: *To determine the efficacy of EMCO therapy with limited Actinomycin D on serum β-hCG levels in Gestational Trophoblastic Neoplasm (GTN) cases at Dr. M. Djamil Padang Hospital in 2019-2021.*
Methods: *The type of research used is numerical comparative analytics with a cross sectional approach. The number of samples was 17 GTN patients who had done EMCO chemotherapy and checked β-hCG levels before and after chemotherapy. The research was conducted from April to October 2022 at Dr. M. Djamil Hospital Padang. Data processing using total sampling technique and tested using Wilcoxon Test.*
Results: *Most GTN patients were found to be 5 cm (58,8%), metastasis location in the internal genital tract (35,5%), and patients who did not have metastasis (52,9%).*
Conclusion: *There was a significant decrease in β-hCG levels after chemotherapy using EMCO for three cycles in patients with a diagnosis of GTN.*

Keywords: *Gestational Trophoblastic Neoplasm (GTN), EMCO Chemotherapy, Serum β-hCG Levels*

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INTRODUCTION

Gestational trophoblastic disease is classified into two, benign and malignant. The malignant gestational disease is commonly referred to as Gestational Trophoblastic Neoplasm or Penyakit Trofoblas Ganas (GTN or PTG).[1] Gestational Trophoblastic Neoplasm (GTN) is a collection of malignancies originating from placental trophoblastic cells. The disease group consists of invasive moles, choriocarcinomas, and Trophoblastic Tumor Intermediates (TTI) namely Placental Site Trophoblastic Tumor (PSTT) and Epithelioid Trophoblastic Tumor (ETT).[2]

Frequent gestational trophoblastic neoplasms are Choriocarcinoma and invasive mola with a percentage of 50% due to previous benign molar pregnancies, while Placental Site Trophoblastic Tumor (PSTT) and Epithelioid Trophoblastic Tumor (ETT) originate from at term pregnancies or abortions.[1] Choriocarcinoma was found in 3/100.000 pregnancies in North America and Europe and 23/100.000 pregnancies in Southeast Asia, while PSTT and ETT were found with a prevalence of PSTT of 1/100.000 pregnancies and ETT of 0,5/100.000 pregnancies.[3] Supporting examinations that can be done for GTN patients are blood β-hCG levels and normal serum β-hCG levels <5 mIU/mL.[4] The patient should also have a pelvic ultrasound (ultrasound) with da oppler to look at the existing tissue, measure the uterus, and evaluate for metastasis.[5] The gold standard examination of GTN is the histologic examination, which can determine the type of GTN suffered.[4]

Gestational Trophoblastic Neoplasm (GTN) treatment generally uses chemotherapy, but not all regimens can be given to all GTN patients, rather the regimen is adjusted according to the stage and classification of GTN occurrence.[6] Gestational trophoblastic neoplasm chemotherapy is classified into two: low-risk chemotherapy and score value 0-6 with stage I, given with single-agent methotrexate and actinomycin D.[7] Most patients diagnosed with low-risk GTN have a good prognosis without the need for hysterectomy.[8] In GTN with stage IV and high risk or FIGO score ≥7 can be given multi-agent chemotherapy, namely EMACO (Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide, and Vincristine) without radiation or surgery. According to research conducted in the last 20 years, the effectiveness of this therapy has reached 67%-78% with 85%-94% survival.[7] Gestational trophoblastic neoplasm patients at Dr. M. Djamil Padang Hospital do not use EMACO chemotherapy but EMCO chemotherapy (Etoposide, Methotrexate, Cyclophosphamide, and Vincristine) as an alternative regimen because Actinomycin D has not been included in the National Formulation (FORNAS).

METHODS

The type of research used in this study is numerical comparative analytics with a cross sectional approach using medical record data of patients with Gestational Trophoblastic Neoplasm (GTN) who were given EMCO chemotherapy at Dr. M. Djamil Padang Hospital. This study was conducted in the Obstetrics and Gynecology department of Dr. M. Djamil Padang Hospital which was held from April to October 2022. This research method uses the Total Sampling technique. The samples in this study are medical records of all patients diagnosed with GTN by obgyn specialists who perform EMCO chemotherapy at Dr. M. Djamil Padang Hospital who meet the inclusion are not included in the exclusion criteria. This study has a flow that starts from looking at medical record data of patients suffering from GTN with high risk who have undergone chemotherapy, then entering data on β-hCG levels before and after chemotherapy. After obtaining the data, then the data is processed using SPSS

with the dependent T-test and if the data is not normally distributed, it can be processed using the Wilcoxon test.

RESULT AND DISCUSSION

A. Characteristics and Classification of Gestational Trophoblastic Neoplasm (GTN) at Dr. M. Djamil Hospital Padang in 2019-2021

The results obtained in Table 1 below regarding the characteristics of the most patients suffering from GTN at Dr. M. Djamil Padang Hospital are patients with age <40 years with 11 patients (64,7%), history of previous pregnancy with hydatidiform mole with 8 patients (47,1%), last pregnancy interval <4 months as many as 10 patients (58,1%). Djamil Padang is patients with age <40 years with 11 patients (64,7%), previous pregnancy history of mola hydatids with 8 patients (47,1%), last pregnancy distance <4 months as many as 10 patients (58,8%), β-hCG levels before therapy 10^4-10^5 (mIU/mL) as many as 9 patients (52,9%), tumor size >5 cm as many as 10 patients (58,8%), the location of metastases in the internal genital tract as many as 6 patients (35,3%), and as many as 9 patients (52,9%) did not experience metastasis. Choriocarcinoma was the most common GTN classification found in 11 patients (64,7%).

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Table 1. Frequency distribution of patient characteristics and GTN classification

Characteristic	Total (n)	Percentages (%)
Age		
1. <40 years old	11	64,7%
2. ≥40 years old	6	35,3%
History of Previous Pregnancies		
1. Mola Hidatidosa	8	47,1%
2. Abortus	4	23,5%
3. Kehamilan Aterm	5	29,4%
Distance of Last Pregnancy		
1. <4 months	10	58,8%
2. 4-6 months	7	41,2%
3. 7-12 months	0	00,0%
4. >12 months	0	00,0%
β-hCG Levels before Treatment (mIU/mL)		
1. $<10^3$	3	17,6%
2. 10^3-$<10^4$	2	11,8%
3. 10^4-10^5	9	52,9%
4. $>10^5$	3	17,6%
Size of Tumor		
1. 3-5 cm	7	41,2%
2. >5 cm	10	58,8%
Location of Metastases		
1. Lungs	3	17,6%
2. Lymph Nodes and Kidneys	0	00,0%
3. Internal Genitalia Tract	6	35,3%
4. Brain and Liver	0	00,0%
The Number of Metastases		
1. 0	9	52,9%
2. 1-4	8	47,1%
3. 5-8	0	00,0%
4. >8	0	00,0%
Classification of GTN		
1. Choriocarcinoma	11	64,7%
2. Invasive Mole	6	35,3%
3. PSTT	0	00,0%
4. ETT	0	00,0%

The research results that have been obtained, these results are similar to the results of research conducted by Jareemit et al. (2020) in Bangkok Thailand, where patients with a diagnosis of GTN who received EMACO chemotherapy were 32 patients (82,1%) at the age of <40 years and 7 patients (17,9%) were found at the age of >40 years.[9] Research conducted by Wang et al. (2020) in Hangzhou China, found that patients with GTN disease occurred more at the age of <40 years with details of 17 cases (65,4%) and at the age of >40 years as many as 9 cases (34,6%).[2] Furthermore, the results in this study are reinforced by research

conducted by Sirimusika et al. (2022) in Songkhla Thailand, which stated that High Risk Gestational Trophoblastic Neoplasm (HRGTN) of 40% developed through hydatidiform molar pregnancy.[10] These results are also in line with those obtained by Jareemit et al. (2020) in Bangkok Thailand which states that the most common pregnancy history is a hydatidiform mole with 16 cases (41%).[9]

This study also has the same results as those conducted by Jareemit et al. (2020) in Bangkok Thailand, which found that GTN patients with the most recent pregnancy distance were <4 months in 15 patients (38,5%).[9] Research conducted by Sinaga et al. (2018) at Dr. Hasan Sadikin Hospital Bandung that GTN patients who have the most pregnancy distance are <4 months with details of 24 cases (52,5%).[11] In a study conducted by Wang et al. (2021) in Hangzhou China, the highest β-hCG level before chemotherapy obtained was 10^4-10^5 with details of 13 cases (50%).[2] But in contrast to the results obtained by Jareemit et al. (2021) in Bangkok Thailand, namely the highest β-hCG levels were >10^5 (mIU/mL) with 13 cases (33,3%) and followed by 10^4-10^5 with 10 cases (25,6%).[9]

In contrast to research conducted by Gupta et al. (2022) in India, which states that metastasis to the lungs is more common, namely 80% but still found metastasis to the vagina by 30%. Gestational trophoblastic neoplasm patients with choriocarcinoma classification often experience metastasis due to hematogenous spread.[12] The results obtained in this study are in line with research conducted by Wang et al. (2021) in Hangzhou China, namely, the classification of GTN that often occurs is choriocarcinoma with 9 cases (34,6%) and invasive mola as many as 3 cases (11,5%).[2] It is also proven by research conducted by Pierre et al. (2021) in France the most common GTN found was choriocarcinoma with details of 7 cases (35%).[13]

B. Comparison of β-hCG Levels Before and After EMCO Chemotherapy

The results obtained in this study were that all patients who performed EMCO chemotherapy experienced a decrease in β-hCG levels after chemotherapy in three cycles. It can be seen in table 2 that the average β-hCG level before chemotherapy was 54751,82 mIU/mL and after chemotherapy became 69,11 mIU/mL. The average percentage of decrease obtained is 96,7003%.

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Table 2. Frequency distribution of percentage decrease in β-hCG levels

No.	β-hCG Levels (mIU/mL)		Percentage Reduction (%)
	Before Chemotherapy	After Chemotherapy	
1.	256,10	99,00	61,3000%
2.	256,80	2,38	99,1000%
3.	274,20	3,00	98,9000%
4.	1473,80	0,21	99,9860%
5.	5520,00	742,50	86,5500%
6.	10000,00	0,20	99,9980%
7.	10000,00	0,46	99,9950%
8.	10000,00	1,20	99,9880%
9.	10000,00	3,00	99,9700%
10.	10000,00	7,53	99,9200%
11.	10000,00	9,00	99,9100%
12.	10000,00	23,84	99,7600%
13.	10000,00	128,00	98,7200%
14.	76000,00	138,10	99,8200%
15.	125000,00	14,40	99,9885%
16.	210000,00	1,20	99,9994%
17.	432000,00	0,91	99,9998%
Average	**54751,82**	**69,11**	**96,7003%**

Research conducted by Jareemit et al. (2020) in Bangkok Thailand found that chemotherapy using EMA or EMACO has a comparable reduction rate as a first-line treatment in GTN patients.[9] This is also reinforced by research conducted by Winata et al. (2022) in Denpasar on the comparison of EMA and EMACO in GTN patients with high risk. If high-risk GTN patients are given EMA or EMACO therapy, a good prognosis is obtained. Both regimens are very effective in treating GTN but have some differences in treatment schedules, hospitalization requirements, and toxicity between regimens. It is also important to consider the patient's social circumstances to support the treatment.[14]

C. Analysis of β-hCG Level Decrease Before and After EMCO Chemotherapy

The results of the study obtained after data analysis using the Wilcoxon test are in table 3 below with a sample of 17 patients.

Table 3. Analysis of the decrease in β-hCG levels before and after EMCO chemotherapy

Variable	*Negative Ranks*	*Positive Ranks*	*p Value*
β-hCG levels before chemotherapy β-hCG levels after chemotherapy	17	0	0,000
Totally		**17**	

In this study, a Wilcoxon test was conducted to see the significance of the decrease in β-hCG levels in GTN patients after EMCO chemotherapy, and the results were found to be very significant, which means that all β-hCG levels in GTN patients who underwent EMCO chemotherapy decreased.

CONCLUSION

Based on the research results that have been obtained, the following conclusions are obtained:

1. The characteristics of patients with Gestational Trophoblastic Neoplasm (GTN) at Dr. M. Djamil Padang Hospital are patients with age <40 years, a history of previous pregnancies with molar hydatids, the last pregnancy interval <4 months, β-hCG levels before chemotherapy 10^4-10^5 mIU/mL, tumor size >5 cm, the location of metastases in the internal genital tract, and no metastases.
2. There was a significant decrease in β-hCG levels after chemotherapy using EMCO in GTN patients at Dr. M. Djamil Hospital Padang.

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