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Effectiveness and Efficiency Comparison of One-Day vs Eight-Day Methotrexate Protocols in Managing Low-Risk Gestational Trophoblastic Neoplasia

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Background: Gestational Trophoblastic Neoplasia (GTN) has a high incidence in Bandung, Indonesia, with a mortality rate between 31% and 51%. The most common type is low-risk GTN with various treatment protocols available. The 8-day Methotrexate (MTX) 50 mg protocol has been implemented at our center; however, due to limitation of government insurance, this study aims to compare its effectiveness against the 1-day Methotrexate (MTX) 300 mg/m² protocol.

Methods: A retrospective cohort study compared two protocols for low-risk GTN treatment at Dr. Hasan Sadikin General Hospital from January 2020 to December 2023: a 1-day Methotrexate (MTX) 300 mg/m² protocol and an 8-day MTX protocol (50 mg MTX IM on days 1, 3, 5, 7 with folinic acid 15 mg orally 24 h after MTX on days 2, 4, 6, 8) and repeat every 2 weeks. Data on patient characteristics, chemotherapy response, side effects, and treatment costs were analyzed.

Results: The 1-day MTX 300 mg/m² protocol achieved similar remission with fewer cycles, milder side effects, and reduced costs compared to the 8-day MTX 50 mg protocol, supporting it as an effective treatment option for low-risk GTN.

Conclusion: The 1-day MTX 300 mg/m² protocol is as an effective treatment option for low-risk GTN compared to the 8-day MTX 50 mg protocol.

Keywords: gestational trophoblastic neoplasia, low risk, chemotherapy, methotrexate

Introduction

Gestational trophoblastic disease (GTD) is a placental disorder consisting of a spectrum of premalignant and malignant abnormalities called gestational trophoblastic neoplasia (GTN). The spectrum of premalignant tumors is complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM), and malignant ones are invasive mole, choriocarcinoma, *placental site trophoblastic tumor* (PSTT), and *epithelioid trophoblastic tumor* (ETT). The evacuation of a complete hydatidiform mole carries a 15% risk of progressing into an invasive mole, a malignant form of gestational trophoblastic neoplasia (GTN).[1]

The incidence of benign and malignant gestational trophoblastic neoplasia (GTN) remains significantly higher in Indonesia and other developing countries compared to developed nations. Although hydatidiform mole cases in Indonesia have declined over the years, choriocarcinoma rates remain high. WHO reports estimate hydatidiform mole incidence in Western countries at 1:1,450–1:2,000 pregnancies and choriocarcinoma at 1:14,000–1:40,000, while Southeast Asia reports GTN rates of 9.2 per 40,000 pregnancies. In Indonesia, hydatidiform mole cases occur in 1:51 to 1:141

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pregnancies, and in West Java, at 1:28 to 1:105 childbirths. Bandung shows an incidence of 1:427 for hydatidiform mole and 1:822 for GTN, with a mortality rate of 31–51%. These high rates underscore the need for effective treatment.[2]

GTN management is based on staging and risk stratification, with cases categorized as low-risk or high-risk. Risk assessment considers factors like age, antecedent pregnancy, time since pregnancy, pre-therapy serum hCG levels, tumor size, metastasis sites and count, and history of chemotherapy failure. For low-risk GTN cases (stages I–III, risk score <7), single-agent chemotherapy is preferred, primarily using methotrexate or actinomycin-D. Methotrexate has multiple administration routes and dosage options, typically given intravenously or intramuscularly. Oral methotrexate, however, is linked to higher resistance and more side effects.[3]

Methotrexate was first used in metastatic choriocarcinoma cases in 1956, and intramuscular five-day methotrexate administration has shown a 76–98% cure rate for non-metastatic GTN. Folic acid supplementation reduces methotrexate toxicity. The eight-day methotrexate-folinic acid (MTX-FA) protocol provides high remission with low systemic toxicity. Weekly intramuscular methotrexate offers a cost-effective option by reducing hospital stays. Additionally, a study on 300 mg/m² methotrexate infusion in low-risk GTN suggests that higher doses can speed remission and reduce therapy duration. Omitting consolidation chemotherapy and folinic acid, as systemic methotrexate toxicity remains low, further reduces costs and treatment duration.[4–6]

A study at the New England Trophoblastic Disease Centre (NETDC) from 1974 to 2014 examined 325 patients with low-risk GTN, comparing an eight-day intramuscular MTX-FA regimen to a one-day 300 mg/m² MTX-FA infusion. The eight-day regimen was associated with more side effects—including gastrointestinal issues, abnormal lab results, visual disturbances, and other general complaints—compared to the one-day infusion, though the need to switch regimens was higher with the eight-day protocol but not statistically significant. Side effects were temporary, resolving post-treatment with no long-term sequelae.[7]

In order to achieve cost and service efficiency, single chemotherapy MTX 30–50 mg/m^2 is an option, with minimal chemotherapy toxicity and patient comfort. However, this chemotherapy regimen has the lowest complete chemotherapy response rate when compared to other MTX chemotherapy regimens.[8]

A meta-analysis comparing chemotherapy with the MTX-FA regimen with Actinic D in low-risk GTN cases showed that the administration of Actinixin D resulted in a better rate of remission compared to the administration of the MTX-FA regimen, although the administration of Actinixin D was associated with higher side effects when compared with the administration of the MTX-FA regimen. However, the determination of chemotherapy in low-risk GTN cases is also based on the ability and availability of each GTN treatment centre. Other studies also showed that chemotherapy with a single regimen of MTX was still reliable when compared to a combination regimen of MTX with Actinixin D.[3,8,9]

Methotrexate is widely used as first-line chemotherapy for low-risk GTN cases, though no international consensus exists on the optimal regimen for maximum response with minimal residual risk. While a single-dose approach is common, some protocols adjust doses based on body surface area (BSA) or weight. Parker et al found that in low-risk GTN, single-dose methotrexate—whether standardized, BSA-based, or weight-based—does not impact complete response rates or recurrence. The number of chemotherapy cycles and complications also showed no significant difference between dosing approaches.[10]

The Universal Health Coverage\Jaminan Kesehatan Nasional (JKN) in Indonesia aims to increase public access to quality health services, including for people with catastrophic diseases such as cancer. Services available to cancer patients include outpatient care, hospitalization, surgery, and chemotherapy. However, this financing has been widely studied, and it is said that the direct-cost of treating cancer patients is higher than the INA-CBG (Indonesian Case Base Groups) bill used in this JKN program. One of the factors that affects this is the length of stay (LOS) of the cancer patient.[11]

Dr. Hasan Sadikin General Hospital (RSHS) Bandung, as a GTN treatment centre in West Java, has long used methotrexate as a therapy option for low-risk GTN. There are two protocols commonly used in RSHS, namely the eight-day MTX-FA protocol and the 300 mg/m2 infusion MTX protocol. Although studies show that the eight-day MTX-FA protocol is superior in remission rates, the 300 mg/m2 infusion MTX protocol can provide efficiency in terms of length of stay in patients. Efficiency is certainly expected in the mechanism of RSHS as a JKN provider. Therefore, the

researcher intends to conduct a study on the use of the methotrexate protocol in RSHS to determine the effectiveness and efficiency of each methotrexate chemotherapy protocol given.

Method

Sample Collection

The inclusion criteria for this study are women diagnosed with low-risk gestational trophoblastic disease (FIGO score <7) scheduled for single-agent methotrexate chemotherapy, either via a one-day (MTX 300 mg/m²) or eight-day (MTX 50 mg) protocol. Participants must have complete medical records and β-hCG test results. Exclusion criteria include women who have undergone a hysterectomy, had secondary curettage before chemotherapy, have recurrent GTD, or have unrelated comorbid conditions.

The sample size for this study was calculated based on the requirements for unpaired categorical analytical research. Using the standard sample size formula and Z values from the normal distribution (Zα = 1.96 and Zβ = 1.64), the minimum sample size was determined. Given that the proportion of patients resistant to the eight-day MTX protocol (P1) is 12%, and the recurrence rate (P2) is 45%, the minimum required sample size for each group is 38 participants.

A retrospective cohort study was done to two groups of low-risk GTN patients that were given a one-day MTX protocol or an eight-day MTX protocol. The protocol therapy that was given followed the FIGO and NCCN guidelines, even though the 300 mg/m^2 is no longer recommended due to lesser efficacy, it is still used due to limitation coverage of the government insurance. The first group was given a one-day MTX protocol (300 mg/m^2 6–12 h IV infusion with leucovorin 15 mg orally or IM every 12 hours for 4 doses start 24 hours after MTX infusion; while the second group was given an eight-day MTX protocol (50 mg MTX IM on days 1, 3, 5, 7 with folinic acid 15 mg orally 24 h after MTX on days 2, 4, 6, 8). The frequency of β-hCG monitoring to evaluate chemotherapy response was done two-weekly. Consolidation therapy in our protocol was given for 2–3 cycles after the β-hCG value has returned to normal.

Result

A total of 88 patients met the inclusion and exclusion criteria; 43 patients received management with a 1-day MTX 300 mg/m^2 protocol; and 45 patients received management with an 8-day MTX 50 mg protocol. There was no difference in the characteristics of pre-treatment serum β-hCG levels, stages, or FIGO scores of the two protocols (Table 1). The results of patient management with the 1-day MTX 300 mg/m2 protocol and the 8-day MTX 50 mg protocol included: primary remission, 76.7% and 75.6%, respectively (OR 1.068, P value 0.896); chemoresistance, 23.3% and 24.4% (OR 0.937, P value 0.896) (Table 2); recurrence at three months after chemotherapy, 6.9% and 8.9% (P value 0.721) (Table 3);

Table 1 Characteristics of the Research Subject

Characteristic	Total	1-Day Protocol MTX 300 mg/m^2	8-Day Protocol MTX 50 mg	*p*
Serum β-hCG level				
Mean ± SD	240146±368,676*	126,829.42±252,574*	348,427.08±428,160.14*	0.268
Median	61360,20*	21013,80*	71,557,80*	
Range	999,988*	999,883*	999,988*	
Metastatic disease				
Stage I	76	39(51,3)	37(48,7)	0,035
Stage II	6	0(0,0)	6(100,0)	
Stage III	6	4(66,7)	2(33,3)	
Stage IV	0	0(0,0)	0(0,0)	
FIGO Score				
0–4	54	28(51,9)	26(48,1)	0,480
5–6	34	15(44,1)	19(55,9)	

Notes: *abnormally distributed β-hCG levels test continued to Mann Whitney test.

Table 2 Results of MTX Chemotherapy Remission and Chemoresistance

Outcome	Total	Variable	Variable	OR	*p*
		Primary Remission	No Remission		
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	33(76,7) 34(75,6)	10(23,3) 11(24,4)	1,068 Reff	0,896
		Chemoresistance	Chemosensitivity		
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	10(23,3) 11(24,4)	33(76,7) 34(75,6)	0,937 Reff	0,896

Table 3 MTX Post-Chemotherapy Follow-Up

Outcome	Total	Variable	Variable	OR	*p*
		Remission	No Remission		
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	40(93.0) 41(91.1)	3(6.9) 4(8.9)	1.300 Reff	0.721

the average number of chemotherapy cycles was 6.77 ± 3.25 and 8.82 ± 4.79 (P value 0.040); the average total treatment cost was Rp 18,659,867±8,961,724 and Rp 37,527,968± 20,386,168 (P value 0.000) (Table 4).

The side effects that occurred included: gastrointestinal 46.5% and 64.4%, abnormal lab values 32.6% and 15.6%, eyes 4.7% and 13.3%, general complaints 9.3% and 0, infections 7.0% and 24.4%, respiration 9.3% and 13.3%, skin 2.3% and 0 (Table 5).

Discussion

Low-risk GTN cases at Dr. Hasan Sadikin General Hospital Bandung, Bandung are still quite high. There have been many studies that discuss the risk factors for chemoresistance events in GTN.

Low-risk gestational trophoblastic neoplasia (GTN) is considered chemoresistance if there is a poor response, which means there is an inadequate reduction of β-hCG; either when the β-hCG level plateaus (<10% change) after 3 treatment cycles or when the β-hCG level rises (>10% change) for 2 treatment cycles. This resistance indicates that tumour cells are not being effectively eliminated and that the disease may progress or remain persistent despite ongoing chemotherapy. In such cases, alternative therapeutic strategies, including switching to more potent drugs or combination regimens, are necessary to achieve remission and manage the condition effectively.

Table 4 Results of the Management of the Number of Chemotherapy Cycles and MTX Chemotherapy Financing

Outcome	1-Day Protocol MTX 300 mg/m^2	8-Day MTX 50 mg Protocol	*p*
Number of chemotherapy cycles			
Mean ± SD	6.77±3.25	8.82±4.79	0.040
Median	6.00	8.00	
Range	13.00	21.00	
Total fees			
Mean ± SD	18659867±8,961,724	37,527,968±20,386,168	0,000
Median	16543800	34,030,400	
Range	35844900	89,329,800	

Table 5 Side Effects After Treatment with MTX Chemotherapy

Outcome	Total	Side effects		OR	*p*
		Yes	Not		
Gastrointestinal					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	20(46,5) 29(64,4)	23(53,5) 16(35,6)	0,480 Reff	0,090
Abnormal lab values					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	14(32,6) 7(15,6)	29(67,4) 38(84,4)	2,621 Reff	0,061
Eye					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	2(4,7) 6(13,3)	41(95,3) 39(86,7)	0,317	0,157
General Disorders					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	4(9,3) 0(0,0)	39(90,7) 45(100,0)	NA*	0,036
Infection					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	3(7,0) 11(24,4)	40(93,0) 34(75,6)	0,232	0,025
Nerve					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	0(0,0) 0(0,0)	43(100,0) 45(100,0)	NA*	NA*
Respiration					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	4(9,3) 6(13,3)	39(90,7) 39(86,7)	0,667	0,551
Skin					
1-day protocol MTX 300 mg/m2 8-day MTX 50 mg protocol	43 45	1(2,3) 0(0,0)	42(97,7) 45(100,0)	NA*	0,304

Notes: *NA=not applicable.

Among other factors that are considered to be influential namely serum β-hCG levels pre-treatment and FIGO scores.

In this study, the average β level of -hCG in patients given the 1-day MTX protocol of 300 mg/m2 was 126,829.42 ±252,574, while the patients who were given the 8-day protocol of MTX 50 mg were 348,427.08±428,160.14. There was no significant difference in mean β-hCG levels between patients with a 1-day MTX protocol of 300 mg/m^2 and patients with an 8-day MTX protocol of 50 mg. This result was also obtained in the study.

Stage I patients who received the 1-day MTX 300 mg/m^2 protocol were 51.3%, and stage III patients who were given the 1-day MTX 300 mg/m^2 protocol were 66.7%. Stage I patients who received the 8-day MTX 50 mg protocol were 48.7%, and stage III patients who were given the 8-day MTX 50 mg protocol were 33.3%. Stage II patients who were given an 8-day MTX 50 mg protocol as much as 100%. Low-risk GTN patients are given chemotherapy with a single regimen, although there are other criteria for chemotherapy administration where chemotherapy will be given with multiple regimens, as in Hammond's criteria. However, from various studies that have been published, the effectiveness of a single chemotherapy regimen in low-risk GTN patients at various stages gives quite good results.

Patients with FIGO scores 0–4 who received a 1-day MTX protocol of 300 mg/m^2 were 51.9%, while patients with FIGO scores of 5–6 who received a 1-day protocol of MTX 300 mg/m2 were 41.1%. Patients with FIGO scores 0–4 who

received the 8-day MTX 50 mg protocol were 48.1%, while patients with FIGO scores of 5–6 who received the 8-day MTX 50 mg protocol were 55.9%. Before using the FIGO 2000 risk scoring criteria, the risk division was divided into three, namely a score of 0–4 as low risk, a score of 5–6 as medium risk, and a score of >6 as high risk. A FIGO score of 5–6 is associated with an increased risk of chemoresistance events, although this is not always the case.

MTX chemotherapy has been widely studied as a single therapy in low-risk cases of GTN. Even with different levels of effectiveness, the use of MTX chemotherapy is still relied on in various trophoblastic centre around the world. Until now, there has been no consensus that states that the use of chemotherapy is declared the most effective for the management of GTN cases; therefore, the use of chemotherapy in low-risk GTN cases can vary in each Trophoblast flashlight.

Dr. Hasan Sadikin General Hospital Bandung, Bandung itself has long used MTX chemotherapy as a single therapy in low-risk GTN cases. The protocol that has been used for a long time is the 8-day MTX 50 mg protocol. The use of this protocol has long proven to be quite satisfactory as management in low-risk GTN cases, although there are other protocols that can be used as management in low-risk GTN cases.

The research by Wong et al obtained the results of administering intravenous MTX chemotherapy at 300 mg/m^2 plus folinic acid, providing effective results in the management of low-risk GTN cases, while the reduction in cost and duration of treatment can be reduced by eliminating the administration of consolidation chemotherapy and folinic acid, which in the study is not always given after the administration of methotrexate because systemic methotrexate levels do not reach toxic levels. The study by Ngu et al also obtained similar results, namely that in the administration of single MTX chemotherapy at 300 mg/m^2, complete remission was obtained in 85.2% of patients (a total of 115 patients), and 60.9% of patients only needed a single dose of the chemotherapy protocol. MTX chemotherapy with a one-day protocol has been shown to have a fairly good remission rate by providing the advantage of fewer chemotherapy cycles and less financing when compared to MTX chemotherapy with an eight-day protocol. This is similar to what was obtained in this study.[4–6,12]

In other studies, the rate of remission from MTX chemotherapy can be increased by the administration of actinomycin-D chemotherapy, which can be given as a replacement if the MTX chemotherapy response is not appropriate. The administration of actinomycin-D chemotherapy as a replacement chemotherapy can increase the remission response by up to 100%. Although the use of actinomycin-D chemotherapy as a replacement chemotherapy has not been established as a protocol for the management of low-risk GTN at Dr. Hasan Sadikin General Hospital Bandung, Bandung, this can certainly be a consideration for providing replacement chemotherapy compared to giving multi-agent chemotherapy after the MTX single chemotherapy response is not as expected.[8,12–14]

Different results were obtained in other studies. In a study conducted at the New England Trophoblastic Disease Centre (NETDC) based on patients treated between 1974 and 2014, which included 325 patients with low-risk GTN, it was found that patients who received chemotherapy with an intramuscular MTX-FA regimen for eight days had a better rate of complete remission compared to patients who received chemotherapy with an infusion MTX regimen of 300 mg/m2-FA for one day. However, in this study, the incidence of changes in chemotherapy regimen with intramuscular MTX-FA for eight days to a different regimen was higher than chemotherapy with an infusion MTX regimen of 300 mg/m2-FA for one day, although it was not statistically significant.[7]

The incidence of chemoresistance in MTX single chemotherapy has been extensively studied. Although it provides different results on risk factors that may affect the incidence of chemoresistance in the administration of MTX monotherapy, risk factors that are currently considered to be influential include β-hCG levels before therapy and FIGO scores. However, in this study, there was no significant effect of β-hCG levels before therapy and FIGO scores on the incidence of chemoresistance in MTX single chemotherapy in either the one-day protocol or the eight-day protocol. The incidence of chemoresistance in the administration of the 1-day MTX 300 mg/m^2 protocol was 23.3%, and the number of patients who received the 8-day MTX 50 mg protocol was 24.4%, which was statistically no significant difference. The incidence of chemoresistance in the administration of MTX single chemotherapy tends to remain constant when compared to previous studies conducted at Dr. Hasan Sadikin General Hospital Bandung, Bandung. Even so, the incidence of this chemoresistance is still in accordance with what was obtained in several studies, ranging from 15.9% to 35.7%.[15,16]

Follow-up in patients with low-risk GTN after primary remission is an important action to take because, although the remission rate in low-risk GTN cases can reach 100%, recurrence can still occur, especially 12 months after primary remission for low-risk GTN cases. The researcher added follow-up results after three months of primary remission in patients who received MTX chemotherapy. The obstacle that occurred was the lack of compliance from patients for routine control up to 12 months after primary remission. This can be seen from data from medical records, where in some patients there are no follow-up data for up to 12 months after remission. Patients carry out routine control to carry out anamnesis examinations for recurrence symptoms, physical examinations, and serum β-hCG levels every two weeks for the first three months, followed monthly for up to twelve months. After a three-month follow-up, as many as 40 (93.0%) patients who received the 1-day MTX 300 mg protocol remained in remission, while as many as 3 (6.9%) patients experienced an increase in β-hCG levels. Meanwhile, in patients who received the 8-day MTX 50 mg protocol, as many as 41 (91.1%) patients remained in remission, and 4 (8.9%) patients experienced an increase in β-hCG levels. In patients who received a 1-day MTX 300 mg/m^2 protocol and patients who received an 8-day MTX 50 mg protocol, there was no difference in risk for remission.

The financing issued by the hospital in one cycle of chemotherapy comes from the cost of accommodation, pharmacy, medical procedures, and medical support. Financing is certainly one of the problems, both on the patient and hospital sides. The more cycles of chemotherapy given and the complications that occur, the greater the financing. The average amount of treatment costs for patients who were given the 1-day MTX 300 mg/m^2 protocol was IDR 18,659,867 ±8,961,724, while those given the 8-day protocol MTX 50 mg were IDR 37,527,968± 20,386,168. The total cost of treatment for patients who were given a 1-day MTX protocol of 300 mg/m2 was cheaper compared to patients who were given an 8-day MTX protocol of 50 mg. From the results of *the Mann–Whitney* test, there was a significant difference in the average amount of treatment costs between patients with a 1-day MTX protocol of 300 mg/m2 and patients with an 8-day MTX protocol of 50 mg. The cheaper financing of the 1-day MTX 300 mg/m2 protocol is due to the administration of fewer drugs, shorter treatment duration, fewer total chemotherapy cycles, and milder complications when compared to the 8-day MTX 50 mg protocol.

In other studies, reducing the financing of MTX chemotherapy can be done by not giving folic acid, not giving consolidation chemotherapy, or giving weekly chemotherapy. In the study, the administration of a 1-day MTX protocol of 300 mg/m^2 was carried out to check the level of MTX in the serum after the administration of MTX chemotherapy, but from the examination, there was no increase in serum MTX levels exceeding the toxic level, so it is not always necessary to give folic acid. The administration of consolidation chemotherapy has no effect on remission, but it can affect recurrence, where each cycle of consolidation chemotherapy can reduce the risk of recurrence by 3%. However, current recommendations suggest the administration of consolidation chemotherapy in low-risk GTN at a minimum of three doses to reduce the risk of recurrence.[7,12,13,17,18]

Side effects can always occur in every chemotherapy administered, be it in the form of mild to severe side effects. Side effects obtained from the administration of methotrexate chemotherapy are generally mild and can be overcome either without therapy or with medical therapy. This is also shown by the administration of chemotherapy, either with a 1-day MTX 300 mg/m^2 protocol or with an 8-day MTX 50 mg protocol.

This study showed that chemotherapy with a 1-day MTX 300 mg/m^2 protocol has a protective effect against the side effects of gastrointestinal disorders, eye disorders, general complaints, infections, nervous system disorders, respiratory disorders and skin disorders. Numerous other studies have supported this, such as the New England Trophoblastic Disease Centre (NETDC) study, which included 325 patients with low-risk GTN and was based on patients treated between 1974 and 2014. The study found that patients who received chemotherapy with an intramuscular MTX-FA regimen for eight days experienced more side effects than patients who received chemotherapy with an MTX regimen infusion of 300 mg/m2 -FA for one day. When compared to chemotherapy with an infusion MTX regimen of 300 mg/m2-FA, complaints of these side effects are more common when the chemotherapy is administered with an eight-day intramuscular MTX-FA regimen. Common side effects include abnormal laboratory findings, visual impairment, and other common disorders. However, the side effects that appear can be recovered after the completion of treatment, and there is no long-term sequel to the side effects that appear.[7]

Minimal adverse effects were also observed in the Wong et al research when chemotherapy was administered with a 300 mg/m^2 MTX treatment for one day. In this study, 1 patient with side effects of Steven Johnson syndrome was obtained after chemotherapy with a 1-day MTX protocol of 300 mg/m2, the same thing also happened in the study of Wong et al. However, patients can be given appropriate therapy until they recover and resume chemotherapy with a different regimen.[4–6]

On the other hand, patients who received an 8-day protocol of 50 mg of MTX and experienced adverse effects at aberrant lab values were 15.6%, compared to 32.6% of patients who received a 1-day protocol of 300 mg/m^2. It can be concluded that patients who received the 1-day MTX 300 mg/m^2 protocol had a higher risk of adverse events with abnormal lab values than patients who received the 8-day MTX 50 mg protocol. A side effect that often occurs is anemia. This study did not find any further adverse effects with abnormal laboratory values, specifically hepatotoxicity, thrombocytopenia, or granulocytopenia.

Research Limitations

This study took retrospective data from the medical records of patients who received MTX chemotherapy in low-risk GTN cases. Post-chemotherapy monitoring in low-risk GTN patients was carried out for twelve months, but from the data obtained by the researchers, not all patients had post-chemotherapy monitoring data for up to twelve months. This causes not all low-risk GTN patients who have completed MTX chemotherapy to be assessed until a complete response. This can occur due to patient non-compliance to conduct monitoring for up to twelve months, or it can occur that the patient conducts monitoring at other hospitals that are closer to where they live so that the post-chemotherapy monitoring data are incomplete for up to twelve months. However, in patients who have recurrence or a partial response, the patient will return again for treatment at Dr. Hasan Sadikin General Hospital Bandung, Bandung.

Conclusion

MTX 300 mg/m^2 1-day protocol chemotherapy has the same primary and recurrence rates, fewer chemotherapy cycles, and cheaper financing compared to MTX 50 mg 8-day protocol chemotherapy.

Suggestion

Chemotherapy 1-day protocol MTX 300 mg/m2 can be a therapeutic option in the management of low-risk GTN cases. The need to increase patients confidence in the importance of monitoring up to twelve months post-chemotherapy.

Ethics Approval and Consent to Participate

This research has been reviewed and approved by the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung (Ethical Approval Number: DP.04.03/D.XIV.6.5/27/2024). All patients have agreed and signed the consent form. This research has complied with the guidelines outlined in the Declaration of Helsinki.

Disclosure

The authors report no conflicts of interest in this work.

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