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Effects of *Momordica charantia* (MC) Extract on Clinical Symptoms, Parasite Account, Thrombocytes, Total Bilirubin and Direct Bilirubin in Patients with Uncomplicated *Plasmodium falciparum* Malaria: A Case Report

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A B S T R A C T

Clinical symptoms during the treatment of uncomplicated *P. falciparum* malaria have been reported in several studies. Parasite density in the blood is associated with clinical symptoms, platelet, and bilirubin count. A 52-year-old male, weighing 52 kg, was given one capsule containing 325 mg bitter melon (*Momordica charantia*) extract for 3 days of treatment. Patients were followed up for 28 days, days 1,2,3,4,7,14,21,28, and peripheral blood microscopic examination and clinical symptoms were carried out. Measurement of platelets, total bilirubin, direct bilirubin D0, D14 and D28. Naranjo Scale, adverse events measurements were taken on D7, no signs of severe malaria, no comorbidities, no history of malaria, blood pressure 110/80 mmHg, peripheral blood parasite examination on D0 found *P. falciparum* parasites of 31,714/µL, D0 platelet value of 94x10 /mm^3, D0 total bilirubin value of 1.3 mg% and D0 direct bilirubin value of 0.6 mµ/mL. On D1 parasite count was 2,400/µL, D2 was 372/µL, D3, D4, D7, D14, D21, D28 no asexual parasites were found again. Clinical symptoms that arose on D0 were nausea, no appetite, sweating, chills, sleep disturbance, dizziness, headache, and weakness with a body temperature of 37°C. After D3 of bitter melon extract treatment, no clinical symptoms were found again. Naranjo scale score based on nurse and pharmacist agreement was 6 (probable) at D7 for the adverse events of nausea and vomiting. There were no reported adverse events such as nausea, vomiting, diarrhea, abdominal pain, cough, sleep disturbance, dizziness, headache and weakness on D2 treatment. Bitter melon extract is effective for uncomplicated malaria *P. falciparum*, reduces clinical symptoms, and is safe.

1. Introduction

Malaria is a deadly disease caused by plasmodium parasites. One of the plasmodium species that causes malaria is *Plasmodium falciparum*. Early diagnosis and appropriate treatment is one of the effective weapons used in the fight against this disease. Artemisinin, quinine, mefloquine, lumefantrine, amodiaquine, sulfadoxine, piperaquine, primakuine are currently used in the treatment of malaria.[1] A looming part of the failure to control malaria is the spread of antimalarial drug resistance. Although there have been no reports related to resistance to artemisinin derivatives in Indonesia, reports of resistance cases in Myanmar and the tendency of malaria parasites in the Southeast Asian region to develop resistance to antimalarials need to be well anticipated, one of which is the development and discovery of new antimalarials.[2,3] The development and discovery of

antimalarials is one of them with an ethnopharmacological approach. Bitter melon fruit extract (*Momordica charantia)* invitro with the smallest concentration IC_{50} (0.0178µg/mL) and invivo ED_{50} (113.50mg/kgbb) inhibits the growth of *P. falciparum* strain 3D7 and *Plasmodium berghei.*[4] Syamsudin et al's other research on acute and subchronic toxicity tests showed that bitter melon fruit extract is safe to use.[5] Syamsudin et al's research in Manokwari, West Papua showed that the combination of bitter melon extract with primaquine reduced and eliminated *P. falciparum* asexual parasites at H3 and at H7 there were no reports of clinical symptoms.[6] *P. falciparum* parasite density is associated with clinical symptoms, platelet and bilirubin parameter values.[7-9]

2. Case Presentation

This report is about a 52-year-old male weighing 52 kg, based on a doctor's diagnosis and microscopic examination he was suffering from *P. falciparum* malaria. He was previously given an explanation and information on a leaflet before the action and examination. Clinical symptoms that arose before treatment (D0) were nausea, no appetite, sweating, chills, sleep disturbance, dizziness, headache, and weakness without fever. Platelet, total bilirubin and direct bilirubin examinations D0, D14, and D28 were performed. Peripheral blood parasite examination and clinical symptoms were performed on D1, D2, D3, D4, D7, D14, D21, and D28. Examination of adverse events arising after treatment was carried out on D7 using the Naranjo scale.[10]

The blood pressure check result was 110/80 mmHg. Clinical symptoms before treatment (D0) were nausea, palpitations, no appetite, sweating, chills, sleep disturbance, dizziness, headache, and weakness. Clinical symptoms arising at follow-up D1, D2, D3, D4, D7, D14, D21 and D28 can be seen in table 1. Table 1 shows that clinical symptoms began to disappear at D2.

Table 1. Clinical symptoms.

Descriptive	D0	D1	D2	D3	D4	D7	D14	D21	D28
Nausea	v	v	-	-	-	-	-	-	-
Vomit	v	v	-	-	-	-	-	-	-
Pounding	v	-	-	-	-	-	-	-	-
No appetite	v	v	-	-	-	-	-	-	-
Cough	-	-	-	-	-	-	-	-	-
Sweating	v	-	-	-	-	-	-	-	-
Chils	v	-	-	-	-	-	-	-	-
Sleep disorder	v	v	-	-	-	-	-	-	-
Dizzines	v	v	-	-	-	-	-	-	-
Headache	v	v	-	-	-	-	-	-	-
Weak	v	v	-	-	-	-	-	-	-
Abdominal pain	-	-	-	-	-	-	-	-	-
Diarrhea	-	-	-	-	-	-	-	-	-
Muscle pain	-	-	-	-	-	-	-	-	-

Microscopic parasite count before treatment (H0) was 31,714/µL, D1 was 2400/µL, and D2 was 372/µL. The result of platelet examination D0 was 94 x 10^3 /mm^3, D14 was 297 x 10^3 /mm^3, D28 was 186 x 10 /mm^{33} (normal platelet value: 150-400 thousand / mm^3). Laboratory examination results of total bilirubin value D0 by 1.3 mg%, D14 by 0.6 mg%, D28 by 0.3 mg% (normal value of total bilirubin: 0.2-1.0 mg%). D0

direct bilirubin examination result of 0.6 mμ/mL, D14 of 0.2 mμ/mL, D28 of 0.2 mμ/mL (normal value of direct bilirubin 0.05-0.3 mμ/mL). Parasite count, total bilirubin and direct bilirubin values can be seen in Table 2.

Table 2. Parasite count, thrombocytes, total bilirubin and direct bilirubin.

Descriptive	D0	D1	D2	D3	D4	D7	D14	D21	D28
Parasite count/μL	31714	2400	372	-	-	-	-	-	-
Platelets $(mm)^3$	94 x 10^3	-	-	-	-	-	297 x 10^3	-	186 x 10^3
Total bilirubin (mg%)	1,3	-	-	-	-	-	0,6	-	0,3
Bilirubin direct (mμ/mL)	0,6	-	-	-	-	-	0,2	-	0,2

The results of the examination of adverse events of bitter melon (*Momordica charantia*) extract treatment with the Naranjo scale with patients by nurses and pharmacists during the D7 follow-up were agreed to a score of 6 (probable) for the adverse events of nausea and vomiting in Table 3.

Table 3. Results of adverse event screening using the Naranjo scale (vomit and nausea).

No	Descriptive	Scale			
		Yes	No	Don't know	Score
1	Are there previous conclusive reports on this reaction?	1	0	0	1
2	Did the adverse event appear after the suspected drug was administered?	2	-1	0	2
3	Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	1
4	Did the adverse event reappear when the drug was readministered?	2	-1	0	-1
5	Are there alternative causes that could on their own have caused the reaction?	-1	2	0	2
6	Did the reaction reappear when a placebo was given?	-1	1	0	1
7	Was the drug detected in blood or other fluids in concentrations known to be toxic?	1	0	0	0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0	0
10	Was the adverse event confirmed by any objective evidence?	1	0	0	0
Total					6

Score	Interpretation of scores
Total Score ≥9	**Definite**. The reaction (1) followed a reasonable temporal sequence after a drug or in which a toxic drug level had been established in body fluids or tissues, (2) followed a recognized response to the suspected drug, and (3) was confirmed by improvement on withdrawing the drug and reappeared on reexposure.
Total Score 5 to 8	**Probable**. The reaction (1) followed a reasonable temporal sequence after a drug, (2) followed a recognized response to the suspected drug, (3) was confirmed by withdrawal but not by exposure to the drug, and (4) could not be reasonably explained by the known characteristics of the patient's clinical state.
Total Score 1 to 4	**Possible**. The reaction (1) followed a temporal sequence after a drug, (2) possibly followed a recognized pattern to the suspected drug, and (3) could be explained by characteristics of the patient's disease.
Total Score ≤0	**Doubtful**. The reaction was likely related to factors other than a drug.

3. Discussion

This report looks at the effect of clinical symptoms before and after treatment for uncomplicated *P. falciparum* malaria. At H0, there were 9 (nine) clinical symptoms reported by patients. Clinical symptoms that arise in patients are related to the density of *P. falciparum* parasites in the blood.[7] Parasite density, endemicity level, antimalarial concentration in the blood, patient immunity, the presence of other severe diseases, pharmacodynamic profile of drugs affect the success of malaria parasite elimination which affects the clinical symptoms that arise.[3,6] In uncomplicated *P. falciparum* malaria patients without symptoms, parasite density is not always related to the clinical symptoms that arise, but many research reports reveal that in non-immune patients as the number of parasites increases, the length of time and clinical symptoms that arise is getting longer.[11] Parasite density is associated with the development of complications and disease severity.[11,12] Mangal et al's research shows that there is a relationship between parasite density and platelet values. In patients with *falciparum* malaria as the parasite density increases, the platelet value of *P. falciparum* malaria patients decreases.[7]

This report shows that bitter melon fruit extract (*Momordica charantia*) is able to improve platelet values, reduce and eliminate *P. falciparum* parasites followed by a decrease in clinical symptoms. This is in line with the research of Syamsudin et al in Manokwari, West Papua showing that the combination of bitter melon extract with primaquine was able to eliminate clinical symptoms that arose at D7 and improve platelet values at D14, D28, and D42.[6] Al Salahy et al's research in Yemen showed that parasite density affects the value of total bilirubin and direct bilirubin. Patients with parasitemia tend to have low total bilirubin and direct bilirubin values.[13] Patients with high parasitemia tend to have high bilirubin values.[14] Syamsudin et al research in vivo showed that bitter melon fruit extract (*Momordica charantia*) 320 mg/Kg/bb had no effect on AST/SGOT and ALT/SGPT values. Table 2 above shows that bitter melon fruit extract (*Momordica charantia*) improves the value of total bilirubin and direct bilirubin. The content of bioactive compounds from *Momordica charantia* as anti-inflammatory, anti-oxidant and immunomodulator is likely to improve the total bilirubin and direct bilirubin values of patients.[15,16] The possibility of *Momordica charantia* extract has an antimalarial effect through modulation of cytokine mediation.[16] The content of *Momordica charantia* extract in the form of alkaloids, flavonoids, terpenoids as antimalarial by forming chelates of parasite nucleic acid bases.[17] The decrease in parasite density may be related to the measurement of blood chemistry values (total bilirubin and direct bilirubin).[11,12]

The efficacy of safe and convenient-to-use therapies is associated with the effectiveness of malaria therapy. The Naranjo scale method is used for the estimation of drug reaction adverse events.[10] Syamsudin et al research on uncomplicated *Plasmodium falsciparum* patients in Manokwari, West Papua, reported weakness, headache, dizziness, sleep disturbance, chills, sweating, no appetite, nausea, vomiting, abdominal pain, diarrhea, muscle pain and cough.[6] It is likely that these clinical symptoms are clinical manifestations of uncomplicated falciparum malaria.[7,12] The use of bitter melon (*Momordica charantia*) extract needs to be followed by the use of anti-nausea and vomiting drugs to optimize therapeutic efficacy. It is likely that bitter melon fruit extract causes nausea and vomiting in patients with the results of measuring the Naranjo scale the total score is 6. Syamsudin et al research on uncomplicated *Plasmodium falciparum* malaria patients using a combination of bitter melon fruit extract (*Momordica charantia*) and primaquine in Manokwari, West Papua clinical symptoms of nausea on day 7 and vomiting on day 3 were reported to disappear.[6]

4. Conclusion

This case report is very special because this treatment of uncomplicated *P. falciparum ma*laria patients with bitter melon fruit extract (*Momordica charantia*) has never been done before. Bitter melon extract can be used as an alternative treatment for uncomplicated *P. falciparum* malaria in combination or alone. The results of the measurement of adverse events that occur need the addition of anti-nausea and vomiting drugs to avoid this so that the expected efficacy is more optimal. The measurement of adverse events with the Naranjo scale has limited resources that only involve nurses and pharmacists in determining adverse events that occur. Further research is needed with a larger number of patients, specialized laboratories, doctors, laboratory technicians, nurses and pharmacists who are specifically involved in the study.

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