PENGARUH KOMBINASI TABLET FRAKSI ETIL ASETAT SAMBILOTO DAN DIHIDROARTEMISININ-PIPERAKUIN TERHADAP EKSPRESI IFN-γ, TNF-α, IL-10, JUMLAH PARASIT PLASENTA DAN MORFOLOGI JANIN MENCIT BUNTING YANG DIINFEKSI *PLASMODIUM BERGHEI*

ABSTRAK

Latar belakang: Pengembangan obat antimalaria yang efektif dan aman untuk terapi malaria pada kehamilan sangat diperlukan. Model terapi kombinasi dari bahan alam seperti sambiloto *(Andrographis paniculata)* dengan dihidroartemisinin-piperakuin (DHP) diharapkan dapat menjadi satu alternatif untuk meningkatkan efektifitas terapi, mengurangi toksisitas, dan mencegah terjadinya resistensi pada obat standar malaria.

Tujuan: Tujuan penelitian ini adalah meneliti efek dari kombinasi tablet fraksi etil asetat sambiloto (FEAS) dengan DHP terhadap aktivitas antimalaria di plasenta, dan pengaruhnya terhadap sistem imun (IFN-γ, TNF-α, dan IL-10) di plasenta serta efeknya terhadap morfologi janin.

Metode: 30 ekor mencit BALB/c bunting terinfeksi *P. berghei* dibagi dalam 6 kelompok, K1, K2, K3, K4, K5 dan K6 dengan randomisasi. K1 adalah kelompok kontrol negatif diberi plasebo CMC Na; K2 diberi tablet FEAS; K3 diberi tablet DHP. Kelompok K4 diberi kombinasi pertama dari tablet FEAS dan DHP; K5 diberi kombinasi kedua dari tablet FEAS dan DHP; K6 diberi kombinasi ketiga dari tablet FEAS dan DHP. Selama terapi diambil sampel darah tepi untuk menghitung parasitemia. Sampel jaringan plasenta diambil untuk diperiksa ekspresi IFNγ, TNF-α, IL-10, jumlah parasit plasenta dan morfologi janin.

Hasil: K4 dan K5 mampu menghambat ekspresi IFN-γ, dan IL-10, sedangkan ekspresi TNF-α tidak berbeda dengan kelompok kontrol. Pada K6 tidak tampak penghambatan terhadap ekspresi IFN-γ dan IL-10, dan TNF-α. Pemberian kombinasi pertama, kedua dan ketiga dari tablet FEAS dan DHP mampu menurunkan jumlah parasit di perifer dan plasenta secara signifikan, namun pengaruhnya pada janin menimbulkan abnormalitas morfologi. Persentase abnormalitas morfologi paling rendah terdapat pada K4. K2 tidak mengalami abnormalitas morfologi janin.

Kesimpulan: Kelompok kombinasi pertama (K4) merupakan kelompok kombinasi yang lebih potensial dibandingkan dua kelompok kombinasi lainnya. Perlu dilakukan penelitian lebih lanjut dengan menaikkan dosis tablet FEAS pada kelompok kombinasi pertama dari tablet FEAS dan DHP ini sehingga didapatkan model terapi kombinasi yang aman dan efektif untuk pengobatan malaria plasenta.

Kata kunci: Malaria plasenta malaria, DHP, *A. paniculata*, sistem imun, morfologi janin

EFFECT OF COMBINATION BETWEEN ETHYL ACETATE FRACTION OF *ANDROGRAPHIS PANICULATA* AND DEHYDROARTEMISININ-PIPERAQUIN TABLET AGAINST IFN-γ, TNF-α, IL-10, PLACENTAL MALARIAL PARASITE AND FOETAL MORPHOLOGY ON PREGNANT MICE INFECTED WITH *PLASMODIUM BERGHEI*

ABSTRACT

Background: Development of an effective and safe drugs for therapy of malaria in pregnancy is quite needed. Combination model of standard antimalarial such as, DHP with herbal drugs, e.g. *A.paniculata* is expected to be an alternative for increasing the therapeutic effectivity, minimizing the toxicity and preventing the resistance of standard antimalarial drugs.

Purpose: to study the effect of the combination between ethyl acetate fraction of *A. paniculata* (FEAS tablets) and DHP against the malarial activity on placenta, immune system (IFN-γ, TNF- α, and IL-10) and foetal morphology in pregnancy.

Methods: Thirty BALB/c pregnant mice infected with *P. berghei*, divided into 6 groups (n = 5). Group K1 was infected pregnant mice; K2 was infected pregnant mice treated with FEAS tablets; K3 was infected pregnant mice treated with DHP tablets; K4 was infected pregnant mice treated with first combination of FEAS tablets and DHP tablets; K5 was infected pregnant mice treated with second combination of FEAS tablets and DHP; and K6 was infected pregnant mice treated with third combination of FEAS tablets and DHP. Pheripheral blood were collected during therapy for bloodsmear to counting parasitemia.Placental samples were taken and analyzed regarding the expression of IFN-γ, TNF- α, IL-10, placental parasite counts and foetal morphology.

Results: The group treated with first and second combination of drugs (K4 and K5) were able to reduce the expression of IFN-γ and IL-10, whereas the expression of TNF-α was not significantly different with control group. There was no significant inhibition to the expression of IFN-γ, TNF- α, and IL-10 observed in the third combination of drugs (K6). The treatment of first, second and third combination (K4, K5 and K6) decreased both peripheral and placental parasite counts significantly. The effects to fetus gave rise morphologic abnormalities. The lowest percentages of morphologic abnormalities was observed in K4. The only group that foetal morphologic abnormalities were not observed is K2.

Conclusion: The present study demonstrated that the first combination (K4) is more potential compared to the other two combinations. Further studies should be done by increasing doses of FEAS of the tablet in the first combination to find the more efective and safe combination therapy model for the treatment of the malarial placenta.

Keywords: Placental malaria, DHP, *A. paniculata*, immune system, foetal morphology