ABSTRAK

Malaria masih merupakan salah satu jenis penyakit mematikan di dunia. Sekitar setengah populasi dunia mengalami resiko malaria. Kasus infeksi ini mengakibatkan 863.000 kematian pada tahun 2008 di dunia. Di Indonesia, sekitar 35 persen penduduk tinggal di daerah endemis dan dilaporkan 38.000 orang meninggal pertahun karena malaria akibat plasmodium falciparum. Invasi plasmodium terhadap eritrosit merupakan proses senrtal dari permulaan pathogenesis malaria. Faktor genetik merupakan salah satu faktor yang penting dalam pemberian obat dimana gen berperan dalam mengkode protein dan enzim yang mempengaruhi farmakokinetika obat yaitu absorpsi, distribusi, metabolisme, dan eliminasi (ADME). Farmakokinetika obat kombinasi anti malaria DHA, Piperakuin dan Primakuin belum pernah dilakukan pemeriksaan di Indonesia.

Tujuan penelitian ini adalah untuk mengetahui profil farmakokinetika kombinasi DHA Piperkuin dan Primakuin pada malaria falciparum tanpa komplikasi, hubungan antara kadar obat yakni Cmax (kadar Puncak) dengan klirens parasit dari kombinasi DHA (*Dihydroartemisinin*), Piperakuin dan Primakuin serta efek farmakologis yakni efek terapi, efek samping dan kegagalan terapi pada malaria falciparum tanpa komplikasi di Halmahera.

Dilakukan penelitian uji klinik secara acak dengan metode eksperimen guna mengetahui farmakokinetika kombinasi DHA, Piperakuin dan Primakuin dan efek farmakologisnya terhadap malaria falciparum sebelum dan sesudah diberi obat terapi ACT (*Artemicin Combination Therapy*) pada 12 penderita malaria falciparum tanpa komplikasi di RSUD Tobelo Halmahera Utara pada bulan September - Desember 2014. Pada penelitian ini dilakukan pengambilan sampel darah malaria secara serial hari 0 - 28, dilakukan pemeriksaan darah tetes tebal dan tipis, fungsi hati, fungsi ginjal, leukosit, erytrosit dan haemoglobin, dilakukan pengujian serial sampel untuk mengukur kadar kinetik dari kombinasi ACT hari 1 jam ke 0.25; 0.5; 0.75; 1; 1.5; 2; 3; 6; 8; 12; 18; 24, hari ke 2; 3; 7; 14 dan 28 dengan menggunakan LCMS untuk menganalisa parameter farmakokinetiknya.

Hasil penelitian ini menunjukkan bahwa profil farmakokinetika DHA, Piperakuin dan Primakuin pada 12 penderita malaria falciparum tidak saling berkontradiksi dalam darah atau saling melengkapi dimana penderita mengalami kesembuhan tanpa efek samping yang berarti. Profil farmakokinetika DHA, ka 2,24 jam, Cmax 495,80 ng/ml, Tmax 1,25 jam, t ½ 0,81 jam, AUC 559,18 ug jam/liter, VD 1.193,60 liter, Cl 582,12 liter/jam. Farmakokinetika piperakuin Ka 2,63 jam, Cmax 1.576,25 ng/ml, Tmax 1,50 jam, t ½ 7,37 jam, AUC 3.312,39 ug jam/liter, VD 1.481,53 liter, Cl 371,15 liter/jam. Farmakokinetika Primakuin Ka 2,63 jam, Cmax 330,06 ug/ml, Tmax 1,25 jam, t ½ 6,22 jam, AUC 1.237,24 ng jam/ml, VD 67,99 liter, Cl 20,78 liter/jam. Kombinasi ACT sangat baik dengan efek farmakologis termasuk kategori pada APCR *(Adecuat clinical and parasitological respo*n*)*, tingkat keberhasilan pengobatan tergolong tinggi yakni 100 persen pada 12 subjek. Disimpulkan bahwa pada penderita malaria falciparum tanpa komplikasi yang diterapi dengan kombinasi ACT DHA Piperakuin dan Primakuin sangat efektif dengan terjadi pembersihan klirens parasit.

Kata Kunci: Malaria falciparum, farmakokinetika, DHP, Primakuin, klirens parasit, APCR.

ABSTRACT

Malaria is still one of deadly diseases worldwide since half of its population risks on the malaria. In 2008, the infection caused 863.000 deaths globally. In Indonesia, about 35% of people lives here and 38,000 people was reported died each year because of the plasmodium falciparum malaria. The invasion of plasmodium on erythrocyte was the central process of initial malaria pathogenesis. Genetic factor then is one of significant drug distributions where the gene acting in protein and enzyme coding influences the drug namely absorption, distribution, metabolism, and elimination (ADME). The pharmacokinetic combination of anti-malaria of DHA, piperaquine and primaquine that have not been any investigation conducted in Indonesia.

The purpose of this research is to know the profile of combination pharmacokinetic of DHA, piperaquine and primaquine in the falciparum malaria without complicated, relation of drug content, Cmax (peak content) and parasite clearance with DHA (Dehydroartemisinin), piperaquine and primaquine combination and its pharmacology effect that is therapy, side effect, and therapy failure on falciparum malaria without complicated in Halmahera.

The research conducts randomly clinical test with experimental method in order to know pharmacokinetic combination of DHA, piperaquine, primaquine and its pharmacology effect to falciparum malaria before and after distribution of ACT theraphy (Artemycine Combination Therapy) toward 12 patients of falciparum malaria without complicated in RSUD Tobelo, North Halmahera during September to December 2014. In this research, it is conducted the blood sample taken from those malaria patients sequentially started from serial 0 to 28, the investigation of thick blood drop, liver function, kidney function, leucocyte, erythrocyte and hemoglobin, the series of sample test was done to account the pharmacokinetic concentration of act combination at day 1 of hour at 0.25, pharmacokinetic .0.5; 0.75; 1; 1.5; 2; 3; 6; 8; 12; 18; 24 and at day 2; 3; 7; 14 and 28 by using LCMS to analyzing the parameters of its pharmacokinetic.

As result, it showed that the pharmacokinetic profile of DHA, piperaquine, and primaquine to the 12 patients suffered falciparum malaria there was no contradiction within the blood and it was mutually completing where the patients experience the cure without any side effect. The pharmacokinetic profile of DHA comprised of Ka = 2,24 hours, Cmax = 495.80ng/ml, Tmax = 1,25 hours, $t_{1/2}$ = 0,81 hour, AUC = 559,18 ng/hour/liter, VD = 1.193,60 liter, Cl = 582,12 liter/hour. The piperaquine pharmacokinetic consisted of Ka = 2,63 hours, Cmax = 1.576,25 ng/ml, Tmax = 1,50 hours, $t_{1/2}$ = 7,37 hours, AUC = 3.312,39 ng/hour/liter, VD = 1.481,53 liters, Cl = 371,15 liters/hour. The primaquine pharmacokinetic included Ka = 2,63 hours, Cmax = 330,06 ng/ml, Tmax = 1,25 hours, $t_{1/2}$ = 6,22 hours, AUC = 1.237, 24 ng/hour/ml, VD = 67,99 liters, Cl = 20,78 liters/hour. The pharmacology effect including APCR category (Adequate clinical and parasitological respond), clean level of the highest treatment which is 100% > 95% (12 sampels). In conclusion, the patient of falciparum malaria without complicated cured with the combination of ACT DHA, Piperaquine, and Primaquine works synergic to clean parasite clearance.

Keywords: Falciparum malaria, pharmacokinetic, DHA, Piperaquine, Primaquine, Parasite Clearance, APCR