CHAPTER 5

DISCUSSION

5.1 The Effectiveness of Two Regimens

From clinical observation, orally administered artemisinin + doxycycline drug regimen was found to be more effective against resistant falciparum malaria than orally administered quinine + doxycycline drug regimen. The parasite clearance time (2 days) in the Art + Dox drug regimen was shorter than the parasite clearance time (3 days) in the Qui + Dox drug regimen. This result conformed to the results of efficacy of artemisinin reported by Hien TT (1992) and Sy (1993).

The cure rate of Art + Dox drug regimen (95.4%) was significantly higher than the cure rate of Qui + Dox (83.1), $p < 0.05$. With this cure rate, Art + Dox drug regimen will be a major antimalarial drug for resistant falciparum malaria or multiple resistant falciparum treatment. A suggestion from Looreesuwan and Chongsuphajaisiddhi for measures to combat drug resistance was to encourage the use of tested effective drug regimen (90-100% cure rate) for treatment.

The recrudescence rate within 28 days observation follow up with the Art + Dox drug regimen was 4.6% lower than the recrudescence rate (16.9%) with the Qui + Dox drug regimen. This involved the provider costs and costs incurred by patient because in normal condition recrudescence patients should come back hospital to be treated again within the third week after the first treatment time, therefore the costs in the Qui + Dox drug regimen should be higher.

No side effects were observed with the Art + Dox drug regimen, so artemisinin may be a high safety antimalarial drug. In chemotherapy of malaria, chloroquine seemed to be the less toxic antimalarial drug than any other (Bruce-Chwatt, 1986; Brewer, 1993). Acute toxicity study in animals indicated that artemisinin and its derivatives have higher LD50s and better chemotherapeutic indices than chloroquine. And in some recent studies (Li Guo Qiao, 1990 and Hien TT, 1992) transient first-degree heart block was documented in one patient administered artemisinin and in three patients receiving artemether at the standard dose. A transient dose-related reduction in reticulocyte counts was noted in volunteers administered dose above 4 mg/kg/day for 3 days. Tenesmus, abdominal pain and diarrhoea were reported in a minority (<6%) of patients administered artemisinin suppositories.

In the Qui + Dox group, the side effects were very high (63.08%), some patients (40% of side effects) with slight side effects did not need treatment, but 60% of side effect patients were treated by drug. Although the cost of side effects treatment was not high, side

effects had an impact on the patients and the doctor is always careful when using quinine in malaria treatment.

It is clear that artemisinin used at a dose of 10 mg/kg/day for 5 days in combination with doxycycline was more effective (95.45%) than artermisinin used alone with dose of 10 mg/kg/day for 5 days (85.3%) reported by Sy (1993).

Quinine, a main antimalarial drug for resistant falciparum malaria, in combination with doxycycline for uncomplicated falciparum malaria treatment was significantly lower than artemisinin in combination with doxycycline. The Art + Dox drug regimen can be used to treat uncomplicated falciparum malaria instead of quinine in hospital to avoid and to prevent development of severe and complicated malaria from uncomplicated malaria. This can also reduce mortality rate due to malaria in hospital.

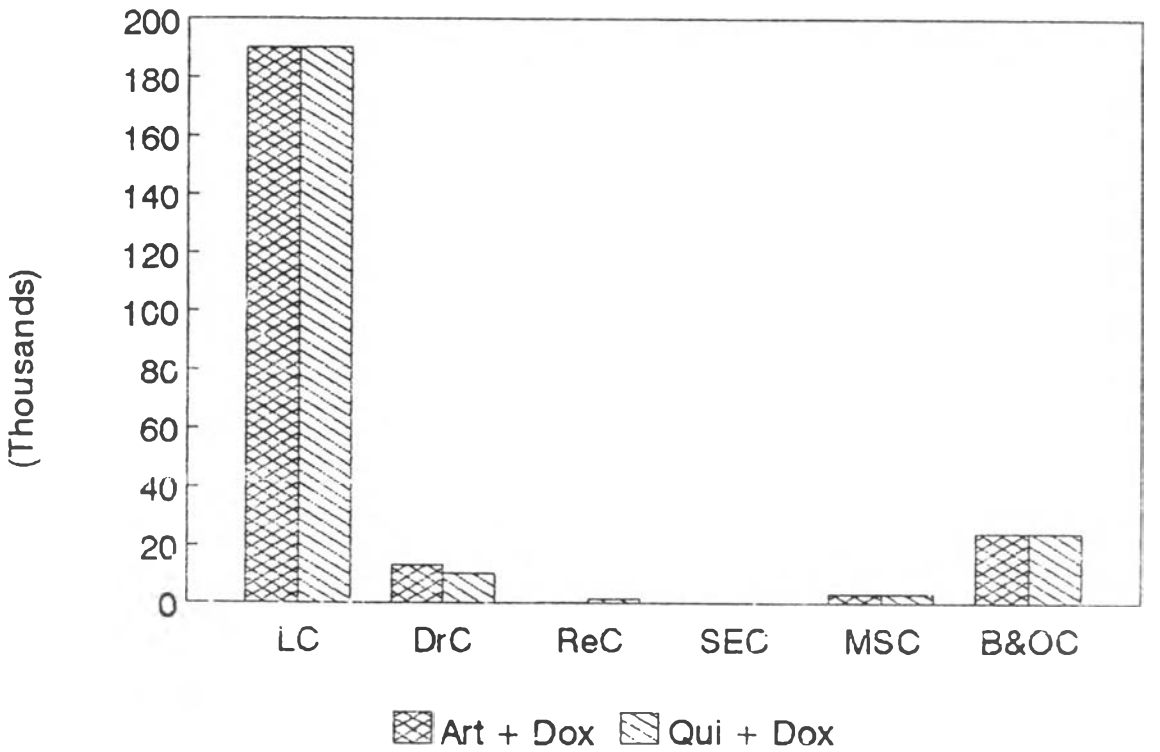
5.2 The costs of two regimens

In this study, the costs were very high from both the provider and patient perspectives because of protocol driven costs. Figure 5.1 and fig 5.2 present comparisons of the components of provider costs and costs incurred by patient between two drug regimen groups in 28 days followed up in hospital.

Although the price of artemisinin is more expensive than quinine (878,460 VN dong in the Art + Dox regimen group was compared with 683,540 VN dong in the Qui + Dox regimen group). The average provider costs per patient in the Art + Dox group (232,381 VN dong = $22.13) were only a little higher than average provider costs per patient in the Qui + Dox group (231,089 VN dong = $22.01).

Since malarial patients in the two drug regimen groups were followed up 28 days in hospital and number of diagnosis tests were the same between patients in two groups. The cost of personnel (191,940 VN dong =$18.3), the operating cost (4,867 VN dong = $0.4) and maintenance cost of building (19,425 VN dong = $1.8), cost of medical supply (VN dong) were the same to each patient in both drug regimen groups. Average cost of drug per patient treated by Art + Dox drug was higher than average of cost of drug per patient treated by Qui + Dox.

Figure 5.1 Comparison of Components of Provider Costs Between Two Drug Regimen Groups (28 days).



* VN dong.

Where:

LC	=	Cost of personnel.
DrC	=	Cost of antimalarial drug (except ReC).
ReC	=	Cost of recrudescence treatment.
SEC	=	Cost of side effects treatment.
MSC	=	Cost of medical supply.
B&OC	=	Building maintenance & operating costs.

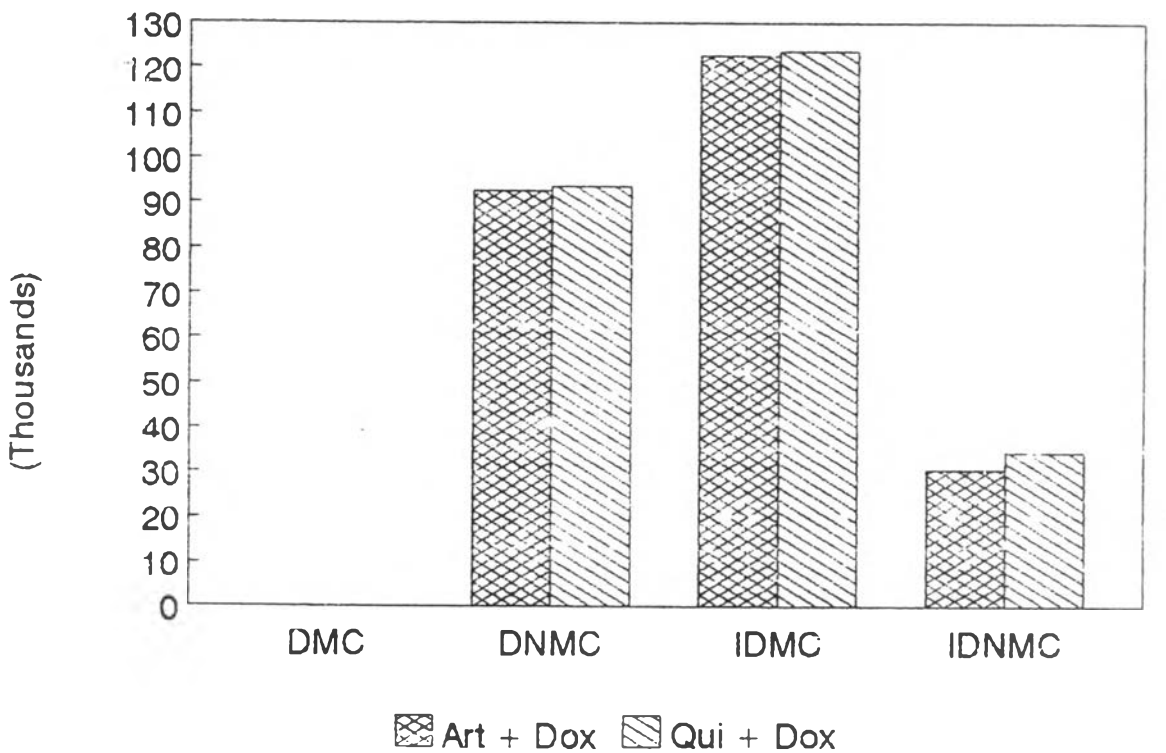
In Figure 5.2, direct costs incurred by patient were 0 because these costs were covered by provider.

- Average direct non medical costs including travel cost, cost of food of patient treated by Art + Dox drug (92,803.03 VN dong) were slightly lower than patient treated by Qui + Dox drug (93,772.0 VN dong) because cost of food of accompanying person of patient treated by Qui + Dox was higher due to stay in hospital with patient longer.

- Average indirect medical costs incurred by patient treated by Art + Dox drug was approximately the same as for patient treated by Qui + Dox drug (122,852.55 VN dong and 123,769.05).

- Average indirect non medical cost incurred by patient treated by Art + Dox drug (30,696.92 VN dong) was lower than patient treated by Qui + Dox (34,478.23 VN dong).

Figure 5.2 Comparison of Components of Costs Incurred by Patient Between Two Drug Regimen Groups (28 days).



* VN dong.

Were:

DMC = Direct medical costs.
DNMC = Direct non medical costs.
IDMC = Indirect medical costs.
IDNMC = Indirect non medical costs.

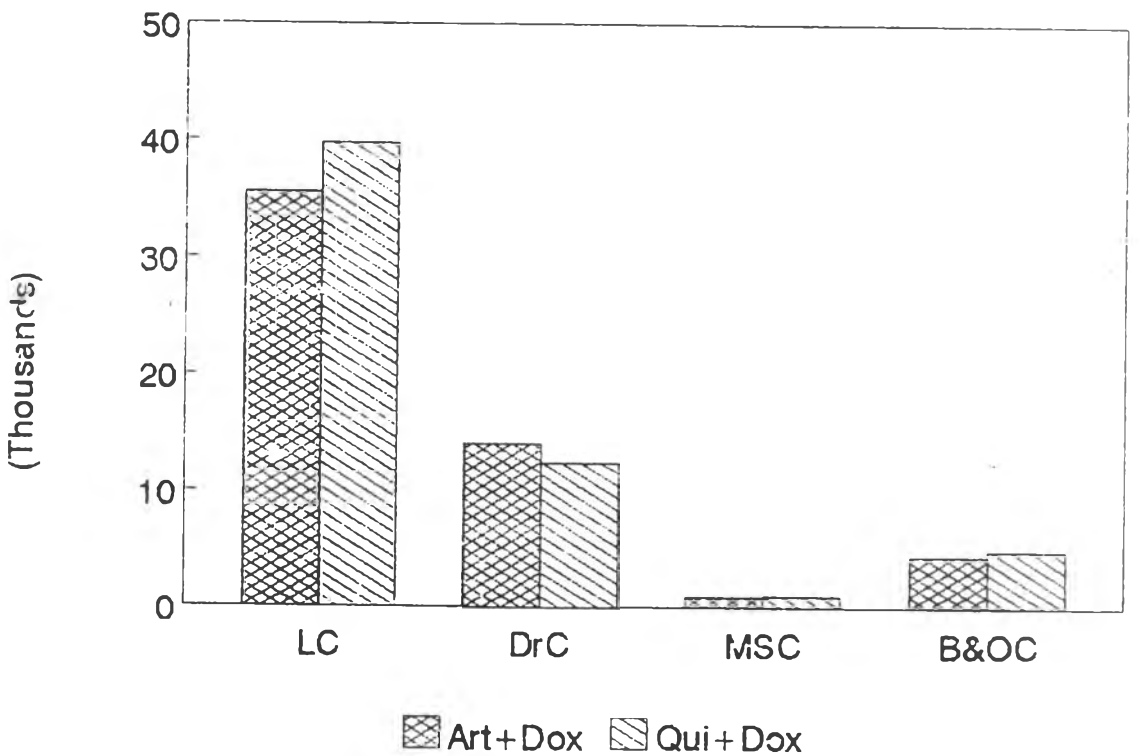
In normal treatment practice conditions, malarial patients are only treated 5 days in hospital, with this treatment duration, Figure 5.3 and Figure 5.4 are present comparison of provider costs and costs incurred by patients in normal treatment conditions (recrudescence treatment included).

Figure 5.3 present the average provider costs per patient treated by Art + Dox drug which were lower than patient treated by Qui + Dox drug (71,916.46 VN dong in comparison with 94,109.64 VN dong).

- Average costs of personnel, maintenance cost of building, operating cost and cost of medical supply per patient treated by the Art + Dox drugs were lower than patient treated by the Qui + Dox drugs, because of the recrudescent patients in the Qui + Dox drugs group were higher than recrudescent patients in the Art + Dox drugs group.

- Average cost of drug per patient treated by the Art + Dox drug was higher than patient treated by the Qui + Dox drug because the price of artemisinin was more expensive.

Figure 5.3 Comparison of Components of Provider Costs in Normal Condition Between Two Drug Regimen Groups.



* VN dong.

Where:

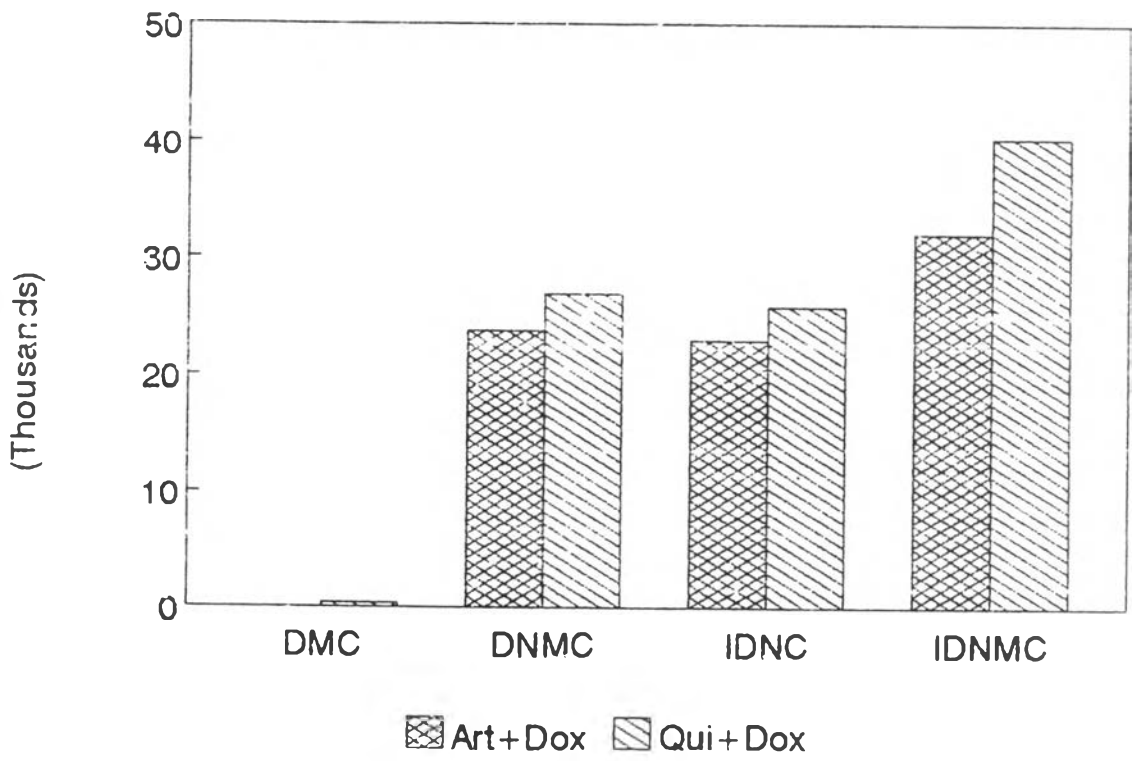
LC = Cost of personnel.
DrC = Drug cost.
MSC = Cost of medical supplies.
B&OC = Building maintenance & operating costs.

In Figure 5.4, average costs incurred by patient treated by Art + Dox drug in normal treatment condition (the cost of recrudescence treatment included) were lower than patient treated by the Qui + Dox

drug (82.487 VN dong = $7.8 in comparison with 97,118 VN dong = $9.2).

- Average of each component of the cost incurred by patient treated by Art + Dox drug was also lower than patient treated by Qui + Dox drug. The reason was the number of recrudescence patient (11 patients) treated by Qui + Dox drug was higher than number recrudescence treated by Art + Dox drug (3 patients) and additional costs of patients treated by Qui + Dox drug due to side effect treatment.

Figure 5.4 Comparison of Components of Costs Incurred by Patient in Normal Condition (Include Cost of Recrudescence Treatment)



* VN dong.

Where:
DMC = Direct medical costs.
DNMC = Direct non medical costs.
IDMC = Indirect medical costs.
IDNMC = Indirect non medical costs.

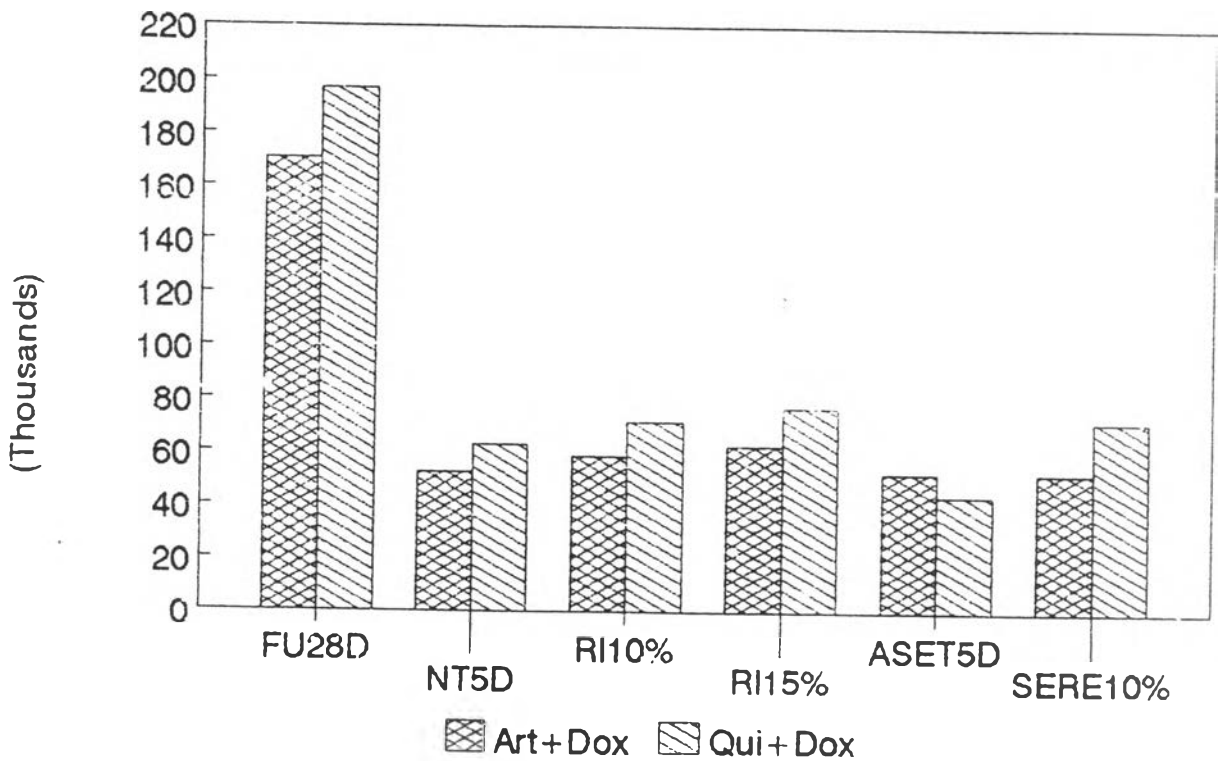
5.3 The cost-effectiveness ratio

The cost-effectiveness ratio of Art + Dox was lower than that of the Qui + Dox from both provider perspective and patient

perspective. The cost-effectiveness ratio to provider in the Art + Dox drug regimen was 160.766 VN dong ($15.3) compared with 180,755 VN dong ($17.2) in the Qui + Dox drug regimen.

The cost-effectiveness ratio to patient in Art + Dox drug regimen group was 170,432 VN dong ($16.2) lower than 197,127 VN dong ($18.7).

Figure 5.5 Cost-Effectiveness Ratio to Provider under Different Conditions.



Where:

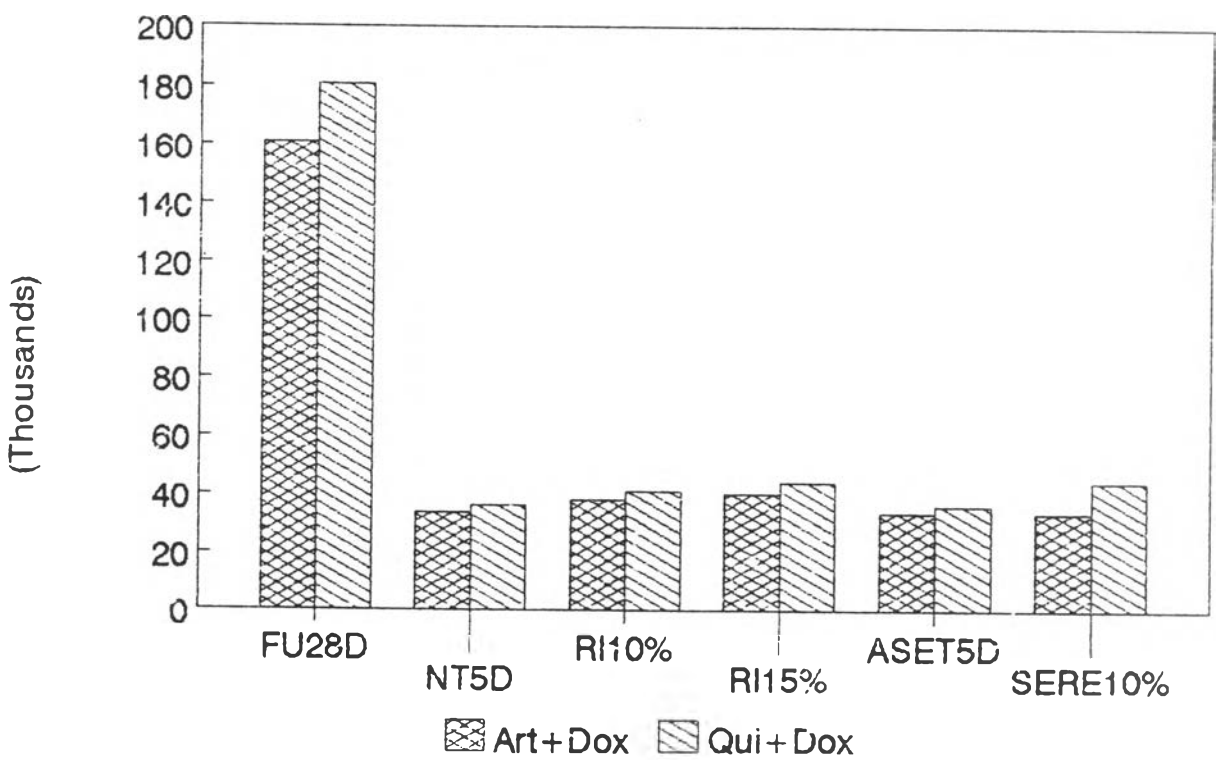
FU28D	=	Follow up 28 days in nospital.
NT5D	=	Five days in normal treatment practice.
RI10%	=	Resistance increase 10%.
RI15%	=	Resistance increase 15%.
ASET5D	=	Side effects treated in 5 days.
SERE 10%	=	Side effects reduce E 10%.

In cost-effectiveness analysis, the more cost-effective is the lower cost per unit of effectiveness achieved, the lower cost-effectiveness ratio is better drug regimen. Therefore the artemisinin with dose of 10 mg/kg/days for 5 days combined with doxycycline dose of 2 mg/kg/day for 5 days was more cost-effective than quinine dose of 30 mg/kg/day for 5 days combined with doxycycline dose of 2 mg/kg/day for 5 days.

From the result of this study we can say that from the provider side the use artemisinin - doxycycline drug regimen in falciparum treatment is better because the effectiveness of this drug regimen is high and the costs of this regimen are lower than quinine - doxycycline. Furthermore the artemisinin - doxycycline drug regimen is more safe than the quinine - doxycycline regimen.

From the patient side, Figure 5.6 shows that the artemisinin + doxycycline regimen is also better, the cost-effectiveness ratio of Art + Dox drug regimen is also lower than the Qui + Dox drug regimen in different conditions. Besides that Art + Dox has no side effect, it is more readily accepted by patient in compared with Qui + Dox drug regimen.

Figure 5.6 The Cost-Effectiveness Ratio to Patients.



Where:

FU28D	=	Follow up 28 days in hospital
NT5D	=	Five days in normal treatment practice
RI10%	=	Recrudescence increase 10%
RI15%	=	Recrudescence increase 15%

The Art + Dox drug regimen should be chosen to treat resistant falciparum malaria in uncomplicated cases in hospital instead of Qui + Dox.

With important advantage of oral artemisinin in combination with doxycycline is rapid onset of action, it is particularly effective against severe cases of falciparum malaria. Furthermore, since it is a safe antimalarial drug with no side effects and is well tolerated, oral artemisinin + doxycycline regimen can play an important role in chemotherapy of malaria and antimalarial drug policy of the national malaria control programme.