EDITORIAL

Artimisinin in the Treatment of Falciparum Malaria

Malaria remained as one of the most important infections causing huge health burden in the tropical world to the extent of more then one million deaths per year. The strategies for its control were changed by the World Health Organization (WHO) on several occasions with limited success each time. Present strategy of malaria control has important elements of early diagnosis and effective treatment by drugs coupled with promotion of use of insecticide impregnated mosquito nets. Using the available technology WHO has targeted to reduce the burden and mortality by 50% by the year 2010[1].

Until recently, diagnosis of malaria in most cases in endemic countries including Bangladesh was clinical and malaria including dreadful falciparum malaria was being treated with drugs like chloroquine or sulfadoxine pyremethamine against which the parasite has already developed resistance[2]. Many cases, even up to 60-70%, treated as malaria on clinical diagnosis were not really malaria at all[3]. Present day treatment of choice in falciparum malaria is artemisinin based combination treatment either artemether lumefantrine or artesunate mefloquine which has high degree of efficacy with relative safety but at the same time very expensive for the countries most in need. Bangladesh has already changed the regimen for treatment of uncomplicated falciparum malaria and recommended for using six dose artemether lumefantrine but yet to use and implement it widely[4]. The drug has been found to be effective to the extent of more then 97% and is equivalent to artesunate mefloquine in areas of multi-drug resistance[5]. Due to availability of easy method of rapid diagnostic test based on HRPII of falciparum antigen, diagnosis of malaria can be done at patient's home and a new challenge of providing effective treatment has been suggested. The spread and increase of malaria were contributed by the development of resistance of the parasite to the commonly used antimalarials. It has been found that use of effective combination treatment in infectious diseases could prevent development of resistance. Rediscovery of artemisinin, a very potent antimalarial, now gives a hope of containment of malaria. Artemisinin is a plant derived (*Artemisia annua*) sesquiterpine lactone containing antimalarial discovered by Chinese scientists and now available in most malaria endemic countries. Delay in development of resistance to this class of antimalarial could be made possible by combination with other slow acting effective drugs. Currently, WHO has recommended such of combinations for effective treatment of falciparum malaria by using artemisinin with lumefantrine, mefloquine, amodiaquine, or S-P. Based on the available local evidence of increasing chloroquine and S-P failure, and also as per WHO recommendations the antimalarial regimen recommend in Bangladesh for treatment of falciparum malaria was adopted in 2004, and it recommends using an artimisinin based combination antimalarial, artemether-lumefantrine. The drug also has potentiality of reducing transmission due to gametocytocidal effects. It is essential to use the artemisinin based antimalarial treatment in confirmed falciparum cases in complete dose only, thus not to abuse the drug which is expected to delay the development of resistance. Considering the cost of the drug and RDT the poor countries and people in malaria endemic region need subsistence in order to provide the community with optimal benefit of the strategy. We cannot afford to use the artemisinin-based drug on clinical diagnosis alone. It is expected that the malaria control programme will carefully deploy and extend the access to rapid diagnosis and ACT based treatment for the treatment of uncomplicated malaria (UM) down to the periphery involving different types of health care providers from government and non-government sectors.

The antimalarial drug used for the management of severe malaria was evaluated by a number of trials

before without finding any significant superiority of artemether over quinine[6,7]. The exception was some indication of better outcome in adult patients of severe malaria particularly with multiple organ involvement in Asia. This finding along with availability of better artemisinin with water soluble formulation artesunate prompted the scientists to compare artesunate with quinine in an open-label randomised control trial among 1461 adults and children with severe malaria in four countries of Asia including Bangladesh. The findings show a reduction of mortality by 34.7% compared to quinine[8]. Artesunate has been found to be well tolerated and was not associated with hypoglycaemia as has been found in quinine group. The new WHO guideline for management of severe malaria promptly accepted the results and recommended artesunate over quinine in the treatment of severe malaria in adults in Asia and travelers world wide[9]. Such a study involving children is in progress in Africa. Many cases of severe malaria used to die before arrival or in early period of treatment in hospital. The treatment delay includes arrival delay for parenteral treatment in the hospital. Intramuscular quinine was recommended as a pre referral treatment, which was not really in practice in remote rural areas. Per rectal formulations of artesunate has been found to be effective as good as parentral quinine in severe malaria in hospital setting[10]. This could be an alternative to parenteral quinine in remote areas. How far it is effective in community setting while using as a pre-referral treatment in preventing death in malaria is yet to be seen.

The present day treatment of falciparum malaria is thus based on artimisinin compounds both for uncomplicated and severe malaria. For the treatment of UM combination ACT is recommended, for the treatment of SM artesunate is the preferred drug. The availability of antigen based rapid diagnostic test for the diagnosis of falciparum malaria along with highly potent ACT based therapy is expected to contribute significantly in achieving the target of 50% reduction of mortality due to malaria. At the same time insecticide impregnated mosquito net or long lasting nets would be used as an important element of integrated vector control. It is high time to act now for using this knowledge base in malaria diagnosis, treatment and prevention for achieving the target before it is too late.

M A Faiz[a], Emran Bin Yunus[b]
M Ridwanur Rahman[a]

[a]Department of Medicine, Dhaka Medical College, Dhaka; [b]Department of Nephrology, Chittagong Medical College, Chittagong.

(J Bangladesh Coll Phys Surg 2005; 23 : 99-100)

References:

1. WHO. World Malaria Report. Roll Back Malaria/World Health Organization/UNICEF, 2005.
2. Rahman MR, Paul DC, Rashid M, Ghosh A, Bangali AM, Jalil MA, Faiz M A. A randomised controlled trial on the efficacy of alternative treatment regimens for uncomplicated falciparum malaria in a multidrug-resistant falciparum area of Bangladesh - narrowing the options for the National Malaria Control Programme? Trans R Soc Trop Med Hyg 2001; 95: 661 - 667.
3. Faiz M A, Yunus E B, Rahman MR, Hossain MA, Pang LW, Rahman M E, Bhuiyan SN. Failure of national guidelines to diagnose uncomplicated malaria in Bangladesh. Am J Trop Med Hyg 2002; 67: 396-399.
4. DGHS. Malaria Treatment Regimen-2004. Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, Bangladesh, 2004.
5. van den Broek IV, Maung UA, Peters A, Liem L, Kamal M, Rahman M, et al. Efficacy of chloroquine + sulfadoxine-pyrimethamine, mefloquine + artesunate and artemether + lumefantrine combination therapies to treat Plasmodium falciparum malaria in the Chittagong Hill Tracts, Bangladesh. Trans R Soc Trop Med Hyg 2005; 99: 727-735.
6. Artemether-Quinine Meta-analysis Study Group. A meta-analysis using individual patient data of trials comparing artemether with quinine in the treatment of severe falciparum malaria. Trans R Soc Trop Med Hyg 2001; 95: 637-50.
7. Faiz M A, Rahman E, Hossain M A, Rahman MR, Yunus EB, Samad R, Hossain M A. A randomized controlled trial comparing artemether and quinine in the treatment of cerebral malaria in Bangladesh. Indian J Malariol 2001; 38: 9 - 18.
8. South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet 2005; 366: 717-25.
9. WHO. WHO Guidelines for the Treatment of Malaria, 2005. Roll Back Malaria Department, Geneva, 2005.
10. Barnes K I, Mwenechanya J, Tembo M, Mcllleron H, Folb P I, Ribeiro I et al. Efficacy of recital artesunate compared with parenteral quinine in initial treatment of moderately severe malaria in African children and adults: a randomized study. Lancet 2004; 363: 1598-1605.