

Role of pyrethroids in control of malaria amongst refugee population

Seemin Jamali

Jinnah Post Graduate Medical Centre, Karachi, Pakistan.

Abstract

Malaria is a human disease caused by sporozoan parasite belonging to genus plasmodium. According to World Health Organization (WHO) estimates for year 2006, there were 247 million clinical infections and 0.88 million deaths due to malaria. Malaria control programmes aim to contain the disease and reduce its burden on the refugees by adopting various methods to reduce the incidence of malaria by targeting the mosquitos. Most of the displaced people live in Asia and Africa, where host countries lack the resources to support them. Under these conditions, the methods adopted for control of malaria should be both effective and safe.² Pyrethroids form the mainstay of preventive measures due to their efficacy and safety in mammals. They can be used as (a) indoor residual sprays, (b) impregnation of bednets, blankets/top sheets, curtains and personal clothing, (c) pyrethroid containing coils, mats and vaporizers and (d) livestock sponging.

Keywords: Malaria control, Refugees, Pyrethroids, Indoor residual spray, impregnated nets/ curtains/blankets/ sheets, livestock sponging.

Introduction

Malaria is a human disease caused by sporozoan parasite belonging to genus plasmodium. It is a significant global health problem and is common in displaced population. It flourishes during the conditions of crisis and mass movement due to breakdown of health services, displacement/concentration of non-immune population in the areas prone to the vector breeding, lack of protective shelter and non-availability of medicines.¹ Most of the displaced people live in Asia and Africa, where host countries lack the resources to support them. The recent UNHCR report in 2009 estimated the number of refugees to be 15.2 million and 26 million internally displaced people globally as a result of significant surge in the number of refugees noted between 1978 till 1993.

The refugees/internally displaced people live in countries that are endemic with malaria and are at high risk of morbidity and mortality. This can be seen from the figures that the number of malaria cases increased tenfold from 1978 to 1991 amongst the Afghan refugees.² Malaria accounted for 21% of all deaths and 26% of deaths in the children under the age of five amongst the refugees during 2007. Africa bears

the most burden of malaria with more than 90% share with 500 million clinical cases and up to 2 million deaths annually being contributed due to reasons^{1,3-8} such as; presence or absence of immunity, movement of refugees, resistance to drugs and resistance to insecticides. WHO has reduced the figures to 247 million clinical infections and 0.88 million deaths due to malaria in year 2006. Insecticides form the cornerstone of malaria control programmes and a number of compounds like organophosphates carbamates, pyrethroids and phenyl pyrazoles are used for this purpose.⁹ Dichlorodiphenyltrichloroethane (DDT) is still useful for indoor sprays and recommended by WHO, though there are issues due to its long term toxicity because it accumulates in environment. Pyrethroids are preferred for their efficacy and safety.¹⁰ They can be used as sprays, impregnated materials, vaporizers and for livestock sponging.

Pyrethroids

History:

Pyrethroids are a group of synthetic pesticides similar to the pyrethrum a natural pesticide produced by chrysanthemum flowers and containing pyrethrin and cinerin. About 200 years ago, people in Central Asia discovered that the crushed flowers of chrysanthemum were toxic to the insects.¹¹

Pyrethrum compounds are odourless and pose a far less risk to the mammals,¹¹ having short term residual properties. Pyrethroids were developed to improve the stability, efficacy and duration of action of these compounds. Allethrin was the first pyrethroid identified in 1949. Since then over 1000 pyrethroids have been found but only few are used.

Basic Structure:

The basic structure of all pyrethroids has several common features (an acid moiety, a central ester bond and an alcohol moiety)¹¹ and exist as stereo isomeric compounds with different insecticidal activity. There are two types of pyrethroids; type 1 with basic cyclopropane carboxylic ester structure and type 2 with an alpha-cyano phenyl acetic 3-phenoxyl benzyl ester structure.

Mode of Action:

Pyrethroids slow the kinetics of both activation and inactivation of the voltage sensitive sodium channels

(VSSCs) resulting in prolonging the opening of the individual channels.¹¹ This allows the sodium ions to cross and depolarize the neuronal membrane and cause repetitive discharge and synaptic disturbances leading to the hyper excitatory symptoms of poisoning. Type II Pyrethroids also inhibit the calcineurin by delaying the dephosphorylation process and affect the chloride channels.¹² This may explain some of the features of toxicity of type 2 pyrethroids. The actions of pyrethroids can be increased by sensitizing the target area by synergists (piperonyl butoxide) or by decreasing the metabolic rate by carboxylase inhibitors (organophosphates).^{6,8}

Biodegradation of pyrethroids:

The two main routes of degradation of pyrethroids, photo- and biodegradation, are often superimposed.¹³ Different pyrethroids retain insecticidal activity for a variable period due to difference in the biodegradation rate.

Insecticidal activity:

The insecticidal activity of the pyrethroids is mainly neurotoxic resulting in hyper excitation and tremors followed by paralysis due to change in membrane permeability. Pyrethroids have excitatory/ repellent action on mosquitoes⁹ as a result two types of toxic effects, the T (Tremors) syndrome by type 1 and CS (Choreoathetosis and seizures) syndrome by type 2 pyrethroids.^{11,14}

Pyrethroid resistance:

Pyrethroid resistance means a reduced excitorepellency and mortality in mosquitoes exposed to pyrethroids.¹⁰ It is either due to decreased sensitivity of the target site due to presence of knock down resistance (Kdr) gene or increased metabolism or combination of the two.^{7,8,11,15} However there are conflicting reports about the impact of pyrethroid resistance.^{7,8,16} This is said to be counteracted by using pyrethroids with a synergist or in combination with other insecticide.

Toxicity to the human beings:

Pyrethroids are generally safe. Less than ten deaths have been attributed to the pyrethroids.²⁴ Pyrethroid toxicity can occur as a result of inhalation, ingestion or direct contact. The details on this aspect can be seen in an article by Kodiaga.¹⁷

Ways of using of Pyrethroids:

(A) Indoor residual spray (IRS) with pyrethroids:

Indoor residual spray with insecticides is the mainstay of the malaria control programme and

recommended by the World Health Organization.^{10,18} Pyrethroids and DDT are mostly used and recommended; however pyrethroids with long residual effect such as deltamethrin are preferred.¹⁰ There is no concrete evidence to support efficacy of outdoor residual spraying in vector control and pyrethroids are less useful as an outdoor residual spray because of their accelerated biodegradation in the presence of light and high temperatures.^{1,19} IRS is possible under stable conditions in refugee camps and is very effective against susceptible indoor resting species of the mosquitoes. Being an effective mass exterminating agent, indoor residual spray pyrethroids should be used as a preemptive measure in early stages of refugee camps.

Prerequisites for carrying out Indoor residual spray with pyrethroids in refugee camps are: (a) Size and shape of the tent, (b) ability to retain and maintain adequate level of insecticide for vector control on plastic sheets, (c) adsorption/ absorption on mud surfaces, (d) replastering/ painting or washing of the walls and (e) thickness of the tent fabric.^{1,20} Spraying of the mud walled dwellings with deltamethrin killed only 40% of the mosquitoes on the first day.²⁰ Double sheet tents sprayed with permethrin or deltamethrin retained their insecticidal activity for one year, while single sheet tents retained the same activity for approximately six months.^{1,21} Over 50% reduction in the burden of malaria was achieved in Afghan refugees after IRS.^{2,3} Another study on the Afghan refugees reported reduction in the prevalence of the *P. Falciparum* from 46.9% to 16.3% after spraying of the tents with permethrin.²⁰ IRS with Malathion and lambda cyhalothrin gave a protective efficacy of 66% against *P. Falciparum* in the refugee camps.¹⁹ Pyrethroids are less effective against resistant mosquitoes, particularly *Anopheles Gambiae*.^{6,7,15} IRS with pyrethroids is considered cheaper.

(B) Impregnated Materials:

(1) Insecticide treated plastic sheet tents (ITPSTs):

Pyrethroid treated plastic sheet tents (ITPSTs) with insecticide impregnated during manufacturing process are showing better results.¹⁸ Mean 24 hour mortality of 50.8% for the wild *Anopheles* was observed in the treated tents as compared to 25.7% in untreated tents in a refugee camp,²² while in another refugee camp, the mortality rate of mosquitoes was 80%-100% for deltamethrin impregnated tents/ tarpaulins as compared to 5% in the untreated ones.²³ Other studies have also reported similar results. Plastic sheets are cheaper than the canvas sheets.

(2) Insecticide (Pyrethroid) treated nets (ITNs):

ITNs are as effective as IRS in reducing the incidence of malaria.²⁴ Pyrethroids are the only compound recommended for this purpose.²⁵ They require community cooperation for their proper use, retention and retreatment.²⁴

Poor retention of the ITNs was observed under the conditions where community engagement was lacking and competing survival priorities existed.²⁴ However, many studies have reported high retention and use of ITNs.^{1,3,18} ITNs have longer residual insecticidal activity and may be effective up to 13 months.²⁰ Washing and exposure to high temperatures and sunlight reduces the efficacy of ITNs and requires retreatment at an appropriate interval.²⁰

ITNs act as a chemical and physical barrier. They not only provide cover to the users but to other refugees by virtue of mass killing action. ITNs,^{2,25} reduced the density of vector by 67%^{4,16} and consistently gave 70% protection. The prevalence of malarial parasitaemia was significantly lower (9.3%) in the ITN users as compared to 13.8% in non-users amongst the internally displaced people in Uganda.²⁶ The number of blood fed mosquitoes found in places with ITN use was seventeen times lower than those without ITN use amongst the refugees in Uganda.²⁶ ITNs provided 61% protection against P- Falciparum and 40% against P- Vivax in Afghan refugees.¹ A reduction of 87% in the annual incidence of the malaria was reported with IRS and ITNs in the Afghans.²⁴ ITNs are reported to be less effective in protecting pregnant women. The use of ITNs may put the nonusers at the increased risk of malaria, though this was not observed during a study which showed that with 75% coverage of the population with ITNs, 98% protection for the ITN users and 90% protection for the nonusers was seen.²⁷

The efficacy of pyrethroid treated nets decrease significantly in the presence of pyrethroid resistance,¹⁵ though others have reported their continuous efficacy despite presence of Kdr gene.⁷ In an attempt to overcome this problem, the nets can be dually impregnated (pyrethroids with a synergist or another insecticide.^{6,8,25} PermaNet (polyester net coated with polymer resin containing deltamethrin) belongs to new category of Long Lasting Insecticidal Net (LLIN).²⁵ The new PermaNet 3 is impregnated with piperonyl butoxide (synergist) and pyrethroid achieved 90% and 81.2% blood feeding inhibition in Tanzania and Vietnam for the susceptible vectors. In areas with high pyrethroid resistance (Burkina Faso) 72.6% reduction was achieved.²⁵

The initial cost of the nets is high¹⁹ but the retreatment costs only 10% of the initial outlay.¹ The issues related to ITNs usage amongst the refugees include the initial cost of the net, their availability at the time of need, social acceptance, retention and retreatment of the nets.^{1,3,28}

(3) Insecticide (pyrethroid) treated curtains (ITCs):

Insecticide treated nets can be useful for the control of malaria amongst the refugees as they are socially acceptable and easy to use.¹ Treated curtains are more effective in cool weather.

Permethrin treated curtains offered better protection

than the electric fans, pyrethrum coils, untreated curtains, pyrethroid vaporizing mats in reducing the number of blood fed *Anopheles stephensi* in Afghan refugee camps.²⁹ A reduction of 67% in the blood fed mosquitoes was reported from Afghan refugees with treated curtains. However, they are not superior to the ITNs, though a study from Kenya, which reported better efficacy of the permethrin treated curtains over permethrin treated nets. Studies from India and Sudan have reported significant reduction in the density of indoor resting and man biting species of mosquitoes with over 50% mortality with the use of pyrethroid treated curtains.

Pyrethroid treated curtains are more effective against the *Anopheles* than the *Culex* species of the mosquitoes. They are also cheap, easily available, easy to impregnate and retain insecticidal activity for long periods, hence, very useful for malaria control among refugees.

(4) Pyrethroid treated blankets/ top sheets/ chaddars:

Pyrethroid treated blankets and sheets have a great potential in the management of malaria control during the acute phase and later on as they are always needed in such situations and are retained/ used by the refugees. They can be used in all types of the shelters.

A single treatment of blanket gives protective efficacy for four months.¹ Residual insecticidal activity can be extended by the use of factory based permethrin impregnation using a new polymer coat. This type of fabric retains insecticidal activity for up to 100 washings.

Pyrethroid treated cotton sheets performed significantly better than the untreated sheets in deterring or killing mosquitoes in an Afghan refugee camp.³⁰ Permethrin treated sheets and blankets reduced the chances of malaria infection by 70% among the Somali refugees.³¹ Blankets, top sheets and chaddars gave 64% protective efficacy against P- Falciparum and 38% against P- Vivax in refugees.¹⁹ Permethrin treated chaddars caused 64% reduction in the malaria among the children aged between 0-10 years but were less effective in those aged over 20 years.¹⁹ Permethrin treated top sheets/ chaddars provided protection against malaria similar to ITNs.³

The treatment cost of the blankets/ top sheets is approximately a quarter of a dollar or less and is around 15% of the cost of an ITN.¹⁹ Permethrin or cypermethrin are preferred pyrethroids for this purpose as some side effects were reported with deltamethrin.^{1,30}

(5) Pyrethroid impregnated personal clothing:

Pyrethroid treated personal clothing have not been used on a large scale among the refugees, possibly due to the cost of repeated impregnation and loss of residual insecticidal

activity due to washing.³¹ A study on Somali refugees reduced the odds of malaria by 70%, but required daily treatment with permethrin.³¹ Studies on the soldiers wearing pyrethroid treated dresses have reported good protection against malaria.³² Factory based permethrin impregnated military uniforms retained the residual insecticidal activity even after one hundred washings. This technology may be applicable in refugees in future.

(C) Pyrethroid treated coils, mats and vapourizers:

There is very little literature on this subject among the refugees. They are not useful during acute emergencies as other priorities take over. However, once refugees are settled with some degree of self-sustainability, these measures can be used on individual basis. Pyrethroid vapourizing mats gave better protection than the others.^{29,33} Hewett reported 56% reduction in blood fed mosquitoes in the Afghan refugee camps.²⁹ Another similar study reported over 60% mean reduction in the indoor biting mosquitoes.³³ An improved method of pyrethroid vapourizer was reported from Tanzania which gave efficacy of 90%. Pyrethroid coils are less effective and achieved only 36% reduction in blood fed mosquitoes³³ and 52% reduction in bite rates.

(D) Livestock sponging with pyrethroids:

Cattle tend to increase the human biting rate by mosquitoes and the prevalence of malaria.^{34,35} A study from an Afghan refugee camp reported 38% increase in human biting in the presence of a single cow and 50% in the presence of two goats.³⁴ Livestock sponging with pyrethroids is an effective way of controlling malaria in areas where the vector is zoophilic.^{1,34} It is cheap and easy to apply method, costing only 20% of the cost of IRS.³ It has become popular among the Afghan refugees.¹ Livestock sponging with deltamethrin four times a year reduced the incidence of P- Falciparum malaria by 56% in a refugee camp. It is suggested that the pyrethroid treatment of cattle should be done every three weeks. It is as effective as a house spray.

Conclusion

The current approach to the control of malaria among the refugees is based upon targeting the vector and has achieved a limited success. With emergence of resistance to the pyrethroids in mosquitoes, the success rate will further decline. It is imperative to find ways to not only deal with this resistance but point towards complete eradication of malaria.

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