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Uncomplicated Plasmodium Vivax Malaria Treatment in India

Arvind Nath

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Arvind Nath/Uncomplicated Plasmodium Vivax Malaria Treatment in India/J Microbiol Relat Res. 2022;8(1): 9–10.

Abstract

Background: Uncomplicated P. vivax Malaria treatment in India is straightforward because the same regime exists for the North-eastern part of the country and the rest of the country unlike treating uncomplicated P. falciparum Malaria where different regimes exist for these two areas. However, a slightly different approach is needed for the treatment of pregnant patients.

Objectives: To find out what are the antimalarials prescribed in India for treating uncomplicated Vivax Malaria.

Methods: By reviewing documents prepared by WHO and NVBDCP.

Results: It is found that the same regime exists for treating uncomplicated Vivax Malaria whether the patient comes from any part of the country. However, some modifications are made depending on the pregnancy status of the female patient.

Conclusions: Some more education is required among health care providers on how to treat uncomplicated P. vivax Malaria. This paper addresses this concern.

Keywords: Malaria, Plasmodium vivax, Chloroquine, Primaquine, Hypnozoite.

INTRODUCTION

Treatment of Malaria depends on the species of Plasmodium causing it. If the species is P. vivax, the treatment is by giving Chloroquine and Primaquine. If the patient is pregnant, she is treated with Chloroquine only but no Primaquine. If the patient is an infant, it is also treated with Chloroquine only but no Primaquine. Primaquine is also not given to known G6PD-deficient individuals.[1]

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MATERIAL AND METHODS

The study design included analysis of the documents of the WHO and NVBDCP pertaining to treating P. vivax Malaria that is uncomplicated.

RESULTS

Guidelines for the treatment of Malaria published by the WHO in 2015 dealt with treating P. vivax Malaria that is uncomplicated, in the following manner.[2]

Table 1: Dosage of Chloroquine for Uncomplicated P. vivax Malaria.

A total of 25 milligrams of Chloroquine base per kilogram of body weight over three days as follows:		
Day 1	**Day 2**	**Day3**
10 milligrams per kilogram bodyweight	10 milligrams per kilogram bodyweight	5 milligrams per kilogram bodyweight

In addition to the above, it was also advised to give a fourteen-day course of Primaquine at a dose of 0.25 milligrams per kg of body weight to prevent relapses due to the release of hypnozoites from the liver.

The country's Drug Policy on Malaria 2013 dealt with treating uncomplicatedP. vivaxMalaria in the same way as was given in the WHO guidelines above.[3]

The 2014 guidelines for diagnosis and treatment of Malaria covered treating uncomplicated P. vivax Malaria in the same way as was done by the WHO document described above. It was recommended that patients stop Primaquine in case patients notice any (i) dark-colored urine, (ii) yellow eyes, (iii) blue discoloration of the lips, pain in the abdomen, nausea, vomiting, and breathlessness.[1]

The operational document on Malaria Elimination in India, published in 2016, also covered treating uncomplicated P. vivax Malaria in the same way as was done by the WHO guidelines given above. It also advised patients to stop Primaquine in case they noticed high coloration of urine or blue coloration of lips.[4]

DISCUSSION

The Government of India, in 2016, adopted aframework for Malaria Elimination in India covering the period 2016 – 2030.[5] This was based on WHO's Global Technical Strategy for Malaria, covering the same period, adopted in 2015 and updated in 2021.[6]

The aim is to reach no Malaria cases by 2027 and then wait for three years before WHO can grant Malaria-free status certification. It is already the beginning of 2022 and India is about to reach the halfway mark of this period from 2016 to 2027. The Annual Parasite Incidence (API) has also come down significantly (it was 0.32 during 2018).[7]

CONCLUSION

If a medical practitioner, whether in government service or in private practice, comes across an uncomplicated case of P. vivax Malaria, he/she can manage the patient using the drugs at the dosages recommended above. This will be a step towards reaching the target of zero Malaria cases in the country by 2027.

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Severe Plasmodium Falciparum Malaria and Severe Plasmodium Vivax Malaria Treatment in India

Arvind Nath

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Abstract

Background: The treatment of severe P. falciparum Malaria and severe P. vivax Malaria is identical. Their treatment in India is complex because different regimes exist for the North-eastern part of the country and for the rest of the country. Also, different drugs are needed for the treatment of pregnant patients.

Objectives: To find out what are the antimalarials prescribed in India for treating severe Falciparum Malaria and severe Vivax Malaria.

Methods: By reviewing documents prepared by NVBDCP.

Results: It is found that different regimes exist for treating severe Falciparum Malaria and severe Vivax Malaria depending on where the patient comes from, and the drugs differ based on the pregnancy status of the female patient.

Conclusions: More education is required among health care providers on how to treat severe P. falciparum Malaria and severe P. vivax Malaria. This paper addresses this concern.

Keywords: Malaria; Plasmozzdium falciparum; Plasmodium vivax.

INTRODUCTION

Treatment of severe P. falciparumMalaria and severe P. vivax Malaria consists of an initial parenteral phase and a follow-up oral phase. While the parenteral phase is the same irrespective of where the patient lives, the oral phase, consisting ofgiving Artemisinin-based Combination Therapy (ACT) and Primaquine, differs based on the place of residence. If the patient resides in any part of the country except the North-East, he/she is treated with an ACT consisting of three days treatment with Artesunate and one-day treatment with Sulphadoxine-Pyrimethamine (SP). If the patient lives in the North-East, he/she is treated with Artemether and Lumefantrine for three days.[1]

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MATERIAL AND METHODS

The study design included analysis of the documents of the NVBDCP pertaining to treating severe P. falciparum Malaria.

RESULTS

The country's Drug Policy on Malaria 2013 for severeP. falciparumMalaria:[2]

A. Table Showing the Three Available Initial Parenteral Regimes (to be given for at least 48 hours even if the patient can tolerate oral medication earlier than this)

Drug (for at least 48 hours)	Dosage
Inj. Artesunate	2.4 milligrams/kilogram body wt. IV or IM at diagnosis (0 hrs). Next at 12 hrs, then 24 hrs, After that, once a day.
Inj. Artemether	3.2 milligrams /kilogram body wt. IM at diagnosis. After that, 1.6 milligrams/kilogram body wt. daily.
Inj. Arteether	150 mg IM daily for three days (for adults only; not for children)

B. Follow-up Oral Regimes (at the time the patient can take oral medication):

Treatment in those States other than the North-Eastern States:

Here, the ACT used consists of the following drugs in the given dosages:

- Artesunate: 4mg/kg body wt. daily for three days PLUS
- SP consisting of 25 milligrams per kilogram body wt. Sulfadoxine plus 1.25 milligrams per kilogram body wt. Pyrimethamine on Day One.

In addition, 0.75 milligrams per kilogram body wt. Primaquine is given on the second day. The function of Primaquine is to kill the gametocytes.

Note:

(i) SP not to be prescribed for children under the age of 5 months. In such cases, they should be given an ACT not containing SP.

(ii) The above ACT should not be given during the first trimester of pregnancy. Instead, in the first trimester, Quinine salt is to be given at 10 mg per kg body wt. TDS for one week. During the second and third trimesters, the above ACT can be given. However, Primaquine is not to be given in any trimester.

Treatment in the North-Eastern States:

Here, the ACT used consists of the following drugs in the given dosages:

Artemether-Lumefantrine prescribed as per body weight:

5 kilograms to 14 kilograms	20 mg Artemether plus Lumefantrine 120 mg BD X 3 days
15 kilograms to 24 kilograms	40 mg Artemether plus Lumefantrine 240 mg BD X 3 days
25 kilograms to 34 kilograms	60 mg Artemether plus Lumefantrine 360 mg BD X 3 days
35 kilograms & above	80 mg Artemether plus Lumefantrine 480 mg BD X 3 days

In addition, Primaquine is given at a dose of 0.75 milligrams per kg body wt. on the Second day.

Note:

(i) Artemether-Lumefantrine is not to be given to children weighing less than 5 kilograms.

(ii) The above ACT should not be given during the first trimester of pregnancy. Instead, in the first trimester, Quinine salt is to be given at 10 mg per kg body wt. TDS for one week. During the second and third trimesters, the above ACT can be given. However, Primaquine is not to be given in any trimester.

QUININE REGIME

This consists of an Initial Parenteral Phase of 20 mg Inj. Quinine salt/kilogram body wt. IV infusion or IM to be given at diagnosis followed by a maintenance dose of 10 milligrams/kilogram body wt. TDS.

Note:

(a) Infusion rate should not exceed 5 milligrams/kg body wt. per hour.

(b) If the patient received Quinine earlier, then the Loading dose of 20 milligrams/kg body wt. should not be given.

The Follow-up Oral Phase is given when the patient can take oral medication. It consists of:

Tab Quinine 10 milligrams/kg body wt. TDS till seven days of Quinine therapy (including parenteral Quinine therapy) is completed AND Cap Doxycycline 3 milligrams/kg body weight once a day for one week.

For Pregnant Women and Children under the Age of Eight Years: Instead of Doxycycline:

Cap or Syrup Clindamycin 10 milligrams/kilogram body weight TDS for one week.[3]

The diagnosis and treatment of Malaria guidelines (2014) covered treatingsevere P. falciparum Malaria in the same way as was done by the National Drug Policy on Malaria 2013 given above. An additional point made in this document is that in the first trimester of pregnancy, parenteral quinine is to be preferred. Only if it is not available should Artemisinin derivatives be given. However, in the second and third trimesters, parenteral Artemisinin products are preferred.[1]

The operational document on Malaria Elimination in India, published in 2016, alsocovered treating severeP. falciparum Malaria in the same way as was done by the National Drug Policy on Malaria 2013 given above.[4]

DISCUSSION

The Government of India, in 2016, adopted aframework for Malaria Elimination in India covering the period 2016 – 2030.[5] This was based on WHO's Global Technical Strategy for Malaria, covering the same period, adopted in 2015 and updated in 2021.[6]

The aim is to reach no Malaria cases by 2027 and then wait for three years before WHO can grant Malaria-free status certification. It is already the beginning of 2022 and India is about to reach the halfway mark of this period from 2016 to 2027. The Annual Parasite Incidence (API) has also come down significantly (it was 0.32 during 2018[7]),

CONCLUSION

If a medical practitioner, whether in government service or in private practice, comes across a severe case of P. falciparum Malaria or P. vivax Malaria, he/she can manage the patient using the drugs at the dosages recommended above. This will be a step towards reaching the target of zero Malaria cases in the country by 2027.

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Conflict of Interest: There is no conflict of interest.

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Micro Encapsulation for Ultraviolet Protection and Activity Enhancement of Baculoviruses

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Abstract

Baculoviruses are dsDNA viruses and universally used biological control agents in the integrated pest management programmes. The foremost drawback of these viruses is their sensitivity towards ultraviolet radiation. Different materials have been tested by different workers to influence the sunlight protectant activity. Microencapsulation is currently an extensively studied approach in protecting baculoviruses from UV light as well as enhances the activity, efficiency and performance of baculoviruses formulations. Findings suggest that the microencapsulation technique could reduce the cost and enhance the efficacy of baculoviruses. On the other hand, it can also reduce the use of agrochemicals and their residues in the environment and food materials.

Keywords: Microencapsulation; baculovirus; biological control.

INTRODUCTION

Biological control of agricultural pests has gained importance in recent years due to increased pressure to reduce the use of agrochemicals and their residues in the environment and food. Over the past two decades, baculoviruses have been commercialized for the control of codling moth (*Cydia pomonella*), gypsy moth (*Lymantria dispar*), corn earworm (*Helicoverpa zea*), tobacco budworm (*Heliothis virescens*), beet armyworm (*Spodoptera exigua*), and the cabbage looper (*Trichoplusia ni*) in the United States; the rhinoceros beetle (*Oryctes rhinoceras*) in the Pacific; the velvetbean caterpillar (*Antacarsia gemmatalis*) in Brazil. In addition, large scale control programs for periodic forest pests, such as the Douglas-Fir tussock moth (*Orgyia pseudotsugata*), Eastern Spruce Budworm (*Choristoneura fumiferana*), and European pine sawfly (*Neodiprion sertzfer*), have been conducted in countries worldwide, including Canada, the United States, the United Kingdom, Finland, Norway, Sweden, Austria, Italy, Poland, and the Soviet Republic (former USSR). Although insect viruses are highly effective against their target insects, until today, baculovirus insecticides and their application as bio-insecticides was limited to control pest insects worldwide as the performance of these viruses are susceptibility to ultraviolet (UV) radiation. For commercialization, formulations that provide protection from sunlight and rainfall can significantly improve the residual activity of baculoviruses. Following application to plant surfaces, baculovirus occlusion bodies (OBs) are rapidly inactivated by solar ultraviolet (UV) radiation, particularly in the UV-B range of 280–320 nm. This radiation directly affects the nucleic

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acids, modifying or denaturing them, preventing virus infection and replication. Formulation of insect pathogens is recognized as one of the most important priorities in biopesticide research, especially for developing countries (Harris and Dent, 2000). It is well established that the efficacy of entomopathogens that act by ingestion can be improved by the use of formulations that include feeding stimulants which increase the consumption of the pathogen resulting in enhanced prevalence of disease and improved pest control. In this respect, the use of flour and starch-based granular formulations has been the subject of recent interest for the delivery of *Bacillus thuringiensis* and nucleopolyhedro viruses to noctuid pests.

CASE REPORT

Certain formulations can improve the degree of pest control through the use of baits or feeding stimulants that enhance the pest's consumption of viral inoculum while simultaneously protecting. Commonly used unpurifed aqueous preparations typically have high levels of bacterial contaminants, often making them unpleasant to handle, as well as potentially hazardous to human health (Grzywacz *et al.*, 1997), yet purification of baculoviruses prior to formulation is expensive, and leads to large losses of polyhedra (Guillon, 1997). Recent studies have indicated that phagostimulant maize flour-based formulations of *Bacillus thuringiensis* Berliner and nucelopolyhedrovirus resulted in improved control of various species of noctuid pests (Morales Ramos *et al.*, 1998, Tamez-Guerra *et al.*, 1998). Moreover, the maize flour formulation o-ered increased protection from UV radiation and improved the rainfastness of the inoculum during simulated rainfall (Tamez-Guerra *et al.*, 2000 a, b). The use of granular feeding stimulants has a number of advantages that may compensate for the increased formulation cost. These include the ability to use a lower quantity of pathogen inoculum to achieve satisfactory pest control (Bartelt *et al.*, 1990) and the ability to target applications precisely to the feeding site of the pest (e.g., application of granules directly to the maize leaf whorl) (McGuire *et al.*, 1994). Moreover, the opacity of granules may protect the pathogen from UV degradation (Bartelt et al., 1990) and may improve the rainfastness of the application (McGuire *et al.*, 1996; Tamez-Guerra *et al.*, 2000 a, b). Past attempts have been made to provide formulations wherein an insecticidal virus and a sunscreening agent are maintained in close contact after dispersion of the formulation onto vegetation. However, when formulations containing both virus and sunscreening agent were dispersed in the field, the sunscreening agent was no longer in close enough contact to the virus to be effective at reducing the exposure of the viruses to the damaging effects of ultraviolet light. Therefore, microencapsulation - a process in which tiny particles or droplets are surrounded by a coating to give small capsules of many useful properties has been employed. Spray drying serves as a microencapsulation technique when an active material is dissolved or suspended in a melt or polymer solution and becomes trapped in the dried particle. Microcapsules containing virus and sunlight protectant were found to be more stable than virus alone. Very promising results have been obtained by the Agricultural Research Service of the USDA regarding the encapsulation of biopesticides made of species-specific nucleopolyhedroviruses (NPV) isolated from several insects, including celery looper *Anagrapha falcifera* alfalfa looper *Autographa california*, codling moth *Cydia pomonella* and fall armyworm *Spodoptera frugiperda*. Microencapsulation of the UV sensitive *Cydia pomonella* granulovirus in powder form with the encapsulated virus showed increased photostability and strongly enhanced half-life of the encapsulated virus compared to the untreated virus in Germany. Similarly a desirable formulation through microencapsulation of CuniNPV (mosquito) occlusion bodies together with magnesium into a particle that is being developed for delivery to the larval mosquito. Since, inactivation of baculoviruses may be also caused by plant metabolites such as peroxidases which generate free radicals (Hoover *et al.*, 1998), it can be reduced by addition of free radical scavengers such as mannitol or enzyme superoxide dismutase to baculovirus preparations (Zhou *et al.*, 2004). Additives such as Lysine KKL, polyglucine, a by-product of citric acid production and molasses of peat increased the retaining of viral polyhedrae on apple leaves after artificial rainfall and gave 0.5 to 3 times higher larval mortality than that in the control. Luo *et al.* (2021) prepared *S. litura* nucleopolyhedrovirus microcapsules by the complex coacervation method using *S. litura* nucleopolyhedrovirus as the core material, gelatin, and CMC as the wall materials, and tea polyphenols as the curing agent. The particle size of the prepared virus microcapsules was 13 μm, the drug loading was 43.87%, the embedding rate was 62.53%, and LC50 of the microencapsulated virus was 8.36 × 104 (PIB/ml) after 192 h of treatment. The survival ability of microencapsulated *S. litura* nuclear polyhedrosis virus in the field environment was significantly higher than that of unembedded

virus. Similarly, Wilson *et al.* (2020) prepared micro-encapsulated baculovirus in an ENTOSTAT wax combined with a UV absorbant (titanium dioxide, TiO2). Importantly, this capsule protects the sensitive viral DNA from degrading in sunlight, but dissolves in the alkaline insect gut to release the virus. The new formulation has a shelf-life at 30°C of at least 6 months, which is comparable to standard commercial biopesticides and has no phytotoxic effect on the host plants. Taken together, these findings suggest that the new formulation technology could reduce the costs and increase the efficacy of baculovirus biopesticides, with the potential to make them commercially competitive alternatives to synthetic chemicals.

GOALS AND NOVELTY OF APPROACH

- To develop standard formulation for precise delivery of the baculovirus to the feeding site of the target.
- To develop improved formulations for ultraviolet protection and activity enhancement using microencapsulation technique.
- To develop phagostimulant nucleopolyhedrovirus formulations for control semi-cryptic pests such as baits or granules.
- To compare improved formulations of viruses for storage and efficacy.

Typically, baculoviruses have a narrow host range that limits the potential market size of the product when compared with broad spectrum products such as *Bacillus thuringiensis* and chemical pesticides. Therefore, improved formulation technology is required for taking advantage of the unique properties of baculoviruses. It is well established that the efficacy of entomopathogens that act by ingestion can be improved by the use of formulations that include feeding stimulants which increase the consumption of the pathogen resulting in enhanced prevalence of disease and improved pest control. Formulation research proposal presented here addressed to incorporate potent additives of virus preparations retain virus persistence on plants after the rain such as Lysine KKL, polyglucine, a by-product of citric acid production and molasses of peat. Besides, novel adjuvants that improve the pathogenicity of the virus to late instar larvae and improve the persistence of the virus on leaf surfaces. One group of adjuvants of particular interest has been the optical brighteners, derived from stilbene compounds, such as Tinopal LPW or Blankophor BBH. These compounds appear to degrade the peritrophic membrane in the insect midgut, thus increasing the probability of infection of midgut epithelial cells. They can also reduce the rate of sloughing of infected cells and inhibit the suicide response of infected cells, known as apoptosis, thereby increasing the number of foci of infection in each insect that consumes viral OBs. The ingredients used to produce these formulations will be selected based on previous research for extended residual activity (Tamez-Guerra *et al*., 2000, McGuire *et al*., 2001) virus encapsulation, and storage stability (Tamez-Guerra *et al*., 2002). These shall include Baculovirus: for selective insects adjuvants as stickers, UV protectants and phagostimulants antioxidants or radical scavengers besides the addition of folic acid, pyridoxine, riboflavin and charcoal.

DISCUSSION

The methodology will be focused on the preparation of granular/bait formulation by mixing optimized quantity of ingradients like pregelatinized cornstarch, oil, and distilled water to form a paste and its subsequent transformation into bait/granules followed by air drying through fan ventilator. Feeding stimulants that use a lower quantity of pathogen inoculum to achieve satisfactory pest control and the ability to target applications precisely to the feeding site of the pest (e.g., near the base of plant for *Agrotis ypsilon* and application of granules directly to the maize leaf whorl for *Chilo partellus* besides coddling moth *Cydia pomonella.* Another important approach envisaged in this is encapsulation which is the process of mixing microbes with a matrix-forming material, such as cornstarch, that has been partially gelatinized that is, heated to enable water absorption. When the cornstarch-microbe mixture is added to water and then dried, the microbes become entrapped in protective particles so small they can barely be seen without a microscope. Natural (lac or lignin) or synthetic acrylic based polymeric encapsulating agent which is generally soft and thus easily ingested by a target insect.The method will involve (i) mixing (A) an encapsulating polymer comprising (B) a sunscreening agent and (C) a solvent comprising at least one of polyethylene glycol, propylene glycol, a methylene chloride and appropertiate solvents like propylene glycol mixture, tetrahydrofuran, tetrahydropyran, furan, and pyran; A number of schemes for preparing microencapsulated viruses are now described. Among them spray drying is most common.

Finally the formulations of biopesticides can be tested on farmer scale and shall be made available to them by blending the microbial component with carriers and adjuvants for better protection from unfavourable environments, enhanced survival of the bio-agent, controlled rates of release, as well as improved bioactivity, shelf life, and stability.

CONCLUSION

Baculoviruses have been commercialized and gained prime importance worldwide in recent years for the control of many pests. Although baculoviruses are highly effective against their target insects, until today, their application as bio-insecticides was limited as the performance of these viruses is susceptible to UV radiation. Therefore, microencapsulation a process in which tiny particles or droplets are surrounded by a coating to give small capsules of many useful properties has been employed. Microcapsules containing virus and sunlight protectant were found to be more stable than virus alone. Very promising results have been obtained by the Agricultural Research Service of the USDA regarding the encapsulation of biopesticides made of species-specific nucleopolyhedroviruses (NPV) isolated from several insects. The findings discussed above suggest that the new formulation technology could reduce the costs and increase the efficacy of baculovirus biopesticides, with the potential to make them commercially competitive alternatives to synthetic chemicals.

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