Tulip Group

TECHNOTES

Malaria Diagnosis

Importance of 'True speciation' of *P. falciparum* and *P. vivax* - Perspective.

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Setting Trends

Overview

In India both *P. falciparum* and *P. vivax* malaria incidences are very high and there is evidence of mixed infection cases also. Rapid test for malaria has played a crucial role in diagnosis as efficacy of smear microscopy is expertise-dependant and the method has some limitations that can affect the result. But rapid test for Pf antigen and Pan malarial antigen detection has a limitation also. It gives similar signals/ results for mono falciparum infection and mixed infection with vivax, therefore cannot differentiate the two of them.

Specific diagnostic speciation of malarial parasites is very important from therapeutic point of view as treatments are different for *P.f., P.v.* and mixed infection. Mixed infection cases should be treated by Artimicimine combination therapy (ACT), followed by radical therapy for 14 days to prevent relapse of the disease. On the other hand, only ACT is required to treat *falciparum* cases. It does not need radical therapy because there is no chance of relapse in *falciparum* infection. In fact, mixed infection cases should be identified specifically to prevent relapse.

Specific detection of mixed infection can be done by speciation (identifying) the infected parasites (such as *P.f.* and *P.v.*). First generation rapid test for detection of Pf and Pan cannot fulfill the need of speciation between *P.f.* and *P.v.* infection. Therefore second generation rapid antigen detection test that can speciate between *P. falciparum* and *P. vivax* is considered to be an ideal choice of testing for appropriate diagnosis of malaria and its anti relapse treatment.

What is Relapse? How does relapse happen?

After getting initial therapy clinical symptoms may disappear but fall back of disease in patient is possible after a certain period of time. This recurrent disease condition is termed as relapse.

In human life cycle of *P. falciparum*, all merozoites (stage of parasite) infect RBCs, and the pre-erythrocytic schizogony phase disappears completely after initiation of erythrocytic schizogony. In case of *P.vivax* and *P.ovale*; most of the merozoites infect RBCs but some merozoites (known as macromerozoites) re-enter in the liver again and become dormant. This stage is termed as exo-erythrocytic schizogony. After certain months or even after years, these merozoites change their characteristics and enter the blood stream again, thus leading to relapse of the disease.

Relapse is observed in case of *P.vivax* and *P.ovale* infection only. There is no exo-erythrocytic schizogony stage in *P.falciparum*, so there is no chance of relapse in *P.falciparum* infection.

Importance of specific speciation of malarial parasites

Let us take an example of an individual who is suffering by malarial infection. If he is suffering from falciparum infection, treatment by ACT for 3 days is sufficient for his complete cure. If he is suffering from vivax infection, treatment by chloroquine for 3 days followed by radical treatment with primaquiene for 14 days is required for his complete cure. As we discussed, in vivax infection, a specific stage of parasite (macromerozoite) may survive in the liver even after 3 days of chloroquine therapy and this may lead to relapse after some time. So radical therapy (also known as anti-relapse therapy) is required to eradicate those parasites (or we can say macromerozoites) from liver to prevent relapse of the disease.

If that individual is suffering from mixed infection of falciparum and vivax, he should be given ACT as initial 3 days treatment to take care of both falciparum and vivax infection. But ACT cannot eradicate the macromerozoites of vivax (as we discussed earlier, falciparum does not have macromerozoites stage) from liver; so 14 days of radical treatment also should be given to eradicate the vivax macromerozoites completely from liver and prevent relapse.

As the treatments for *P. falciparum*, *P. vivax* and mixed infection are different, therefore specific differentiation of *P.f.* and *P.v.* is very important for taking a correct decision on therapy. Mixed infection can be identified only by specific speciation of *P.f.* and *P.v.*, either by smear microscopy or by specific rapid antigen tests.

Diagnostic challenge for detection of mixed infection

Efficacy of smear microscopy method is subject to many vital factors; such as time of blood collection, density of parasites, quality of stains used, and also the technical skill of microscopist. Moreover microscopic evidence may be negative in patients with severe infections due to sequestration of parasites and partial treatment. Hence, rapid test for malaria has become the most admired test for prompt diagnosis of malaria

Rapid Tests for the detection of *P.falciparum* specific antigen and pan malaria specific antigen have some limitations.

The test system can detect *P. falciparum* through Pf and Pan band, and other infection (such as *vivax, ovale* and *malariae)* through only Pan band. If the patient's specimen is positive for P.falciparum, in addition to Pf band, the pan malarial band will also appear since pan specific antigen is also secreted by *P. falciparum*. In case of mixed infection cases *P.f.* specific band will be present due falciparum infection and Pan specific band will also appear as pan specific antigen is secreted by all both *P.f.* and *P.v*. Therefore mixed infection of *P.f.* and *P.v.* cannot be identified separately. For identification of mixed infection, smear microscopy has to be done parallely in cases where both Pf and Pan Bands appear, especially in endemic areas.

This diagnostic challenge has been successfully addressed by rapid antigen detection test that can speciate clearly between *P falciparum* & *P.vivax*, (also termed as TRUE SPECIATION). The test can differentiate between mono infection of *P.falciparum* and mixed infection with *P. vivax*. Specific identification of P.f. and *P.v*. and mixed infection helps medical practitioners to prescribe appropriate and complete therapy.

A brief characteristics of Pf / Pan and Pv/ Pf rapid antigen tests is described at below table,

	First generation Pf / Pan rapid test	**Second generation Pv/ Pf rapid test**
Detection capacity	Falciparum & other than falciparum	Falciparum & Vivax (clear cut differentiation)
Signal/ band appearance		
In *P. vivax* infection	Band in Pan marked area	Band in Pv marked area
In *P. falciparum* infection	Band in Pf and Pan marked area	Band in Pf marked area
In Mixed infection of *P.f.* & *P.v.*	Band in Pf and Pan marked area	Band in Pf and Pv marked area
True speciation of Pf & Pv	Not possible	Possible

Treatment of malaria

Artemisinin Combination Therapy (ACT) should be given to all confirmed *P. falciparum* cases found positive by microscopy or Rapid test. This is to be accompanied by single dose primaquine (0.75 mg/kg body weight) on Day 2.

Confirmed *P. vivax* cases should be treated with chloroquine in full therapeutic dose of 25 mg/kg divided over three days. After successful treatment of malarial infection; radical treatment has to be given to eradicate parasite from liver completely, which prevent the relapse.

Mixed infections of *P. vivax* and *P. falciparum* should be treated as falciparum malaria. Anti-relapse treatment or radical treatment with primaquine should be given for 14 days after initial therapy, to prevent relapse of *P. vivax* infection.

Conclusion

From the above discussion it is evident that specific detection of types of malaria (especially *P.f.* & *Pv.*) is essential from treatment point of view. So it is imperative that a rapid test of malaria that can speciate between *P.falciparum* and *P.vivax* (True speciation) should be used for specific detection of parasites and to identify the mixed infection cases. Specific identification of mixed infection cases aids clinicians to initiate prompt and effective treatment to the patients.

References and suggested reading

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