Journal of Bioterrorism & Biodefense

Research Article Open Access

Transmission of Rapid Malaria Test

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Abstract

The biggest cause of disease and mortality worldwide is malaria. Improved control methods and a decrease in morbidity and death would outcomes from a swift and accurate diagnosis of malaria. Objective. This study sought to determine the frequency of malaria in high-risk areas of Egypt and the efficiency of quick diagnostic tests in identifying the disease and subsequently controlling it. Methodology. The current study comprised a total of 600 patients of both sexes with various ages. Cases were divided into two groups: the first group, which consisted of 500 cases, was chosen at random from families in the Fayoum Governorate; the second group, which consisted of 100 cases, had malarial symptoms and had been admitted to the Fayoum Fever Hospital. In-depth case histories, clinical examinations, microscopic examinations of thin and thick blood films, and immunological tests to identify plasmodial antigens were all performed on the cases. Rapid diagnostic tests identified a total of 3 positive cases (RDTs). One of these three instances tested positive for the malaria parasite when blood films were examined under a microscope. All of the study's positive cases had a history of visiting regions where malaria is common. RDTs are easy to use and efficient for diagnosing malaria quickly so that control actions can be implemented in various areas. A very sophisticated approach can be used to effectively treat malaria: The complicated life cycle between mosquitoes as the vectors and vertebrates as the hosts allows for the development of Plasmodium parasites in many stages. A potent medication must be active against the liver, blood, and gametocyte stages of the Plasmodium infection in order to completely and effectively eradicate the parasites. In order to accomplish this, we provide here the design, synthesis methods, and characterisation of new hybrid compounds having combined action against Plasmodium liver stages, blood stages, and gametocytes. Access to variously linked primaquine-chloroquine hybrid templates is made possible by the divergent synthesis technique in as few as eight steps.

Keywords: Parasites; Plasmodium

Introduction

WHO estimates that malaria caused 1.2 million deaths globally. The second most common infectious cause of death in Africa, behind HIV/AIDS, is recognised to be malaria [1]. Given that malaria is mainly preventable and treated, WHO defines malaria control as "reducing the disease burden to a level at which it is no longer a public health hazard." ITNs, indoor residual spraying, first-line medication with an artemisinin combination, and enhanced diagnosis with rapid diagnostic testing are only a few of the many malaria control methods available. Since the overlap of malaria symptoms with those of other tropical diseases, diagnostic specificity is compromised, which might encourage the indiscriminate use of antimalarials and degrade the standard of care provided to patients in endemic areas who have nonmalarial fevers [2]. By combining clinical and parasite-based findings, malaria diagnostic accuracy can be significantly increased. Giemsa-stained blood smears under a microscope are the standard diagnostic tool for diagnosing malaria. The stage of the parasite and parasitaemia are revealed by expert microscopy. However, to maintain a high grade of microscopy, qualified technicians, a steady supply of high-quality staining chemicals, and properly maintained microscopes are all necessary. Since ancient times, Egypt has been plagued by the malady malaria [3]. Prior to the disease's eradication in Egypt, high malarial infection rates seemed to have been restricted to a few regions and were only related to the country's geology. Due to a robust national control programme implemented by the Ministry of Health in collaboration with WHO, Egypt was certified as malaria-free in 2008 [4]. The last focus for malaria was in Fayoum, which has been free of transmission of the disease since 1998. The prevention of reintroduction phase of malaria control is currently underway in Egypt and other countries, according to WHO, where transmission has been stopped. As the ability to control malaria increases, surveillance will be required to locate hotspots of infection that are persistent and isolated regions where control efforts are failing so that appropriate control measures can be implemented when infection is discovered. To do this, clinical data and laboratory diagnostic techniques can be used to support and estimate the burden of malaria [5]. With an estimated 207 million clinical cases and 627,000 fatal cases each year, malaria remains one of the most dangerous infectious illnesses in the world. Because of the pathogen's distinct biological traits and the growing emergence of drug resistance, treating malaria is made more difficult. In a convoluted life cycle including mosquitoes as vectors and vertebrates as hosts, the intracellular and unicellular Plasmodium parasites evolve [6]. Humans contract Plasmodium sporozoites from the bite of anopheles mosquitoes, which are then carried to the liver cells by the circulation. There they grow into preerythrocytic forms and then change into erythrocytes that infect merozoites. Thousands of merozoites that reinfect erythrocytes are released after red corpuscles rupture as a outcomes of the maturation of these merozoites into schizonts [7].

Plasmodium falciparum, which causes more than 90% of all cases of malaria-related death, is the most lethal human pathogenic malarial parasite. Plasmodium vivax and Plasmodium ovale, in contrast to P. falciparum, have a unique trait in that they create hypnozoites. The hypnozoites can be dormant in the liver cells for a few weeks to a number of years until activation outcoming in a relapse without a fresh infectious bite [8]. The surface antigens of Plasmodium parasites

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Received: 09-Sep-2022, Manuscript No: jbtbd-22-74925, **Editor assigned:** 13-Sep-2022, PreQC No: jbtbd-22-74925 (PQ), **Reviewed:** 19-Sep-2022, QC No: jbtbd-22-74925, **Revised:** 23-Sep-2022, Manuscript No: jbtbd-22-74925 (R) **Published:** 29-Sep-2022, DOI: 10.4172/2157-2526.1000310

Citation: Mahejbeen K (2022) Transmission of Rapid Malaria Test. J Bioterr Biodef, 13: 310.

differ significantly at different stages of development, which is another unusual trait. Because of their intricate life cycle, parasites can be thought of as different organisms at each stage even if they all share a single genome. This makes treating malaria more difficult because it needs to be effective at all stages.

In perspective of this, we have described the design, synthesis, and characterisation of novel hybrid molecules made of the well-known antimalarial medications primaquine (1) and chloroquine (2). The most effective hybrid compounds in our research exhibit actions against the liver, blood, and gametocyte stages of Plasmodium, making them possible novel therapeutic templates for the treatment of malaria [9]. The technique of synthesis employs a divergent synthetic approach to variously coupled primaquine-chloroquine hybrid templates, outcoming in a number of compounds based on a single important intermediate. The new hybrids described in this work demonstrated good to exceptional biological activity against liver stages, blood stages, and gametocytes; the activity is superior to that of the parent medications primaquine (1) and chloroquine (2) taken together [10].

Material and Methods

Clients and Techniques [11]

The current study was conducted from March 2014 to December 2014 on a total of 600 cases from Egypt's Fayoum Governorate. Two groups of cases were included in the current study. The first group consisted of 500 cases drawn at random from residents of the villages of Abou Shanab and EL-Khaldia in the Abshoy district of Fayoum. 100 cases from the second group were chosen from those Fayoum Fever Hospital patients who had been admitted and had malaria-like symptoms and signs. A thorough history was taken in all cases, paying particular attention to the use of antimalarial medications and travel to regions with a high malaria incidence. Clinical examinations of the cases were conducted in-depth to look for malaria infection symptoms.

Examination

Blood was applied to the spreader slide's edge and distributed around the surface to create thin blood films. The films were repaired with pure methanol after letting them air dry. When working with thick blood films, a blood spot was agitated in a circular motion with the slide's corner before the slides were allowed to dry naturally without being fixed. The blood films were washed in buffered water after being stained for 20 minutes with diluted Giemsa after they had dried.

Microscopic Examination Standardization

Blood was used to create blood films, especially thick films, and it was placed evenly over a designated region of the slide (15 15 mm for thick films) to ensure high quality staining and standardisation of blood film examination and reporting. Each slide was first screened using low power objectives (10 and 40), and then at least 100 microscopic fields were examined using high power objectives (100). Two microscopists reviewed the slides, while a third expert looked at the suspicious slides [12].

Immune Evaluation

The commercially available malaria pf/pan one-step rapid test [Abon Biopharm (Hangzhou) Co., Ltd., China] was used to test stored blood samples for plasmodial antigens. This test allows for the detection of malaria antigen in blood flowing along a membrane containing specific anti-malaria antibodies and allows for the differentiation of Plasmodium species in blood samples [13]. By injecting 10 L of blood sample into the sample well and three drops of lysis buffer into the buffer well, the test was carried out in accordance with the manufacturer's instructions. The sample well received one whole drop of buffer after five minutes, and the put comes were read fifteen minutes later.

Hybrid Molecule 30 with an Aromatic-Type Linkage: Synthetic Method

Ongoing research on the impact of linkage composition on bioactivity values led to the design and synthesis of a hybrid molecule with a nonbasic, simple aromatic linker moiety. It was found that the distance between the primaquine and chloroquine pharmacophore linkage locations roughly matched the distance in the original hybrid molecule. Although the amount of nitrogen atoms was left unchanged, the formal para-xylene component was expected to increase the lipophilicity beyond that of the actual molecule 5.

Fundamental Data

Prior to usage, every solvent underwent distillation. Without further purification, Sigma-Aldrich employed compounds that were readily available commercially. Use of silica gel 60 or alumina with fluorescent indicator was used for thin layer chromatography. The chemicals could be identified by staining with iodine or ninhydrin, fluorescence quenching at 254 nm, or fluorescence at 356 nm. ICN neutral, basic alumina, deactivated with 15% H2O, deactivated silica gel, and deactivated silica gel were all used in the flash chromatography process. The coupling constants in NMR spectra are presented in ppm relative to internal solvent signal and in Hertz. The NMR spectra were produced using a Bruker DMX 600 instrument. Normal spectral measurements were made at 25 °C. On a Bruker Daltonik micrOTOF-focus, ESI-HRMS measurements were made, whereas EI mass spectrometry was performed on a Finnigan MAT 8200 [14].

Result

The current investigation covered 600 patients in all. In terms of gender, there were 70.7% female cases and 29.3% male cases, with a mean age of 23.7 years (SD: 17.9 years). The average age of the cases in groups 1 and 2 was 23,30 17,7 and 25,89 18,7 years old, respectively. All cases were residents of Egypt's Fayoum Governorate, and 14.8% of them revealed a history of travel to Sudan's El Khartoum.

20.5% of cases in Egypt received antimalarial medications as part of the country's malaria control programme. Chloroquine, Coartem, which contains artemether and lumefantrine, and Larum, which contains mefloquine, were the medications that were administered in 16.7%, 0.3%, and 0.8% of the cases, respectively. Patients were looked into as such and admitted to the Fayoum Fever Hospital for additional treatment. When the patients in the first group were microscopic examined, neither the thin nor the thick blood films had any plasmodial parasite stages. One instance of Plasmodium falciparum in the ring stage was found in the second group after microscopic analysis of a thick blood film. Malaria pf/pan one-step fast test was used to examine blood samples from cases for plasmodial antigens. Although they tested negative for other plasmodial antigens, three cases in the second group of patients had P. falciparum antigen positivity. Males having a history of travel to Sudan's El Khartoum made up the three positive cases. Following their return from Sudan, they received Coartem for 4 weeks. Fever was the predominant clinical presenting symptom in each of them. A compelling target for the creation of novel medications is sporozoites and liver stages. Drug molecules that are effective in the earliest stages would stop or even prevent the development of blood stages, which would then finding in clinical signs. Additionally, the parasites would be completely eliminated by active chemicals against

gametocytes, effectively stopping the transmission cycle. On the other hand, the blood stages are the focus of more than 90% of all ongoing drug development initiatives globally. There isn't a drug on the market right now that works equally well against all Plasmodium species and stages of the life cycle. In 2001, the World Health Organization suggested combining antimalarial medications rather than using a single therapy to improve the treatment of malaria. In the past ten years, the hybrid concept has become more popular. The creation of hybrid molecules from the synthesis of natural product structures and two or more well-known medications led to a rise in their use, and these new structures were especially effective against resistant species. A hybrid medication is superior to a traditional combination therapy because it has a single pharmacokinetic profile that is simple to anticipate and control. Hybrid pharmaceuticals are absorbed, distributed, metabolised, and eliminated at a single rate. Because there is no competition for plasma protein binding as there is with single medications, the danger of drug interactions is lower with hybrid pharmaceuticals.

In a bid to avoid additional structural moieties on the pharmacodynamic and pharmacokinetic aspects of the hybrid drugs, the first dual molecules were produced with an authentic linking portion. Primaquine can be linked via the primary amine without losing any of its action, as evidenced by earlier examples of its derivatives. As a outcomes, primaquine-to-chloroquine pharmacophore ratios of 1:1 and 1:2 were used to synthesise hybrid structures of primaquine and a chloroquine moiety with a linker employing the original side chain of primaquine. Since a Buchwald-Hartwig amination technique only produces insufficient yields, primaquine is substituted nucleophilically.

Discussion

During ancient times, malaria has been known to be a significant source of disease and mortality in Egypt. In two districts in the Fayoum Governorate—Sinnuris and Abshoy—there are still residual foci that are localised. To lessen morbidity and mortality from malaria, a wide range of malaria control strategies have been put into place, including the use of artemisinin combination therapy and enhanced diagnosis utilising quick diagnostic tests. A significant portion of cases (64.7%) in the current study that had fever or a history of fever did not have malaria. Depending on clinical characteristics and acquired immunity associated with transmission, a diagnosis made only on the basis of signs and symptoms may or may not be accurate. Accordingly, the diagnosis of malaria made on the basis of clinical evidence had a relatively poor specificity but a complete sensitivity. The gold standard for laboratory diagnosis continues to be Giemsa-stained thick blood films for screening and thin blood films for species confirmation for microscopic Plasmodium species detection and identification. In our investigation, a thick blood film examination successfully identified one case of Plasmodium falciparum in its ring stage. The predicted sensitivity that may be obtained by using the thick blood film approach is approximately 50 parasites/L of blood, which is comparable to 0.001% of infected RBC. In order to differentiate between cases of falciparum malaria and cases of vivax malaria, rapid diagnostic tests for malaria could help better focus antimalarial medications to real cases of the disease. Both the parasite-specific lactate dehydrogenase produced by all four species and the histidine-rich protein 2 produced exclusively by Plasmodium falciparum are used as the basis for RDTs for malaria. In 3 instances in the current investigation, the malaria one-step fast test pf/pan identified Plasmodium falciparum antigen. The greatest and lowest P. falciparum RDT sensitivity values were 98% and 76%, respectively. PfHRP2 detection tests had good and comparable sensitivity (96%) for the diagnosis of P. falciparum infection. Aldolase-based detection tests on two samples failed to find plasmodial antigen, while one-step malaria pf/pv did. Fever was a common symptom in instances of malaria positivity in the current investigation, and this was consistent with the universal screening symptom for malaria in research studies. The liver's morphology and the overall number of liver-stage parasites were dramatically affected by Hybrid 5, with the number of parasites reduced by a concentration that was significantly lower than that of primaquine needed for the same activity. The size of the liver stages relative to the parasite wildtype and the quantity of liver stages after 24 hours were both affected by the additional hybrid molecules. Comparing amine 13 to amine 14, it was found that amine 13 had a reduced number of liver stages and a larger impact on the growth of the parasite stages with smaller diameters. When compared to 14 with a second C3 linker, the elongated amide 15 marginally reduced the number of liver stages and the parasite growth. In contrast, the amine 16 showed a larger increase in the number of parasites while the diameter did not change considerably. On the action against the quantity and diameter of parasites, the addition of the second elongating linker component as well as the change of the fundamental molecule features of the four examined molecules had very little of an impact. All RDT-positive subjects who had a history of travelling to Sudan were given Coartem as an antimalarial medication. The prevalence of malaria in Sudan is among the highest in Sub-Saharan Africa. The entire population is at danger of infection because the disease is endemic throughout the nation. The endemicity of malaria ranges from hypoendemicity to holoendemicity, via mesoendemicity, hyperendemicity, and hyperendemicity. The frequency of parasites varies greatly amongst the states, ranging from less than 1% to more than 40%, and is higher in rural than in urban areas. Plasmodium falciparum prevalence was revealed by species distinction in positive samples, which is consistent with a high level of Plasmodium.

Conclusion

RDTs were discovered to be straightforward and efficient for the rapid diagnosis of malaria, which may impose the control measures in Egypt against imported malaria, which poses a risk of the disease being reintroduced.We reviewed eleven hybrid primaquine and chloroquine compounds that were produced in eight or fewer steps of the synthesis process and tested for activity against gametocytes, blood stages, and liver stages of the Plasmodium parasite [15]. Finally, we demonstrated that it is feasible to design and create hybrid therapeutic molecules that are effective against various Plasmodium infection stages at good to exceptional levels of bioactivity. In addition, we looked at how three different strains of bacteria affected the maturation of gametocytes as well as how they affected the development of liver stages in hepatocytes. It's vital to note that hybrid compounds frequently deviate from the rules of the separate components' structural activity relationships. The hybrid molecule was the most intriguing structural design of the produced substances.

Acknowledgement

The author would like to acknowledge his Department of Community Medicine, Faculty of Medicine, Iran for their support during this work.

Conflict of Interest

The author has no known conflicts of interested associated with this paper.

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