

Artemisia annua in the Treatment of Malaria, and as Prophylaxis in Case of Travelling to an Endemic Zone; Concerning a Clinical Case

Kamto Fotso C. S.¹, Doumani Metsim L. F.² and Muluh Sandra Menyin³

1. Clinique de Fertilité, HôpitalErasme-Bruxelles, Maternité des Dix Lunes, Centre Hospitalier EpiCURA_Sited'Ath, 7800 Ath, Belgique

2. Université de Mons, Hainaut, Belgium

3. Medicasure

Abstract: Introduction: Artemisia (armoise) is a plant of the Asteracea family with different species all over the world. The *Artemisia annua* species of Chinese origin is known for its medicinal properties, mainly antimalarial. We present the case of a 38-year-old patient who suffered from malaria and was treated with *Artemisia annua*. This plant despite the controversy it creates, proved to be very efficient in the management of the patient from the onset of the symptoms till the recovery, and the patient also used it as a prophylaxis during other travels in an endemic zone. **Objective**: The objective of this study is to present a case of malaria in a patient considered naïve, who was treated with *Artemisia annua*. **Method**: The symptoms and clinical investigations are listed in chronological order of appearance and realization in the patient's consultation book. The tests were done in two different laboratories (one in Africa and the other in Europe), but the interpretation of results are comparable. A reference from the scientific literature on the subject was mentioned. **Results**: The follow-up of this patient showed a progressive subsidization of the symptoms within three days from the onset of symptoms and normalization of the clinico-biological parameters after ten days of treatment at a dose of 4 g of Artemisia leaves in a liter of water daily and consumed as herbal tea. **Conclusion**: The use of *Artemisia annua* as a treatment for malaria in naïve subjects could be effective. Its efficacy and cost-effectiveness need to be investigated in endemic countries, as it may represent an excellent first-line alternative in low-income healthcare systems.

Key words: Artemisia anua, malaria treatment, malaria prophylaxie.

1. Introduction

Artemisia (armoise) is a plant of the Asteracea family with different species all over the world. The *Artemisia annua* species of Chinese origin and *Artemisia afra* which is mainly found in Africa are mostly used for their medicinal properties. Their extracts have reported antimitotic properties [1, 2] and beneficial effects in the management of Buruli ulcers, and other infectious diseases such as tuberculosis, Lyme disease and most recently, Covid-19 [3-5]. They remain nevertheless principally used for their antimalarial effect. If this effect is primarily attributed to its main active ingredient, artemisinin, that derivatives are found in most antimalarials drugs. Other substances in the plant could equally provide in the said effect. Effectively, depending on the culture, the method of preparation and formulation, plants will mainly contain monoterpenes, sesquiterpenes, flavors, sterols coumarins. Monoterpenes and and B-caryophyllene constitute essential oils of the plant. Whilst sesquiterpenes come from artemisinin and its precursor's arteannuin B and artemisinic acid, flavons are artemetin, chrysosplenol D and casticine which are principally responsible for antiplasmodial activity [2].

The principal action of artemisinin is the reduction of peroxyde which leads to the formation of alkaline radicals which react with heme as well as with some parasitic proteins and obstruct the detoxification of

Corresponding author: Kamto Fotso C. S., Medical Doctor, Master in Hospital Management (MD, MHM), research fields: obstetrics, fertility, hospital management, humanitarian medicine. Email: dr.kamtofotso@gmail.com.

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heme, lethal to the parasite [2]. As for the flavons, they speed the action by catalysing the reactions and ameliorating the solubility of artemisinin.

We are presenting to you a clinical case of a naive patient (19 years without a malaria infection) with malaria who used *Artemisia annua* to treat himself.

The patient is a professional in the amateur health field of phytotherapy, who follows scientific literature and the media on the evolution of the use of Artemisia annua. He informs himself notably with the "La association Maison de l'Artemisia" (https://maison-artemisia.org/). Thus, he cultivated in his garden Artemisia annua using the seeds from this association. He harvests the leaves just before the flowering, chops them and dries them in his cellar, away from the sun. Thereafter, he uses a precision scale to make 4 g sachets of these leaves. To prepare his herbal tea, he boils a liter of water, puts off the fire and puts one sachet of 4 grams of Artemisia annua, then allows infusing for ten minutes and filters. He then pours this tea in a thermostatic gourd and consumes it all day.

2. Clinical Case

This is the case of a male patient aged 38 years old, weighing 82 kg and 170 cm tall. He has lived in Europe for 19 years and has never had malaria for these 19 years. Between 2005 and 2018, he has traveled several times to Cameroon for duration two to three weeks. On each trip, he was mainly active in the center, western and littoral regions and took antimalarial prophylaxis.

During a travel to Cameroon in the summer of 2019, the patient did not take any prophylaxis for malaria. On the 20th day of his travel in a malaria-endemic zone, the patient started manifesting symptoms such as joint pains, asthenia and fever (up to 41 °C). He started auto medication with ibuprofen tablets 400 mg, a tablet thrice daily and *Artemisia annua* 4 g in a liter of warm water which the patient drinks for the whole day as an herbal tea. This treatment improved the symptoms temporally for three days. The recrudescence of symptoms prompts the patient to go for a consultation and do some tests.

3. Paraclinic

The patient consults at a clinic in Yaoundé where a malaria microscopy test is done and confirms a high level of trophozoites at 5,257/microliter of blood. The diagnosis of malaria is made. The patient continues to consume his *Artemisia annua* herbal tea (4 g/liter of warm water) and paracetamol 1 g/6 h to control fever and returns to Europe on day 5 of treatment. When he returns, he does a complete blood workup comprising:

• Malaria parasite which was positive at 0.9%

• C-Reactive Protein (CRP) which was positive at 354.2mg/L

• The remaining tests unremarkable, mainly renal function (urea, creatinine, uric acid and Serum electrolytes), hepatic transaminases, infectious serology (Hepatitis B and C, HIV, Syphilis), fasting blood glucose, and urine culture.

The patient continued his treatment and from day 7, the fever subsided, and control tests were carried out at day 10, still under treatment. CRP was still positive but reduced to 44.87 mg/L, and a Malaria parasite test negative. The symptoms disappeared and the patient was clinically well.

Two weeks after the treatment, a final control showed a negative malaria parasite, PCR to search for genetic material of the parasite was positive and CRP negative at 6.96 mg/L (normal value < 10 mg/L) (Table 1).

Table 1 Biological evolution.

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|------------------|-------------------------------|-------------|--------------|----------|
| Day of treatment | Malaria parasite | CRP | Parasite PCR | RDT |
| Day 3 | 5,257trophozoites/ul of blood | Not done | Not done | Not done |
| Day 5 | Positive at 0.9% | 354.21 mg/L | Positive | Not done |
| Day 7 | Positive at 0.1% | 127.35 mg/L | Not done | Not done |
| Day 10 | Negative | 44.87 mg/L | Positive | Not done |
| Day 16 | Not done | 6.92 mg/L | Positive | Not done |

4. Discussion

In several studies notably that of Munyangi et al in 2019 which showed that the consumption of Artemisia annua in herbal tea form was effective in the treatment of malaria compared to treatment with ASAQ (Artesunate-Amodiaquine) [6]. The studies of Mueller et al in 2004, Blanke et al in 2008, Zime Diawara et al in 2015 and Daddy et al in 2017 equally showed efficacy in the use of Artemisia annua in herbal tea form in the curative treatment of malaria in infected patients [7-10]. This is the same as the clinical and biological observations made by our patient throughout his illness. Effectively on the 7th day of his treatment with Artemisia annua herbal tea, we noticed an improvement in the clinical symptoms of the patient and the results of his tests. As the treatment continued until the symptoms disappeared, the situation improved.

Also we noticed that the patient used *Artemisia annua* 4 g sachets infused in a liter of warm water to obtain favorable results after 7 days of treatment. This is similar to different studies such as Blanke et al and Mueller et al who infused 5 g of *Artemisia annua* diluted in water for 7 days and obtained favorable results on the parasitemia and symptoms of the patient [9, 10].

The use of this treatment by the patient for prophylaxis is also interesting because looking at the data given by this patient; he didn't have malaria when he was taking *Artemisia annua* for prevention. This observation is similar to the study by Ogwang et al in 2021 on 132 subjects in Uganda who showed a weekly consumption of *Artemisia annua* herbal tea at a dose of 5 g diluted in 250 ml of warm water, reduced the risk of contracting malaria by 55% in 9 months compared to the control group [11].

However, the use of *Artemisia annua* as a preventive method was contradicted by the results of studies by Lagarce et al in 2016 and Argemi et al in 2019 that showed a failure in malaria prophylaxis with

the consumption of *Artemisia annua* by the patients in their cohort [12, 13].

In fact, the study of Argemi et al in 2019 is a retrospective study which includes 12 patients with imported malaria (5 severe) of *Plasmodium falciparum* while returning from Africa and hospitalized between 2016 and 2019. Argemi consuming *Artemisia annua* in different forms either tea (73% of patients), capsules (13% of patients), syrups (7% of patients) and 7% of patients without prophylaxis. During their hospitalization, they all received a curative treatment conforming with the French recommendations (artesunate injections) which led to recovery in 100% despite the development of a complication in one of the patients.

The second study contradicting the preventive effects of Artemisia annua was written by Lagarce et al in 2016. Indeed, it is a retrospective study which reports two cases of severe malaria by P. falciparum in two French women who traveled to Sub-Saharan Africa. The two young women declared to have taken Artemisia annua for prevention against malaria during their stay and after their return to France before their hospitalization. The first patient, 17 years old traveled to Benin during which she took an Artemisia-based prophylaxis. Eight days after her return to France, she presented with a high-grade fever (40 °C), headache, joint and muscle pains and digestive troubles. Following a medical opinion, she started her treatment with A. annua then was hospitalized urgently in an intensive care unit for severe malaria (parasitemia at 12.5%) where she was treated with quinine intravenously then Atovaquone-Proguanil. No mention of the year or the form of medication (tea, capsule) of Artemisia used. The second case also concerns a young woman of 18 years who was in Togo. Alongside a prescription with Atovaquone-Proguanil which we don't know if she took well, she bought through the internet some capsules of Artemisia annua. She took the latter during her stay in Togo and five days after returning

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to France. Three days after stopping them, she presented with asthenia, digestive troubles, and then fever four days later. The parasitemia with *P. falciparum* was estimated at 0.34%. She was prescribed quinine, but since she was indebted at her usual pharmacy, she continued her treatment with *Artemisia annua* capsules. The patient was later taken to the hospital in hypotension (60/34 mmHg). She received a unique dose of quinine IV before being treated with artesunate IV for 4 days then by artemether-lumefantrine until her recovery.

The contradictions with the observations of our case can be explained. Firstly, the data observed during these studies were incomplete and partial, not permitting a global analysis on the efficacy of Artemisia annua. In these two studies, it is not mentioned anywhere the duration of Artemisia consumption, the dose, the compliance to treatment by the patients. Also, the quality of information gotten from the consumption of Artemisia notably in the study by Lagarce et al, comes from the words of the patients and are not reliable. We also question ourselves on the pertinence of the second case of this study, for we note the fact that the patient took another antimalarial treatment without being sure of her compliance to the treatment. More so, the patients in these studies were not well informed on the subject. In our clinical case, the patient is trained medical personnel and well informed on Artemisia. He carried out his investigations himself and his own measures to evaluate if the plant was effective. The involvement of the patient can be at the same time a bias, with relation to his preference to phytotherapy! Hence, the need to carry out further research on the subject.

Despite the interesting observations of this clinical case, it reveals some limitations remarkably the fact that we can't affirm that the treatment will be effective in the management of severe malaria. Actually, other studies carried out showed the efficacy of *Artemisia annua* in the management of simple

malaria. It will be more interesting to investigate the efficacy of *Artemisia annua* in the management of severe malaria clearly. Though our patient was naive and presented with clinical features (hyperthermia at 41°C) which could let one think its server malaria, but it wasn't, for he didn't present with other symptoms of severity which is necessary to make this diagnosis.

Concerning the usage of *Artemisia annua* as prophylaxis of malaria, we have to remain prudent for the are few studies which have explored this aspect and so the conclusions permit one to formally say this plant protects against malaria. Also, the two studies which affirm are inefficiency as prophylaxis for malaria is based on partial and incomplete information. Therefore, it is necessary to explore the true preventive potential of *Artemisia annua*.

5. Conclusions

This clinical case brings new perspectives despite contradictory opinions on the use of *Artemisia annua*. On one side, we have authors who affirm that *Artemisia annua* is a plant with multiple virtues among which are its anticancer and antimalarial effects, and on the other side, we have authors who affirm that its antimalarial effects are much reduced. It springs from this case that *Artemisia annua* can be used in herbal tea form as a curative means for naive travelers who travel into endemic zones for malaria and who contract malaria during their stay, which had already been demonstrated by this described study. *Artemisia annua* could be used as a preventive measure taking into account the patient's observation.

We can say it will be interesting to further studies in order to broaden especially the preventive aspect of *Artemisia annua* on malaria, in order to validate the observation of this patient in our clinical case. Very limited studies approach this aspect.

Also, its affordability (cost compared to other treatments) has to be studied for it could be an excellent alternative for low-income countries.

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Disclosures

Medicasure is consultant for the company Pat and Win, which markets herbal teas and the author, is co-founder of the company Medicasure.

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