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https://doi.org/10.22239/2317-269X.01254

Factors that influence blood replacement of mosquitos of medical importance: a bibliographical survey

Fatores que influenciam no repasto sanguíneo de mosquitos de importância médica: um levantamento bibliográfico

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Received: Jan 03, 2019
Approved: Jun 28, 2019

ABSTRACT

Introduction: Mosquitoes belonging to the Culicidae family gather arbovirus vectors and cause great annoyance to human populations, due to hematophagous habits of females and transmission of diseases such as dengue, yellow fever, zika, chikungunya and malaria. **Objective:** To analyze, through a bibliographical survey, the factors involved in blood preference by mosquitoes, in addition to the main studies that discuss this theme. **Method:** The survey was carried out in the PubMed, Google Academic and SciELO databases, in the Portuguese, English and Spanish languages, selecting articles published between the years 2004 and 2018, which brought together the oldest study, up to the most current one found in the searches on the topic. **Results:** Of the analyzed studies, 13 articles that presented a relation with the theme were selected. In these studies, it has been shown that in different parts of the world, the main factors responsible for blood preference are odor, genetic factors, ABO system, availability of hosts in the area and the pheromone produced by females that attracts other individuals to the site. **Conclusions:** The existence of different factors influencing the preference of mosquitoes for human blood is a fact, and despite this, the subject still needs more conclusive analysis. Thus, knowledge of the factors involved may be used mainly in the prevention of mosquito-borne diseases.

KEYWORDS: Culicidae; Blood; Preference; Prevention

RESUMO

Introdução: Os mosquitos pertencentes à família Culicidae reúnem espécies vetoras de arbovírus e causam grande incômodo às populações humanas, devido aos hábitos hematófagos das fêmeas e à transmissão de doenças como dengue, febre amarela, zika, chikungunya e malária. **Objetivo:** Analisar, por meio de um levantamento bibliográfico, os fatores envolvidos na preferência sanguínea por parte dos mosquitos, além dos principais estudos que discutem esta temática. **Método:** O levantamento foi realizado nos bancos de dados PubMed, Google Acadêmico e SciELO, nos idiomas português, inglês e espanhol, selecionando artigos publicados entre os anos de 2004 a 2018, período que reuniu o estudo mais antigo até o mais atual encontrado nas buscas sobre o tema. **Resultados:** Dos estudos analisados, 13 artigos que apresentaram relação com o tema foram selecionados. Neles foi demonstrado que, em diferentes partes do mundo, os principais fatores responsáveis pela preferência sanguínea são: o odor, os fatores genéticos, o sistema ABO, a disponibilidade de hospedeiros no local e o feromônio produzido pelas fêmeas que atrai outros indivíduos ao sítio. **Conclusões:** A existência de diferentes fatores que influenciam na preferência dos mosquitos por sangue humano é um fato e, apesar disso, o tema ainda carece de análises mais conclusivas. Assim, o conhecimento dos fatores envolvidos poderá ser utilizado principalmente na prevenção de doenças transmitidas por mosquitos.

PALAVRAS-CHAVE: Culicidae; Sangue; Preferência; Prevenção

INTRODUCTION

Mosquitoes of the *Diptera* order and *Culicidae* family, commonly known in Brazil as *muriçocas* or *pernilongos*, are among the most important arthropod groups for public health, since they are vector species of arboviruses and cause great discomfort to people due to the haematophagous habits of the females[1,2]. These animals are found in tropical and subtropical regions and predominate in urban and semi-urban areas. They came from Africa and were probably introduced in the American continent shortly after its "discovery"[1,3].

The first three species were described in the mid-eighteenth century and some general knowledge of their biological cycle was also known. For many years, the only known nuisance caused by these insects was their bite. However, in the last decades of the nineteenth century, the role of mosquitoes acting as disease vectors was discovered. Since then, scientists have been studying the biology and systematics of these animals in detail to discover their most vulnerable points and fight them effectively. Today, there are more than 3,000 described mosquito species, although the biology and control forms of a large portion of them are still unknown[4].

The *Aedes*, *Anopheles* and *Culex* genera are very important in medicine because of their role in the cycle of several human and animal diseases, like dengue, yellow fever, zika, chikungunya and malaria. These diseases are transmitted by the females and cause clinical conditions with various degrees of complexity[2]. Only the females are hematophagous. They feed on blood before reproducing to ensure the development and fertility of eggs and their own survival. Males, however, do not have mouthparts adapted to puncturing or consuming blood. Their diet is restricted to plant sap[1,2,5].

According to the World Health Organization (WHO), the diseases transmitted by these vectors represent 17% of the estimated global burden of all infectious diseases, especially malaria and dengue, that today are endemic in more than a hundred countries in the Americas, Africa, Pacific Islands, Asia and the Mediterranean[3,6].

Regarding the relationship between different mosquito species and the forms of transmission, studies conducted in different parts of the world analyzed the factors that interfere in mosquito blood preference at the time of the bite[7,8]. These studies have shown that genetic factors such as odor, ABO blood group system and onsite host availability stand out[9,10]. Although some studies described these factors as influencers, little is known about them because research on this subject is scarce and the results are inconclusive. Thus, this study analyzed the main papers that address this topic and the factors involved in the blood preference of mosquitoes of medical importance through bibliographic survey.

METHODS

Study type

This study is a literature review of the main factors that affect mosquito blood preference. We performed it in specialized scientific databases.

Data collection

We selected the papers from the following electronic databases: PubMed, Google Scholar and Scientific Electronic Library Online (SciELO). The studies were published from 2004 to 2018, that were the publication dates of the oldest and newest studies found during the searches. We performed the following steps sequentially: proposal identification; search for studies on the subject; evaluation of the papers regarding their inclusion or not in the review; and analysis of the results found, considering the factors related to possible blood preferences.

Regarding the inclusion criteria, we considered the publications in English, Portuguese and Spanish submitted from 2004 to 2018 that analyzed the main factors of mosquito blood preferences, demographic regions and ethnicity of people affected by the female haematophagous habit.

We excluded thesis, dissertations and papers that did not fit with the proposed topic. For the introduction of the paper and its enrichment, we included the general characteristics of the mosquitoes of medical importance and the main diseases transmitted by these vectors. After searching and analyzing the subject, we selected 13 papers.

RESULTS AND DISCUSSION

After thorough research about the topic in the databases, we selected and analyzed 13 papers. Among them, we did not find any papers that used keywords in Portuguese. In this language, we found only a few studies that addressed the feeding behaviors of mosquitoes in relation to other animal species, and also about the diseases possibly transmitted by them. We did not find any papers or dissertations in Spanish, unlike English, that was the language of all the papers selected for this study. We found five papers in PubMed[7,8,10,11,12] and seven in Google Scholar[13,14,15,16,17,18,19], as shown in tables 1 and 2.

The largest production of papers about the subject occurred between 2004 and 2018 and from 2010 to 2014, three in each year, followed by 2004, when two papers were published. During the other years, only one paper was published, except 2018, when we did not find any studies, as shown in the chart.

There are few studies in the literature regarding the possible mosquito blood preferences and the mechanisms that make them choose a host. However, authors from different countries did experimental studies to investigate these questions.

Influence of blood typing on host choice

In vivo studies conducted in Japan[7] and Iran[12] using *Aedes albopictus*, *Anopheles gambiae* and *Anopheles stephensi* raised some hypotheses to support the idea that blood typing influences

Table 1. Papers found at PubMed.

Keywords	Title	Author	Preference factor
"Blood preference of mosquitoes"	*Landing preference of Aedes albopictus (Diptera: Culicidae) on human skin among ABO blood groups, secretors or nonsecretors, and ABH antigens*	Shirai et al., 2004[7]	Blood typing
	Blood-feeding behavior of Anopheles gambiae and Anopheles melas in Ghana, Western Africa	Tuno et al., 2010[11]	Onsite Host Availability
	Host preferences of blood-feeding mosquitoes	Takken, Verhulst, 2013[10]	Genetic Factors
	ABO blood groups of residents and the ABO host choice of malaria vectors in southern Iran	Anjomruz et al., 2014[12]	Blood typing
"ABO system and mosquito preference"	*Preferential feeding success of laboratory reared Anopheles stephensi mosquitoes according to ABO blood group status*	Anjomruzet al., 2014	Blood typing and odor

Table 2. Papers found on Google Scholar.

Keywords	Title	Author	Preference factor
"Blood preference of mosquitoes"	*No accounting for taste: host preference in malaria vectors*	Besansky et al., 2004[13]	Genetic Factors
	Vector host-feeding preferences drive transmission of multi-host pathogens: West Nile virus as a model system	Simpson et al., 2012[14]	Onsite host availability and heterogeneity
	Notes on blood-feeding behavior of Aedes albopictus (Diptera: Culicidae) in Cameroon	Kamgang et al. 2012[15]	Odor
	Evolution of mosquito preference for humans linked to an odorant receptor	McBride et al., 2014[16]	Odor
	Divergent host preferences of above-and-below-ground Culex pipiens mosquitoes and their hybrid offspring	Fritz et al., 2015[17]	Genetic Factors
"ABO system and mosquito preference"	*Blood feeding patterns of mosquitoes: random or structured?*	Chaves et al., 2010[18]	Onsite Host Availability
	Attraction of Culex mosquitoes to aldehydes from human emanations	Leal et al., 2017[19]	Odor

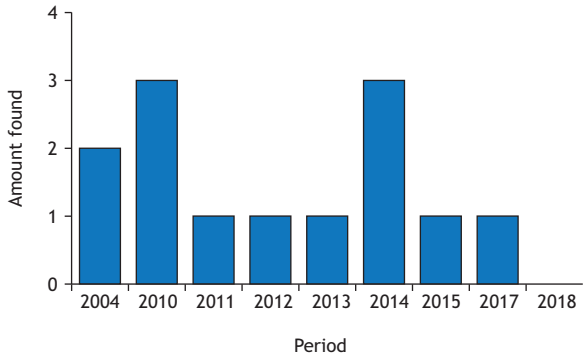

Chart 1. Papers found in indexing databases from 2004 to 2018.

mosquito host choice, since, according to the authors, these insects showed some preference for some of them.

In these studies, after *Aedes albopictus* and *Anopheles gambiae* preferred O-type blood individuals over other types, the researchers described that this choice possibly happened because: 1) of the mosquito attraction to these individuals due to the disaccharide that is present in the O blood group (antigen H). However, the researchers also highlighted that the observations and data collected after the experiment did not explain the preference for O-type blood, and that there may be other unknown influences underlying blood preferences. They also believe that there are ABH antigens in human skin at low concentrations that are imperceptible to mosquitoes; 2) *A. gambiae* geographical distribution is restricted to Africa, a region where O-type blood is highly prevalent, thus inducing mosquitoes to interact more with this blood type and, consequently, prefer it. However, this hypothesis would not explain the preference of the *A. albopictus* species, which comes from Asia, where there is a higher prevalence of A-type blood in the population, not O-type blood[7,10].

In contrast to the results found about the species cited above, another in vivo study conducted with *A. stephensi* showed that these mosquitoes prefer AB-type blood. To try to explain that, the authors cited a theory developed by other researchers that says that mosquito behavior is mediated by semiochemicals and that possibly the first females who came into contact with AB-type blood individuals produced an aggregation pheromone that attracted other mosquitoes to that same host. So perhaps the mosquitoes prefer not the type itself but the pheromone that attracted them to that same site[8]. Another study that presented results different from those previously mentioned described that *Culex quinquefasciatus* prefers blood of other vertebrates, not necessarily humans, such as the *Galliformes*, which were the preferred animals by the mosquitoes according to the study[20].

Genetic factors associated with blood preferences

Still in an attempt to explain the possible factors involved in mosquito blood preferences, some authors raised the hypothesis that human genetic factors are involved in this process[10].

The most commonly raised hypotheses for explaining blood preferences involve the: 1) mosquito eyesight, that allows them to successfully explore their surroundings. Their color perception, however, is poor and unlikely to play a role in host preference and choice. For this reason, the hypothesis that there is a preference for a particular race, color or ethnicity was rejected[21]; 2) mammalian and poultry body heat, that is a result of their metabolic activity. Scientists, however, do not know whether the differences in body heat affect blood preference in situations of choice. Nevertheless, body heat creates convection currents that affect the dispersion of the semiochemicals and, thus, the host searching behavior[22,23]; 3) individual body mass, that may also affect blood preference because one can assume that a larger host leaves more olfactory cues like, for example, metabolic carbon dioxide, that is associated with body size and, consequently, mosquito attraction[24,25]; 4) gender, because odors differ between men and women and between people of the same gender[26,27]; 5) effectiveness of the immune system. Studies performed with healthy and malaria infected mice have shown that animals without the disease were bitten significantly less frequently due to their good immune response. Thus, individuals with a good immune system are less bitten and, as a result, may be less likely to contract diseases[28,29].

Influence of odor on blood preferences

Olfaction is the main way through which mosquitoes detect a host[30,31]. Olfactory receptors located on the antennae, maxillary palp and lip[32,33,34] are tuned to respond to the specific odors released by the host[9], mainly carbon dioxide[35].

Different studies highlighted odor as the main method for choosing the ideal host because it serves as a guide to reach the individual, since the preference for humans may be closely related to the increase in both expression and sensitivity to the Or4 odorant receptor ligand present in mosquitoes. These changes can help mosquitoes distinguish humans from nonhuman animals and increase behavioral sensitivity at the time of choice due to a substance called sulcatone, that we secrete through skin and that characterizes us as humans to these animals. However, sulcatone is unlikely to be the only odorant that differentiates us from other animals[16].

Host availability associated with blood preference

According to Tuno et al.[11] and Simpson et al.[14], the availability of a certain host is closely related to the preference at the time of choice. Not only the availability, but also the heterogeneity and the direct contact between hosts and mosquitoes may play a role in blood preferences because, according to the authors, if a mosquito species lives in an environment where there are more humans than other vertebrates, the mosquito blood preference will be the host that is most abundant there, in this case, humans. However, if this situation changes and another animal species becomes more abundant, the mosquito blood preference will also change to that species because it is now the most abundant one in that place.

CONCLUSIONS

Genetic factors, odor, host availability and the pheromone produced by females that attract other individuals to the site are incentives for the mosquito to prefer one host over another. So far, blood typing seems to have no influence on preference, which does not exclude the need for further studies. Therefore, in vitro tests should be performed using only the individual blood, so that the odor does not interfere with the mosquito choice. The literature lacks more detailed descriptions of the methodologies used in the studies. So, for better analysis, it is important to include detailed information about gender, body mass, presence or absence of hair in the organ analyzed and the use of perfumes by the participating individuals. The existence of different factors that influence mosquito human blood preferences is a fact, however, this topic still needs more conclusive analysis that could be used to prevent diseases transmitted by these vectors.

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Conflict of Interest

Authors have no potential conflict of interest to declare, related to this study's political or financial peers and institutions.