View Point: Ethical dilemmas in malaria vector research in Africa: Making the difficult choice between mosquito, science and humans.

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Abstract

Malaria vector studies are a very important aspect of malaria research as they assist researchers to learn more about the malaria vector. Research programmes in various African countries include studies that assess various methods of preventing malaria transmission including controlling the malaria vector. Various institutions have also established mosquito colonies that are maintained by staff from the institutions. Malaria vector research presents several dilemmas relating to the various ways in which humans are used in the malaria vector research enterprise. A review of the past and present practices reveals much about the prevailing attitudes and assumptions with regard to the ethical conduct of research involving humans. The focus on the science of malaria vector research has led some researchers in African institutions to engage in questionable practices which reveal the ethical tensions inherent in the choice between science and the principles of justice, nonmaleficence and respect for individuals. The analysis of past and present choices in malaria vector research has relevance to broader questions of human dignity and are in line with the current emphasis on ethical research worldwide.

Introduction

Malaria research continues to be a top priority across Africa since malaria continues to be one of the major killer diseases. Despite the current knowledge on how to treat and prevent malaria, it still accounts for approximately one and half million deaths every year across Africa[1]. In the fight against malaria, vector studies are an important aspect of the malaria research agenda as they assist researchers to learn more about the malaria vector. Through vector studies conducted in the past, it is now known that certain mosquito species are responsible for malaria transmission[2]. Current malaria vector research is therefore aimed at further understanding these species while some is aimed at controlling them. Various institutions conducting research on malaria, maintain mosquito colonies as part of research programmes. Mosquitos from these colonies are used in different types of vector studies including those that are aimed at understanding the biology of the vectors, to that aimed at studying feeding patterns and behaviors, to those aimed at exterminating the vectors. Vector studies employ humans in different ways. In some studies, humans are used in learning more about the vectors, whilst in some studies humans are used for catching the vectors. In institutions that maintain colonies of the vectors, humans play the very important role of maintaining these colonies. This paper discusses ethical dilemmas and unethical practices in malaria vector research in Africa. It critically looks at how human beings have been involved as participants (subjects or volunteers) in malaria vector studies. The paper also critically looks at the role of research staff in malaria vector studies.

Materials and Methods

Interest in the ethics of malaria vector research was motivated by concerns raised by some junior staff working in malaria research during research oversight site visits to some African institutions engaged in malaria vector research. Consequently, focus group discussions were held with malaria researchers and research staff during a series of Research Ethics training workshops held in various African countries by AMANET Trust between 2007-2009. During these focus group discussions, participants were requested to describe and discuss practices in their own institutions. Subsequently, observations were made by the authors during visits to malaria research institutions in various African countries that were conducted as part of Research Ethics capacity building efforts. During these visits, authors interacted with malaria researchers and staff to learn more about how the malaria vector studies were conducted and how mosquito colonies were established and maintained in those institutions. During these visits, authors also observed and noted the facilities that were used for malaria vector research. Literature on alternative methods and best practices in malaria vector research and mosquito colony maintenance was reviewed.

Results and Discussion

In order to learn more about the mosquitos that spread malaria, it is necessary to catch some of the mosquitoes. Human landing catch (HLC) method is the gold standard in malaria research as it allows the researchers to catch the malaria transmitting culprit in the act. This method allows researchers to get more facts on the mosquito feeding habits and patterns. Consequently, it leads to better understanding of the problem mosquito and yet it involves sacrificing humans as bait to attract the malaria transmitting adult mosquitoes. The collection of malaria vectors by human landing-biting catches therefore has numerous direct ethical implications. Over the years alternative vector collection methods have been developed including light traps, double nets, Mbita traps, odour-baited traps, animal baiting and other methods which do not expose "human bait" [3-5]. Unfortunately studies comparing HLC and other methods conducted in Kenya, Senegal, Tanzania have reflected the superiority of the HLC method over the other methods.[6-10] These findings, place malaria researchers in an awkward position.

It is an obvious fact that the mosquitoes that are captured using the HLC method, may transmit pathogens to collectors. Many people serving as human baits may be repeatedly infected by malaria and receive treatment. This reality raises the question of drug resistance; What role have vector studies contributed towards the development of drug resistance in Africa? The bites may lead to pain, damage to skin, swelling and other problems. Questions also need to be asked concerning who serves as bait in these studies. Very often, it is the junior employees at the research sites who play this role while the principal investigators and other researchers who would have written the protocols will be resting in their comfortable homes.

In one particular study, 236 human-night outdoor mosquito captures in three villages yielded 13,536 mosquitoes. Human bite rates (HBRs) of up to 75.8 bites per human per night were recorded during this study. In the same study 72 human-night indoor captures in three villages yielded 6,013 mosquitoes. Indoor HBRs were 84.9 and 82.1 bites per human per night in traditional housing and modern housing, respectively. Outdoor HBR was 141.8 bites per human per night[11]. In this study, the researchers report that landing

catches were performed outdoors from 18:30-06:30hrs by 2 teams of adults "legally" employed by the institute and working in pairs. The first team was working from 18:30-00:30hrs while the second team was working from 00:30-06:30hrs. In this study, it was reported that the collectors were local residents that had already been exposed to the circulating plasmodium parasites. They were supervised during the captures by technical and/or scientific staff.

The above study raises various questions; Does working for an institution mean that one can be used in risky research activities? By being outside during the night, the staff are at the risk of snake bites and other threats. Does pre-exposure to the circulating plasmodium parasites make one resistant to malaria? Are scientists adopting new methods of catching mosquitos? Are current publications based on the new methods? Why are some scientists not adopting the new methods? Are scientists working on new methods? It is evident that HLC while being the best method leads to various ethical challenges relating to the principles of justice and nonmaleficence. In studies that involve catching of the vectors in households, families and individuals staying near research centres are often the volunteers for such and as a result end up bearing all burdens. For such families and individuals, besides the issue of inconvenience (having someone catching mosquitos in your bedroom while you are sleeping), there are also issues of privacy, confidentiality.

In some cases, research proposals that deal with HLC are not reviewed by research ethics committees as researchers try their best to bypass research ethics committees. Where they are reviewed by ethics committees, they may not go through stringent review due to various reasons including lack of knowledge on the part of the research ethics committee members. During discussions on the review of malaria vector studies by Research Ethics Committees (RECs), a staff member from an institution conducting malaria vector research, cited the case of one proposal using human landing catches. During review, the REC asked about the protection and treatment of the people involved as human baits. The researchers responded that they were going to follow the WHO guidelines on the ethical treatment of humans serving as bait in malaria vector research. The proposal was approved and subsequently other proposals which relied on the non-existent WHO guidelines were approved.

Very often, malaria research institutions breed mosquitoes for research. Some of the mosquitos may be infected while some may not be. It is also possible that uninfected mosquitoes can be infected during feeding if an infected individual is used in the feeding. For such programmes, there is need to pose questions relating to the safety of the facilities; Are facilities leak proof? What measures have been put in place to ensure that there is no leakage? Are staff protected? Regarding feeding - How are the mosquitoes fed? Who is involved in feeding them? In some institutions, mosquitoes were fed by junior staff employed by the institutions. Such institutions also did not allow the use of any kind of insecticide to control any other pests due to fears that the pesticide could affect the breeding colonies in some way. Hence one could find corridors that were infested with mosquitos and other insects – in the interest of protecting the research colonies.

In looking at practices in various institutions in Africa, raw questions had to be asked including whether principal investigators were involved in HLC and human feeding? One PI responded that she fed the mosquitoes when she was studying for her PhD. Implying that she had to do it because there was no way for her to earn the PhD. We asked; Are researchers taking advantage of the least educated in their institutions by using them as bait and feed for mosquitos? Is serving as bait and feeding of mosquitos written in their job descriptions? The answer was – in any contract, there is the "Any other duty" phrase which means that an employee can be assigned to any other duty. We asked; Is it acceptable to use general staff as feed and bait? If one works for an institution does it mean they can be used for any risky activities? If one is from the study area does that make him appropriate for baiting? Is there any other way around this "exploitation"? We ask; In order to avoid this problem, why not consider what is done in phase I trials where healthy volunteers are paid more for participating in high risk studied?

Due to some research conducted by other scientists, now there are some alternative feeding methods that can be used in feeding research colonies. One of the methods is the membrane feeder using human blood that is obtained from the transfusion services. The other method is animal feeding using animals such as hamsters. For this method, the animal is shaved on the parts that are going to be exposed for mosquito feeding. The animal is then anaesthetized and placed on top of the cage so that the mosquitos can feed through a net. While this method ensures that humans are not used for feeding, it may create problems with animal welfare groups who may feel that animals are being handled in a cruel manner. In some institutions, the researchers just fasten the shaved animal to the cage without anesthetics. Importantly, where animals are used in research, institutions need to set up animal care and use committees that look into the welfare and use of animals. Such institutions also have to work closely and keep their doors open for organisations that oppose animal cruelty. That way, society and animal lovers can be assured that animals are being used in appropriate ways.

At a particular laboratory we met a junior staff member who reported that he intended to take legal action against his institution because of damage to his skin. He had fed mosquitoes for several years. Feeding mosquitoes was part of his duties. His title was Lab Assistant. Was he being paid to feed them using his own blood? At another institution, staff raised some concerns about whether mosquitoes are capable of transmitting HIV from an infected person to an uninfected person. At that institution, the mosquitos were being fed by different staff members depending on who was on duty. Research staff were concerned that some of their colleagues had been infected by HIV due to human feeding and landing catches. Where they getting the HIV from the mosquitoes? It is known that mosquitoes can transmit some viruses. HIV is supposedly not able to survive inside the body of the mosquito[12-14]. However some cockroaches and ticks have already been implicated in the spread of HIV.

In studies that deal with GMO mosquitoes, there are also many ethical questions. The GMO mosquitos that have been labeled flying syringes by some as they are expected to kill the other natural mosquitos, are not yet fully understood. There are various questions including; What if we end up creating another problem that we are going to fail to eradicate? What if the natural mosquito develops supressors to the gene? What other diseases may the GMO mosquitos be capable of transmitting? What if we end up failing to control

them? What are the effects to the environment? What are their possible interactions and mutations with the existing ecosystem? How far will these mosquitoes travel? How does one select the site for trials? [15-17] All these questions relate to fear of the unknown.

From the side of the research ethics committees, the researchers have to be prepared to face another barrage of questions. How are you going to ensure that GMO mosquitoes will not escape? What will you do if some GMOs do escape? How will you tell the modified mosquitoes from wild ones? Have the authorities responsible for GMO policy in each country been involved? If they fail to answer any of these useful questions, the ethics committees may not be prepared to approve the research. Related to the issue of informed consent for GMO mosquito trials, researchers also have to think about cluster mobilization. In field experiments with GMO mosquitoes how will one get assent from the community at the test site? Do they also need to obtain the assent of the neighbouring communities? What about the neighbouring districts? What about the neighbouring countries? Is there any room for individual informed consent since the mosquitos will be released within the community? What about those who raise objections to the release of the mosquitos in their community? Is there a right to withdraw for individuals or for communities or countries? There is need to convince the public and other stakeholders before initiation of any research involving GMO mosquitos and any plan to release GMO mosquitoes would have to include meaningful local involvement through culturally sensitive communication and education.

Dilemmas in malaria research have extended to other areas. A case in point is the use of DDT which pits humans against the environment. Malaria treatment & prevention research also presents unique challenges. It is now a requirement that a proven standard should be provided as an alternative method to the study community[18,19]. Provision of the proven method may alter the dynamics of the disease and confuse the interpretation of the data. An example could be a study testing a new malaria drug. In that study insectide treated nets (ITNs) and education have to be provided to the control group. One can then ask; Is research ethics interfering with science? The researchers who conducted the early ITN trials "fortunately" did not go through these "ethical" requirements as they were not required to compare the new intervention (ITNs) with existing strategiesthat are known to be effective, e.g., residual spraying.[20]

Conclusion

From the above, it is evident that malaria vector researchers in African institutions face numerous ethical dilemmas and they have to make difficult choices in their research. These choices reveal much about attitudes and assumptions with regard to research involving human beings. The analysis of past and present choices has relevance to broader questions of human rights as it allows society to reflect on the past, as part of the current emphasis on ethical research worldwide. Malaria vector researchers have to consider the ethical dilemmas they face and come up with appropriate answers. Vector studies need due caution. With more and more research scandals being reported, research in general has become a sensitive field. Mistakes will cost researchers and institutions and even the whole malaria research community. The principles of respect for persons, beneficence, nonmaleficence and justice need to continuously guide research. Certainly where one has to make a choice between science, mosquito and human being, the answer has to be an obvious one since all vector research has ultimately to benefit humankind. The agenda of trust (trust by staff, individuals and communities) has to be maintained.

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