ISSN: 2573-9565

Review Article

Journal of Clinical Review & Case Reports

Trypansoma Cruzi Integrated Vector Management in Latin America

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Submitted: 15 July 2018; **Accepted**: 30 July 2018; **Published**: 06 Aug 2018

Introduction

The protozoan parasite Trypansoma Cruzi causes Chagas Disease in humans, which is known to be a disease of the Americas. Chagas Disease primarily affects rural and poor regions of Latin America [1]. Chagas Disease is a zoonotic disease with an interesting life cycle and is spread to humans via reduviid otherwise known as kissing bugs or triatomines [1]. This bug gets its name by taking its blood meal from a human host near the mouth and then releasing the parasite in its feces by the bite. The bites are typically painless but the parasite is further tunneled into the bite when the host scratches the area of the bite. Initially the patient could be asymptomatic; however ten to twenty years later he or she may develop symptoms that can be severe such as mega colon, dilated cardiomyopathy, and mega esophagus [1]. There is no treatment for chronic Chagas Disease; however this disease is extremely preventable making it a topic of public health interest and action [1].

The World Health Organization reports that 8 to10 million people are infected with Chagas Disease worldwide and 10,000 people die from the disease every year [2]. It is estimated that over 300,000 people are infected with Chagas in the United States while 30,000 to 45,000 have undiagnosed Chagas cardiomyopathy [3]. Most of the individuals with Chagas Disease reside in Latin America where it is considered endemic; however Chagas is still being seen in developed countries due to immigration patterns [3].

The economic burden and cost of Chagas disease is considered greater than many other diseases such as cervical cancer and rotaviruses [3]. Chagas disease tends to lead to early mortality and disability in young adults who tend to be the most economically productive population [3]. Cost of long term treatment for individuals who begin to have cardiac complications is high and not effective when the disease has progressed, whereas early diagnosis and treatment or prevention is more effective. Early diagnosis can prove to be very difficult since most are asymptomatic and serology screening can be laborious and difficult to achieve in the remote areas where Chagas Disease is highly prevalent [4].

Research shows that insecticides can be very effective in mitigating Chagas Disease; however there are still many setbacks. It has been reported that the population most effected by Chagas Disease is poor and rural South America, and there are special challenges they face [5]. One of which being the quality of their housing being susceptible to reduviid. This population also tends to have more interaction with domestic or per domestic animals that could also be reservoirs for T. Cruzi. Thus, despite insecticide use indoors this population is still severely at risk for contracting Chagas Disease [6].

Goals and Objectives

This paper aims to investigate various integrated vector management program approaches encompassing vector control, education, treatment, screening for seroprevalence, housing, and wildlife reservoirs. This paper also aims to point out the gaps in information as well as the latest developments in relation to Chagas Disease in hopes of providing a platform to help better tailor a gold standard for vector management where the burden is highest.

Methods

First, the CDC website was used to find basic information about the protozoan parasite and methods of disease transmission for background and understanding. Next, keywords such as "Chagas Disease", "Trypansoma cruzi and vector control" were used in databases such as EBSCO, PubMed, and Google Scholar to find peer reviewed articles for more background and general insight on what types of article titles were relevant. Next, keywords such as "Chagas disease treatment", "Chagas disease in rural Latin America" and "Chagas disease burden of disease" were utilized. Once the setting and burden of disease was identified "Chagas Disease serology screening" was the next keyword search on the EBSCO database to find information on screening and new tests being done to replace serology as the key diagnostic factor. Lastly, a search on "vector management Chagas" was done and following what was learned through that a search on "Rhodococus rhodnii genetic modification" was done to target the latest research in genetic engineering in relation to the triatomine bug. Articles were selected on the basis of how relevance and importance to creating a gold standard vector management program, and also how current the information was based on publication date of the articles.

Analysis

Findings

The burden of Chagas Disease lies disproportionately heavy on Latin America. Figure one depicts the regions heavily affected by Chagas Disease in red and orange. These countries include Mexico, Panama, Peru, Bolivia, Peru, Ecuador, Argentina, Colombia, and Venezuela to list a few (PANHO, figure 1). The primary risk factors tend to be living in these countries in rural areas and poverty. Poor housing conditions related to poverty is major risk factors due to structures

such as mud walls and thatched roofs [1]. The poor tend to live in rural areas with poor housing conditions, have closer contact with animals, live in homes that bugs can easily enter, and do not use mosquito nets all increasing their odds of infection.

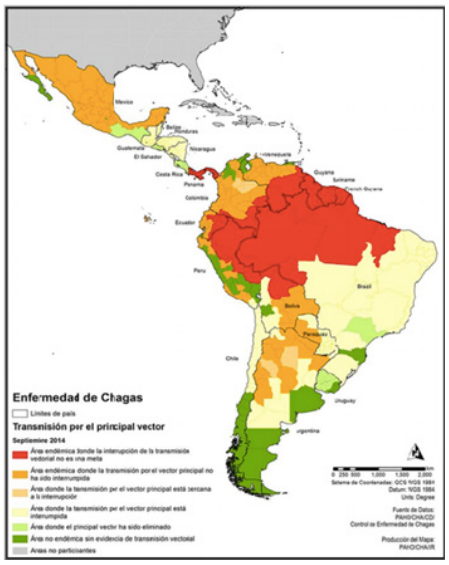

Figure 1: Chagas Disease Vector Transmission (2014)

Another significant risk factor is the role of close contact with peridomestic animals, such as dogs, cats, sheep, and pigs that individuals in rural Latin America are susceptible to [6]. These animals may harbor the triatomines on them allowing the bug closer access to the human via animal contact. If the animals such as dogs can roam freely in and out of the home it can make the use of insecticides and mosquito nets in the home obsolete [6].

Serology screening is a helpful tool in mitigating the disease burden of Chagas disease. An individual may be infected with Chagas disease and be asymptomatic for decades, however the treatment options for Chagas disease are not nearly as effective the longer a person is infected with the parasite. Regular serology screening in regions with known high burden of disease would help eliminate chronic Chagas disease by allowing cases to be diagnosed earlier, thus having a much better prognosis [7]. However, serology screening requires equipment and trained personnel accessing remote areas where Chagas is most prevalent, which can be a time consuming and expensive process [8]. A rapid screening test would be ideal in these areas to cut costs and increase access in remote regions. In Bolivia where seroprevalence is especially high the National Chagas Program diagnosis guideline is that a rapid test must be confirmed by serology or ELISA in order to begin treatment, which means multiple visits to a health center by the patient delaying efficiency and access of proper diagnosis to many who are at high risk [4].

Genetically modified insects have been a very popular field of research in regard to vector transmitted diseases. In regard to the triatomine bug, researchers have been targeting genetic engineering of symbionts, or the gut bacteria of the insect, to be lethal to the parasite T. Cruzi since the early 2000's [9]. Research and testing is still being done on Rhodococcus rhodnii, the triatomine's resident symbiont bacterium of the gut [10]. Since the early 2000's the goal has been to use the genetically modified R. rhodnii to export cecropin A, an active immune peptide against T. cruzi, to eliminate the parasite from the triatomine bug [10].

Advances

Insecticide usage within the home in rural Latin America is on the rise with united efforts from Latin American countries to educate and prevent Chagas Disease. This is an effective and important way to prevent contact with bugs harboring the parasite, but individuals are still very much at risk to Chagas infection [3]. Many of those living in rural Latin America have farms and peridomestic animals such as dog or sheep that they come in contact with on a daily basis creating another avenue for infection [6]. A study was done in hopes of combating this problem by treating dogs with insecticides to prevent them from infection so that the dogs could not transmit the parasite to their owner [6].

The study comprised of a trial with a sample of 12 dogs split up into three groups. Each group consisted of three dogs treated with a specific insecticide and one untreated dog to determine if insecticides in general are successful in killing triatomines and if a particular insecticide was more superior to another [6]. The study was successful in showing that the dogs treated with insecticides, specifically Bravecto, knocked out more of the triatomine bugs thus having less of an opportunity to be infected with T. Cruzi [6]. The use of insecticides on peridomestic animals in conjunction to home insecticide usage and mosquito nets could be a more effective prevention campaign specifically targeting those in rural Latin America.

Screening for Chagas disease is done through serology which can be laborious and expensive [4]. A study published this year aims to eliminate this barrier to screening by using two different rapid tests together instead of serology in order to diagnose Chagas and begin treatment immediately [4]. The two rapid tests selected in the study allow for "diagnosis of whole blood samples, generate results within an hour, not require instrumentation for results readout, have long shelf life at room temperature, and be based on distinct sets of parasite antigens," making it a very realistic and effective option for screening in rural Latin America [4].

In this study, a group of 342 patients in Bolivia were selected to participate ranging from 1 to 59 years old. In this double-blind trial blood samples were taken via fingertip puncture and venous extraction for the two rapid tests, Chagas Stat-Pak (CST) and Chagas Detect plus (CDP), and conventional serology [7]. The results from this, as seen in figure 2, show that both rapid tests and the conventional serology all yielded the same results, making a strong case for the usage of rapid tests CDP and CST as a diagnostic tool to begin treatment over serology for screening in rural Latin America [7].

CST and/or CDP	Conventional serological tests		
	Positive	Negative	Total
Positive	208	1	209
Negative	0	133	133
Total	208	134	342

Figure 2: Rapid diagnostic tests duo as alternative to conventional serological assays for conclusive Chagas disease diagnosis (2017)

The research and trials being done for genetically modifying the gut microbiota of the triatomine bug against T. Cruzi have been promising [9]. Many of the trials show success of the bug's symbiont forming cecropin A and clearing the parasite from the insect [10]. There is still much research to be done on ensuring that the change in the triatomine's gut symbiont will not have any severe adverse effects on its natural environment and ecosystem.

Challenges

Ensuring a collaborative system of education and access to insecticides both to people and their homes and their peridomestic animals can be costly and difficult [6]. It would take many public health professionals and volunteers to regularly go into these areas to ensure they have adequate supplies to keep the insects out of their homes and away from their animals. The information that we have regarding the use of insecticides on peridomestic animals comes from a study with a very small sample size of just dogs that was not blinded [6]. It would be helpful to have more studies done on the effectiveness of insecticides on a variety of peridomestic animals before implementing this as commonplace in an integrated vector management program.

Egüez's study showed very promising results of duo rapid tests having the credibility to be used as a confirmatory Chagas disease diagnosis on their own without serological confirmation. This would provide faster results and a greater range of access which is positive; however there are some drawbacks as well. The rapid tests are more expensive than the conventional serology, running from $4 to $7 USD while the cost of a conventional serological test is merely $1 [7]. Overall, T. Cruzi has high genetic and antigenic diversity that makes it challenging to confirm at times even in conventional serology [8]. Rapid tests can target distinct strains, however the strains of T. Cruzi vary geographically, thus making it necessary to first validate seroprevalence in specific areas to ensure that the rapid tests have a high sensitivity and specificity [7]. There is also the issue of T. cruzi's overall high genetic and antigenic diversity that makes it challenging to confirm at times even in conventional serology [8]. More extensive research into specific seroprevalences will be necessary in order to have the information needed to develop a standard regarding rapid tests in various regions throughout Latin America.

The primary challenge facing the real-life application of genetic modification of the symbiont R. rhodnii is the threat of horizontal gene transfer to other organisms in its environment [10]. This technology has proven to have little risk associated with horizontal gene transfer in the laboratory setting, but needs much more additional research under field conditions [10]. This research can be very costly, time consuming, and is only the first step towards implementation. After the proper research has been done a comprehensive risk assessment must be passed, and then extensive and precise planning must be done before this technology can be implemented in a vector management program [10].

Conclusion

Solutions

Latin America has been battling Chagas disease with prevention and vector control via insecticides and mosquito nets with success, however there is still a high burden of disease indicating that more can be done to reach optimal success. This paper aims to show avenues of research that may help enhance the ongoing effort to minimize the burden of disease in rural Latin America. Insecticide treatment of peridomestic animals in conjunction to domestic insecticides and mosquito nets could enhance current prevention protocol [6]. Vector management programs should consider more research into this avenue with a bigger sample sizes and a variety in animals before potentially implementing.

Another major hurdle vector management programs encounter is surveillance of Chagas due to the silent nature of disease progression. Screening has proven to be difficult to do in rural Latin America because of the time, labor, expense, and access of serological surveillance in these remote areas. Egüez's study shows that rapid tests can be just as effective in diagnosing Chagas as conventional serology without the burden of complicated equipment and personnel being transported in remote areas [7]. More research would have to be done to replicate Egüez's study and specific seroprevelances would have to be identified in varying geographical locations before implementing. A single rapid test is more expensive than the serological alternative; however it would minimize the cost of transporting equipment and trained personnel which could be of equal or greater cost in total [7]. Chagas disease is very expensive on the individual patient's level when it becomes chronic as well as its economic burden in a society (Nunes, 2013). Chronic Chagas disease costs a society productive work in young people as well as the expense to treat them, thus an effective and accessible screening system should be the integral point of development for a vector management program to mitigate these adverse effects [3].

Implications

A successful integrated vector management program will prevent further Chagas disease cases through education, insecticide and mosquito net usage. It will also allow for screening which can help prevent any current cases of T. Cruzi infections from progressing to chronic and having severe effects such as dilated cardiomyopathy [1]. This will increase the health status of these regions and allow for the burden of disease to be lowered.

Significance

Chagas Disease can have a very detrimental impact on an individual's quality of life, yet it is extremely preventable. An integrative approach in vector management focusing on surveillance development can greatly impact the quality of life of so many individuals in rural Latin America. This in turn could allow these individuals to have a higher quality of life, be higher functioning members of their society and country's economy [3]. Having a strong surveillance and screening system in place will also help avoid accidental infection through blood transfusions and vertical transmission [3].

Recommendations

Current vector management programs have focused primarily on prevention through the use of insecticides and mosquito nets domestically, which has shown success however the burden of disease is still very high especially in rural Latin America. Development of a strong surveillance system of Chagas disease will help manage the burden of disease. Regular screening for Chagas in rural Latin America will ensure that patients can receive effective treatment and avoid progression to chronic Chagas disease [7]. National initiatives to fight Chagas disease would benefit most by teaming with researchers on creating rapid tests that are effective and relevant to specific strains and geographical regions to serve as a primary diagnostic factor [7]. Next, the vector management

team should continue to monitor and work with researchers on the latest developments on genetically modifying the triatomine gut symbiont R. rhodnii in the hopes of ridding the parasite from these bugs in the natural environment all together [10]. Lastly, the vector management team can focus on more research into the usage of insecticides on peridomestic animals to further strengthen their prevention efforts. A combination of a strong prevention initiative and an accessible screening system would greatly impact the burden of disease experienced by rural Latin America.

In order to create an integrated vector management program a very cohesive team needs to be put in place to address all aspects of the program. The team needs to have a collaborative approach including public health workers, physicians, veterinarians, scientists and members of the affected communities. This will allow a better tailored approach for each community when members of the community are involved and can give input on how education and resources can be best accessible to the people. Physicians will be important in consulting the individuals of the communities before and after their screenings to let them know how they can be treated or what they can do to better their current health status or state of infection. Veterinarians will be important in targeting how best to keep peridomestic animals triatomine free thus preventing the spread of Chagas disease. Scientists will be important in continuing efforts towards genetically modifying triatomine to impair it from ever harboring the parasite T. Cruzi. Each component of the vector management program will depend on the other in order to truly be effective in the battle against Chagas disease [11].

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