Opinion article

Changes in the paradigm of clinical and therapeutic management of Chagas' disease: progress and perspectives in the pursuit of comprehensive health

doi: 10.5123/S1679-49742016000500003

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The epidemiological profile of Chagas' disease in Brazil has changed considerably due to great results of control actions, besides environment and socioeconomic changes that have been happening in the country.[1] The traditional scenario of domestic vectorial transmission, which has been the main transmission form since the disease discovery, and has been responsible for thousands of annual cases has changed, and nowadays, the sylvatic transmission of the parasite, mainly orally is concentrated in the Amazon region, and is responsible for about 150 new cases/year.[2,3]

The prevalence of infection by the *Trypanosoma cruzi*, which is a marker of the control, together with low domestic triatomine infestation, was estimated in more than 5% for children in endemic areas during the 1960s, and was reduced to less than 2% in the 1990s. The findings of the last national survey, conducted in 2008, showed that, nowadays, this prevalence is below 0.1%.[4]

Besides the progress in the control, we can also mention the change in the traditional profile of the disease as a consequence of the rural-urban migratory movements that occurred in the Latin America in the 1970s and 1980s. In a first moment, the urbanization of the disease increased the infection prevalence through blood transfusion.[5] Since this is a relevant problem, in the context of transfusion-transmitted infections – especially the Human Immunodeficiency Virus (HIV) from 1980 on –, this transmission form started to be controlled.[6]

However, even with the great impact of the prevention and control activities adopted under the national policies, it is estimated that about one million people live with the *T. cruzi* infection in Brazil, which shows the chronic condition of this disease.[7] Between 2009 and 2013, 23,568 deaths whose underlying cause was the Chagas' disease were registered.[8] This mortality rate demands coordination efforts of the health surveillance, with multisectoral involvement, especially focused on the participation of the primary health care services of the Brazilian National Health System (*SUS*).

These efforts involve the decision making processes, which are based on scientific evidence. The challenges for its achievement are the control or elimination of neglected diseases. For instance, despite of the increasing global investments on health, we still notice the inequality of financial resources directed to the neglected diseases.[9]

In Brazil, the State role is indispensible to overcome this gap and to give priority and fund researches on neglected diseases and conditions. With regard to Chagas' disease, the National Council of Scientific and

Technological Development (*CNPq*) of the Ministry of Science, Technology and Innovation (*MCTI*) and the Ministry of Health (*MS*), through the Department of Science and Technology of the Secretariat of Science, Technology and Strategic Inputs (*Decit/SCTIE/MS*) published public notices for researches on neglected diseases and, more recently, a specific notice for Chagas' disease.

The role of national and international institutions is noteworthy. They have been conducting clinical trials of new components for treating Chagas' disease, seeking a better profile of security and efficacy than the current treatment, and evaluating its association with other drugs.[10]

In 2015, the results of a multicenter randomized controlled trial named BENEFIT showed that, in patients with heart disease, the clinical deterioration did not present great reduction with the use of Benznidazole, although there was reduction in the parasite detection, evaluated by polymerase chain reaction (PCR). That study also revealed regional differences in the therapeutic response and tolerance to the drug used.[11] With regard to the clinical benefits, the results go against other studies and the experience from other countries that strongly recommend the etiological treatment as a procedure capable of (i) minimizing or slowing down the progression of the disease in cases of indeterminate form and those with the absence of advanced heart disease,[12-14] besides (ii) reducing the odds of congenital transmission when infected women are treated before the pregnancy.[15,16]

Therefore, it is clear that the inclusion and exclusion criteria in the antiparasitic therapy must be revised, taking into account the scientific evidence available and the indication accuracy. Concerning the current situation of the disease, especially in Latin America, we are at risk of losing the timely opportunity of treating millions of infected people that fit into the undetermined form or even in the clinical initial forms.

In this context, we can see how important a Clinical Protocol and Therapeutic Guidelines of Chagas' disease (*PCDT*) can be. This protocol is of responsibility of the Ministry of Health that conducts a periodic update and revision of the national guidelines for diagnosis, treatment and monitoring of individuals infected and their different stages and clinical forms. The Ministry of Health has been working on this protocol, aiming at ensuring that the national guidelines cover all the health services and help managers, professionals and users of *SUS* in accomplishing its principle.

The same way, the revision and update of the Brazilian Consensus on Chagas' disease[17] is necessary and well-timed, because it can match the continuous scientific progress, and also answer to the challenge of the eco-epidemiological and social scenarios of this disease in the country.

The Brazilian Consensus on Chagas' disease, published in 2005, was formulated by the academic community together with *SUS* institutions, and changed the way Chagas' disease was seen in Brazil, summarizing it in three big groups: the (i) need of keeping the surveillance in areas of domestic transmission control; the (ii) emergency of transmission forms related to the sylvatic cycle, especially the oral transmission, which is not easily covered by the traditional control strategies; and the (iii) care for individuals with chronic infection.

It has been highlighted that the treatment of people infected by the *T. cruzi* cannot be restricted to specific and symptomatic pharmacotherapy; they must receive comprehensive care, regardless of the clinical form.

The Decree No. 7,508, dated 28 June, 2011 treats about *SUS* organization and health care. It also advocates that, to ensure its comprehensive health, the services must be organized in the form of a Health Care Network (*RAS*), characterized by the proposition of horizontal relations among the health care services, the centrality of the population's health needs and the accountability for the continuous quality, responsible and humanized care.[18,19]

From the basic and operational concepts, essential to the organization process of the Health Care Network, the Ministry of Health has prepared some guidelines for the assistance of individuals with chronic diseases, with priority care lines[20] for the most prevalent diseases/risk factors: heart and kidney diseases; diabetes; obesity; respiratory diseases; and cancers (breast and cervical).

Although these diseases and conditions are non-communicable, the guidelines also apply to Chagas' disease, because its chronic characteristics – despite its clinical specificity –, are mainly related to heart and stomach diseases. Moreover, the World Health Organization (WHO) brought a new and more comprehensive contribution to the definition of the chronic conditions, when considering that when the communicable diseases become chronic, this distinction between 'communicable' and

'non-communicable' is artificial and unnecessary, and may not be as useful as the terms 'acute' and 'chronic' to describe the specter of the health problems.[21]

The health care of individual with Chagas' disease in the Brazilian National Health System demands the development of a wide services network that, once it is geographically distributed, according to the endemic areas, it can provide primary health care, in various clinical modalities of the infection. At the same time, Public Health interventions [22] must be developed by involving multidisciplinary teams, not only for antiparasitic therapy, but also to promote the improvement on life quality, considering the psychosocial aspects and all the stigma related to this disease.

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