CHAGAS DISEASE: IMMUNOADSORPTION STRATEGY

Prof. Dr. Jorge Yanovsky

American tripanosomiasis, also known as Chagas diseases, is one of the most important endemic diseases in the Americas, with over 15,000,000 people infected with Tripanosoma cruzi (T. cruzi) parasite. Approximately 30% of chagasic patients develop some sort of cardiomyopathy, with different evolutions in terms of lesions and clinical symptoms. These cardiac alterations may lead to an acute arrhythmia, which causes sudden death, or progressive cardiac failure[1-2]

An important amount of evidence has been accumulated over the last two decades showing similarities among cardiomyopathies, regardless of their etiology. Indeed, it has been shown that people affected with dilated cardiomyopathy, as well as many people suffering chagasic cardiomyopathy, present IgG antibodies that react against adrenergic or muscarinic receptors, eliciting agonist-like effects. Thus, these antibodies have immunopharmacological activity.[3-4]

The experimental reproduction of dilated cardiomyopathy in rats immunized with peptides corresponding to the second loop of the β1-adrenergic receptor, and the ability of sera from immunized rats to elicit the same effect in normal rats by passive transference, clearly indicates that antibodies against the β1-adrenergic receptor are responsible for the development of experimental dilated cardiomypathy.[5]

Along the same line, it has been shown that during experimental infection with T. cruzi, infected mice develop antibodies that react both against β1-adrenergic as well as M2-muscarinic receptors. These autoantibodies can be absorbed by peptides representing the second loop of each receptor and their pharmacological activity can be blocked, or their production limited respectively, by the systemic administration during infection of the peptide representing the second loop of the M2-muscarinic or receptor β-blockers (such as atenolol)[6-7-8]

The presence of antibodies against β1-adrenergic and M2-muscarinic receptors has been well documented in humans infected with T. cruzi. The pharmacological evaluation of the above antibodies using isolated rat heart shows a simultaneous adrenergic and muscarinic agonist-like activity. This agonist-like activity is enhanced when an antagonist is added to the system to verify the remaining agonist-like function. The same behavior is shown by sera that have been immunoadsorbed against an affinity column containing peptides resembling the second loop of each receptor.[9]

The development of an ELISA reagent, highly specific and prepared using industrial norms, which is based on a selected antigen resembling the M2 muscarinic receptor that

is capable of inhibiting the agonist-like muscarinic activity of chagasic sera (Chagacor Laboratorio Lemos), is allowing the evaluation of a high number of people infected with T.cruzi. This approach has allowed us to verify that approximately 30% (from 2.000) chagasic patients have positive serologic antimuscarinic reactivity. The same result is found among infected individuals from different Latin American countries, from Mexico to Argentina.[10] The frequency of the antimuscarinic activity increases up to 80% when individuals infected with T. cruzi also show disautonomic clinical manifestations and growth up to 95% among subjects for whom electrocardiographic repolarization studies have been conducted and show a QT dispersion of more than 65 miliseconds.[11-12] The last observation is quite significant given that a tight association between sudden death and an increment in QT dispersion has been recently reported.[13]

The hemodynamic improvements that have been observed after immunoadsorption in people with dilated idiopatic miocardyopathy, suggest that antibodies against neurotransmitter receptors play a significant role in the development of the disease. The above is likely to be the result, as is the case with the chronic adrenergic stimulation, of a perturbation in the synchrony of contraction of miocytes, with the following impact on systolic function.[14-15]

The effect immunoadsorption has not been studied so far in T. cruzi infected individuals. The observation of the presence of antibodies against β1-adrenergic and M2-muscarinic receptors in this disease, together with their likely association with sudden death, suggest that the immunoadsorption of circulating autoantibodies against neurotransmitter receptors may have a strong positive effect on chagasic patients with cardiac alterations. Therefore, the evaluation of this approach is really important both for academic purposes (i.e. increasing our knowledge of the origin of cardiac problems in a disease like chagas, whose etiology is well documented), but also for the development of a therapeutic solution much more accessible operatively and economically than the installation of cardiac defibrilattors, or cardiac transplants.

To achieve the above aim, we are organizing a working group of cardiologists, as well as hemotherapy centers, that will coordinate and conduct immunoadsorptions with Protein A, as well as a detail follow up of the patients.

Jorge F. Yanovsky
President
Polychaco SAIC
Center for Research and Development

of Biotech Strategies

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