EVIDENCE-BASED CONTROL STRATEGIES TOWARDS ELIMINATION OF SCHISTOSOMIASIS IN THE PHILIPPINES

Remigio M. Olveda, MD

Member, National Academy of Science and Technology Philippines (NAST PHL) Former Director, Research Institute for Tropical Medicine, Department of Health

Summary

In the Philippines, schistosomiasis due to *Schistosoma japonicum* remains a public health problem in many areas affecting 12 million people in 28 endemic provinces. To interrupt schistosomiasis transmission in the country, interventions should target three parasite pathways of transmission. These are the pathway from humans (definitive host) to snails (intermediate host), pathway from animals (definitive animal host) to snails and the pathway from snails to humans and animals. For more than 35 years, control measure for schistosomiasis in the country has been directed only to the schistosome pathway from humans to snails using community-based chemotherapy with the drug praziquantel. Despite the findings that bovines, carabaos in particular, play a significant role in the transmission of the disease, the pathway of transmission from bovines to snails has not been adequately addressed. Control of disease transmission from snail intermediate host was implemented but this measure has been found to be very expensive and difficult to sustain.

The recommended policy actions include the following: (1) Continue mass drug administration (MDA) in humans with the drug praziquantel covering 85% of the people in endemic communities and replacing animals with mechanized tractors; (2) annual MDA in humans (85% coverage) and annual treatment of bovines (carabao and cattle) (85% coverage) in endemic areas where mechanized rice farming cannot be carried out; and (3) Combined MDA in humans (85% coverage) and vaccination of bovines (carabao and cattle) (85% coverage) with anti-schistosome transmission vaccine. This shall be accompanied by continuous health education on behavioral changes and improved sanitation for each of the recommended actions.

NAST PHL SCIENCE ADVISORY 2020-01

Published by the National Academy of Science and Technology, Philippines (NAST PHL). A contribution from the Health Sciences Division of NAST PHL.

NAST PHL is the country's premier advisory and recognition body on science and technology. NAST PHL is an attached agency to the Department of Science and Technology.

Introduction

Schistosomiasis japonica, caused by the parasite called Schistosoma japonicum, remains a major health problem in the Philippines. Approximately 12 million people, residing in 28 endemic provinces, are at risk of infection (Figure 1) (1-3).

Infection of humans with this parasite can lead to serious disease affecting the liver, lungs, and brain. The disease can also cause growth retardation, anemia, and poor cognitive functions in children and can induce poor outcomes in infected pregnant women. Infected individuals can die from rupture of blood vessels in the upper portion of the gastrointestinal tract (Figure 2) (4-10).

There are two major pathways in the transmission of *S. japonicum* infection in the Philippines: the parasite's pathway from humans or bovines (definitive hosts) to snails (intermediate hosts) and the pathway from snails to humans/bovines (Figure 3) (*11*). Control measures for schistosomiasis in the Philippines have been directed mainly at the schistosome pathway from humans to snails

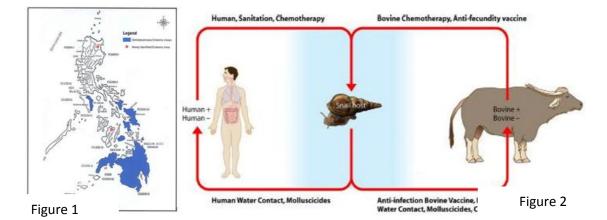


Figure 1. Map of the current Schistosomiasis-endemic areas in the Philippines highlighted in blue. Schistosomiasis is endemic in 12 regions and in 28 provinces with an estimated 28 million people at risk of infection. The red dots represent new foci of infection (*3*).



Figure 2. Transmission pathways and various control measures in schistosomiasis (11).

Figure 3. Hepatosplenic form of Schistosomiasis japonica in children and adult.

using community-based chemotherapy with praziquantel (PZQ). Other control measures like health education, behavioral modification, improved sanitation, and snail control cannot be sustained (12).

After more than three decades of community-based chemotherapy, significant reduction in schistosome-induced morbidities was demonstrated but disease transmission remains uninterrupted. Clinically apparent and subtle morbidities persist in many endemic zones. Innovative control measures are needed if schistosomiasis elimination in the Philippines is the goal (12).

RECOMMENDED POLICY ACTIONS

 Continue mass drug administration (MDA) in humans with the drug praziquantel (PZQ) (85% coverage) plus removal of carabaos from endemic areas and replacing these animals with mechanized tractors.
Yearly treatment of cattle with PZQ. Continue health education on behavioral modification and improved sanitation.

2. In endemic areas where mechanized rice farming cannot be carried out, continue MDA in humans (85% coverage), annual treatment of 85% of the bovines (carabao and cattle), and behavioral modification and improved sanitation.

3. In endemic areas where mechanized rice farming cannot be carried out and yearly treatment of bovines cannot be sustained, the long-term solution is combined MDA in humans and vaccination of bovines with anti-schistosome transmission vaccine.

Pros and Cons of the Policy Actions

1. The first action has been found to be highly effective in China as demonstrated in the study that curing and removal of water buffalos from endemic areas immediately resulted in a profound reduction in the transmission of *S. japonicum* to humans by 75 to 95%.

However, this control approach would be a costly endeavor for the Philippines because rice farming is the major source of income in endemic areas and carabaos are extensively used for tilling and other rice farming activities. This action will also require a comprehensive and more effective phase of disease control and will require incremental expense, but this would ultimately be offset by the greater health benefits achieved with complete elimination of parasite transmission and alleviation of poverty in the endemic areas.

For example, mechanized rice farming is being implemented in a pilot scale by a private company in the town of Alang-Alang, a schistosomiasis endemic village in the Leyte province. Mechanized farming in this endemic area increased the income of 2000 farmers involved in the project up to ten times compared to their income when they were using the traditional rice farming method. In this endemic area, carabaos are no longer a major contributor to *S. japonicum* transmission.

On the other hand, the local government unit (LGU) of the municipality of Javiar (another schistosomiasis endemic area in Leyte) has expressed its willingness to start mechanized farming to help eliminate schistosomiasis in their endemic villages. With strong government support, this strategy will not only dramatically reduce transmission of S. *japonicum* infection but will also alleviate poverty in schistosomiasis endemic zones in the country.

2. The second option is feasible for implementation. Bovine treatment with PZQ has been accepted by animal owners in schistosomiasis endemic areas. The

Department of Agriculture (DA) has also conveyed its willingness to treat bovines with PZQ. However, treating bovines will impose additional budget for DA. One tablet of PZQ costs PhP25.00. Humans will require an average of six tablets while bovines will need 35 tables. The huge manpower requirements to implement the action will be a challenge to DA.

3. The third approach will be the long-term solution. By mathematical modeling, this option can result into sustainable control. However, it is difficult to predict when this control approach can be used in schistosomiasis-endemic zones. During the last 35 years, only three promising transmission blocking anti-schistosome vaccines have reached field trials in carabaos in endemic areas in the Philippines. Continuing support for vaccine development against schistosomiasis is needed. Two promising transmission blocking anti-schistosome vaccines have been tested in carabaos in endemic areas in the Philippines. They are the triose-phosphate isomerase (SjCTPI), a DNA primed vaccine fused with heat-shock protein 70, and the full length recombinant paramyosin (rSj87) (13-14).

Only SjCTPI reached a phase III clinical trial in the field. A five-year phase III cluster randomized control trial was conducted among 18 schistosomiasis endemic barangay comprising 18,221 residents in Northern Samar, Philippines. The impact of a combination of human mass chemotherapy, snail control through mollusciciding, and SjCTPI bovine vaccination on the human incidence of infection was determined. Snail mollusciciding and human mass treatment on their own had no statistically significant impact on the human incidence of infection. However, when bovine vaccination was combined with human mass treatment, there was a significant drop in the human incidence across all follow-ups. This is the first trial to successfully demonstrate the impact of a bovine transmission blocking vaccine on reducing the human incidence of infection. However, additional studies are needed for this bovine vaccine to become part of a future integrated control strategy for the elimination of schistosomiasis in the Philippines (15).

Conclusion

A multi-component integrated approach towards the control of S. japonicum transmission in the Philippines is critical for its long-term sustainable control and eventual elimination. Key to such an approach is ensuring high praziquantel coverage in endemic populations and targeting of bovines (carabao) through their removal and replacement with mechanized tractors and yearly treatment of cattle with the anti-schistosome drug. When anti-schistosome transmission vaccines for bovines become available, the long term control measure towards elimination of schistosomiasis in endemic areas in the Philippines will be treatment of humans, removal of carabaos and replacing these animals by machines, and vaccination of cattle.

Acknowledgments:

The author thanks the National Academy of Science and Technology (NAST) Philippines for providing a fellowship grant that supported the formulation and writing of the policy brief towards elimination of schistosomiasis in the country on which this Science Advisory is based.

References:

- 1. Santos AT. The present status of schistosomiasis in the Philippines. Southeast Asian J Trop MedPublic Health 1984;15:439-45.
- 2. Blas BL, Rosales MI, Lipayon IL, Yasuraoka K, Matsuda H, Hayashi M. The schistosomiasis problem in the Philippines: a review. Parasitol Int 2004;53:127-34.
- Leonardo L, Rivera P, Saniel O, Antonio Solon J, Chigusa Y, Villacorte E, Christoper Chua J, Moendeg K, Manalo D, Crisostomo B, Sunico L, Boldero N, Payne L, Hernandez L, Velayudhan R. New endemic foci of schistosomiasis infections in the Philippines. Acta Trop 2015;141, Part B:354-60.
- 4. Olveda R, Icatlo Jr F, Domingo E. Clinical aspects of *Schistosomiasis japonica*: a review. Philippine Journal of Internal Medicine. 1986;24:147–50.
- 5. McGarvey ST, Aligui G, Daniel BL, Peters P, Olveda R, Olds GR. Child growth and schistosomiasis japonica in northeastern Leyte, the Philippines: cross-sectional results. Am J Trop Med Hyg 1992;46:571-81.
- 6. Leenstra T, Acosta LP, Langdon GC, Manalo DL, Su L, Olveda RM, McGarvey ST, Kurtis JD, Friedman JF. *Schistosomiasis japonica*, anemia, and iron status in children, adolescents, and young adults in Leyte, Philippines 1. Am J Clin Nutr 2006;83:371-9.
- 7. Ezeamama AE, Friedman JF, Acosta LP, Bellinger DC, Langdon GC, Manalo DL, Olveda RM, Kurtis JD, McGarvey ST. Helminth infection and cognitive impairment among Filipino children. Am J Trop Med Hyg 2005;72:540-8.
- Ezeamama AE, McGarvey ST, Hogan J, Lapane KL, Bellinger DC, Acosta LP, Leenstra T, Olveda RM, Kurtis JD, Friedman JF. Treatment *for Schistosoma japonicum*, reduction of intestinal parasite load, and cognitive test score improvements in school-aged children. PLoS Negl Trop Dis 2012;6:e1634.
- 9. Kurtis JD, Higashi A, Wu HW, Gundogan F, McDonald EA, Sharma S, PondTor S, Jarilla B, Sagliba MJ, Gonzal A, Olveda R, Acosta L, Friedman JF. Maternal Schistosomiasis japonica is associated with maternal, placental, and fetal inflammation. Infect Immun 2011;79:1254-61.
- 10. McDonald EA, Pond-Tor S, Jarilla B, Sagliba MJ, Gonzal A, Amoylen AJ, Olveda R, Acosta L, Gundogan F, Ganley-Leal LM, Kurtis JD, Friedman JF. Schistosomiasis japonica during pregnancy is associated with elevated endotoxin levels in maternal and placental compartments. J Infect Dis 2014;209:468-72.

- 11. Ross AG, Olveda RM, Acosta L, Harn DA, Chy D, Li Y, Gray DJ, Gordon CA, McManus DP, Williams GM. Road to the elimination of schistosomiasis from Asia: the journey is far from over. Microbes Infect 2013;15:858-65.
- 12. Olveda RM, Tallo V, Olveda DU, Inobaya MT, Chau TN, Ross AG. National survey data for zoonotic schistosomiasis in the Philippines grossly underestimates the true burden of disease within endemic zones: implications for future control. Int J Infect Dis 2016.
- 13. Da'dara AA, Li YS, Xiong T, Zhou J, Williams GM, McManus DP, Feng Z, Yu XL, Gray DJ, Harn DA. DNA-based vaccines protect against zoonotic schistosomiasis in water buffalo. Vaccine 2008; 26:3617-25.
- 14. Jiz M, Friedman JF, Leenstra T, Jarilla B, Pablo A, Langdon G, Pond-Tor S, Wu HW, Manalo D, Olveda R, Acosta L, Kurtis JD. Immunoglobulin E (IgE) responses to paramyosin predict resistance to reinfection with Schistosoma japonicum and are attenuated by IgG4. Infect Immun 2009; 77:2051-8.
- 15. Ross AG, Harn DA, Olveda RM, Chy D, Inobaya M, Jjiz M, Guevarra J, Li Y, Shollenberger L, Gray DJ, McManus DP, Williams GM. Is a bovine transmission blocking vaccine the missing link for the elimination of human schistosomiasis from Asia?

ABOUT NAST PHL

The National Academy of Science and Technology Philippines (NAST PHL) is mandated to recognize outstanding achievements in science and technology and to serve as reservoir of competent scientific and technological manpower for the country (Presidential Decree No. 1003-A, December 17, 1976). By virtue of Executive Order 818 (July 16, 1982), the Academy was formally charged with the function of advisory body to the President and the Cabinet on policies concerning science and technology in the country.

3rd Level, Science Heritage Building, DOST Complex, General Santos Avenue, Bicutan, Taguig City 1631 Philippines Telephone Nos.: (632) 837-2071 locals 2170-73 Telefax Nos.: (632) 837-3170; 838-7766 e-mail address: secretariat@nast.ph; website: www. nast.ph Facebook: fb.com/nast.phl Instagram: @nast.phl Twitter: @nast.phl