ORIGINAL PAPER



Long-term effectiveness of the integrated schistosomiasis control strategy with emphasis on infectious source control in China: a 10-year evaluation from 2005 to 2014

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Received: 22 September 2016 / Accepted: 26 October 2016 / Published online: 3 November 2016 © Springer-Verlag Berlin Heidelberg 2016

Abstract Schistosomiasis is a neglected tropical parasitic disease of great public health significance worldwide. Currently, mass drug administration with praziquantel remains the major strategy for global schistosomiasis control programs. Since 2005, an integrated strategy with emphasis on infectious source control was implemented for the control of schistosomiasis japonica, a major public health concern in China, and pilot studies have demonstrated that such a strategy is effective to reduce the prevalence of Schistosoma japonicum infection in both humans and bovines. However, there is little knowledge on the long-term effectiveness of this integrated strategy for controlling schistosomiasis japonica. The aim of this study was to evaluate the long-term effectiveness of the integrated strategy for schistosomiasis control following the 10-year implementation, based on the data from the national schistosomiasis control program released by the Ministry of Health, People's Republic of China. In 2014, there were 5 counties in which the transmission of schistosomiasis japonica had not been interrupted, which reduced by 95.2% as compared to that in 2005 (105 counties). The number of schistosomiasis patients

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and acute cases reduced by 85.5 and 99.7% in 2014 (115,614 cases and 2 cases) as compared to that in 2005 (798,762 cases and 564 cases), and the number of bovines and S. japonicuminfected bovines reduced by 47.9 and 98% in 2014 (919,579 bovines and 666 infected bovines) as compared to that in 2005 (1,764,472 bovines and 33,736 infected bovines), respectively. During the 10-year implementation of the integrated strategy, however, there was a minor fluctuation in the area of Oncomelania hupensis snail habitats, and there was only a 5.6% reduction in the area of snail habitats in 2014 relative to in 2005. The results of the current study demonstrate that the 10-year implementation of the integrated strategy with emphasis on infectious source has greatly reduced schistosomiasisrelated morbidity in humans and bovines. It is concluded that the new integrated strategy has remarkable long-term effectiveness on the transmission of schistosomiasis japonica in China, which facilitates the shift of the national schistosomiasis control program from transmission control to transmission interruption and elimination. However, such a strategy seems to have little effect on the shrinking of areas of snail habitats.

Keywords Schistosomiasis japonica · Integrated strategy · Long-term effectiveness · Infectious source · China

Introduction

Schistosomiasis is a neglected tropical disease which affects over 200 million people worldwide (Colley et al. 2014). In China, schistosomiasis japonica, caused by the trematode *Schistosoma japonicum*, has a history of over than 2100 years, as detected by the parasite eggs in the liver of an ancient corpse (Chen 2014). Since the initiation of the national schistosomiasis control program in 1950s, schistosomiasis had never been neglected but given a high priority in China (Zhou et al. 2005). In 2004, the central government defined schistosomiasis, together with HIV/AIDS, tuberculosis, and hepatitis B, as the highest priorities in communicable disease control (Wang et al. 2008), and in 2014, schistosomiasis was ranked among the five major diseases (cancer, schistosomiasis, tuberculosis, viral hepatitis, and severe mental illness) with the top priority for the control in China (Liu 2014). Due to strong political will, adequate financial support and effective control strategy (Wang et al. 2014; Zhu et al. 2016), great success has been achieved in schistosomiasis control in China (McManus et al. 2009; Yang et al. 2014; Zhu et al. 2010).

There have been three shifts in the national schistosomiasis control strategy in China, namely snail control-based transmission control strategy, praziquantel chemotherapy-based morbidity control strategy, and integrated strategy with focus on infectious source control (Collins et al. 2012; Xu et al. 2015, 2016a). In 2004, the integrated strategy was proposed for schistosomiasis control in China and it was implemented across the country since 2005 (Liu et al. 2012; Qian et al. 2014; Wang et al. 2009a). Pilot studies have shown that the integrated control strategy is effective to reduce the prevalence of S. japonicum infection in both humans and bovines (Wang et al. 2009b). However, there is little knowledge on the longterm effect of this integrated strategy on the transmission of schistosomiasis japonica. The current study was therefore designed to evaluate the long-term effectiveness of the new integrated strategy for schistosomiasis control following the 10-year implementation, based on the data from the national schistosomiasis control program released by the Ministry of Health, the People's Republic of China.

Materials and methods

Data source

The data pertaining to the national schistosomiasis control program of China during the period from 2005 through 2014 (Hao et al. 2006, 2007, 2008, 2009, 2010; Lei et al. 2011, 2014, 2015; Li et al. 2013; Zheng et al. 2012), which were released by the Ministry of Health, the People's Republic of China, were collected. The prevalence of *S. japonicum* infection in humans and bovines, and areas of snail habitats were captured from the publications and used for the evaluation of the effectiveness of the integrated strategy for schistosomiasis control.

Evaluation of the effectiveness of the integrated strategy for schistosomiasis control

The following parameters were calculated: (1) annual number of counties with transmission interruption (<1% prevalence of *S. japonicum* infection in humans and domestic animals, no

local acute cases, and no *S. japonicum*-infected *Oncomelania hupensis* detected for successive 2 years) (NHFPC 2016) and transmission control of schistosomiasis japonica (no local *S. japonicum* infections in humans and domestic animals and no *S. japonicum*-infected *O. hupensis* detected for successive five years) (NHFPC 2016) from 2005 to 2014; (2) annual number of schistosomiasis patients and acute cases from 2005 to 2014; (3) annual number of bovines and *S. japonicum*-infected bovines fenced in endemic foci from 2005 to 2014; and (4) annual areas of snail habitats from 2005 to 2014. We compared the dynamic changes of these parameters during the 10-year implementation of the integrated strategy from 2005 through 2014 to evaluate the long-term effectiveness of the integrated strategy for schistosomiasis control.

Data management

All data were entered into the software Microsoft Excel version 2007 (Microsoft Corporation; Redmond, WA, USA), and all graphs were plotted with GraphPad Prism 5.0 software (GraphPad Software, Inc.; San Diego, CA, USA).

Results

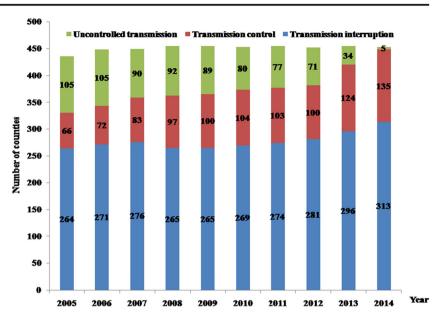
Overall status of schistosomiasis control in China from 2005 to 2014

During the 10-year implementation of the new integrated strategy from 2005 to 2014, there were 435 to 454 counties that were endemic for S. japonicum in China, in which 264 to 313 counties achieved transmission interruption of schistosomiasis japonica, 66 to 135 counties achieved transmission control, while the transmission of schistosomiasis remained uncontrolled among 5 to 105 counties. In 2014, when the integrated strategy had been implemented across China for 10 years, there were 313 counties achieving transmission interruption and 135 counties achieving transmission control, which increased by 18.6 and 104.5% as compared those in 2005, and there were only five counties where the transmission of schistosomiasis japonica had not been controlled, which reduced by 95.2% relative to in 2005 (Fig. 1). The results indicate that the implementation of the integrated strategy greatly facilitates the control of schistosomiasis transmission in China.

S. japonicum infection in humans in China from 2005 to 2014

During the 10-year implementation of the new integrated strategy, there were 798,762, 671,265, 515,971, 412,927, 365,770, 325,824, 286,836, 240,597, 184,943, and 115,614 cases with schistosomiasis japonica in China annually from 2005 to 2014, which appeared a decline in the annual number

Fig. 1 Annual number of counties achieving transmission interruption and transmission control and counties with uncontrolled transmission of schistosomiasis in China during the period from 2005 to 2014



of schistosomiasis cases year by year over the 10 years. Following the 10-year implementation of the integrated strategy, the number of cases with schistosomiasis japonica reduced by 85.5% in 2014 as compared to that in 2005. In addition, there were 564, 207, 83, 57, 77, 43, 3, 13, 9, and 2 acute cases in China during the period from 2005 through 2014, appearing an overall decreasing tendency. There were only two acute cases found in 2014, which reduced by 99.6% relative to that in 2005 (Fig. 2). Our findings demonstrate that the integrated strategy is effective to greatly reduce the morbidity due to *S. japonicum* human infection.

S. japonicum infection in bovines in China from 2005 to 2014

During the 10-year implementation of the integrated strategy, there were 1,764,472, 1,586,715, 1,496,477, 1,468,669, 1,570,300, 1,476,606, 1,410,936, 1,189,829, 962,065, and 919,579 bovines fenced in the schistosomiasis-endemic regions of China annually from 2005 to 2014, which appeared a reduction tendency in the number of bovines. Following the 10-year implementation of the integrated strategy, the number of bovines fenced in the schistosomiasis-endemic regions of

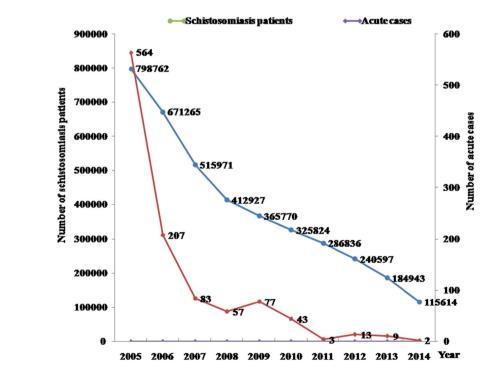


Fig. 2 Annual number of schistosomiasis patients and acute cases in China during the period from 2005 to 2014

China reduced by 47.9% in 2014 as compared to that in 2005. In addition, there were 33,736, 24,855, 16,624, 9988, 7753, 7173, 5146, 3297, 633, and 666 S. japonicum-infected bovines in the endemic foci of China during the period between 2005 and 2014, appearing a decline in the number of infected bovines year by year from 2005 to 2013; however, there was a 5.25% increase in the number of S. japonicuminfected bovines in 2014 as compared to that in 2013. Following the 10-year implementation of the integrated strategy, the number of S. japonicum-infected bovines fenced in the schistosomiasis-endemic regions of China reduced by 98% in 2014 as compared to that in 2005 (Fig. 3). Our findings indicate that the integrated strategy shows a clear-cut effect on the reduction of the number of bovines and S. *japonicum*-infected bovines that are fenced in the endemic regions of China.

Dynamic shifts in area of snail habitats in China from 2005 to 2014

During the 10-year implementation of the integrated strategy from 2005 to 2014, there were 364,324.42 to 494,673.1 hm² snail habitats in China. There was a minor fluctuation in the area of snail habitats over the 10 years except a slight rise in 2007 (494,673.1 hm²) and 2008 (477,852.6 hm²). Following the 10-year implementation of the integrated strategy, there was only a 5.7% reduction in the area of snail habitats in 2014 as compared to that in 2005 (Fig. 4). The results demonstrate that the integrated strategy has no remarkable effect on the shrinking of areas of snail habitats.

Discussion

The national schistosomiasis control strategy has shifted three times in China since the initiation of the national schistosomiasis control program at 1950s to present (Collins et al. 2012;

Fig. 3 Annual number of bovines and *Schistosoma japonicum*-infected bovine fenced in the endemic foci of China during the period from 2005 to 2014

Xu et al. 2015, 2016a). From mid-1950s to early 1980s. transmission control strategy with emphasis on control of the snail populations was implemented, which greatly shrunk the snail habitats and reduced the number of cases infected with S. japonicum; however, this strategy resulted in environmental pollution (resulting from extensive use of chemical molluscicides) and ecological damage (caused by environmental modification) (Xu et al. 2016a). During the period between mid-1980s and 2004, morbidity control strategy based on praziquantel chemotherapy was implemented, leading to a great reduction in the prevalence of S. japonicum infection in both humans and bovines; however, praziguantel treatment cannot prevent re-infection with the parasite (Jiang et al. 2002). In addition, the termination of the World Bank Loan Project for Chinese Schistosomiasis Control Program (Xianyi et al. 2005), frequent flooding along the Yangtze River basin (Wu et al. 2008), and other natural and social factors (Zhou et al. 2012) resulted in a resurgence of schistosomiasis japonica in China at early 2000s (Liang et al. 2006). In terms of bovines identified as the primary source of infection in the marshland and lake regions (Gray et al. 2008), a new strategy, which integrates an intervention package of prohibition of bovines from snail-infested grasslands, replacement of bovines with mechanized farm equipments, access to safe water, building lavatories and latrines, praziquantel chemotherapy, snail control, and health education, was developed for schistosomiasis control in China in 2004 (Wang et al. 2009a). Targeting the transmission pathway of S. japonicum, this integrated strategy aims to eliminate humans and bovines as the major source of infection in O. hupensis snails, so as to control the transmission of S. japonicum (Wang et al. 2009b).

Previous studies have examined the effectiveness of the integrated strategy for schistosomiasis control in the main endemic foci of China (Liu et al. 2013; Qian et al. 2014; Wang et al. 2009b). In Poyang Lake regions, the 4-year implementation of the integrated strategy reduced human *S. japonicum* infection from 11.35 to 0.18 and from 4 to 0%

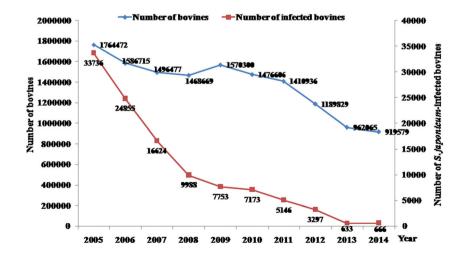
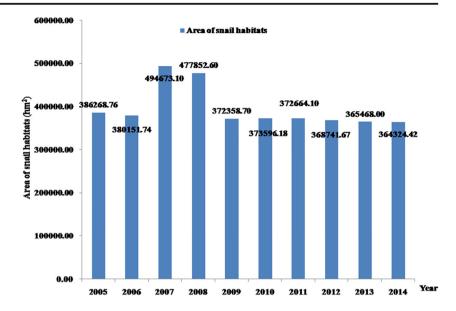


Fig. 4 Annual areas of snail habitats in China during the period from 2005 to 2014



and intensity of infection (EPG) from 1.33 to 0.01 and from 1.14 to 0 in the two pilot villages and decreased snail infection to 0 in both villages (Chen et al. 2009). In a pilot around the Dongting Lake regions, the 3-year implementation of the integrated strategy reduced human S. japonicum infection from 8.36 to 1.06% and snail infection from 0.68 to 0.11% (Yi et al. 2009), and another pilot study showed a reduction from 7.51 to 0.95 and 7.8 to 0% in the prevalence of S. japonicum infection in humans and bovines, and a reduction from 0.693 to 0% in snail infection following the 5-year implementation of the integrated strategy, while a human infection reduction from 7.79 to 2.31%, a bovine infection reduction from 5.81 to 2.33% and a snail infection reduction from 1.118 to 0.869% were observed in the control village (Zhu et al. 2011). In Anhui Province, the 2-year implementation of the integrated strategy reduced the prevalence of human S. japonicum infection from 4.57 to 1.76% and snail infection from 0.28 to 0.04% (Cao et al. 2012). Following the 32-month implementation of the integrated strategy in Jiangsu Province, there were 47.88, 94.29, 92.55, 96.94, and 100% reductions in the areas of snail habitats, areas of infected snail habitat, snail infection rate, and human S. japonicum prevalence and bovine infection (Sun et al. 2011). Finding from a cluster randomized controlled trial revealed a human S. japonicum infection reduction from 3.41 to 0.81%, bovine infection reduction from 3.3 to 0% and snail infection reduction from 0.18 to 0% following the 3-year implementation of the integrated control strategy, while there were no statistically significant reductions of S. japonicum infection in humans, bovines, and snails in the control group (Hong et al. 2013). An 8-year longitudinal survey showed the integrated control strategy reduced the prevalence of human S. japonicum infection from 1.7% in 2005 to 0.4% in 2012 (P < 0.001) and bovine infection from 11.7% in 2005 to 0.6% in 2012 (P < 0.001) (Chen et al. 2014).

Results of these pilot studies demonstrate the short- and midterm effectiveness of the integrated control strategy to reduce *S. japonicum* infection in humans, bovines, and snails in the marshland and lake regions of China.

Since the integrated strategy was developed to target the marshland and lake regions, the effect of this strategy on the transmission of schistosomiasis is questionable in the plain regions and hilly and mountainous regions (Seto et al. 2011), due to the great variation in the environmental conditions and epidemiology of schistosomiasis transmission (Zhou et al. 2007). In Oianjiang City, a plain region with waterway networks, the 7-year implementation of the integrated strategy resulted in transmission control of schistosomiasis, with 89.13 and 100% reductions seen in the prevalence of S. japonicum infection in humans and bovines (Zhu and Wang 2014). Another pilot study showed 94.2, 100, and 100% reductions in the rates of S. japonicum infection in humans, bovines, and snails in the plain regions following the 4-year implementation of the integrated strategy (Deng et al. 2012). In hilly regions of Yunnan Province, the 2-year implementation of the integrated strategy reduced the prevalence of human S. japonicum infection from 11.3 to 0.95%, bovine infection from 17.36 to 4.92%, and snail infection from 0.48 to 0.14% (Yang et al. 2009), and in plateau regions of Yunnan Province, the 7-year implementation of the integrated strategy reduced human S. japonicum infection from 4.94 to 0.06%, bovine infection from 1.11 to 0% and snail infection from 5.87 to 0% (Chen et al. 2015). In addition, the 4-year implementation of the integrated strategy was found to achieve 93.91, 94.69, and 100% reductions in the rates of S. japonicum infection in humans, bovines, and snails in a mountainous endemic focus of Sichuan Province, respectively (Yihuo et al. 2009). These results indicate that the integrated strategy is also effective to reduce S. japonicum infection in humans, bovines, and snails in other two endemic types of plains regions and hilly and mountainous regions.

There is increasing evidence from field data proving that the integrated strategy has remarkable effects on schistosomiasis control in all endemic foci with various environmental conditions across China, as long as various combinations of the intervention packages are employed tailored to local settings (King 2009; Seto et al. 2011). However, there is little knowledge on the long-term effectiveness of the integrated control strategy on the transmission of schistosomiasis japonica, as evaluated at a national level to date. Based on the 2005-2014 data captured from the national schistosomiasis control activities, which were annually released by the Ministry of Health, the People's Republic of China, the present study aimed to examine the long-term effectiveness of the integrated strategy for schistosomiasis control through analyzing and comparing the annual number of schistosomiasis patients and acute cases, annual number of bovines and S. *japonicum*-infected bovines, and annual areas of snail habitats during the 10-year implementation of the integrated strategy from 2005 to 2014. Our findings showed a decline in the annual number of schistosomiasis cases year by year over the 10 years, with a 85.5% reduction in the number of schistosomiasis cases seen in 2014 as compared to that in 2005, and an overall decreasing tendency was observed in the number of acute cases during the period from 2005 through 2014, with a 99.6% reduction in the number of acute cases in 2014 relative to that in 2005. In addition, the 10-year implementation of the integrated strategy resulted in a great reduction in the number of bovines (by 47.9% as compared to 2005) and S. japonicuminfected bovines (by 98% relative to 2005) in the endemic foci of China. Following the 10-year implementation of the integrated strategy, there were 313 counties achieving transmission interruption and 135 counties achieving transmission control, which increased by 18.6 and 104.5% as compared to 2005, and there were only 5 counties where the transmission of schistosomiasis japonica had not been controlled, which reduced by 95.2% relative to in 2005. However, there was only a minor fluctuation in the area of snail habitats over the 10 years, with a 5.7% reduction in the area of snail habitats in 2014 as compared to that in 2005. The results of the current study demonstrate that the integrated strategy is effective to control the transmission of S. japonicum in China; however, such a strategy seems to have no clear-cut effect on the areas of snail habitats.

Currently, mass drug administration (MDA) with praziquantel remains the primary strategy for schistosomiasis control across the world (Ross et al. 2015a, b; Sokolow et al. 2016; Webster et al. 2014). Since praziquantel therapy cannot prevent re-infection, however, schistosome re-infection may occur upon contact with cercariae-infested water, thereby resulting in re-emergence and resurgence of schistosomiasis (Lo et al. 2015; Olveda et al. 2016; Secor 2015). Lessons from the national schistosomiasis control programs in the Philippines and Africa have shown that MDA alone cannot lead to sustainable schistosomiasis control (Hodges et al. 2012; Inobaya et al. 2015; Ross et al. 2015b; Wang and Liang 2015), and the elimination of schistosomiasis requires a multifaceted integrated approach (Gray et al. 2010; Rollinson et al. 2013; Savioli et al. 2015). Currently, China is transferring its experiences of schistosomiasis control to the Philippines and African mainland and will aid the elimination of schistosomiasis in these countries (Xu et al. 2016b, 2016c). It is believed that the successful experiences from the 10-year implementation of the integrated control strategy across all endemic regions of China may provide new insights into the development and adjustment of the global schistosomiasis elimination strategy (Xu et al. 2016a).

In conclusion, the results of this study demonstrate that the integrated strategy has remarkable long-term effectiveness on schistosomiasis control in China, which is effective to control the transmission of *S. japonicum*. Based on the endemic situation of schistosomiasis, the agenda for schistosomiasis elimination was set in China in 2015 to achieve transmission interruption by 2020 and elimination by 2015 in the country (Zhang et al. 2016). During the stage moving from transmission control to transmission interruption and elimination of schistosomiasis, the integrated strategy for schistosomiasis control should be intensified and precision control requires to be implemented (Zhou 2016). We call for randomized, controlled trials to examine the effect of the integrated strategy for schistosomiasis control in the Philippines and Africa.

Acknowledgments This study was supported by the grants from Jiangsu Provincial Department of Science and Technology (grant no. BL2014021) and Jiangsu Department of Health (grant nos. Q201404 and X201117).

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