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Review Article

Schistosomiasis Control Strategies, with Emphasis on Snail Control Using **Molluscicides**

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ABSTRACT

Schistosomiasis is, one of the common infectious diseases, a trematode infection of humans and other animals in the different parts of the world like in Asia, Africa, the Middle East, South America and the Caribbean. About 240 million people in around 78 countries are affected and more than 700 million are at a risk of acquiring this infection. Schistosomiasis control involves the use of chemotherapy, control of the snail intermediate hosts through the application of molluscicides, environmental and biological methods; health education; clean water supply and basic sanitation. Chemotherapy is the efficient and widely used method for the reduction of morbidity of schistosomiasis. As the measures of snail control, the use of synthetic and plant molluscicides, environmental management and biological agents have been effective. These snail control measures must always be considered as complementary to chemotherapy in the control of the disease if the impact of chemotherapy is to be maintains. Health education, water supply and sanitation are also important aspects of disease non-specific methods of schistosomiasis control. In Ethiopia, some pilot control trials have been made in different endemic foci of schistosomiasis in which endod has been recommended as molluscicide to complement chemotherapy. This paper reviews the available information on schistosomiasis control strategies and gives insight into the effective molluscicide approach.

Key Words: Schistosomiasis control, molluscicides, snail control, chemotherapy

INTRODUCTION

Schistosomiasis or bilharzia is an infectious disease affecting many people in developing or tropical countries, caused by blood flukes under the genus Schistosoma. Reports indicated that around 230 million populations need treatment in each year worldwide. Transmission of schistosomiasis has been occurred in 78 countries with are 52 countries at the highest risk of acquiring the infection. (1)

The common schistosome species infecting humans are Schistosoma mansoni, S. japonicum, S. haematobium, S. mekongi, and S. intercalatum. (2) Other species of Schistosoma which have veterinary importance include Schistosoma mattheei, S. bovis, S. sprinadalis and S. rodhaini. These schistosome species may accidentally infect humans. the most relevant snail intermediate hosts of schistosomes are under Biomphalaria, **Bulinus** genera

Oncomelania and responsible for the transmission of this disease. (4)

Schistosome intermediate snails occur in scrupulous ecological circumstances that are subject to rapid change involving in the presence and absence of rainfall. Therefore, one of the challenges to understanding the future of this disease is to try to understand how snails affected by climate changes, (5) elevated aquatic habitats' pollution due to ecologic changes in the environment, sustained transport of exotic species, increase in water related projects, frequent flooding and population movements. Some of the above mentioned factors will have effects on transmission of this disease. (6)

Currently, the development agriculture particularly in irrigation systems in Ethiopia have increased from time to time as well differs from place to place. The existence and construction of hydroelectric power for irrigation and power will maintain the snails in endemic areas of country. Consequently, water production programs have negative impact on the health of the society by maintaining life of the intermediate hosts. (7)

Review METHODS

A systematic literature review was done with the aim to identify all relevant studies that examined the available information on schistosomiasis control strategies, focusing on the effective molluscicide approaches. I did computeraided searches of the different relevant electronic databases: such as Indian Journal of Medical Research, BioMed Central, Pacific Journal of **Tropical** Asian Biomedicine. Journal of Science and Technology, Asian Journal of Epidemiology, PLoS Neglected Tropical Diseases, Online Journal of Health Allied Sciences, Clinical Microbiology Review, East African Medical Journal, etc.

Next, I searched the electronic archives of international organizations, i.e., WHO. dissertations. Books. unpublished documents ("grey literature") were also considered. The following keywords and combinations thereof were used in this review: "schistosomiasis" in combination with "epidemiology", "chemotherapy", "molluscicide (s)", "snail hosts", "and clean water supply", "environmental management", biological control".

Epidemiology of Schistosomiasis:

Schistosomiasis is one of the chronic and the world's most prevalent disease affecting millions of people and is one of the most common among parasitic diseases of public health. (8) The disease is widespread in various parts of the world, especially in the most parts of Africa, South America and Asia. (9) It infects around 240 million people in the world, and over 700 million people are at a risk of the infection. (10) Of 249 million cases of schistosomiasis occurring in 78 endemic countries of the world, 90% (192 million cases) occurs in sub-Saharan Africa. (11) Schistosomiasis is predominantly in the developing countries and more frequent in areas with tropical weather and inadequate sanitation practices, and poor water supply. (10) Schistosomiasis is more predominant in the different parts of Africa, especially in sub-Saharan Africa (80-85%). The disease is more prevalent in Africa, perhaps due to low socio-economy or favorable climate for transmission of the disease. (12)

In Ethiopia, schistosomiasis pose considerable public health problem. (13) Both Schistosoma mansoni (causing intestinal bilharziasis) and Schistosoma haematobium (producing urinary schistosomiasis) are endemic in the different parts of Ethiopia. The increase in construction of dams and

irrigation schemes and population migration, have increased the frequency of schistosomiasis, affecting the productive man power, which affects the economy of the country. (14)

Schistosomiasis transmission takes place where the ecologies of the schistosome parasites, the fresh water snail hosts, and the human hosts meet in space and time in habitat of snail hosts. Both abiotic factors (temperature and rainfall) and biotic factors (host sex and age) play major role in the transmission and spatial distribution of the schistosomiasis. (15) The presence of fresh water is essential to the transmission of the disease as human population contracted the infection by water contact during water related activities. The disease is associated with human excrement and other sources polluted water and poor sanitation practices. After rainfall there are sufficient surface water accumulations in ponds which will provide snail propagation places and facilitate transmission of schistosomiasis. (16)



Fig. 1: Transmission cycle of schistosomiasis, WHO, 2014

Control of Schistosomiasis: Control of schistosomiasis has been likely in certain countries and been achieved in some areas, but there are no agreed approaches for elimination of the disease. But elimination will need a combination of techniques and

approaches, involving chemotherapy, mollusciciding, health education, environmental modification, providing of pure water supply and sufficient hygienic practices. (17)

Schistosomiasis control through mollusciciding is the most important approach in complementing chemotherapy. At present niclosamide is the major molluscicide applied on a large scale. Alternative possibilities for snail control need to be evaluated as this synthetic compound is toxic to other animals like fish and frequently impractical in low income areas, schistosomiasis-endemic areas. Plant molluscicides are available to contribute to schistosomiasis control with environmentally sound and affordable in cost. The advances in the battle against the snails using natural molluscicides must be encouraged in order to minimize the negative side effects to the environment. A number of tropical plants have been investigated for their molluscicidal activity. (19, 20)

In general, mass chemotherapy with praziquantel should be supplemented with adequate sanitation, mollusciciding and provision of pure water, together with health education and promotion and environmental modifications, which play role in interrupting the transmission of the infection. (21, 22)

Chemotherapy: Chemotherapy is the most effective intervention for controlling infection morbidity and rates schistosomiasis. (23) Access to very effective drug in the last three decades has resulted in reducing the prevalence and morbidity of the disease in many areas of the world and reducing the public health importance of schistosomiasis in some countries. Treatment of infected cases provides the most effective short-term results in control of schistosomiasis. Because case detection is the first planning approach for

chemotherapy and selection of most effective chemotherapy, diagnostic techniques available will be described first. (24)

Praziquantel (PZQ) is the mainstay of treatment and a critical part of community-based Schistosomiasis Control Programs. This drug is effective, generally in a single dose, against all species of schistosomes. Reports on praziquantel elucidate its failure to stop reinfection as a result of development of drug resistant Schistosoma strain, beside it induces hemorrhages in the lung tissue of the host as well as abdominal pain and diarrhea by long term application of the drug. (25)

Metrifonate is an organophosphorus compound originally used as an insecticide. It is well tolerated and is very effective in the treatment of S. haematobium mostly in mass chemotherapy programs. After administration, abdominal pain, nausea, vomiting, diarrhea, headache and vertigo may occur. (26)

Oxamniquine is used for the treatment of schistosomiasis due to S. mansoni both in the acute stage and in patients with hepatosplenic involvement. Some strains of S. mansoni are resistant to this drug. Side effects of oxamniquine are dizziness, drowsiness and headache. In more recent years, the price of oxamniquine has not undergone the substantial decrease as seen for praziquantel, so that the latter drug is now less expensive and is likely to replace oxamniquine. (24)

Snail control: The problems in mass treatment with praziquantel that threat of reinfection and absence of a completely and safe schistosomiasis vaccine support the use of snail control as an important means in control programs of schistosomiasis. (27) Snail control may involve the use of synthetic molluscicides, plant molluscicides, environmental management and biological agents. (26) Snail control could be regarded as

a rapid and efficient method of eliminating transmission and remains among the methods of choice for schistosomiasis control. Existing control methods are aimed principally at the management of snail populations that inhabit endemic areas. Where feasible, environmental management including elimination of natural water bodies such as marshes and ponds, and regulation of human settlement in areas with significant risk, has proven to be efficient. (28)

Control by Molluscicides: Molluscicides are crucial for controlling schistosomiasis in complementing chemotherapy. They have a history of success and failure in the control of schistosomiasis. (29) The molluscicides have been using in most areas are either synthetic or natural. (30) The use of molluscicides has always been considered to be a major supportive procedure in integrated schistosomiasis control. Perrett and Whitfield (31) provided an outline of both the synthetic and natural origin of molluscicidal chemicals with their potencies. From synthetic molluscicides, the niclosamide is still the effective molluscicide, being active to interrupt the snail biology and also lethal on the schistosome miracidia and cercariae. Niclosamide is toxic to fish although it is not toxic to humans and other animals. In addition, the use of niclosamide did not prevent recolonization of water bodies by the unaffected snails that may lead to molluscicide-resistant snails. In addition, niclosamide is considered as a teratogen because it possesses developmental toxicity potential indicated by induction of snail embryo abnormalities (teratogenesis, i.e. affecting embryo of the snails). (32)

Natural molluscicides are present in the different molluscicidal plant parts. Even some others are under investigation. For example, saponins (isolated from Phytolacca dodecandra) and isoflavonoids (extracted from Millettia thonningii) have been proved for their anti-mollusc activity. The availability plants having molluscicidal activity in some areas have been studied widely, but their toxicity produced with their large-scale production has considerably limited their exploitation. (28)

Chemical Molluscicides: Application of chemical molluscicides in snail habitats is a method for elimination intermediate snail hosts, in addition to environmental modification such cementing canals, re-adjusting irrigation systems, etc. The use of molluscicides as the strategies schistosomiasis began by using niclosamide. Niclosamide, a chemical molluscicide, is recommended by the WHO as a sole chemical molluscicide since the 1960s and is still the molluscicide of choice. (33) The high cost, the possibility of recolonization of breeding grounds by snails and the ecological toxicity of this product were limitations on its use as an official molluscicide program of schistosomiasis control. (34) On the other hand, Takourgang et al. (35) studied the effect of lower Bayluscide doses on snail host and fish. Niclosamide concentration of 0.50 g m⁻³ applied to ponds under investigation resulted in high snail mortality and show low lethality to fish.

Other synthetic organic molluscicides such carbomate, as organophophorus and pyrethoroids are used for the control of harmful snails. However, these synthetic molluscicides are causing serious environmental hazards. (29) And some other synthetic molluscicides like Thymol. Linalool and Eugenol considerable (monoterpenes) showed molluscicidal effect against Biomphalaria alexandrina, Bulinus truncatus and Lymnaea natalensis. (36)

Generally, widespread and heavy use of synthetic molluscicides has been found to

affect water bodies due to their high toxicity, bioaccumulation and long term persistence. The hazardous nature of synthetic molluscicides has prompted the scientists to find out the least disruptive newer options in the field of snail control technologies, especially plant molluscicides. (37)

Plant Molluscicides: The relative high cost of synthetic molluscicides employed in the control schistosomiasis intermediate hosts. serious environmental hazards. and development of snail resistance to these synthetic chemicals and their non-specificity have stimulated in using plant product (29,38) Plant molluscicides molluscicides. have gained better significance due to the above reasons. Different plants and their parts having molluscicidal activity have been identified. The plant phytochemicals derived from plant resources can be used as an alternative to the synthetic anti-mollusc chemicals.

The investigation of potent and snailspecific molluscicides, non-expensive and with environmentally sound encouraged the investigation of active substances from local and their parts. The molluscicidal chemicals are derived from different parts of plants like Phytolacca dodecandra (Endod), Croton macrostachys, Jatropha curcas, Ambrosia maritima, Anarcardium occidentale. These plant parts may have less cost, environmentally safe and locally available and produced products. (39) Tariwari et al., (40) added that extracts of Jatropha curcas leaves have molluscicidal effect presence of some phytochemicals Biomphalaria pfeifferi against snails. Aqueous extract of Solanum nigrum L. leaves have molluscicidal activity against Lymnaea acuminate. (41) El-Saved (42) stated that the dry powder of the plant Cupressus macrocarpa have a significant molluscicidal activity against B. alexandrina snails.

The tannins of Pomegranate (Punica granatum) extracts were completely lethal to

Schistosoma mansoni miracidia with 100% and 50% lethality after exposures of 50-150 minutes and 25.1-48.3 minutes respectively.

Molla et al. (44) considered that the aqueous extracts of seeds and fruits of Balanites aegyptiaca showed practical lethal effect against Schistosoma mansoni and Fasciola gigantic snail hosts and cercariae of Schistosoma mansoni. Similarly, Kiros et al., (45) also observed that Glinus lotoides fruits showed potent effect on Biomphalaria pfeifferi and Schistosoma mansoni cercariae. Nevertheless, further investigation is needed for their possible application against schistosome larvae and their intermediate hosts.

The toxicity of active ingredients of certain plants to freshwater snails usually leads to death or low density of freshwater snails in such an environment. Therefore, the use of plant molluscicides should be justified, i.e., the molluscicidal concentration of the chemical should be non-toxic to other non-target animals, which have the same habitat with snails. Control measure of the freshwater snails is crucial and method with low cost and free of environmental pollution could be adopted. (46)

Endod as Molluscicides: The discovery of molluscicidal properties of endod by Aklilu Lemma in 1964 has been a major breakthrough in combating intermediate snail hosts in schistosomiasis control. (47) Endod (Phytolacca dodecandra), also called the soap-berry plant in Ethiopia, has proven to be a potent molluscicide, killing snail intermediate hosts of schistosomes. The species occurs throughout Africa and is familiar to rural populations. In Ethiopia, the plant has been used by local people as laundry soap for centuries. (48) The fact that endod grows locally and is biodegradable, makes it ecologically and economically more acceptable for use in schistosomiasis

control compared to synthetic molluscicides. (47)

It is the most thoroughly studied and promising of the currently available plant molluscicide. (49) Its berrikes are the most thoroughly studied as source of the molluscicidal saponins with no major toxic properties for other animals and plants. (24,48) Endod is an effective schistosomiasis control agent, particularly when combined with chemotherapy. (50) Its active principle, a monodesmosidic saponin with an oleanolic acid glucoside base, is most concentrated in the pericarp of immature fruits. (49) The plant contains a dozen oleanolic acid glucosides of which five have been chemically characterized. (51)

The water extract of the dried and powdered fruit has a potency of killing snails (Biomphalaria, Bulinus and Lymnaea spp.) at a concentration of 10 ppm within 24 hours at room temperature. Comparisons of the molluscicidal potency of the green leaves lower and buds showed that the green dried fruit extract was the most potent. Heat has no effect on the active ingredient of endod, and the solution remains stable and active over a long period of time. (52)

Different parts of endod have different potencies. Higher potencies were reported from the green and semi-ripe than from the fully ripe berries and female plants are more toxic than male plants. The potency of endod is also dependent on the extraction methods employed. It has been observed that butanol extraction of endod berries increases its potency by 7-10 fold compared to the aqueous suspension. (52)

In the field trials at Adwa, Ethiopia, between 1969 and 1973, application of crude ground endod berries reduced schistosomiasis in children 1-5 years old by 85%. The incidence of the disease among the overall Adwa population (1700) declined from 63% to 34%. Endod concentrations of 10-20 ppm remained lethal for 24 hours. (53)

Compared with more than 1000 molluscicidal plants identified so far, endod ranks as one of the most promising. (48)

Although the preparation and application of the endod berries is a safe procedure and that the molluscicidal saponins are decomposed to water and carbon dioxide in the environment, some outstanding questions are still to be solved. One of the future projects should deal with ecotoxicology in respect of the biological impact of the endod berries on the environment. Toxicity testing of endod is a prerequisite for its safe use as a molluscicide. (54) In addition, it lacks an ovicidal activity. (48)

Environmental Manipulation: The transmission of schistosomiasis is closely related to the daily and frequent contact with contaminated water sources that are used in domestic and recreational purposes. (55) As a avoidance of contact result, contaminated water, provision of protected drinking-water, promoting safe recreational water supply, construction of bridges across infested streams and rivers and clean bathing facilities will reduce the risk of acquiring the disease. (24) It is apparent that since the snails all require water, at least for breeding, reduction in the size and number of potential breeding areas will reduce the total population and so tend to reduce human infection. Generally weed clearance, repeated cleaning of irrigation canals, good ditch and stream management and good practices play significant a reduction in the population of snail intermediate hosts of schistosomiasis. (56)

Chemical and physical properties of fresh water as the major determinants for presence and absence of snail intermediate hosts in aquatic system are magnesium concentration and calcium concentration, dissolved oxygen, pH and current velocity. The high salinity and magnesium/calcium concentrations found to have a negative

impact on the population of snail hosts in water bodies. The level of dissolved oxygen/low oxygen concentration and current velocity will be additional chemical determinants for the availability and distribution of snail intermediate hosts in their foci. Low and high pH could be harmful to snails because there is denaturation of the mucus of the snails. (27)

The distribution of snails is limited by the power of temperature. Schistosoma mansoni snail hosts were not survived in the winter season when the night temperature becomes below 0°C. Temperature can also affect the reproductive potential of these snails. (24) In addition, Coelho and Bezerra (57) reported that temperature affect the infective potential of S. mansoni larvae against Biomphalaria glabrata snail.

Biological Control: Biological control is the control of snails through micro-parasites, trematodes, predators and competitor snail species. (58) and the lists of recommended biological snail control candidates are range from bacteria to birds. The later animals (like turtles, birds, crayfish and fish) have been investigated when they eat eating snail hosts in their habitats. Other animals like leaches, sciomyzid flies, nematodes, rotifers ostracods, have been effective antagonists of snails under laboratory colonies so far identified.

In particular, the snail Marisa cornuarietis snail, first observed in Puerto Rico, will compete with Biomphalaria snail intermediate hosts for food. It can also eat Biomphalaria eggs, and has been used as a biological control agent in the area. (59)

A number of predator and competitors are considered to be the most promising control agents by reducing/eliminating the spread of schistosomiasis for their direct effect on the snails and interference of the infectivity of miracidia. A number of competitors have been observed both in the laboratory and under

field situations. For example, in Puerto Rico, Grenada, Martinique and St. Lucia observed that Pomacea glauca, Marisa cornuarietis, Tarebia granifera and Melanoides tuberculata snail hosts were competed Biomphalaria snail species for food and space. (60)

Health education: Health education and promotion is one of the major strategies in schistosomiasis control programs. It aims to promote and reinforce healthy behavior with full participation of both the individual and the community. This approach could be developed in all endemic areas, with emphasis on personal/environmental hygiene & community's participation in the controlling programs. Schistosomiasis could largely be prevented by changing human behavior, and health education is of paramount importance to achieve this. (26)

In general all control schistosomiasis programs need the knowledge, attitude and practices of the community for their success. There is a need to improve the individual's community's perception towards schistosomiasis. Health education incorporate on proper excreta disposal, avoiding contact with infected water bodies like lakes, rivers, ponds and canals. In countries that have been able to implement such programs, they need to focus on the change of human behavior. Since educated community is able to adopt control strategies at the community and individual level. (24)

Water supply: Schistosomiasis transmission and prevalence is closely linked to any kind of water related activities. Transmission of the disease occurs through parasite infested fresh water contact during our daily routine activities. Studies of human water contact behavior thus have been encouraged in the control of schistosomiasis. Improvements of water supply can be most effective in places where the population is concentrated and the risk of infection is high. (61, 62) Water supply must

be adequate, particularly in the transmission season, and the system must be well maintained with delivery points conveniently located for easy access. (26)

As the transmission of schistosomiasis is caused by pollution of streams and water bodies with excreta and human contact with polluted water, proper waste disposal and provision of safe water supply can significantly contribute to the control of schistosomiasis. (52)

Safe water remains the main concern for most developing countries and demands a great deal of investment. Experience has shown that schistosomiasis control alone is unlikely to provide sufficient motivation for investment in water supply in endemic areas. (26, 63)

Sanitation: Sanitation practices can reduce the prevalence and morbidity schistosomiasis. One of the key control strategies of the disease are practicing personal and environmental hygiene and sanitation. By avoiding defecation of human excrements in fresh waters, we can interrupt the life cycle of the schistosome parasites. The widespread use of improved latrines would, in the long term, have an effect on transmission, although in the short term this is unlikely. The construction and use of private and public latrines in sufficient numbers and the repair and maintenance of such latrines should be encouraged to improve the general standard of hygiene and to reduce canal contamination and postexcretion water contact. (52, 62) Since latrines can also serve as washrooms, their provision additional have an effect schistosomiasis transmission. (64)

Schistosomiasis Control in Ethiopia: Control of schistosomiasis requires sound planning of programs and adequate financial resources. Even though the present economic status of Ethiopia may not provide enough resources to carry out a nationwide campaign, individual and collective

measures should be encouraged and whenever possible should be subsidized by the government. (52) Although there has been no national schistosomiasis control program in Ethiopia, some pilot control trials have been made in different endemic foci of schistosomiasis.

The study conducted in Kemissie indicated that where suspension of ground endod was sprayed on the stream containing infected snails, the prevalence of the disease was reduced from 59% to 53%. In Bati town where endod soap approach was used, the respective reduction in the prevalence and intensity of infection was from 51% to 43%. There was also a significant reduction of the disease in the control town probably due to the effects of praziquantel treatment and other factors. This observation confirms the fact that molluscicides must always be considered supplementary as to chemotherapy in the control of schistosomiasis. (47)

In Adwa town, S. mansoni infection rates were reduced from 64% to 33% after a five year period (1969-1974) of applying crude powder endod. Other measures, guarding and fencing of hazardous sections of the streams, were not successful. High cost and scarcity of endod berries were major constraints of this program. (52)

A pilot control trial of intestinal schistosomiasis was instituted in 1995 to reduce the magnitude of the disease and sustainable schistosomiasis introduce control approaches in Finchaa sugar estate. Following initial parasitological survey of all the camps in the sugar project area in 1995, mass chemotherapy of the heavily infected residents of Camp 7 and selective treatment of lightly infected residents of other camps were made using praziquantel. Endod (type 44) was applied to transmission sites along Fekerie stream in Camp 7 on quarterly basis whenever Biomphalaria pfeifferi was detected. Other inputs to the project included were transplantation of endod cuttings (type 44), training and health education. The results of stool examination showed that the prevalence of schistosomiasis was reduced from 30% in 1995 to 26% in 1998 among residents of Camp 7. Similarly, the prevalence of infection among children in Finchaa Valley Elementary School was reduced from 78% in 1994 to 56% in 1998. (64)

The accumulated results obtained in these various pilot control trials pointed out the need for carefully designed projects, community participation and intersectorial collaboration.

CONCLUSION

Schistosomiasis control involves chemotherapy; control the of snail intermediate hosts using molluscicides, environmental or biological methods; health education; clean water supply and basic sanitation. Chemotherapy is the effective method for reducing morbidity and infection rates of schistosomiasis. Since chemotherapy does not prevent reinfection and there remains a need to reduce snail densities in human water supplies, combining chemotherapy with mollusciciding was successful. more Essentially, control of snail hosts can be achieved through mollusciciding, environmental and biological controlling. The high cost and toxicity to environment of synthetic molluscicides has resulted in renewed interest in plant Molluscicides. molluscicides. however, probably cause stress on the water balance system and toxicity to non-target organisms so that selection of appropriate plant molluscicides and improved application are mandatory. techniques Alternative methods of snail control should also be developed using different biological control agents and environmental management. In addition, basic sanitation and clean water

supply combined with health education potentially constitute the effective approach to schistosomiasis control. In Ethiopia, chemotherapy, snail control using endod, employing disease non-specific methods such as health education, water supply and sanitation should be employed in order to sustain the impact of chemotherapy.

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Conflicts of Interests

I confirm that I don't have any competitive conflict of interest with anybody in all aspects of the manuscript.

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