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FASCIOLOSIS: AN EMERGING ZOONOTIC TREMATODE INFECTION AFFECTING THE LIVER- A REVIEW

FASCIOLOSIS: UNA INFECCIÓN EMERGENTE ZOONÓTICA POR TREMATODOS QUE AFECTAN AL HÍGADO- UNA REVISIÓN

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ABSTRACT

Zoonotic trematodiasis has emerged at a rapid pace and frequently with significant human and financial costs. The most important and well-known human zoonoses caused by trematodes affecting liver is Fasciolosis. The present work has been carried out to review on the extensive literature on Fasciolosis in detail that is increasing rapidly in incidence and geographic range. Reasons for the increase in the infection caused by *Fasciola* spp. are likely to be multifactorial. The use of parasitoproteomics as a powerful experimental approach, and its potential benefits to trematode biology are also discussed in relation to the future control of trematode infections of animals and humans. The aim is to make more young researchers vigilant about the importance of this critical issue. Global efforts to expand joint planning, information sharing, and financial support of a range of global efforts aimed at detection, verification, and response are increasingly important. Failure to jointly pursue these goals in a balanced approach has already contributed to new, re-emerging, and drug resistant etiological agent causing fasciolosis. The current review highlights the need for basic laboratory research to update the knowledge on zoonotic fasciolosis.

Keywords: Aetiological agent - Fasciolosis - Parasitoproteomic - Re-emerging - Zoonosis

RESUMEN

Las trematodiasis zoonóticas han surgido a un ritmo rápido y frecuente con un importante costo humano y financiero. La más importante y conocida zoonosis humana causada por trematodos, que afectan al hígado es la fasciolosis. El presente trabajo ha sido realizado para tener una revisión exhaustiva de la extensa bibliografía sobre la fasciolosis en detalle que está aumentando rápidamente en incidencia y alcance geográfico. Las razones para el aumento de la infección por *Fasciola* spp son probablemente multifactoriales. El uso de la parasitoproteómica como un poderoso enfoque experimental, y sus potenciales beneficios para la biología de trematodos también se examinan en relación con el control futuro de las infecciones por trematodos en animales y en seres humanos. El objetivo es hacer a los jóvenes investigadores más vigilantes sobre la importancia de esta temática crítica. Los esfuerzos mundiales para ampliar la planificación conjunta, el intercambio de información, y el apoyo financiero a una serie de esfuerzos mundiales encaminados a la detección, verificación y respuesta son cada vez más importantes. El fracaso por perseguir estos objetivos conjuntamente con un enfoque equilibrado, ya han contribuido a nuevas, a re-emergentes, y a agentes etiológicos resistentes terapéuticamente causantes de fasciolosis. La actual revisión resalta la necesidad de investigación básica de laboratorio para actualizar los conocimientos sobre la fasciolosis zoonótica.

Palabras clave: agente etiológico - fasciolosis - Parasitoproteomic - re-emergentes - Zoonosis

INTRODUCTION

Zoonoses are infections and diseases that are transmissible between animals and humans. The severity of these diseases in humans can vary from mild symptoms to life-threatening conditions. Zoonotic infectious agents are among the most prevalent on earth and are thought to be responsible for >60 per cent of all human infections and 75 per cent of emerging human infectious diseases (Cunningham, 2005). With the inherent complexity of the biological and social systems involved in disease emergence, it is not possible to accurately predict the infectious agents destined to emerge. Yet, the probable reasons for the emergence of new zoonotic diseases are many and include, changes in social, dietary or cultural mores, environmental changes, and the improved recognition of heretofore neglected infections often coupled with an improved ability to diagnose infection (McCarthy & Moore, 2000). Increased demand for livestock products in many developing countries is viewed as a market, which can potentially be exploited by poor livestock keepers and offer a pathway out of poverty for some (Delgado *et al*., 1999). However, the zoonotic diseases may lead to restrictions on the sale of livestock products and therefore limit the access of the poor to these new markets An emerging zoonosis is defined as 'a zoonosis that is newly recognized or newly evolved, or has occurred previously, but shows increases in incidence or expansion in a geographic, host or vector range (Slingenbergh, 2004). Fascioliasis is among one such emerging zoonotic diseases.

Fasciolosis

Fasciolosis, a major veterinary problem worldwide due to the economic losses it causes in animal husbandry, has recently become

increasingly important in public health, with human reports increasing in number and the description of human endemic areas (Mas Coma *et al*., 2009). The epidemiological picture of human Fasciolosis has changed in recent years. The number of reports of humans infected with *Fasciola hepatica* (Linnaeus, 1758) has increased significantly since 1980 and several geographical areas have been described as endemic for the disease in humans, with prevalence and intensity ranging from low to very high (Mas Coma *et al*., 1999). In the past, Fasciolosis was limited to populations within well-defined watershed boundaries; however, recent environmental changes and modifications in human behaviour are defining new geographical limits and increasing the populations at risk (*Soliman, 2008)*. In recent times, human Fasciolosis has apparently emerged or re-emerged as well recognized neglected zoonotic infection because of improved diagnosis. Thus, human Fasciolosis can no longer be considered merely as a secondary zoonotic disease but must be considered to be an important human parasitic disease.

Etiology

Fasciola hepatica and *Fasciola gigantica* (Cobbold, 1855) are the two trematodes which cause human and animal Fasciolosis. These hepatic helminth parasites are present around the world infecting a great variety of mammals as definitive hosts, but using only some species of snails which act as their sole intermediate host. *F. hepatica* is found in the five continents; however, *F. gigantica* is primarily distributed in tropical regions excluding America (Fuentes, 2006). Throughout the greater parts of world, *F. hepatica* is mainly transmitted by *Galba truncatula* (Müller, 1774) or by snails not readily distinguishable from it on grounds of morphology or ecological requirements,whereas, *F. gigantica* is transmitted by varieties of the super species *Lymnaea auricularia* (Linnaeus, 1758) as reported by Kendall, 1954. However, Soliman (2008) indicated that *Radix auricularia* (Held, 1836) also acts as intermediate host for *F. hepatica* in Oman.

Life cycle of *Fasciola* spp.

The life cycle of *Fasciola* spp is complex and includes a snail and a mammal as intermediate and definitive hosts respectively. Mammals (human, cow, sheep, rabbit, etc.) get infected by ingestion of the quiescent larvae (metacercariae) encysted in the vegetation. Infection has also been reported in birds (Despommier, 1987). An interplay of extrinsic signals from the host (digestive enzymes, bile salts, redox potential, pH, and temperature among others) and intrinsic factors from the parasite (enzymes and secretions) determine the emergence of motile larvae (Fried, 1994). The newly excysted juveniles (NEJ) actively penetrate and transverse the gut wall into the peritoneal cavity within two or three hours. By four or five days post-infection the parasites reach and penetrate the liver, and continue burrowing through the parenchyma for several weeks. Within the major bile ducts the parasites mature and start to release eggs, that can be found in the bile and feces from 8 weeks post-infection (Andrew, 1999).

Factors affecting the emergence of zoonotic diseases

Factors associated with the emergence of Fascioliasis in human, wildlife and domestic animals have been explored by various researchers. According to one perspective, disease emergence is the result of two sequential processes:

***a*) Adaptation of a pathogen (*Fasciola*) to a new host:** As elegantly demonstrated by, pathogen strains entering a new host population may initially have an overall reproductive number of less than one ($R0 < 1$) that leads to the extinction of the pathogens, but prior to extinction, some may evolve and increase their virulence to give $R0 > 1$, allowing them to persist and spread into a new

host population (Antia *et al*., 2003).

***b*) Spread of the *Fasciola* into the new population**

Diagnosis of Fascioliasis

The traditional way for diagnosis of Fascioliasis is coprological examination. But during the acute phase, no eggs can be seen because the parasites have not yet matured, and thus positive reactions may not appear at such an early stage. Moreover, consumption of beef or lamb's liver may cause trematode eggs to appear in feces and consequently give a false positive result in the coprological examination. A number of immunobiological tests have been used in an effort to diagnose the infection during the prepatent period, including a skin test, complement fixation, immunofluorescence, immunoelectrophoresis, counterimmunoelectrophoresis, enzyme-linked immunosorbent assay (ELISA), and immunoelectrotransfer. The search for appropriate antigens has improved the specificity and sensitivity of these tests, but there are still cross-reactions, especially with schistosomiasis (WHO, 2003). PCR techniques are also used for identification of *F. hepatica* and *F. gigantica* infections (McGarry *et al.*, 2007). Several ELISAs for *Fasciola* have been developed and most rely on the detection of antibodies against fluke-secretory proteins (Espinoza *et al*., 2007). An accurate serological test using recombinant cathepsin L protease produced in yeast has been developed by Dalton and colleagues (O'Neill *et al*., 1999).

Control of Fascioliasis

As Fascioliasis falls under three typological diseases, i.e., neglected zoonoses, emerging zoonoses and foodborne diseases (WHO 2003), so it requires diversified approaches to combat it which include:

Better health systems,

- Development and poverty alleviation measures, Public awareness, Emergency preparedness,
- Early detection and rapid responses and
- Control via the food chain, consumer empowerment and certification.

Fasciolosis can be controlled by adopting the following parameters:

Use of Molluscicide

Application of molluscicides in bait form is a new approach and technique for the control of fascioliasis for controling of harmful snails. Active components ferulic acid, umbelliferone (*Ferula asafoetida*), eugenol (*Syzygium aromaticum*) and limonene (*Carum carvi*) are very effective molluscicides when release directly in aquatic environment (Kumar *et al*., 2006)

Phytotherapy of Vector Snail to Kill *Fasciola* Larva

Phytotherapy of infected snails by the active components is one of the new method to control the fascioliasis without killing the vector snail, an important components of the aquatic ecosystem. Sunita & Singh (2011) during their study clearly indicated that the *Zingiber officinale (*citral), *Ferula asafoetida* (ferulic acid, umbelliferone), *Azadirachta indica* oil (azadirachtin), and *Allium sativum* (allicin) have sufficient larvicidal activity against different larva of *F. gigantica* in *in vivo* and *in vitro* treatments.

Myrrh (Mirazid) which is an oleo-gum resin from the stem of Commiphora molmol tree (Family Burseraceae) has been used in folk medicine since ancient Egyptians (Myrrh) and registered in Egypt for the treatment of schistosomiasis and fascioliasis. (Yakoot, 2010). The majority of these studies reported that Mirazid® has higher than 90% cure rates, that even higher in mixed than single trematodal infections in humans and in farm animals.

Chemotherapy

A series of chemotherapeutic agents are

available for the treatment of animal Fasciolosis, including closantal, clorsulan, rafoxanide, nitroxynil and triclabendazole (Boray, 1999). However, triclabendazole resistant parasites have been reported in Europe and Australia. The experimental fasciolicides such as artemether and OZ78 have activity against TCBZ-resistant flukes (Keiser *et al.*, 2007).But, chemicals runoff into water supplies will make the chemical control of fasciolosis more difficult in the future (Dalton *et al.*, 2003b). Most importantly, government and consumer concern about chemical and antibiotic residues in animal foods (milk and meat). For high efficacy and safety, triclabendazole (Egaten) in dose 10–12 mg/kg is the drug of choice in human fasciolosis (Savioli *et al.*, 1999).

Anti *Fasciola* vaccines: An additional advance in the control of animal fasciolosis will be provided by the development of anti-Fasciola vaccines against species specific antigens. Although a range of vaccines against *F. hepatica* infections have been developed by several laboratories (McManus & Dalton, 2006) but none are commercially available at present. Fatty acid binding protein (FABP) is an attractive vaccine candidate and a drug target for controlling Fasciolosis caused by *F. gigantica* in ruminants (Sriveny *et al*., 2003).

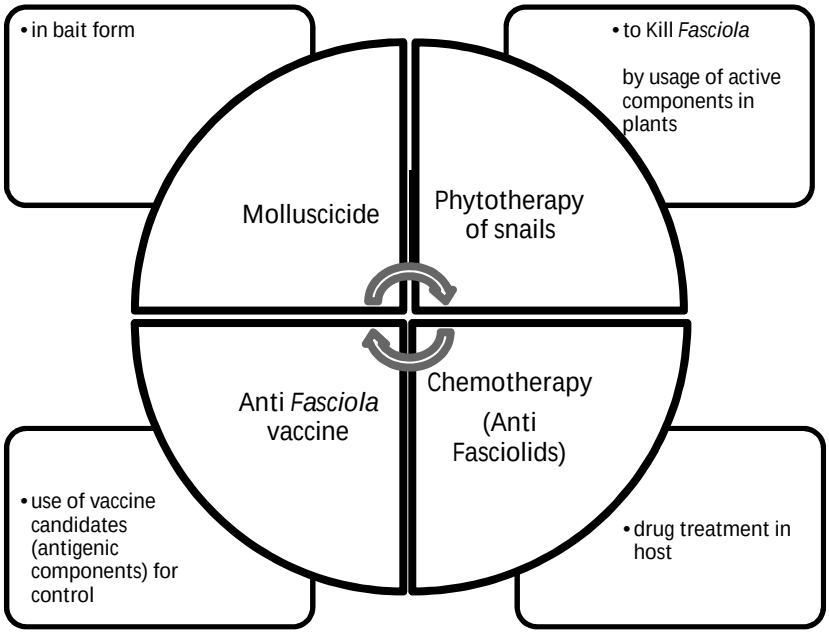

Figure 1. Parameters for control of fascioliasis.

Though there is advance in our understanding of biology of helminth parasites, Zoonotic Fasciolosis remain endemic in many parts of world. Thus the need for basic laboratory research on zoonotic Fasciolosis is stronger than ever. Experimental approaches should be armed with recent advanced technologies like post genomics and proteomic analysis to combat such global issue in the future.

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