Modulatory Role of Immunization with Secretory-Excretory Products of Schistosoma haematobium Eggs on Morbidity in Infected Hamsters

THESIS

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Abstract

The present work was carried out to evaluate the possible anti-morbidity effect of secretory-excretory products (SEP) of *Schistosoma haematobium* eggs, when given to hamsters prior to infection. Multiple small doses of SEP were injected intra-peritoneally into laboratory bred hamsters (100 µg of purified SEP followed 2 weeks later with 2 booster doses of 50 µg at weekly intervals). Animals were infected with *S. haematobium* cercariae 1week following last booster immunization dose, and the experimental design included three groups of 10 hamsters each; SEP immunized group, infected immunized group and infected control group. All animals were sacrificed 12 weeks post infection. The results revealed significant reduction in worm load (61.37%), tissue egg loads were also the reduction in tissue egg loads was significant (54.85% and 41.57% for hepatic and intestinal ova, respectively) in addition to decreased percent of immature stages and increase in the percent of the dead ova in Oogram pattern. Pathological examination also revealed significant reduction in number of hepatic granuloma (46.06 %). This study could represent an immunization model as a trial to decrease severe morbidity of schistosomiasis *haematobium* which may be aggravated by serious sequellae.

Key words

S. haematobium- Anti-morbidity- Hamster- Antigen

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List of abbreviations

AIDS: Acquired immunodeficiency syndrome

ANOVA: Analysis of variants

BSA: Bovine serum albumin

BCG: Bacillus Calmette-Guérin

^{O}C: Degree celcius

cDNA: Complementary Deoxyribonucleic acid

cm: Centimeter

CNBr: Cyanogen bromide

CSAg: Circulating Schistosome antigens

DALY: Disability-adjusted life- year

DNA: Deoxyribonucleic acid

E/S: Excretory-Secretory

EITB: Enzyme linked immunoelectrotransfer blot

ELISA: Enzyme-linked immunosorbent assay

FABPs: Fatty acid binding proteins

Fc: Fraction crystallization

Fig: Figure

GBD: Global burden of diseases

HIV: Human immunodeficiency virus

Hx & E: Haematoxylin and Eosin

IFN- γ: Interferon gamma

IgG: Immunoglobulin G

IL: Interleukin

IVC: Inferior vena cava

kDa: kilodaltons

Kg: kilogram

KOH: potassioum hydroxide

MAbs: Monoclonal antibodies

MAMA: Mansoni adult microsomal antigen

mRNA: Messenger ribonucleic acid

NaOH: Sodium hydroxide

NO: Nitric oxide

No.: Number

OPD: O-phenylene diamine dihydrochloride

P: Protein

PBS: phosphate buffered saline

pH: Hydrogen potential

PM: Postmortum

P value: Probability value

PZQ: Praziquantel

RA cercaria: Radiated attenuated cercaria

Rpm: Round per minute

RPMI: Roswell Park Memorial Institute medium,

rRNA: Recombinant Ribonucleic acid

SBSP: Schistosome biological supply program

SCC: Squamous cell carcinoma

SDS-PAGE: Sodium dodecyl sulfate polyacrylamide gel electrophoresis

S. mansoni: *Schistosoma mansoni*

Sm: *Schistosoma mansoni*

Sm28GST: *Schistosoma mansoni* 28 Gluatthion S -Transferase

S. haematobium: *Schistosoma haematobium*

Sh28GST: *Schistosoma haematobium* 28 Gluatthion S -Transferase

S. japonicum: *Schistosoma japonicum*

SWAP: *Schistosoma* Worm Antigen Preparation

SEA: Soluble Egg Antigen

SEP: Secretory-excretory products

SOD: Superoxide dismutase

SD: Standard deviation

Spp: Species

Tab: Table

TBRI: Theodor Bilharz Research Institute

TDR: Tropical Disease Research

Th: T-helper

TIS: Total immature stages

TNF-α: Tumor Necrotic Factor Alfa

TWB: Total worm burden

U: Unit

USA: United States of America

WHO: World Health Organization

µ: Micron

µg: Microgram

µl: Micro liter

µm: Micrometer

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Introduction

Schistosomiasis is a human disease caused by infection from one of several species of parasitic trematodes of the genus *Schistosoma*. It is also referred to as bilharziasis or snail fever (Mostafa et al., 1999). It is named bilhaziasis after Theodor Billharz, who described the infection in 1851. It is a major source of morbidity and mortality for developing countries in Africa, South America, the Caribbean, the Middle East, and Asia (Ross et al., 2002).

In the developing world, parasitic infections such as schistosomiasis are common; recurrent and long-lasting health problems due to such infection represent an ongoing inflammatory challenge and a significant health threat to the populations who are exposed to continuing daily risk of infection. Currently more than 200 million people worldwide are affected (Garcia, 2001). An estimated 600 million people are at risk of infection in 79 endemic countries, the disease continues to spread to new geographic areas (WHO, 2002 and Hotez et al., 2008).

Factors that favor spread include growth in international travel, refugee and population migration, and the development of new water resources, schistosomiasis is increasingly found in travelers returning from the tropics (Ross et al., 2002).

Although it has a low mortality rate, schistosomiasis is often a chronic illness that can damage internal organs and, in children, impair growth and cognitive development (Garcia, 2001). The urinary form of schistosomiasis is associated with increased risks

for bladder cancer in adults (Michaud, 2007). Schistosomiasis is the second most socioeconomically devastating parasitic disease after malaria (King and Dangerfeild-Cha, 2008).

Most human schistosomiasis is caused by *Schistosoma haematobium*, *Schistosoma mansoni*, or *Schistosoma japonicum*. Less prevalent species such as *Schistosoma mekongi* and *Schistosoma intercalatum* may also cause systemic human disease. Less importantly, other *Schistosomes* with avian or mammalian primary hosts can cause severe dermatitis in humans (e.g. swimmer's itch secondary to *Trichobilharzia ocellata*). Schistosomal infection with either *S. mansoni* or *S. japonicum* is associated with chronic liver and intestinal disease, whereas chronic *S. haematobium* infection can lead to fibrosis and calcifications of the urinary tract (Gryseels et al., 2006).

Schistosomiasis is a silent and neglected pandemic disease and priorities for treating it should be re-assessed (Van der Werf et al.,2003), the authors estimated the mortality rate from haematemesis caused by *S. mansoni* as 130 000 per year according to their collected data. King et al., (2005) attributed a disability weight of 2–15% to schistosomiasis. There is also growing evidence of the potential interaction between schistosomiasis and other diseases such as malaria, HIV/AIDS and tuberculosis (Brown et al., 2006).

Chronic endemic schistosomiasis may be causing significant morbidity and mortality due to the high incidence of dangerous complications. The disease caused by *Schistosoma* has been a major health problem throughout the developing world including Egypt (Kamel et al., 1999).It is not only a prime health problem but also an