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Vaccination of cattle against bovine schistosomosis: current status and future prospects: a review

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Abstract

Bovine schistosomosis, caused by *Schistosoma bovis*, constitutes a serious veterinary problem in many parts of the world. The vaccination approaches for the control of bovine schistosomosis include the use of irradiation-attenuated *S. bovis* cercarial or schistosomular vaccines, *S. bovis* adult worms or whole-egg antigens and defined antigen vaccine. Irradiated *S. bovis* cercarial or schistosomular vaccines provide partial protection against *S. bovis* infection. However, this type of vaccine requires live infectious cercariae or viable schistosomula for induction of protection. Unfortunately, experimental immunizations with dead schistosome antigens have been largely unsuccessful. The surge of new techniques in cellular immunology and molecular biology has made possible the development of potential candidate vaccine antigens from various species of schistosomes including *S. bovis*. The efficiency of these vaccines has been evaluated in experimentally infected calves. These vaccines will probably replace the irradiated *S. bovis* vaccines. A broad-spectrum antischistosome vaccine which can kill a variety of human and animal schistosome species is yet to be produced.

Keywords: Schistosoma bovis; Cattle; Vaccines

1. Introduction

Bovine schistosomosis, caused by *Schistosoma bovis*, is one of the major veterinary problems in many parts of the world including the Sudan (Hussien, 1968; Bushara et al., 1978; Saad et al., 1980; Aradaib, 1988, 1992; Aradaib et al., 1993,

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1994a). The economic importance of the disease is attributed mainly to losses occurring in animals 6–30 months of age, which are due to morbidity, mortality, retarded growth, liver condemnation and poor reproductive performance (McCauley et al., 1984).

Several studies on *S. bovis* in various regions of the Sudan have estimated prevalence rates based on abattoir records. In the southern region of the Sudan, the prevalence rates of the disease were 53% in the province of Equitoria, 62% in Bahar Elghazal and 47% in the Upper Nile (Elbadawi and Slepov, 1976). In the western region, the parasite was first reported in the Nyala and Elfashir central abattoir during a survey for helminth parasites. *S. bovis* constituted 89.7% of the internal parasites of ruminants (Malik, 1969). In an endemic area of the White Nile province of the Sudan, the prevalence rate of the infection was very high, approaching 90% in 1.5-year-old calves, as judged by fecal egg counts. Monthly incidence rates estimated from fecal examinations of initially uninfected calves showed a marked seasonal pattern, with the infection level being much higher in the rainy months. This coincided with a high snail infection rate (Majid et al., 1980b). In the vicinity of Khartoum, internal parasitic infections including *S. bovis* were diagnosed at the University of Khartoum Veterinary Medical Teaching Hospital, and the prevalence rate was 8% in resident dairy farms (Aradaib and Abbas, 1985). This constitutes a newly reported focus of the disease. In general, the prevalence of bovine schistosomosis increases in areas where development in agriculture and industry depends on construction of new dams and irrigation canals, which provide a suitable habitat for the snail intermediate host, the *Bulinus* spp. Therefore, it is not surprising for the disease to be encountered in the vicinity of Khartoum, as there is a growing livestock industry based on plant agriculture.

Special attention has been paid to the control of the disease in the Sudan for the last two decades (Hussien, 1973). The control of contaminated water and/or destruction of the snail intermediate host were impractical and not economical (Bushara, 1976). In spite of the development of effective and relatively safe drugs, prevention of rapid reinfection has remained a problem which requires repeated drug applications over a long period of time. Partial protection develops in cattle following prior exposure to *S. bovis* (Hussien, 1968). This indicates that vaccination could be a feasible and effective method for limiting the extent of pathology and level of transmission (Hussien and Bushara, 1976; Taylor and Bickle, 1986). The vaccination approaches for the control of bovine schistosomosis include those described in the following sections.

2. Irradiation-attenuated *Schistosoma bovis* vaccines

Irradiated *S. bovis* cercarial or schistosomular vaccines sensitized the host to schistosome antigen without acquisition of a patent infection (Hussien and Bushara, 1976). At least partial immunity to infection can be induced in laboratory animals by using irradiated schistosomular vaccine (Murrell et al., 1975; Mad-

dison et al., 1978; James et al., 1981; Smithers and Doenhoff, 1983). In cattle, *S. bovis* infestation can be partially prevented by prior immunization with homologous irradiated cercariae. Irradiated cercarial vaccines have shown their greatest promise in the control of bovine schistosomosis; experimental immunization of zebu calves with *S. bovis* cercariae irradiated at 3 or 20 krad induced partial protection against homologous challenge as judged by parasitological and hematological parameters (Bushara, 1976). Under field conditions in the endemic area of the White Nile province of the Sudan a single i.m. injection of 10 000 cercariae of *S. bovis* irradiated at 3 krad induced a 60% reduction in worm recovery and 80% reduction in fecal egg counts. Improved survival and body weight in the vaccinated calves were also recorded. The protection lasted at least 40 weeks (Majid et al., 1980a). The efficacy of the vaccine was 70% (McCauley et al., 1984). Similar results were obtained when Sudanese desert sheep were immunized with irradiated cercariae and challenged with normal cercariae of *S. bovis* (Bushara, 1976). However, the shorter life-span of the normal cercariae or the shistosomula necessitates the need for expensive cryopreservation of the vaccine. In addition, concern about the pathological lesions which may be produced by the irradiated vaccines limit their use as effective vaccines against schistosomosis (Aradaib et al., 1994b). Moreover, thousands of worms were recovered from the immunized calves at the time of perfusion (Bushara et al., 1978; Majid et al., 1980a; Aradaib, 1988). This indicated that the irradiated *S. bovis* vaccines induced immunity against challenge infection by suppressing worm fecundity without having any lethal effect on worm viability.

3. Non-living (dead) *Schistosoma bovis* vaccines

Unfortunately, experimental immunizations with dead antigens have been largely unsuccessful (Murrell et al., 1975; Maddison et al., 1978). However, successful immunization was achieved by Hillyer (1979), who reported significant reduction in the *S. bovis* worm burden of mice vaccinated with a crude antigenic preparation from *Fasciola gigantica*, a trematode parasite closely related to *S. bovis*, in Freund's complete adjuvant. In previous studies, we demonstrated that Nubian goats treated with immunopotentiating drugs such as levamezole (L-tetramezole) developed partial protection to infection with *F. gigantica*. The protection was reflected by reduced worm recovery at necropsy and by the development of less severe hepatic lesions (Goraish et al., 1988). Primary infection of sheep and cattle with *F. gigantica* provided partial protection against *S. bovis* challenge, but not vice versa (Yagi et al., 1986; Rodriguez et al., 1993). In our laboratory, extensive immunization experiments were conducted in the bovine species. Zebu calves were injected with schistosome antigen prepared from adult worms of *S. bovis* in an attempt to stimulate resistance to challenge with this trematode parasite. Unfortunately, the immunization experiments proved unsuccessful. There was no significant difference between the vaccinated and the control groups as determined by fecal and tissue egg counts, worm recoveries and

hematological parameters (Aradaib et al., 1993). In addition, *S. bovis* whole-egg antigen did not protect zebu calves against experimental schistosomosis using homologous challenge as judged by parasitological and hematological parameters (Aradaib et al., 1995). Protection was not achieved in spite of the detection of strong immune responses to both adult schistosomes and whole-egg antigens using the agar gel diffusion (AGID) or the enzyme-linked immunosorbent assay (ELISA).

4. Passive immunization by transfer of immune serum

The mechanism of immunity using passive-transfer experiments has been investigated. It was reported that serum from donors with chronic, naturally acquired infections did not produce a lethal effect on worm maturation when injected intraperitoneally immediately before challenge, but did provide suppression of fecundity of the adult worms in the recipient calves (Bushara et al., 1994). The role of humoral factors in immunity was also investigated in cattle using immune sera from naturally infected cattle. Serum was injected intraperitoneally into recipient calves which had been infected a month earlier. The control calves received either normal serum or saline. No significant difference in worm recovery, fecal egg count or tissue egg count was recorded between the three groups. However, sera from experimentally infected calves 8 and 12 weeks post infection were shown to contain factors capable of causing lethal damage to the worms and suppression of worm fecundity (Bushara et al., 1994).

5. Defined antigen vaccines

The surge of new techniques in cell immunology and molecular biology has made possible development of potential candidate vaccine antigens from complex organisms including schistosomes. A range of defined vaccine antigens has been identified. Two of the antigens which have shown vaccine potential in experimental *S. mansoni* infection are glutathione-S-transferase (GST) and GP38. The *S. mansoni* GST (smGST), developed by Capron and coworkers, is an enzyme of a molecular weight of 26–28 kDa in all species of schistosomes including *S. bovis* (Balloul et al., 1987a). smGST shares cross-reactive epitopes with other schistosome species including *S. hematobium*, *S. bovis* and *S. japonicum* (Balloul et al., 1987b; Trottein et al, 1992). smGST partially protected mice and baboons against homologous challenge. Both worm viability and worm fecundity are affected (Boulanger, 1991). In previous studies, zebu cattle were immunized with a recombinant smGST expressed in *E. coli* or yeast. Using Western blots and ELISA, immunoglobulin G (IgG) antibodies to smGST were detected in sera from the vaccinated calves, but not in sera from control calves. However, the specific IgG antibodies from *S. bovis* infected calves did not recognize smGST as determined by Western blots or ELISA. We suggested that structural variations

between *S. bovis* and *S. mansoni* GST might be responsible for this finding (Aradaib, 1988), and this has been confirmed by Trottein et al. (1992), who reported inter-species variation between schistosome 28 kDa glutathione-S-transferases by demonstrating structural difference within the immunologically essential regions of schistosome 28 kDa GSTs. Therefore, it was concluded that the primary antibody response induced by smGST in vaccinated calves may not have an association with protection against *S. bovis* challenge (Aradaib et al, 1994b). Subsequently, adult *S. bovis* were recovered from experimentally infected cattle and used for preparation of native *S. bovis* GST (sbGST). Zebu calves immunized with sbGST developed partial protection against homologous challenge under laboratory conditions. The protection was due to production of specific anti-sbGST IgG antibodies which have a lethal effect on worm fecundity and thereby induce suppression of egg production, as determined by fecal and tissue egg counts. However, no significant difference was observed in worm recoveries of the vaccinated animals or their controls. The *S. mansoni* GP38 shares protective carbohydrate epitopes with keyhole limpet hemocyanin (KLH) (Grzych et al., 1987). Similar results were obtained when KLH was used as immunizing agent against *S. bovis* infection (Bushara et al., 1993).

6. Conclusions

Experimental immunization against *S. bovis* infection, using non-living schistosome antigens, has been largely unsuccessful. Irradiation-attenuated *S. bovis* cercarial or schistosomular vaccines provide partial protection against challenge with homologous infection. These vaccines showed great promise under field conditions of the White Nile Province of the Sudan, where a single i.m. injection of 10 000 cercariae of *S. bovis*, irradiated at 3 or 20 krad, provided protection which lasted at least 40 weeks. However, production of such vaccines is laborious, time-consuming and expensive. In addition, they only induce egg suppression, but lack lethal effect on worm maturation. Moreover, the pathological lesion that might be produced by the irradiated vaccines limits their use as effective schistosomicidal vaccines. The sbGST or KLH vaccines protected cattle against challenge with *S. bovis* infection. However, the mechanism of protection induced by both types of subunit vaccines is mainly by suppression of egg production without having any effect on worm viability. A schistosomicidal vaccine which can kill *S. bovis* is yet to be produced. At the present time, KLH or sbGST probably will replace the current cumbersome time-consuming procedure required for the preparation of irradiated vaccines. Because of the structural variation within the immunologically essential regions of schistosome 28 kDa GSTs, smGST may not protect cattle against *S. bovis* infection. Nevertheless, because of cross-reactive epitopes between schistosome GSTs, the possibility of developing a broad-spectrum schistosomicidal vaccine exists.

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