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Short Communication

Study on chemotherapeutic value of imidorazi against sheep babesia infection

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ABSTRACT

The activity and efficacy of Iranian synthesized imidocarb dipropionate (imidorazi) has been tested against *Babesia ovis* infection in experimentally and naturally affected sheep. The results indicated that the drug is effective and could be used for treatment of sheep and goats babesiosis. The effectiveness of imidorazi is also similar to the imizol (imidocarb dipropionate) imported from abroad.

Keywords: Babesiosis, Chemotherapy, Imizole, Imidorazi, Feld trial

INTRODUCTION

Babesiosis, known as piroplasmosis, tick fever, texas fever, and splenic fever, is a disease complex caused by different intraerythrocytic protozoan parasites of the genus babesia in the varieties of vertebrate hosts. It induces a formidable problem in tropical and subtropical areas of South America, Africa, Asia, the Middle East and Eurpoe (Adams 1998 & Levine 1985). The most significant symptoms of babesiosis are immediate increasing fever, haemolytic anaemia, haemoglobinuria, icterus, emaciation and in severe cases death (Levine 1985). In Iran variety of babesia species infecting different range of domestic and wild animals are reported. But it is emphasize that sheep and goats babesiosis, in contrast to others, cause problem because rearing sheep and goats are the most important sources of farmers and nomads income (Kuttler 1981). The morbidity and mortality rate of infected animals in Iran approximately reach to 25% and 12% respectively (personal experiences during 43 years research work in Razi Institute) As there is not yet available effective vaccine for sheep and goats babesia infections, chemotherapy and chemoprophylaxis remain the principal defenses against in current control strategies (Kuttler 1981, Mchardy 1974). Numerous chemical compounds have been used for treatment of babesiosis, but imidocarb dipropionate is highly effective without significant side-effects provided that it is injected at accurate dose. The drug fixes on red blood cell membranes, block up the receptors responsible for the incorporation of the inositol which is vital element for the parasite metabolism, consequently death of parasite occurs inside the RBC (Hashemi-Fesharki 1975). Fortunately, our chemists recently

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synthesized the most effective drug named imidorazi (imidocarb dipropionate). This paper describes whether imidorazi could be used as an effective and suitable drug for treatment of affected animals with *B. ovis* infection or not?

MATERIALS AND METHODS

During the last three years (2004-2007), several investigations related to the activity of Iranian synthesized imidorazi (imidocarb dipropionate) and it's adverse effects against sheep babesiosis have been carried out. The effectiveness of imidorazi also was compared with the imizol (imidocarb dipropionate) imported from abroad. Summarized data were described as follows:

Isolation of acute *Babesia ovis* strain. To accomplish the effectiveness of imidorazi against sheep babesiosis, acute *Babesia ovis* strain was isolated from naturally infected sheep. All necessary examinations indicated that the isolated strain was highly virulent for healthy intact sheep and free from other pathogenic micro-organisms. This strain was cryo preserved at liquid nitrogen (-196 ^{o}C) until next use.

Laboratory trials. Totally 12 lambs, aged 6-8 months old were chosen, shearing and spraying with suitable acaricide. They were kept under strict observations in order to be sure that they were free from any infection. The animals were divided into 4 groups and the effectiveness of imidorazi and its side effects were evaluated as follows:

Group one: consisted of 4 lambs which were splenectomized and maintained under strict observations for a period of one month. During this period, a) daily blood smears prepared from peripheral and jugular veins stained and checked microscopically, b) biopsy smears from prescapular lymph nodes also were prepared four times and controlled by light microscopy. All splenectomized lambs were in healthy conditions and pathogen-free.

Firstly. Two splenectomized lambs were infected (IV) by the *Babesia ovis* strain. They showed acute clinical symptoms with rising temperature to 41-41.2 ^{o}C and parasitaemia rate reached to 20% in one animal and 15% in second one. Both animals were treated with imidorazi at concentration level of 1.5 mg/kg. 24 hours later the temperature decreased and reached to normal and parasitaemia rate also reduced to 0.2%. though 0.2% parasitaemia rate was not significant but the animals received imidorazi at level of 1.5 mg/kg 12 days later than first injection. Three days after last injection no *Babesia ovis* was seen in blood smears. The treated animals were kept under observations for a period of 1 month, during which no Babesia have been seen and they were recovered completely.

Secondly. The reminder 2 splenectomized lambs also were infected with *Babesia ovis* strain from the first two infected animals before their treatment with imidorazi. These animals revealed parasitic and thermal reactions and received imidorazi at level of 1.5 mg/kg two times at an interval of 24 hours. 72 hours later no babesia was seen in their blood smears and no symptoms of toxicity were also indicated in both of them. Group two: consisted of four intact lambs were infected (IV) with the isolated *Babesia ovis* strain. Acute clinical symptoms of babesiosis were observed. The animals received imidorazi in concentration level of 1.5 mg/kg, 2 times at an interval of 24 hours. 48 hours later, all clinical symptoms were disappeared and 5 days after the last injection the body temperature reached to normal level and no parasitaemia was seen and no symptoms of toxicity were also indicated. Group three: consisted of 2 lambs which were considered as first controls. They received only the isolated *Babesia ovis* strain. Three days later acute clinical symptoms were observed. One lamb was died from acute babesiosis due to *Babesia ovis* infection. This investigation indicated that the isolated strain was very virulent. Group four: consisted as 2 lambs which were considered as

second controls. They received only imidorazi at concentration level of 1.5 mg/kg two times at an interval of 24 hours. The animals were kept under observations for a period of one month, during which any significant side effects were not observed and the animals tolerated well the drug at concenteration levels used for treatment.

Field Trials. Two sheep herds consisted each approximately 100 animals, located around the institute, were considered for this investigation. Their blood smears were microscopically checked, and found that 10-15% of sheep in each herd were infected with babesia ovis. The parasitaemia rate was 0.5-5% in both herds. All animals were injected with imidorazi at level of 1.5 mg/kg. Their blood smears were taken at 5, 7, 15 and 21 days post treatment, checked microscopically and no babesia was seen. Comparative study on effectiveness of imidorazi and imizol: Laboratory Trials: 15 lambs were chosen and divided in 3 groups. They were infected experimentally with the virulent *Babesia ovis* strain. After appearance of clinical symptoms the animals were injected as follows: First group consisted of 5 lambs were injected (SC) with imidorazi at concentration level of 1.5 mg/kg. Second group consisted of 5 lambs were injected (SC) with imizol at concentration level of 1.5 mg/kg.Third group consisted of 5 lambs which were considered as controls. The first and second groups were recovered and no *Babesia ovis* was seen in their blood smears during one month post treatment. Third group showed acute clinical symptoms of babesiosis and one lamb was died due to acute *Babesia ovis* infection. *Field Trials:* For this purpose two sheep herds each consisted of 50 animals were chosen. All sheep from both herds were checked and 9 sheep from first herd and 12 sheep from second herd were infected with Babesia ovis. The parasitaemia level was 0.5-5% respectively. The infected animals from first herd were injected (SC) by imidorazi at level of 1.5 mg/kg and the infected animals from the second herd were injected (SC) by imizol at level of 1.5 mg/kg. All treated animals from both herds were kept under observation and their blood smears at 7, 14 and 21 days post injection were evaluated microscopically. The results were satisfactory and no Babesia was seen.

RESULTS AND DISCUSSION

The results of laboratory and field trials on activity of imidorazi against sheep infected with *Babesia ovis* showed that it could be used as an effective drug. Its therapeutic value in treatment of babesiosis is similar to imizol, and it has a high safety margin without significant adverse effects in treated animals, provided that it uses under veterinary approval instructions. Recovery from clinical symptoms of babesia infection is the rule of treatment if the drug is given early in the course of infection. Nevertheless if treatment is delayed, supportive drugs should be administered. Imidocarb dipropionate has also successfully used as a chemoprophylactic effect at a dose rate of 2.5-3 mg/kg body weight that prevent babesia clinical symptoms for a period of 6-8 weeks (Bellelic *et al* 2006). However in contrast of differences in depletion of imidocarb residue in meat and milk, it is suggested that great care should be taken in defining the withdrawal time for human consumption. According to the recommendations of scientists from different countries and our experiences, it is emphasized that the curative treatment of babesiosis is valuable aspect of control program that will probably be in use for years in any future eradication effects (Hashemi-Feshaki 1991, Kuhler 1980, Mchaedy & Simpson 1974). Furthermore, it is needed to mention that the ever-broading scope of babesiosis in human and animals has focused attention on the development of appropriate treatment to moderate clinical signs in acutely infected individuals and eliminate or prevent infections. The drug such as imidorazi has these

particularities and accepted as a suitable drug for this purpose.

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