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Comparative Study of Ivermectin and Cypermethrin against *Sarcoptes Scabiei* in Rabbit

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Abstract:

Background: Scabies is a contagious disease caused by microscopic mites which borrow the skin and infect all wild, domestic animals as well as human beings. Which show signs or lesion mostly on ears, eyes, abdomen, nose, and inguinal region. **Objective:** The aim of the present study was to compare the efficacy of single topical dose of ivermectin (1%) in cream form and topical cypermethrin (1%) in spray form per week in the rabbits against scabies. While in this study cypermethrin was used first time against *Sarcoptes Scabiei*. **Methodology:** In this study, total twelfth (12) local varieties rabbits were used by authors. In which eight (08) rabbits (04 naturally infested and 04 in contacts rabbits) were used for *Sarcoptes scabiei* treatment, while four (04) healthy rabbits were kept in separate group as a negative (-) control. In group A, ivermectin (1%) in cream form was used, although, in second group cypermethrin was used in spray form on a weekly base while, group C remained as such fed with food and water ad libitum and no treatment was done. Clinical and microscopic examination was done by weekly base while taking skin scraping samples. **Results:** Furthermore, in both groups treatment was done at the same time and same route. This study shows that cypermethrin is superior in the recovery of scabies than ivermectin. **Conclusions:** Therefore, it was concluded that cypermethrin animal preparation could be effective, safe, and practical treatment alternative for Scabies on weekly base until recovery. However, further studies should be performed for determination of exact therapeutic doses.

Keywords: lesion, *sarcoptes scabiei*, ivermectin, cypermethrin

1. Introduction

Scabies is a contagious skin infection caused by the mite *sarcoptes scabiei* (*S. scabiei*) which is microscopic parasite burrowing under the host's skin (Chosidow, 2006). The Italian physician Giovan Cosimo Bonomo and the apothecary Diacinto Cestonifor the first time described the causative relation between the scabies mite and distinctive lesion appeared on skin after infestation in 1687 (Ramos-e-Silva, 1998).

Scabies is a major public health threat in the developing countries occurring mostly in resource-poor urban and rural communities, with prevalence reaching to 10% in the general population and 50% in children (Chakrabarti, 1985, Heukelbach and Feldmeier, 2006). The incidence in the children younger than 6 years was 952 per 1000 per year in the urban area of Bangladesh (Stanton et al., 1987).

According to 2010 data, scabies affects approximately 100 million people (1.5% of the population) and is equally common in both genders. While according to 2009, worldwide 300 million cases of scabies occurred each year (Andrews et al., 2009, Lim et al., 2013, Abdo et al., 2009).

Sarcoptic mange is a transmittable disease of farm and wild animals. Infested animals can lose body condition, become weak and die. European wild rabbits (*Oryctola- Guscuniculus*) were only recently reported suffering with scabies (Millán, 2010). *S. scabiei* is the agent which causes invasion and affects the ear, nose, eye, abdominal area, feet and area around the genitalia; it also causes dermatitis and itching (Aiello et al., 2002). Animals affected by *S. scabiei* are hypertensive and experience weight loss and invasion may lead to complications and deaths due to development of secondary infections. Mostly peripheral parasites are present, which cause dermatitis. The mite are affecting ear, mouth, perineal region and around the eye (Pandey, 1989).

Due to the availability of effective chemotherapy as well in Northern Australia, the prevalence of the scabies is up to 50% in the children (Walton and Currie, 2007).

Both in animals and human, treatment of scabies may be initiated with avermectin group. This group includes ivermectin, abamectin, doramectin, eprinomectin and celamectin. Any one of these can be use for the treatment of *S. scabiei*. Ivermectin can be obtained from a fungus streptomyces avermitilis. Ivermectin has the potential to show broad-spectrum activity against many internal and external parasites, more especially, nematodes and arthropod parasites. It acts by binding to the glutamate-activated Cl⁻ channels of the parasite, preventing their closure. Therefore, Cl⁻ flows into the cells, the cell membrane is hyperpolarized. The mite is slowly and gradually paralyzed and died (Turner and Schaeffer, 1989).

A study conducted for the treatment of scabies in pig using ivermectin 300 to 500 micro-grams per kilogram ($\mu\text{g}/\text{kg}$) body-weights (BW). The results of this study showed that using ivermectin at the above stated doses cured the scabies in pigs. However, the same drug at 180 $\mu\text{g}/\text{kg}$ BW was found less effective (Lee et al., 1980). Topical ivermectin and permethrin were equally effective against scabies while oral ivermectin was found significantly less effective used for 2 weeks (wks.) (Chhaiya et al., 2012). Moreover, ivermectin has also used in combination therapy with oral ivermectin and topical benzyl benzoate solution (15%) is preferable to single-agent therapy in crusted scabies in human immune-deficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) patients. This therapy has a most advantageous rate of success, without significant side effects (Alberici et al., 2000).

Cypermethrin is a synthetic pyrethroid, synthesized on a large commercial scale, which is used as an insecticide having agricultural use as well as in other products. Its mechanism of action is neurotoxic for insect. Cypermethrin is carcinogenic for human being as well as for other aquatic and domestic flies (Amer and Aboul-ela, 1985). In one study it is shown cypermethrin prevent cellular communication between adjacent cells which play a role cell survival and inhibited by carcinogenic agents (Tateno et al., 1993).

The permethrin is the best therapeutic options use for all forms of scabies, which is a scabicide with low toxicity. The management of crusted (Norwegian) scabies in human immune deficiency syndrome (HIV/AIDS) is more difficult to treat and require, continual treatment with scabicide and occasionally chronological of several agents (Orkin and Maibach, 1993).

The side effect of cypermethrin included licking of the body parts on which side it's applied, muscular tremor, ataxia, salivation and convulsions (Ullah et al., 2006). Cypermethrin cross the blood-brain barrier and induce neurotoxicity and motor deficits. Cypermethrin, which prolong the opening of sodium channel, main site of its action lead to hyper-excitation of the central nervous system. This is causing rhythmic nerve action recovery through persistence of sodium permeability during the recovery stage of the likely of neurons (Singh et al., 2012).

The aim of the present study was to compare the efficacy of single topical dose of ivermectin (1%) in cream form and topical cypermethrin (1%) in spray form per week in the rabbits against scabies.

2. Materials and Methods

The study was conducted in project "Up Gradation of Our Local Rabbits for Meat Production" approved from National Agriculture Research Center (NARC) association with China Organization in Department of Poultry Science, Faculty of Animal Husbandry and Veterinary Sciences (FAH&VS); The University of Agriculture, Peshawar-Pakistan.

2.1. Laboratory Animals

Total of twelfth (12) 0.8-1.5 years old rabbits of local varieties were kept in a separate room for 10 days (d). After ensuring that rabbits were not affected from other diseases for quarantine period, they were taken to another room in which the rabbits of the unit were also kept. Four (04) rabbits were separate and kept as a control negative (-) group. While eight (08) rabbits (Four (04) of the rabbits in the unit were infected by four (04) newcomers) were used for *S. scabiei* treatment as shown in table 02. Food and water were available *ad libitum* and the animals were kept in the dark for 12 hour (h) and in the light for 12 h each day. Macro and Microscopic examination revealed that group A and B were infested with *S.scabiei*. Treatment of these rabbits was scheduled as a part of research.

2.2. Clinical and Laboratory Examinations

After clinical examination, each of the rabbits was marked. Both groups A and B received scores three (03), while group C received zero (0) as shown in table 01, depending on its degree of infestation, as follows:

- Severe (group A and B)
- Control – (group C)

All animals were placed in three cages (each 90 x 90 x 90 cm), with one cage for each group. Skin scrapings from each rabbit were taken from at least two different sites, such as ears, nose, feet, tail, and inguinal region. These scrapings were placed in a petri dish which was closed.

Each sample was dissolved in 5 ml of a 10% solution of potassium hydroxide (KOH). The mixture was stirred, centrifuged and discarded supernatant. From each sample a few drop of solutions were placed on a slide for examination using light/stereomicroscope under x 10, x20 and x 40 magnification. The groups A and B were graded as sever (++++) and group C (-) healthy as shown in table 03.

Clinical and parasitological examinations were conducted at day 0 (prior to treatment) and subsequently weekly before treatment. The lesion score were present on all animals of group A and B according to degree 03 in Table 01.

Lesion	Score
Clear shinny body, no lesions around eye and ear	0
Lesion extending to 2/3 of ear pinna, external genitalia, above nose, around eye, feet and lose body hair/fur	03

Table 1: Lesion score

Treatment protocol	Lesions area	No. of animals affected	Cases	Group
Ivermectin	Ear, nose, feet, around external genitalia & eyes	04	Severe	A
Cypermethrin	Ear, nose, feet, around external genitalia & eyes	04	Severe	B
Control (-)	No lesions	04	Healthy	C

Table 2: Proposed Experimental Layout:

2.3. Treatment

Infected rabbits of group A, received ivermectin (1%) in cream form while group B received topical spray of cypermethrin (1%). The treatment was done thoroughly on weekly interval i.e. on day 0, 7, 14, 21 and 28, while clinical and microscopic examinations of all rabbits were also performed prior to treatment.

Figure 01. Effect of ivermectin and cypermethrin in rabbits. Ivermectin (1%) was topically applied for 4 weeks. Values are expressed as mean ± SEM (n=4).

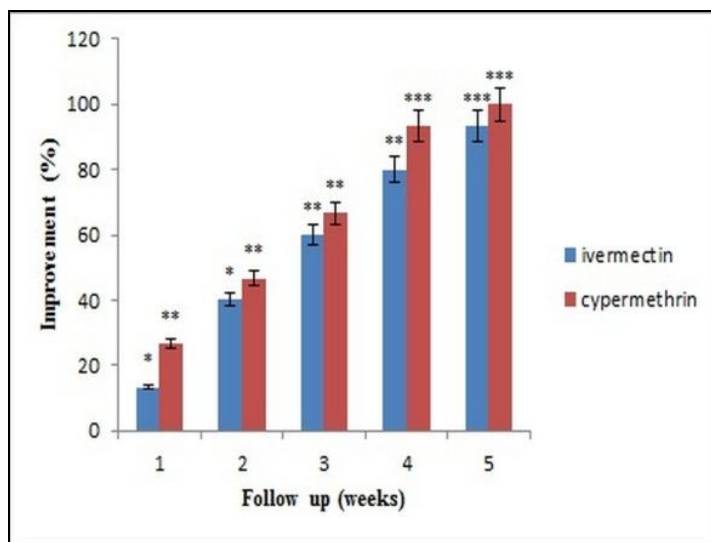


Figure 1

3. Result

In highly infested both groups, ears lobes, around eyes, most of the nose and skin recorded before the treatments are shown in table 03. This was based on degree of alopecia, degree of crust formation, and intensity of lesions.

Intensity of infestation	Group No.	Area of alopecia	Degree of alopecia	Degree of crust formation	Casual species and intensity of lesions
High	Group A	Nose, eyes, ears, inguinal region, paws	++++	++++	Scarcoptes Scabiei (++++)
High	Group B	Nose, eyes, ears, inguinal region, paws	++++	++++	Scarcoptes Scabiei (++++)

Table 3: Clinical and microscopic parasitological examination of the mange-infested rabbits pretreatment + Present, ++ low, +++ medium, +++++ high

In highly infested rabbits, the ear lobes, eyes, skin of the nose, most of the skin of feet were reddish prior the treatment. The mean lesions score of different groups of rabbits (group A and B), recorded before treatment, is shown in table 03.

The clinical and parasitological examinations revealed that these rabbits were naturally infested by eggs, larvae, nymph and adult mites of *S. scabiei* in table 03. While there was an average of 8-10 adult mites per slide each rabbit in both groups prior the treatment. Clinical and parasitological examinations were conducted on day 0, 7, 14, 21 and 28. The percent improvement occurred on weekly base in both groups as a whole is shown in figure 01 which showed that cypermethrin were effective against *S. scabiei*. For parasitological examinations, skin scraping was conducted to identify the mange mites as shown in table 04.

On day 07, the recovery rate, especially among the rabbits of group A was slower that had received ivermectin compared to those which had been spray cypermethrin. The shedding of crust was also slower in ivermectin group in first week than in the group which had cypermethrin spray.

The clinical examination performed on day 14 after commencing treatment revealed that, both drugs had effectively decreased the microscopic mange mites. While, recovery was faster among rabbits in group B than A. As indicated in Figure 01, the comparative improvement occurred in both groups, a significant recovery was observed after 2nd week in cypermethrin group, $p < 0.01$ and $p < 0.001$, respectively. While, animals treated with ivermectin (1%) were slight slow.



Figure 2: Clinical recovery of *S. scabiei* infestation rabbit in group B. left side: Before treatment day (0), right side: After the recovery on day (28)

Group and Animal No.	1 st Week			2 nd Week			3 rd Week			4 th Week		
	Mange agent	Alopecia degree	Shedding of crust	Mange agent	Alopecia degree	Shedding of crust	Mange agent	Alopecia degree	Shedding of crust	Mange agent	Alopecia degree	Shedding of crust
A1	++++	+++	++++	++++	+++	+++	+++	++	+++	++	++	+
A2	+++	+++	++++	++	+++	++	++	++	++	+	+	+
A3	++++	++++	+++	+++	+++	+++	++	+++	+++	+	+	+
A4	++++	+++	+++	+++	++	++	+++	++	++	++	+	+
B1	++++	+++	+++	+++	+++	++	++	++	+	+	+	No crust
B2	++++	+++	+++	+++	++	+++	+	++	++	-	+	No crust
B3	++++	+++	+++	++	+++	+++	++	++	++	+	-	No crust
B4	++++	+++	+++	+++	+++	++	++	++	+	-	+	No crust
C	-	-	-	-	-	-	-	-	-	-	-	-

Table 4: Findings of clinical and microscopic examinations performed at weekly base after commencement of treatment + Present, ++ low, +++ medium, ++++ high

On day 28, all rabbits that had received either ivermectin or cypermethrin had recovered. On parasitological examinations, there was no presence of larvae, nymph, or adult stage of *S. scabiei*. Consequently, it was concluded ivermectin and cypermethrin were effective in both groups. But the ivermectin was little slower in recovery rate, of animal as shown in table 04. The microscopic examinations in group A, revealed presence of some mange mites in rabbits. After termination of study on the 28th day, crust disappears, and hair growth in previously infected area of rabbits was observed in group B as shown in figure 02.

4. Discussion

Previously study showed that rabbits, infected naturally with *S. scabiei*, were injected subcutaneously with a single dose of ivermectin at 200 µg/kg of BW while the other group was administered with 400 µg/kg of BW. The effect of the drug was evaluated clinically,

microscopically and parasitological over 5 weeks. All animals shown significantly recovery in therapy, but the regression of lesion was faster in rabbits administered 400 µg/kg of ivermectin (Pandey, 1989).

Another study suggested that topical application of selamectin at a dose of 6 to 18 mg/kg can completely eliminate mites from rabbits naturally infested with *Psoroptes cuniculi* (ULUTAS et al., 2005).

In one study it's recommended that different dose and administration route of ivermectin and doramectin for ear mange are highly effective (Pandey, 1989). The injection of moxidectin 1% has also effective result against sarcoptic mange (Wagner and Wendlberger, 2000). Doramectin is extremely efficient against various types of ear mange. Particularly, *S. scabiei* and *psoroptes cuniculi* can be treated with the dose rate 200 µg/kg BW infestations (Kaya et al., 2009).

A study was conducted in India, which show that permethrin is superior to a single dose of ivermectin. In which single dose of permethrin is more effective than two doses of ivermectin. Both drugs are effective in prevention over a period of 2 months. But a single dose of permethrin was more effective against scabies (Usha and Gopalakrishnan Nair, 2000).

In our study, after commencing the treatment, itching was still present in group A. On day 14, in group A there were some live mange mites which were dead on day 21 in most of the animals. While, in group B most of the rabbits have no live mange mite on examinations on day 14. The clinical examinations which were performed on day 28 suggest that in group B infestation, the crust had been completely shed and hair had started to grow again in those areas. While parasitological examination revealed that there were dead mange mites in groups B, and all animals were cured and had shed crusts and hair had grown again (table 04).

The laboratory staff and other co-workers should take care when managing the laboratory animals because some time it can also transmitted to human being, but it is not so common. It is very important to wear gloves, laboratory coat and mask, especially during handling *S. scabiei* animals. Although, *S. scabiei* generally does not cause infestation in human, it is better to be cautions when you are not aware of the health status of someone.

5. Conclusions

This study demonstrated that both ivermectin and cypermethrin are effective and safe for clearance of clinical signs and reduce the mange microscopically. However, ivermectin was not effective against all stages in lifecycle of the parasite. Microscopic and clinical examinations showed that there was no significant difference between the effectiveness of cypermethrin and ivermectin; however, cypermethrin faster in regression of crust and adult mites than ivermectin. This study shows that cypermethrin is superior in the recovery of scabies than ivermectin. The rapidity of cure was more in the severe groups B of infestation treated with cypermethrin. Furthermore, controlled prospective studies, including larger groups are needed to further evaluate efficacy of the treatment protocols.

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7. Conflict of interest

The authors declare no conflict of interest.

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