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The efficacy and safety of permethrin 5% vs ivermectin 1% in the treatment of uncomplicated scabies

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Abstract
Human scabies is an intensely pruritic skin infestation caused by the host-specific mite *Sarcoptes scabiei var hominis.* Scabies is a global public health problem, affecting persons of all ages, races, and socioeconomic groups. Scabies impairs the quality of life of patients and their families by the itching. Worldwide, an estimated 300 million cases occur annually. Permethrin 5% has been used widely as scabicidal drug. A new search for alternate scabicidal drugs is a need of the hour due to emerging permethrin resistance. Oral Ivermectin has been used in the management of scabies, with only a little exploration about topical Ivermectin.

Keywords: Scabies, permethrin, ivermectin, permethrin resistance

Introduction
Scabies is a common dermatological problem affecting all races, ages, and social classes. The treatment of Scabies has undergone developments with the evolution of new antiectoparasitic drugs like Permethrin and Ivermectin. Yet the burden of the disease continues to be high in developing countries like India and highest prevalence is present among nursing homes, care centres, orphanages, old age homes and hostels.
Recent observations, have noted emerging drug resistance to Permethrin and oral Ivermectin [1]. Thus, there is a need to research and assess other available therapeutics and to explore newer therapeutic options [2, 3].
This study was done to investigate the safety and efficacy of topical application of Permethrin 5% lotion [2] in comparision with topical application of Ivermectin 1% lotion [1] on the human ectoparasite *sarcoptes scabiei*.

Methods
This was an open label, randomized, comparative parallel group clinical study.
A total of 200 patients were selected from the Outpatient department of Dermatology, Venereology and Leprosy, Narayana Medical College hospital, Nellore from, 20-01-2019 to 19-06-2019. Subjects with clinically diagnosed to have Scabies and were randomly allocated into two groups. First group were presribed Permethrin 5% lotion, second group Ivermectin 1% lotion and were instructed to apply two times one week apart. All the patients received anti-histamines Tab Hydroxyzine hydrochloride according to their body weight for pruritus. The patients were followed up at the end of 2nd and 4th weeks. Primary efficacy was assessed by clinical improvement of skin lesions and itching. Statistical analysis was done by chi square test using SPSS version 20 and t-test.

Inclusion criteria
- Patients
- With uncomplicated Scabies, who were willing to participate in the study voluntarily.
- Did not use any oral or topical medications 1 month prior to the onset of present episode.

Exclusion criteria

The subjects who were

- Pregnant women
- Children < 5 years
- Patients suffering with any systemic diseases.
- People with psychiatric illness
- People with HIV and with other immune compromised diseases.
- People on oral immunosuppressive therapies were excluded from the study.

Severity of itching was graded on qa scale of to 0 – 30. No itching

1. Mild itching (Pruritus with need to scratch but with out excoriation)
2. Moderate itching. (Pruritus unrelieved by scratching accompanied with or without excoriation)
3. Severe / intense itching. (Totally restless, each episode causing sleep disturbances).

Statistical analysis

Statistical analysis of our study was performed using the software Statistical Package of Social Science version 20(SPSS). The demographic data consist of the means of two samples for comparison of functional scores before and after treatment were analyzed using t-test, chi-square. Differences in proportions and efficacy were compared with the Chi-square test and comparison between two groups regarding clinical and functional outcome of our study was done using t-test while considering the initial values of efficacy. $p<0.05$ was considered to be statistically significant. The data were reported as mean ± SD and frequency.

Results

Table 1: Baseline Characteristics of two treatment groups

S.NO		Permethrin 5% (n=100)	Ivermectin 1% (n=100)	p-value
1	Age (years)			
	Mean ± SD	28.58 ± 16.62	22.12 ± 13.66	*p=0.003
	Range	6 – 77	7 - 72	
2	**Sex**			
	Male : Female	66 : 34	76 : 24	@p=0.119
3.	**Nocturnal Variation**			
4.	Yes/No	47/53	49/51	@p=0.777
	Duration	10.54 ± 2.935	10.07 ± 3.715	@p=0.322

*significant at 0.05 level; (P<0.05);@-Not significant (p>0.05)

Patients affected with scabies in the present study were of the ages between 6 to 77 years with the mean age of patients treated with Permethrin was 28.58 years (±16.62) and that of Ivermectin was 22.12 years (±13.66).

This study shows more male patients suffering with scabies who were included in this study with ratio of 66:34 (M:F) in Permethrin group and 76:24 (M:F) in Ivermectin group.

Table 2: Improvement of clinical grade at each follow up visit

	Permethrin5% (n=100)			Ivermectin (n=100)		
	Initial	**2nd week**	**4th week**	**Initial**	**2nd week**	**4th week**
Severe	49	20	3	51	30	18
Moderate	51	21	5	49	33	17
Mild or no itching	0	46	25	0	37	22
Skin Lesions	100	62	93	100	41	65

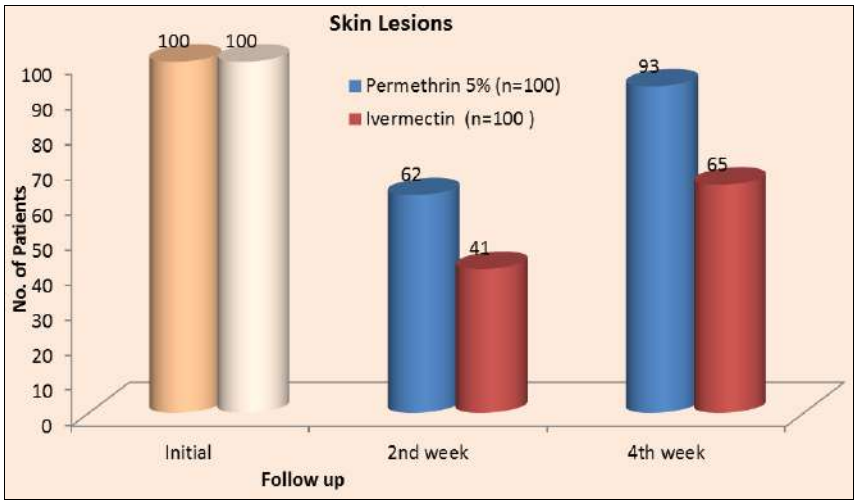

Fig 1: Clinical cure rate at different visits.*shows p=0.013 ($p<0.05$ for permethrin compared to ivermectin lesion at the end of 4 weeks using student t-test.

In group 1 at initial presentation, had skin lesions of various types that include papules, burrows, nodules, excoriations. After usage of two applications of topical Permethrin 5% lotion at the end of two weeks 62% showed complete clearance of their skin lesions and at the end of 4 weeks 93% showed cure of their skin lesions. 7% showed no response to the treatment.

In group 2, at intial presentation had skin lesions of various types that include papules, burrows, nodules, excoriations. After usage of two applications topical Ivermectin 1% lotion, at the end of two weeks 41% showed clearance of their lesions and at the end of 4 weeks 65% showed clinical improvement in their skin lesions. 35% showed no response to the treatment.

In group 1, patients with severe itching were 49%, while with moderate intensity itching were 51%. After using topical permethrin 5% two applications with a gap of one week, 46% showed significant improvement in their severity of itching, 21% had moderate intensity itching and 20% showed no improvement. Those with moderate to severe itching were advised to continue oral antihistamines, tab Hydroxizine Hcl for 2 more weeks. At the end of 4 weeks only 3% showed no response to treatment and continued to have severe itching and 5% experienced moderate itching, while itching subsided completely in the rest of the patients.

In group 2, patients with severe itching were 51%, while with moderate intensity itching were 49%. After using topical ivermectin 1% lotion two applications with a gap of one week, 37% showed significant improvement in their severity of itching, 33% had moderate intensity itching and 30% showed no improvement. Those with moderate to severe itching were advised to continue systemic antihistamines, tab Hydroxizine Hcl for 2 more weeks. At the end of 4 weeks 18% showed no response to treatment and continued to have severe itching and 17% experienced moderate itching, while rest of the patients had no itching.

Thus in present study group 1 showed good clinical improvement in terms of itching and skin lesions at the end of 2nd and 4th week, when compared to that of group 2.

Table 3: Improvement of Itching at each follow up visit

	Permethrin5% (n=100)			Ivermectin (n=100)		
	Initial	**2nd week**	**4th week**	**Initial**	**2nd week**	**4th week**
Itching						
Yes	100	62	93	100	43	69
No	0	38	7	0	57	31

Note: Itching at different visits - * shows $P < 0.05$; for permethrin cream compared to ivermectin lotion at the end of Second and Fourth week using Chi-square test;

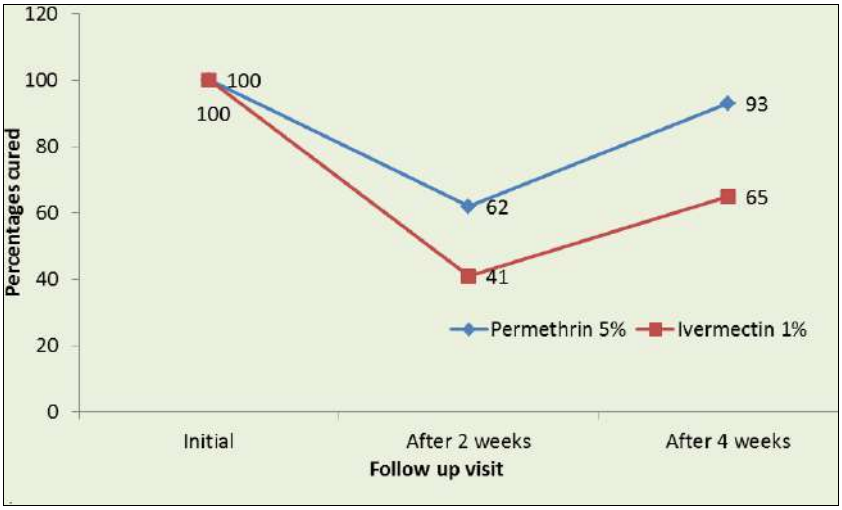

Fig 2: Clinical cure rate at different visits.*shows p=0.013 (p<0.05 for permethrin compared to ivermectin lesion at the end of 4 weeks using student t-test

Considering pruritus as main symptom, the anti scabetic medication, which alleviates it, has greater acceptance in clinical practice. Improvement in itching grade at different visits (Table 2 and table 3), showed that topical permethrin 5% lotion is more effective in releiving itching compared to topical ivermectin 1% lotion.

SAFETY

Table 4: Side effects with topical Permethrin 5% lotion and Ivermectin 1% lotion

Complaints		**Group**		
		Permethrin5% (n=100)	**Ivermectin (n=100)**	
Erythema	Yes	0(.0)	0(.0)	-
	No	100(100.0)	100(100.0)	
	Total	100(100.0)	100(100.0)	
Burning Sensation	Yes	0(.0)	12(12.0)	$\chi 2$= 12.766** (p=0.000) df= 1
	No	100(100.0)	88(88.0)	
	Total	100(100.0)	100(100.0)	
Complaints	Yes	0(.0)	0(.0)	-
	No	100(100.0)	100(100.0)	
	Total	100(100.0)	100(100.0)	

**significant at 0.01 level;

In group 1 individuals who used topical permethrin 5% lotion, showed no localized or systemic side effects.

While that of group 2 individuals who used topical ivermectin 1% lotion,

12 persons reported burning sensation up on intial application which subsided spontaneously did not

experience similar burning sensation on the second application.

Discussion

The word Scabies is derived from latin word "scabere" meaning to "scratch". Scabies is caused by the host-specific mite *Sarcoptes scabiei var hominis*, an obligate human parasite. It is a member of the family *Sarcoptidae*, which belongs to the order *Astigmata*, in the subclass *Acari*, class *Arachnida*.

The mainstay of scabies treatment is the application of topical scabicidal agents, with oral antihistamines for symptomatic relief. Topical drug therapies include Permethrin 5% lotion, precipitated sulfur 6% in Petrolatum, 1% Lindane, 25% Benzyl benzoate, 10% Crotamiton and 1% Ivermectin [5].

Except Permethrin and Ivermectin, all other topical medications have limitation due to more applications, side effects, poor therapeutic and symptomatic response.

Permethrin: It acts by disrupting the sodium channel current, resulting in delayed repolarization, paralysis, and death of the parasite. Sodium channels are ubiquitous and therefore permethrin acts at all stages of the life cycle of the parasite. Furthermore, topical application ensures maximum concentration of the drug in the skin accounting for the superior efficacy. Permethrin's systemic absorption through cutaneous route is very low. It is rapidly metabolized by skin esterases, and excreted in urine. It can be used safely in young children. It has got very rare and mild to moderate side effects with a good safety profile.

Topical Ivermectin

Ivermectin (22, 23 – dihydroavermectin B1b) is a broad spectrum anti parasitic drug. Ivermectin is approved by the US Food and Drug Administration in the year 1996, and used orally worldwide to treat patients with Onchocerciasis and Strongyloidiasis [6]. It is also used against a wide range of endoparasites (nematodes) and ectoparasites (insects, acarine) of animals and humans. It binds to glutamate-gated chloride iron channels, which are present in invertebrate nerve and muscle cells, and causes the paralysis and death of the parasite. For scabies management, it is tried orally at a dose of 200µcg/kg two doses with a gap of 1 to 2 weeks [7]. The drug has a wide margin of safety. However, during clinical trials of the drug, adverse reactions like fever, pruritus, dizziness, and edema were observed. These reactions are generally mild and transient. Occasionally it may cause postural hypotension. Toxic effects include mydriasis, somnolence, depressed motor activity, tremor and respiratory paralysis.

A few studies have reported efficacy of topical Ivermectin in scabies [9, 10, 11].

Our study showed topical Permethrin 5% lotion has got greater efficacy and safety as anti scabitic medication over topical Ivermectin 1% lotion.

This was in contrary to the study done by Chhiaya[8] et al and Patel V [9] et al. which showed topical Ivermectin is as effective as Permethrin with 100% cure rate with topical Ivermectin.

Yerham et al., [10] reported a study of 10 patients with uncomplicated scabies, in which marked clinical improvement was seen after two applications of topical ivermectin 1.8% cream.

Goldust et al. [11, 12] compared the efficacy of topical ivermectin vs permethrin 2.5% cream for the treatment of scabies and demonstrated that two applications of ivermectin was as effective as two applications of permethrin 2.5% cream at the 2nd week and 4th week follow up. The main adverse event was irritation in 30 vs 20 patients treated with ivermectin and permethrin, respectively. This adverse event was not considered serious and did not affect compliance.

Victoria [15] et al, reported that all the patients were cured with the 2 applications of toplical ivermectin at weekly interval.

Limitations

This was an open label study with a small sample size. Though the study showed the superiority of topical Permethrin 5% over topical Ivermectin 1% in uncomplicated scabies, there is a need for further studies in establishing the efficacy of topical Ivermectin as an effective scabicidal agent.

Conclusion

Our study concludes that topical Permethrin 5% as a safer, very effective medication in the management of scabies. Topical Ivermectin 1% can be used as an alternate scabicidal drug with good safety as second line management for those who are not responding to treatment with Permethrin. Topical Ivermectin has got no systemic or cutaneous side effects except for occasional transient burning sensation.

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