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Acomparative Study of Topical Permethrin, Oral Ivermectin and Combination of Permethrin with Ivermectin In Patients Of Scabies.

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Abstract
Background: *Objective of this study was to compare three treatment modalities in scabies for efficacy, safety and cost effectiveness in patients of scabies.*
Materials and Methods: *This was a prospective, randomized, comparative clinical study conducted in 150 diagnosed patients of scabies (5-60 years of age), randomly allocated to three groups. Group A received permethrin 5% cream, group B received tablet ivermectin 200 µg/kg as a single dose, whereas group C received combination of both (Permethrin with ivermectin). The patients were followed up at intervals of one, two, three and four weeks. If there were no signs of cure, the same intervention was repeated at the end of 1 week only once. The participants were followed up for four weeks for cure rate, adverse drug reaction (ADR) monitoring. Cost effectiveness was compared on basis of cost in INR to treat one case successfully. The follow-up was stopped after four weeks.Statistics: Statistical analysis was done by open Epi 3.03 version for percentages and chi-square test.*
Results: *Cure rate at the end of first week was 78% in Group A, 58% in Group B and 86 % in Group C. While cure rate in the three treatment groups at the end of four week was 90% in Group A, 78 % in Group B and 96 % in Group C. The cost (INR) to treat one patient was 61.11 for Group A, 12.82 for group B and 67.70 for group C at the end of four week. Thus tablet ivermectin is more cost effective than permethrin cream. No serious adverse events were observed in any of the group.Conclusion: Permethrin as first line of treatment and ivermectin is moderately efficacious and cost-effective .While combination of both (Permethrin with ivermectin) is very effective in severe form of scabies.*
Key words: *Cost effectiveness,Efficacy, Ivermectin, Scabies, Permethrin.*

I. Introduction

Scabies is caused by Sarcoptes scabiei; it is a parasitic mite that causes intense pruritus (itching), rashes and lesions. Scabies infestation is not life threatening, it is a nuisance disease that is commonly found in health care facilities and can causes crisis, fear and panic. Scabies outbreaks can be costly to control and may easily reoccur if not properly contained and treated.[1] Scabies is transmitted by prolong skin to skin contact,sharing bedding, clothing or other linens with a person who has scabies orsexual contact with infected person. Infestation of immune-competent people is most common on the hands, digits and finger webs and on the wrists. In the elderly, infants and the immunocompromised people the infestation may be more diffuse, affecting the head and neck, and palms and soles.[2]Poverty and overcrowding are the main risk factors, and outbreaks ininstitution, hostels, schools and refugee camps are common.[3] The global prevalence of scabies is estimated at 300 million cases worldwide. Older studies have shown that prevalence is highest in teenagers and schoolchildren.[4, 5, 6]

In India, the incidence ranges from 13% to 59% in rural and urban areas.[4, 5]The disease is reported to be more common in pre-school and school age group though no age is immune to it. A prevalence of 65% in age group of less than 15 years has also been reported by Desai and Nair et al.[6, 7] Prevalence of scabies in one of district in Maharashtra was 12.4%.[8]Treatment of scabies consist of topical anti-scabietic drugs like permethrin 5%, lindane or gamma benzene hexa chloride 1%, benzyl benzoate 10-25%, crotamiton 10%, precipitated sulphure 10%, malathion 0.5% lotion applied all over the body for a specified contact period to patients along with their close contacts. Ivermectin is only orally administered drug for scabies. A single dose 200 mcg/kg or 0.2 mg/kg is used.[9]There are various treatment modalities for scabies but still the searchfor ideal scabicide is going on. An ideal scabicide should be effective againstadult and egg of mite, easily applicable, non-sensitizing, non-irritating, nontoxic, and economical; it should also be applicable in all ages. As yet, no drug can be considered an ideal scabicide.[10]

This study was designed to compare efficacy and safety and cost effectiveness among antiscabetic drugs like topical permethrin 5%, oral ivermectin andcombination of both in patient suffering from scabies, attending skin OPD at Tertiary care hospital.As fewer studies have been done to elucidate the extent of problem,

this study would be helpful in providing some of the verybasic data on the safest scabicide at the lowest affordable cost in our country, which is very necessary as the disease is quite prevalent in the major poor population in India.

II. Aim And Objectives

2.1) To compare efficacy of topical permethrin, oral ivermectin and combination of topical permethrin with oral ivermectin in patients of scabies.
2.2) To compare safety of topical permethrin, oral ivermectin and combination of topical permethrin with oral ivermectin in patients of scabies.
2.3) To compare cost effectiveness of topical permethrin, oral ivermectin and combination of topical permethrin with oral ivermectin in patients of scabies.

III. Materials Andmethods

This was an open-label, randomized, comparative, parallel clinical study. The study was approved by the institutional ethics committee. A total of 150 patients assigned randomly into 3 groups of 50 patients each attending the dermatology OPD of Dr.Shankarrao Chavan Government Medical college, Nanded from March 2013 to March 2014 were included in the study. In **Group A** patients were given topical permethrin 5% cream single application, **Group B** patients were given oral ivermectin 200 microgram/kg single dose, and **Group C**patients were given combination of topical permethrin with oral ivermectin. Patients willing to participate were screened by applying the inclusion and exclusion criteria.

4. Inclusion Criteria:

4.1. New patients of scabies either male or female as diagnosed bydermatologist age between 5 to 60 years.
4.2. History of involvement of family member or similar symptoms in contacts.
4.3. Presence of nocturnal itching.
4.4. Patients, whose microscopic examination was negative, their inclusion instudy was based on clinical criteria.
5.5. Patients who were willing to participate and give written informed consent.

5. Exclusion Criteria:

5.1. Participants with any other associated skin disease, which could alter the picture of scabies; or complications of scabies like pyoderma.
5.2. Known or suspected immunocompromised individuals like HIV.
5.3. History of topical steroid in the previous 4 weeks or patients taking a topical or systemic antibiotic therapy in the week before entry into the study.
5.4. Participants who had taken any antiscabetic treatment in the past 4 weeks.
5.5. Noncompliant participants or guardians.
5.6. Patients not willing to come for follow up.
5.7. Patients having scabies with atypical presentation like crusted scabies or scabies incognito.
5.8. History of allergy to any of the study drugs.
5.9. Pregnant and lactating mother.
5.10. Patients with age less than 5 year and more than 60 year.
5.11. Participants with associated comorbid condition like hypertension, diabetes, liver, kidney disorder.

Parameters were used to assess the efficacy of regimen: Grades of lesion and grades of Itching.
Severity of lesions was clinically graded on a scale of 0 to 3.[11]
Grade 0 - free of lesions (no lesions),**grade 1 -** 10 or fewer lesions (mild) ,**grade 2** - 11 to 49 lesions (moderate), **grade 3** - 50 or more lesions (severe).
The assessment of pruritus was done on a scale of 0 to 10 using visual analogue scale (VAS) score.[11,12]Itching was graded on a Visual Analogue Scale of 0 to 3 on basis of severity. 0 is considered as no itching while 10 worst or severe itching.**Grade 0** - no itching, **grade 1** - mild itching (1-3) ,**grade 2** - moderate itching (4-6)**grade 3** - severe or intense itching (7-10).
After obtaining approval and clearance from the institution ethical committee, the study was started. Informed consent was taken from patients or guardian of the patient and those patients fulfilling the inclusion or exclusion criteria were assigned randomly into groups, treatment was given accordingly.
Efficacy was evaluated by [12, 13]
A. Patient was considered as cured if:1. No new clinical lesions and improvement in pruritus.2. No new lesions like papules, vesicles and classical burrows suggestiveof live parasite should be seen. If any one of the above criteria was not met, patient was termed as notcured.

Efficacy of particular drug was evaluated by cure rate inpercentage that is-Number of patients cured by the particular drug is divided by number of patients on that particular drug multiplied by 100.
Safety was evaluated by : Recording clinical adverse drug reaction and were classified as follows.[14]
Minor: No therapy, antidote or prolongation of hospitalization is required.
Moderate: Requires change in drug therapy, specific treatment or prolong hospital stay by at least one day.
Severe: Potentially life threatening causes permanent damage or requiresintensive medical treatment.
Lethal: Directly or indirectly contributes to death of patients.

Cost effectiveness assessment:

The cost effectiveness was calculated on basis of total expenditure on medicine (in INR) at the end of the fourth week and cure rate (in %) and the three groups were compared on the basis of amount needed to treat one case successfully. [13]The patients were informed and written consent was taken. The selected patients were allocated to any one of the three treatment groups randomly on basis of a computer generated random table. Participants in all three groups were advised to bathe with warm water before application of medication and on subsequent morning. Patients were followed up at the end of first, second, third and fourth week to assess compliance and examine the patient to evaluate efficacy and safety. Primary end point was clinical cure of scabietic lesions and Secondary end point was complete relief of pruritus. At each of the four visits examination of the entire body surface was performed.

All remaining suspected scabies lesions were examined and compared with baseline clinical grading score and itching grading score. The patients were asked for any adverse event occurring during previous week. All the participants were again called for follow up visit after one week. The same intervention was repeated only once, if there were no signs of improvement. The participants were followed up for four weeks for cure rate, adverse drug reaction (ADR) monitoring, and post-intervention observation. The participants who were not cured at the end of fourth week were switched over to standard treatment with 5% permethrin with tab. ivermectin combination.

Statistical Analysis:

The data was entered in excel sheet, tabulated and analysed by open Epi 3.03 version for percentages and chi-square test. The 'P ' value of less than 0.05 was considered as statistically significant. The sample size was calculated taking into consideration the future dropouts and was based on previous similar studies. [13]

Observation and results:

Total 150 patients were enrolled in the study and randomly allocated to three treatment groups, each group having 50 patients.The current study was planned with an objective to study different available treatment modalities in scabies. Baseline characteristics of the patients in three treatment groups were comparable. There was no significant difference between the three study groups at baseline in demographic and clinical characteristics (Table 1).

Table 1. Baseline characteristics of patients:

Clinical parameter	Group A	Group B	Group C	P value
Age (mean ± SD)	(16.74 ± 9.90)	(22.04 ±10.61)	(23.74 ± 9.91)	0.2613
Gender - M/F (%)	60/40	56/44	58/42	0.9212
Residence - U/R (%)	68/32	62/38	62/38	0.7654
Nocturnal pruritus (%)	98	96	98	0.7735
Family history (%)	84	82	84	0.9531
Pruritus grading (mild/ moderate/ severe)	26 /46 / 48	12 /44 / 44	24 /30 / 46	0.1282
Severity of disease (mild/moderate/severe)	24 / 54 / 22	22 / 60 / 18	30 / 56 / 14	0.7838

Table 2. Response to treatment:

Efficacy	Group A	Group B	Group C	P value
At 1st week (%)	78	58	86	0.0045
At 4th week (%)	90	78	96	0.0187

Clinical cure rate was assessed on basis of clinical grading score and itching. Patients showing improvement in both scores were considered as cured.There was statistical significant difference between 3 groups as per efficacy of various regimens at the end of first and fourth week.($P < 0.05$).
Safety: No major adverse events were observed in any of the 3 groups, which subside on its own without any medication.

Table no. 3 .Assessment of safety:

Safety	Group A	Group B	Group C	Total
ADR developed in number of patients	2(4)	1(2)	3(6)	6(4)
No ADR developed in number of patients	48(96)	49(98)	47(98)	144(96)
Total	50(100)	50(100)	50(100)	150(100)

Cost – effectiveness:
Average cost of tab. Ivermectin (6mg/12 mg) – Rs. 10
Cost of Permethrincream (30 gm.) - Rs. 55

Table no. 4. Cost- effectiveness analysis of each drug at end of first week

Parameters	Group A	Group B	Group C
Cost in INR for 100 participants	55 × 100 = 5500	10 × 100 = 1000	65 × 100 = 6500
Cure rate (%)	78	58	86
Cost to treat 100 cases	Rs. 5500 for 78 participants	Rs. 1000 for 58 participants	Rs. 6500 for 86 participants
Cost (INR) to treat one case (Rs.)	70.51	17.24	75.58

Amount needed to treat 1 case of scabies successfully using Permethrin (Group A) at the end of one week was Rs 70.51, for ivermectin (Group B) was Rs. 17.24 and for combination (Group C) of both was Rs. 75.58.

Table no. 5. Cost- effectiveness analysis of each drug at end of four week

Parameters	Group A	Group B	Group C
Cost in INR for 100 participants	55 × 100 = 5500	10 × 100 = 1000	65 × 100 = 6500
Cure rate (%)	90	78	96
Cost to treat 100 cases	Rs. 5500 for 90 participants	Rs. 1000 for 78 participants	Rs. 6500 for 96 participants
Cost (INR) to treat one case (Rs.)	61.11	12.82	67.70

Amount needed to treat 1 case of scabies successfully using Permethrin at the end of four week was 61.11, for ivermectin was Rs. 12.82 and for combination of both was Rs. 67.70. Thus, permethrin and combination of permethrin with ivermectin is approximately 4 to 5 times costlier for treating one scabies case successfully at the end of four week regimen.

IV. Discussion

Permethrin is a neurotoxin and it blocks the movement of sodium ions from outside to inside of the nerve cells. This causes delayed repolarisation and paralysis and death. Permethrin acts on ubiquitous sodium channels so it acts at all stages of the life cycle of the mite. Permethrin has rapid onset of action. It may be due to its topical application which ensures maximum concentration of drug in skin and action at all stages of the life cycle of the parasite.[15]Ivermectin acts by binding selectively and with high affinity to glutamate (or γ-amino butyric acid) gated chloride ion channels, which are present in invertebrate nerve and muscle cells, resulting in paralysis and death of the parasite. Ivermectin is an oral drug, so concentration achieved in skin is variable. Due to its specific site of action, ivermectin may not be effective against the younger stages of parasite inside egg because the nervous sys-tem has not yet developed. So it acts only as miticidal drug.[15]This is the probable reason for its lower efficacy at the end of first week but as it acts through two channels its efficacy increases at end of fourth week.

Cure rate of Permethrin cream:

39 (78%) out of a total of 50 patients responded by 1st week, at the end of 4th week, 45 (90%) patients were cured and 5 (10%) patient failed to respond. No patients were lost to follow up. **Das et al**[16](2006) found 70% improvement at 2nd week and 90% improvement at 4th week. **Maurya et al**[17](2014) found 83.3% cure rate at 1st week and 93.5% cure rate at 4th week. **Taplinet al**[18] (1986), found cure rate of 43% at 2 weeks and 91% after 4 weeks of permethrin 5% application.**Cure rate of ivermectin tablets:**Out of a total of 50 patients 29 (58%) responded by 1st week, at the end of 4th week, 39(78%) patients were cured and 11(22%) patient failed to respond. **Madanet al[19]** (2001) found 82.6% improvement of scabies lesions after 4 weeks**. Usha et al [20](2000)**, found that a single dose of Ivermectin provided acure rate of 70% which increased to 95% with 2 doses at 2 week interval. **Bachewar et al [13](2009)** found 55.5% cure rate after 1 week and 100% curerate after 4th week. **Maurya et al** [17]**(2014)** found 55% cure rate after 1 weekand 98% cure rate after 3rd week.

Cure rate of combination of permethrin with ivermectin:

43(86%) out of a total of 50 patients responded by 1st week, at the end of 4th week, 48(96%) patients were cured and 2(4%) patient failed to respond. No patients were lost to follow up.Previously no study has done

to assess the efficacy and safety of combination of topical permethrin and oral ivermectin in patients of scabies. We did not found any other study to discuss the result of the present study. We evaluated the efficacy of combination of topical permethrin and oral ivermectin in comparison with other 2 groups.

Safety:

In the present study no major adverse drug reaction were observed in any of the group**.** In **Group A (permethrin)** 2(4%) patients developed transient burning sensation after applying drug, which was relieved on its own withoutany medication. 1(2%) patients in **Group B (oral ivermectin)** developed mild headache and increase in pruritus which subsides without any medication. In**Group C (combination of permethrin with ivermectin)** 2(4%) patients developed transient burning sensation and 1(2%) patient mild headachewhich subsides without any medication.Burning or stinging sensation was reported in 9.9%, pruritus in 6.4%, erythema in 2.1%, pain in 1.7%, tingling in 0.9% of patients by **Schultz etal[21](1990)** as side effects of permethrin, while **Chouela et al**[22] **(1999)** reported hypotension, abdominal pain, and vomiting with ivermectin. **Chhaiya etal[12](2012)** found no major adverse effect with topical permethrin, oral ivermectin and topical ivermectin.

Cost effectiveness: The limiting factor in the wide use of any drug is its high cost. When cost effectiveness of the three groups were compared, it was found that **Group B** ivermectin(INR 12.82 per patient) was much more cost effective than both **Group A** permethrin (INR 61.11 per patient) and **Group C** (combination of permethrin with ivermectin) (INR 67.70 per patient). **Bachewar NP et al[13]** found similar results that permethrin gave the fastest symptomatic relief but ivermectin was most cost effective. **Chhaiya et al[12]** found permethrin to be more cost effective than ivermectin. Ivermectin is most suitable drug closely followed by permethrin. Although permethrin has rapid onset of action and at the end of first week its improvement rate was far greater than ivermectin.

V. Conclusion

From this study it can be concluded that Permethrin is highly effective in relieving pruritus in patients of scabies.Ivermectin is moderately efficacious, having minimum side effect and low cost compared to permethrin in the treatment of scabies, in severe form of scabies combination of topical permethrin with oral ivermectin is more effective than permethrin and ivermectin alone. Thus oral ivermectin is more cost effective than topical permethrin in treatment of uncomplicated scabies.

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References

[1]. Scabies Prevention and Control Manual. Michigan Department of Community Health. [Serial online] 2005 May [cited 2014 Dec12] version1.0:[3-50]. Available from: URL: http//www.michigan.gov./documents/scabiesmanual1308667pdf.
[2]. Burgess IF, Scabies. In Williams H, Bigby M, DiepgenT,Herxheimer A,Naldi L, Rzany B, editor, Evidence-based Dermatology. 11th ed London:BMJ Publishing house: UK. 2003:p.515-524.
[3]. Hay RJ, Steer AC, Engelman D, Walton S. Scabies in the developing world its prevalence, complications, and management. Clin Microbiol Infect. 2012; 18: 313–323.
[4]. Sharma RS, Mishra RS, Pal D, Gupta M, Datta KK. An epidemiology study of scabies in rural community in India.Ann Trop Med Parasitol. Apr 1984; 78(2):157-164.
[5]. Nair BKH, Joseph A, Narayanan PL, et al. Epidemiology of scabies. Indian Journal of Dermatology, venereology.1973; 30:101-103
[6]. Desai SG, Nair SS. Ecology and epidemiology of scabies in India.Indian J DermatolVenerolLepr. 1978;44:197-199
[7]. Nair BK, Joseph A, Kandamuthan M. Epidemic scabies. Indian J Med Res. 1977; 65(4): 513–518.
[8]. Yuwnate AH, Chandane RD, Giri KR, Yunati MS, Sirsam SS. A multicentre pharmaco-epidemiological study of dermatological disorders in Wardha district.Int J Basic Clin Pharmacol. 2013;2(6):751-6.
[9]. Tripathi KD. Antiseptics, Disinfectants and Ectoparasiticides.Essentials of medical pharmacology. 7th ed. NewDelhi: Jaypee medical book publisher; 2013: p.902-904.
[10]. Karthikeyan K. Treatment of scabies: Newer perspectives. Postgrad Med J. 2005;81:7-11.
[11]. Chhaiya SB, Patel VJ, Dave JN, Mehta DS, To study cost effectiveness of topical permethrin versus oral ivermectin in patients of uncomplicated scabies. Int J Basic Clin Pharmacol. 2013;2(6):799-803
[12]. Chhaiya SB, Patel VJ, Dave JN, Mehta DS, Shah HA. Comparative efficacy and safety of topical permethrin, topical ivermectin, and oral ivermectin in patients of uncomplicated scabies. Indian J Dermatol Venereol Leprol. 2012;78(5):605-10.
[13]. Bachewar NP, Thawani VR, Mali SN, Gharpure KJ, ShingadeVP,Dakhale GN. Comparison of safety, efficacy, and cost effectiveness of benzyl benzoate, permethrin, and ivermectin in patients of scabies.Indian J Pharmacol. 2009;41(1):9-14.
[14]. Tripathi KD. Adverse drug effect. Essentials of medical pharmacology.7th ed. New Delhi: Jaypee medical book publisher; 2013:p.82-83.
[15]. Campbell WC.Ivermectin, an antiparasitic agent. Med Res Rev 1993;13:61-79.
[16]. Das S, Chatterjee T, Banerji G, Biswas I. Evaluation of commonest site, demographic profile and most effectivetherapy in scabies. Indian J Dermatol. 2006:51(3):186-8
[17]. Maurya M, Kaushik S, Srivastava N, Verma D, Parihar R. An open lable randomized, comparative study of antiscabetic drugs permethrin, gamma benzene hexachloride and ivermectin in patients of uncomplicated scabies. Int J Pharmacol and clinsci.2014;n 3(2):15-21 [18]Taplin D, Meinking TL, Porcelain SL, Castillero PM, Chen JA. Permethrin 5% dermal cream: A new treatment for scabies. J Am AcadDermatol. 1986;15:991-1001.

[18]. Madan V, Jaskiran K, Gupta U, Gupta DK. Oral Ivermectin comparison with 1% topical lindane lotion. Int J Dermatol. 2001;28:481-484.
[19]. Usha V, Nair TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. J Am AcadDermatol. 2000;42(2):236-40.
[20]. Schultz MW, Gomez M, Hansen RC, Mills J, Menter A, Rodgers H et al. Comparative study of 5% permethrin cream and 1% lindane lotion for the treatment of scabies. Arch Dermatol. 1990;126:167-170.
[21]. Chouela EN, Abeldano AM, Pellerano G, La Forgia M, Paple RM, Garsd A, et al. Equivalent therapeutic efficacy and safety of ivermectin and lindane in the treatment of human scabies. Arch Dermatol. 1999;135:6514.