

# **Ivermectin Versus Topical Sulfur in Treatment of Scabies: An Open Therapeutic Trial**

**Ali. H. Hafedh<sup>1</sup>, Maytham M. Al-Hilo<sup>2</sup> and Maysam S. Jassem<sup>3</sup>**

## **Abstract**

**Background:** scabies is still a major public health problem in developing countries. Available antiscabietics are mainly topical. Ivermectin is an oral agent against a variety of endoparasites and ectoparasites. **Objective:** to evaluate the efficacy of oral ivermectin as a therapeutic agent in treatment of scabies and compare its efficacy with the topical sulfur. **Method:** an open labeled comparative therapeutic study was performed in Al-Kindy Teaching hospital. A total of 450 patients with scabies were included in this study: 240 females and 210 males. 225 patients received topical sulfur and 225 patients received oral ivermectin. **Results:** The patients in ivermectin group showed a cure rate of 84%, 94.22% after 2 weeks and 4 weeks follow up respectively. In the sulfur group, the curate rate was 70.67% after 2 weeks follow up that reached 83.11% at the end of 4 weeks follow up. The p-value for difference between two treatment modalities after 2 weeks and 4 weeks was statistically not significant.

**Conclusion:** Oral ivermectin is an effective remedy for the treatment of scabies with excellent compliance and very trivial side effect.

**Keywords:** Scabies, topical sulfur, oral ivermectin.

## **1 Introduction**

Scabies is a highly contagious and intensely pruritic parasitic infestation. It is a re-emerging infection in the new millennium especially with HIV pandemic and a significant health problem in developing countries [1]. Human scabies is caused by the

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<sup>1</sup>MBChB, FICMS, DV, Consultant Dermatologist and Venereologist, Alshaheed Al-Sadr Hospital Baghdad, Iraq.

<sup>2</sup>MBChB, FICMS, DV, Consultant Dermatologist and Venereologist, Al-Kindy Teaching Hospital, Baghdad, Iraq. Corresponding author.

<sup>3</sup>MBChB, Al-Kindy Teaching Hospital, Baghdad, Iraq.

host-specific mite, *S. scabiei* var *hominis*, is an obligate human parasite. It is a member of the class Arachnida, subclass Acari, order Astigmata, and family Sarcoptidae [2].

Treatment options are either topical or oral medication. Topical options include permethrin cream (drug of choice), gamma benzene hexachloride, benzyl benzoate, crotamiton lotion and cream, sulfur, Tea tree oil, or oil of the leaves of *Lippia multiflora* Moldenke, a shrub found growing in West Africa, Savannah. Ivermectin is the only oral option for scabies [3].

**Sulfur in petrolatum** the oldest antiscabietic, one of a few scabidical treatments that may be used safely in very small children (<2 months) and in pregnant women [4, 5].

**Ivermectin** is a synthetic macrocyclic lactone belonging to the avermectin group of antibiotics. It has no antibiotic activity but is active against a number of endoparasites and ectoparasites of humans and animals [6]. Ivermectin is effective in most cases of typical scabies at a dose of 200-250 mcg/kg given at diagnosis and repeated in 7-14 days. Crusted scabies may require 3 or more doses given at 1- to 2-week intervals. Ivermectin is an ideal agent in cases for which topical therapy is difficult or impractical, such as in widespread institutional infestations and bedridden patients [7].

## 2 Patients and Methods

This randomized open labeled comparative study was performed in Al-Kindy Teaching hospital in a period from April 2011 to May 2012.

A total of 450 patients with scabies were included in this study: 240 females and 210 males.

The patient was diagnosed as having scabies if he at least has two of the followings:

Night pruritus, Burrows and Microscopical confirmation of scabitec mite, ova or sybala.

Exclusion criteria include any patient received antiscabietic agent in the last month prior to the study, pregnancy, lactation, children younger than five years , patients older than sixty five years old , patients with central nervous system, hepatic, cardiac, or renal disease and immunocompramized patients.

Full detailed history (name, age, sex, duration of the illness, night pruritus) and physical examination to asses skin eruption (papule, excoriation), burrow and counting of the lesions was done.

The severity of scabies was assessed by counting the number of lesions and assigned a score of 0-3, arranged as follows: 0 =Free of lesions (no scabies), 1= 10 or fewer lesions (mild), 2= 11- 49 lesions (moderate), 3= 50 or more lesions (severe).

A written consent was taken from each patient before starting treatment after a full explanation about the course of the treatment intended, possible side effect of therapy and the follow up.

The patients divided equally into two groups: group A and group B. Each group included 225 patients. Group A represented patients with scabies who received oral ivermectine while group B included the patients with scabies who received topical sulfur.

Any patient with a history of treatment failure with topical agents was only included in group A.

Each patient in group A received oral ivermectin 200 microgram/ Kg in two doses two weeks apart. They were instructed to take the tablet at day 0 and day 14, 1 hour before meal. No antihistamines were given to patients in both groups.

In Group B, each patient older than 12 years was received 10% sulfur ointment, whereas

patient less than 12 years old was received 5% sulfur ointment. They were instructed to apply the ointment after bathing from neck to bottom of feet without bathing for three consecutive days.

## 2.1 Follow Up

Another physical examination was done at 2 and 4 weeks follow up with recording of possible side effect, signs and symptoms including night pruritus, papular eruption and burrows with reassessment of severity with each visit.

Treatment of close contacts, sexual partner and other family members of infested patients in both groups were done at the same time regardless of symptoms.

Patients were advised to wash linen and clothes and those cannot be washed, can be kept in bag for 3 days.

The patients were considered cured only if have no nocturnal pruritus, excoriation and papules and burrows.

## 2.2 Statistical Analysis:

Statistical data were analyzed by using Software Minitab V.16 and percentages were compared Chi-square test. P value < 0.05 is considered statistically significant.

## 3 Results

During the period from April 2011 to May 2012, a total of four hundred fifty patients (two hundred ten male patients (46.66%) and 240 female patients (52.34%) attended the Department of Dermatology and Venereology in Al-Kindy Teaching Hospital/Baghdad, diagnosed as scabies were included in this study.

### 3.1 Age Distribution

Patients in group A (ivermectin group) with total number 225 their ages varied between five years and sixty five years with a median of 34. The highest number of patients was 79 (35.11%) who their ages varied between 5-15 years and the lowest number was 11 patients between 56-65 years. Table 3.1

Table 3.1: Age distribution of patients in group A receiving oral ivermectin

Age group(years)	Number of patients	Percentage %
5-15	79	35.11%
16-25	45	20%
26-35	32	14.22%
36-45	44	19.55%
46-55	14	6.22%
56-65	11	4.88%
Total	225	100%

In group B (sulfur group), the total number of patients in this group was 225 patients; the

age also varied between 5 to 65 years with a median of 37. The number of patients was 97 patients (34.11%) who their ages ranged between 5-15 years and the lowest was 8 (3.55%) patients whose age group ranged between 56 to 65 years. Table 3.2

Table 3.2: Age distribution of patients in group B receiving topical sulfur

Age group(years)	Number of patients	Percentage%
5-15	97	43.11%
16-25	64	22.44%
26-35	30	13.33%
36-45	17	07.55%
46-55	9	04.00%
56-65	8	03.55%
Total	225	100%

### 3.2 Gender Distribution

#### Group A

In all age groups, the number of male and female was nearly equal. Slight female predominance demonstrated in all age groups except that in those groups between 56-65 years where the male gender is predominant, which was statistically not significant. Table 3.3.

Table 3.3: Gender distribution in group A (oral Ivermectin)

Age group(years)	No. of Male (Percentage %)	No. of Female (Percentage %)
5-15	38(16.88)	41(18.22)
16-25	20(8.88)	25(11.11)
26-35	15(06.66)	17(07.55)
36-45	19(08.44)	25(11.11)
46-55	4(01.77)	10(04.44)
56-65	9(04.00)	2(0.88)
total	105	120

**Group B (sulfur group):** Female gender was slightly more than male with the exception in age group ranged from 56 -65 years where male gender was predominant which was statistically not significant. Table 3.4

Table 3.4: Gender distribution in group B (topical sulfur)

Age group	No. of Male (Percentage %)	No. of Female (Percentage %)
5-15	37(16.44)	43(19.11)
16-25	19(08.44)	27(12.00)
26-35	17(07.55)	15(06.66)
36-45	17(07.55)	23(10.22)
46-55	6(02.66)	8(03.55)
56-65	9(04.00)	4(01.77)
Total	105	120

### 3.3 Distribution according to the Severity

The severity was assessed according to the number of lesions. In both groups the number of mild, moderate and severe cases respectively, was as follows 134, 67, 24. Table 3.5 and Table 3.6.

Table 3.5: Severity of disease according to no. of lesions in group A (oral ivermectin)

Age group	Mild	moderate	Severe
5-15	50	20	9
16-25	30	14	1
26-35	18	11	3
36-45	23	15	6
46-55	6	4	4
56-65	7	3	1
total	134	67	24

Table 3.6: Severity of disease according to no. of lesions in group B (topical sulfur)

Age group	Mild	moderate	Severe
5-15	51	19	8
16-25	31	15	2
26-35	18	12	4
36-45	22	13	4
46-55	4	4	4
56-65	8	4	2
total	134	67	24

### 3.4 Duration of Illness

Less than two weeks duration of illness was registered in sixty-four (28.44%) patients in Group A and ninety four (41.77%) patients in Group B; while it was equal to two weeks up to 8 weeks in 95(42.22%) patients, 92(40.88%) patients in Group A and B, respectively. Sixty six patients (29.33%) patients in Group A and 39(17.33%) patients in Group B had the illness in a period more than two months. Table 3.7

Table 3.7: Duration of illness before treatment in group A (oral ivermectin)

Age group	Less than 2 weeks	2 weeks-8 weeks	More than 8 weeks
5-15	21	34	24
16-25	17	18	10
26-35	9	10	13
36-45	14	24	6
46-55	2	5	7
56-65	1	4	6
total	64	95	66

Table 3.8: Duration of illness before treatment in group B (topical sulfur)

Age group	Less than 2 weeks	2 weeks-8 weeks	More than 8 weeks
5-15	40	41	16
16-25	21	24	19
26-35	18	9	3
36-45	7	10	0
46-55	1	7	1
56-65	7	1	0
total	94	92	39

### 3.5 Response to Treatment

#### 3.5.1. Response of patients to treatment regimen according to night pruritus

In Group A, one hundred eighty nine (88%) patients had no nocturnal pruritus at the end of two weeks while it reached 212(94.22%) patients at the end of four weeks follow up. In case of group B, 159(70.66%) patients showed no nocturnal pruritus at the end of two weeks to reach one hundred eighty seven (83.11%) patients at the end of four weeks follow up with ( p value) 0.2, 0.1 respectively. Figure 3.1

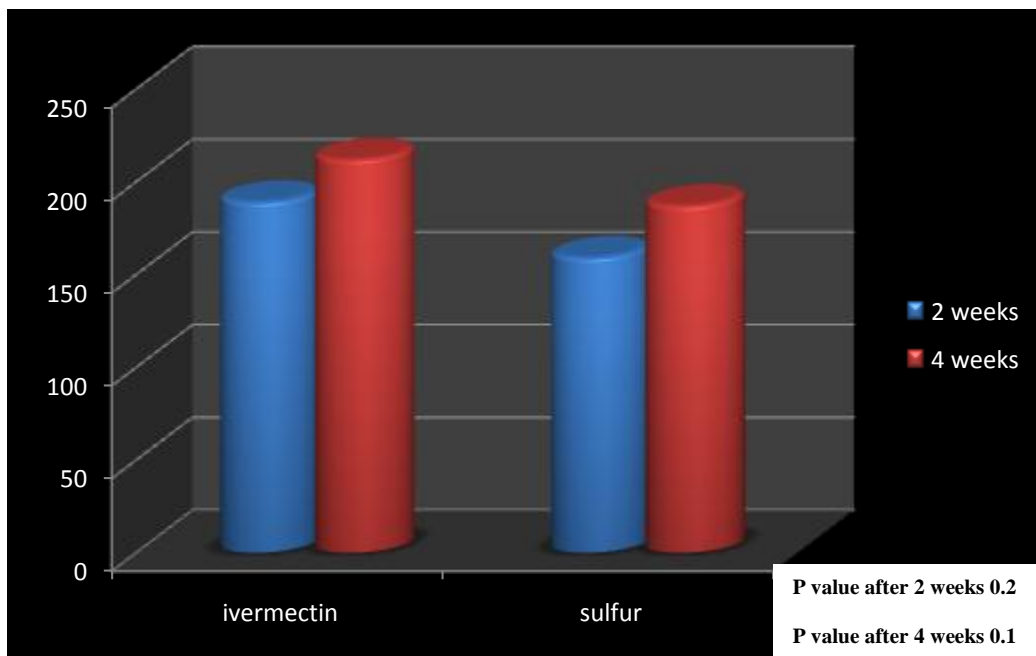


Figure 3.1: Response of patients to treatment regimen with ivermectin and sulfur after two and four weeks follow up according to night pruritus.

#### 3.5.2 Response of patients to treatment regimen according to excoriation and papular eruption

At the end of two weeks follow-up in Group A, one hundred eighty five (82.22%) patients showed no excoriation and papular eruption while two hundred sixteen (96%) patients are free of this lesion at the end of four weeks follow up.

In Group B, the excoriation had not been shown in 130(57.77%) patients, 191(84.88%) patients after two and four weeks follow up with p value of 0.0019 and 0.214 respectively. Figure 3.2.

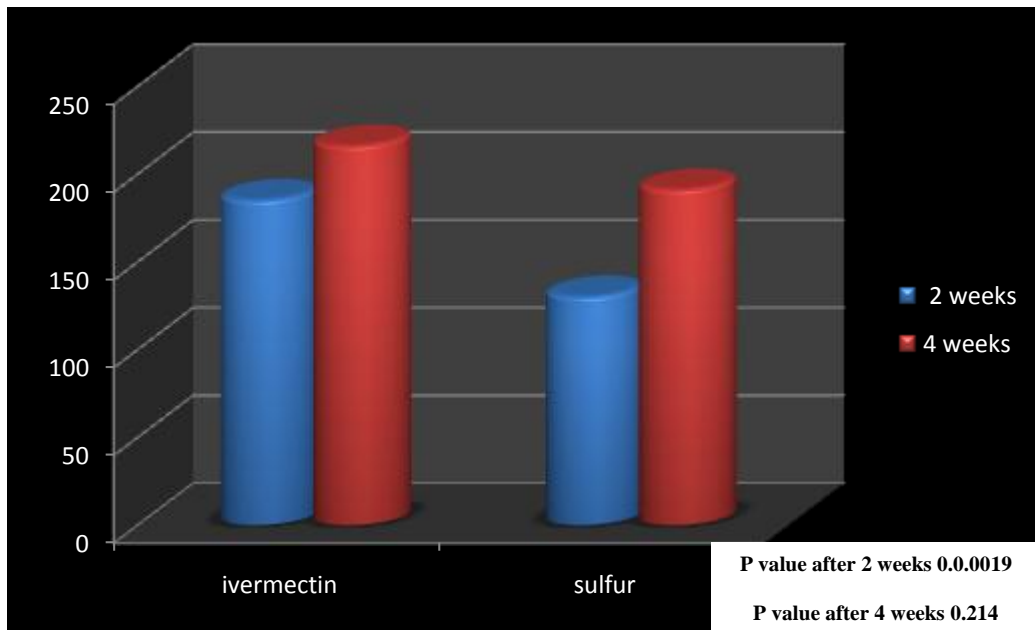


Figure 3.2: Response of patients to treatment regimen with ivermectin and sulfur after two and four weeks follows up according to excoriation and papular eruption.

In Group A, one hundred ninety two (85.33%) patients had no burrows at end of two weeks follow up and two hundred nineteen (97.33%) patients had no burrows at the end of four weeks follow up; while in Group B ,one hundred seventy three(76.88%) patients showed no burrows at the end of two weeks follow up that reached hundred ninety nine(88.44%) patients at the end of the four weeks, with p value 0.243 after 2 weeks and 0.268 after 4 weeks. Figure 3.3.

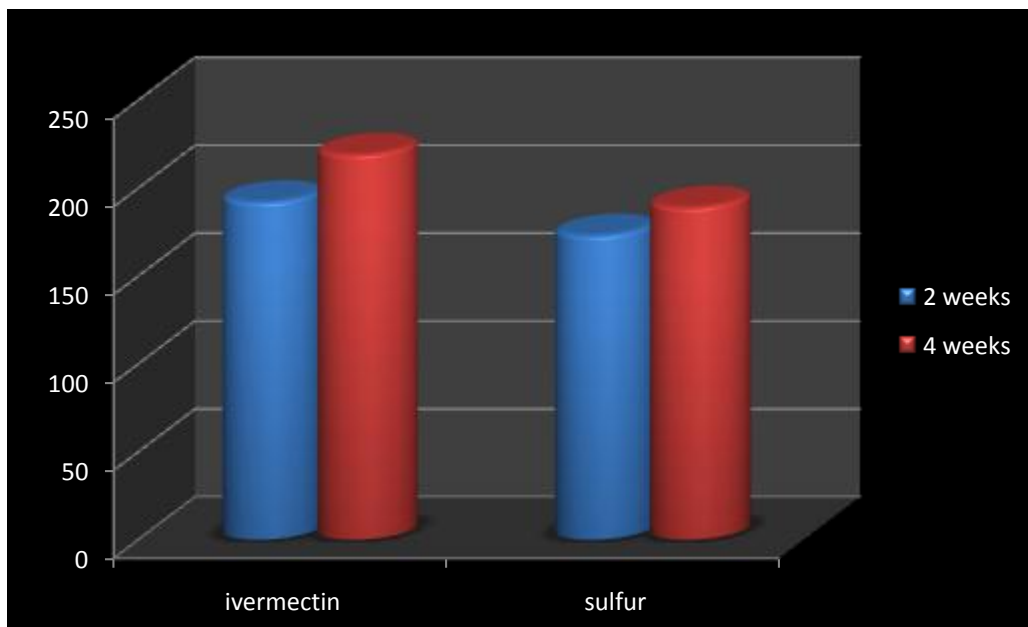


Figure 3.3: Response of patients to treatment with ivermectin and sulfur after two and four weeks follows up according to burrows

### 3.5.3. Response to treatment according to severity of illness

In group A 133(99.25%) patients out of 134 with mild illness show response to oral ivermectin, whereas 59(88.05%) patients and 20(83.33%) patients with moderate and severe illness show response by the end of four weeks table 3-9.

One hundred thirty one (97.76%) patients out of 134 with mild illness in group B show response ,while 41(64.17%) patients and 13(54.16%) patients show response with moderate and sever illness to the topical therapy at the end of fourth week. Table 3.9.

Table 3.9: Response to treatment in group A (oral ivermectin) and group B (topical sulfur) after 4<sup>th</sup> weeks according to severity.

Response to treatment according to severity	Ivermectin group	Sulfur group	P value
Mild	133(99.25%)	131(97.76%)	1.00
Moderate	59(88.05%)	43(64.17%)	0.11
Severe	20(83.33%)	13(54.16%)	0.22

### 3.5.4. Response to treatment according to duration of illness

The response to treatment was relatively higher in all categories with oral ivermectin group than the sulfur group. Table 3.10.



Table 3.10: Response to treatment in group A (oral ivermectin) and group B (topical sulfur) at the end of 4th weeks according to duration of illness.

Response to treatment according to duration	Ivermectin group	Sulfur Group	P value
Less than 2 weeks	61(95.31%)	80(85.10%)	0.11
2 weeks-8 weeks	90(94.73%)	76(80.85%)	0.27
More than 8 weeks	61(92.42%)	31(79.48%)	0.002

### 3.6 Cure Rate

The patients in Group A showed a cure rate (absence of nocturnal pruritus, excoriation and papules and burrows) of 84%, 94.22% after 2 weeks and 4 weeks follow up respectively.

In Group B, the cure rate was 70.67% after 2 weeks follow up that reached 83.11% at the end of 4 weeks follow up.

The p-value for difference between two treatment modalities after 2 weeks was 0.126 and equal to 0.213 after 4 weeks which is statistically not significant.

Table 3.11: Cure rate of patients to treatment regimen of ivermectin and sulfur after 2 and 4 weeks Follow up

Follow up	Group A		Group B	
	No.	%	No.	%
2 weeks	185	84.00	159	70.67
4 weeks	212	94.22	187	83.11

### 3.7 Side Effects

Five patients in group A developed side effects in form of nausea in three (1.33%) patients, headache in two (0.88%) patients and only one patient (0.44%) had gastric upset. In group B, all the patients suffered from the unpleasant odor of the topical medication while the social withdrawal was recorded in 198 patients, 73(32.44%) patients had irritation, five (2.22%) patients stinging sensation; 43(19.11%) patients had drying of the skin and 62(27.55%) patients had contact dermatitis. Table 3.11.

Table 3.12: Side effects of group A, who received oral ivermectin and group B, who received topical sulfur.

Side effect of treatment	Ivermectin group	Sulfur group
nausea	3(1.33%)	0(0.0%)
vomiting	0(0.0%)	0(0.0%)
Headache	2(0.88%)	0(0.0%)
Gastric upset	1(0.44%)	0(0.0%)
Unpleasant odor	0(0.0%)	225(100%)
Social withdrawal	0(0.0%)	198(88%)
irritation	0(0.0%)	73(32.44%)
Stinging sensation	0(0.0%)	5(2.22%)
Dryness	0(0.0%)	43(19.11%)
Contact dermatitis	0(0.0%)	62(27.55%)

## 5 Discussion

Scabies is still a major public health problem in developing countries.

Available antiscabietics are mainly topical and may require repeated application and resistance to some of these drugs has been reported [8].

The topical treatment of scabies includes (sulfur ointment, permethrin cream, gamma benzene hexachloride, benzyl benzoate, malathion, monosulfur and crotamiton).

Topical sulfur ointment is a cost-effective and safe therapeutic agent. It is often applied for the whole body for three successive days [9].

Ivermectin is an oral antiparasitic agent effective against a variety of endoparasites and ectoparasites and the initial reports have highlighted the utility of oral ivermectin in the treatment of scabies [8].

For the best of our knowledge this is the first reported study in Iraqi population sheds the light on the use of oral treatment as scabidicidal agent against this ectoparasite.

In our study the most age group affected was between 5-15 years in both comparative groups which represents (35.11 %) in ivermectin group and (43.11 %) in sulfur group. This finding is compatible with the previous studies that showed significant infestation rate among young age group [10, 11].

Several previous studies showed different results regarding infestation rate among male and females. In this study, there was a slight female predominance in patients of both groups included in this research. This corresponds to the results appointed in some of the previous studies [11] and in contrast to the results reported by other studies [12] which demonstrated that scabies was more commonly seen in boys (50%) than girls (16%) [13]. This variation in different reports might be attributed to the differences in the setting of these studies and limitation of patients' selection.

Most of the patients included in both groups were having mild and moderate disease. The reason behind low number of patients in severe form of illness in our study is that patients that are most likely to be immunocompromised and elderly older than 65 years old were excluded from the start of the study.

In both therapeutic trial groups most patients had duration of disease between 2 weeks to 2 months. This may be due to the delayed presentation related to incorrect diagnosis and symptomatic treatment like antihistamines, topical steroids and emollients.

Sixty six patients in ivermectin group had duration longer than two months in contrast to 39 patients in sulfur group this may be related to that in ivermectin group, patients with history of treatment failure with several topical remedies were included.

Because of the specific site of action, ivermectin may not be effective against the younger stages of the parasite inside the egg related to under development of nervous system. Furthermore, ivermectin may not adequately penetrate the thick egg shell, so the second dose was required to overcome this problem [1]. As Ivermectin is a systemic agent, it is absorbed readily and distributes to all body areas including areas difficult to reach as under the nails and genitalia. In order to overcome the poor compliance, the treatment can be completed at the same minute for the whole family so it's appropriate for mass therapy in prisons, mental institutions and other overcrowding societies.

Regarding the other subset of the study, sulfur is an irritating material that may be not applied properly, odorous that may be regarded social stigmata, required abstinence from job or school, can produce ichthyosis like dermatitis, based on these facts, oral therapy is more superior to sulfur therapy.

The response to treatment was assessed by severity according to the number of lesions.

Although there was no statistical significance between the two groups, there was a higher cure rate in ivermectin group than the sulfur group. This difference may be explained by that ivermectin taken orally and distributed to all body sites which override the possible poor compliance of patients and eliminate the possibility of treatment failure.

Similarly the response to treatment was assessed according to the duration of the disease before treatment. Also, there was no statistical significant difference in response to treatment according to duration in patients with disease duration less than two months between the two comparative groups. On the other hand a significant statistical difference was found in patients with disease duration longer than 2 months. This could be attributed to that most of the patients with duration more than 2 months in ivermectin group had already experienced failure in response to various topical therapies.

After two weeks the overall cure rate in ivermectin group was 84% in contrast to the sulfur group patients where the cure rate was 70%. Although the cure rate was higher in ivermectin group this was statistically not significant P value was (0.126).

By the end of fourth week ninety four percent cure rate was achieved in ivermectin group while it was 83% in sulfur group. Despite this difference, no statistical significance was found; the P value was (0.213).

In our study the cure rate after single dose ivermectin was 84% which is higher than that obtained in previous therapeutic trails which demonstrated that the cure rate after single dose ivermectin was (74%,70%,77.55% and79% respectively) [14, 8, 1, 15].

Several previous studies reported 95% cure rate with oral ivermectin at the end of 4 weeks [14, 8, 15]. Bachewar et al reported 100% cure rate with two doses of oral ivermectin at the end of 2 weeks [16].

The cure rate in sulfur group after two weeks and 4 weeks was 70% and 83% respectively which is lower than that reported by a previous Iraqi study which demonstrated 96.9% cure rate at the end of two weeks [9].

All the patients who received the oral therapy reported beneficial effects, particularly diminished pruritus, which in several patients occurred less than 48 hours after treatment.

In onchocerciasis and other filarial diseases, the majority of side effects of the drug involve eosinophilia and Mazzotti reactions [17].

Although similar dose of ivermectin that used in onchocerciasis was used in our study, only trivial side effects were recorded, 3(1.33%) patients developed nausea, headache in 2(0.88%) patients and only one patient (0.44%) developed gastric upset. This may be explained by that the major side effects like Mazzotti reaction may be attributed to the sudden death of the microfilaria or the release of their toxic products [17].

In the sulfur group all the treated patients suffered from the unpleasant odor of the medication with social withdrawal have been reported in 88% (198) patients, 73 (32.44%) patients developed irritation, 5 (2.22%) patients stinging sensation, 43(19.11%) patients developed dryness and 62(27.55%) patients developed contact dermatitis.

## **6 Conclusion and Recommendations**

Oral ivermectin is an effective remedy for the treatment of scabies with excellent compliance and very trivial side effect.

We recommended the use of ivermectin in the management of scabies and regarded as a first line therapy in prisons, mental institutions and other overcrowded infested families.

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