**BRIEF COMMUNICATION**

# EFFECTS OF IVERMECTIN TREATMENT OF SOWDA (HYPERREACTIVE ONCHODERMATITIS) IN GHANIAN PATIENTS

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## ABSTRACT

***Background:*** *Though Onchodermatitis was a public health problem in Ghana, sowda had never been reported there. Sowda patients have been isolated from and forgotten by society. Thus, it was crucial to find out whether sowda was present in Ghana and, if so, to treat these patients with ivermectin and monitor the outcome.*
***Methods:*** *An active search for patients with sowda was carried out in 16 villages around Hohoe, Volta Region, Ghana. The patients underwent clinical examinations including photographic documentation of their skin lesions. Skin snips were taken and a local Mazzotti test was performed. Blood was drawn for eosinophil count. A single oral dose of ivermectin was administered. Adverse events were monitored over 3 days. Follow-up was carried out one month later and the above examinations repeated.*
***Results:*** *A total of 18 patients, 6 males and 12 females, with an age range from 7-60 years were diagnosed to have sowda. The skin lesions were asymmetric (94%) and involved predominantly the gluteal region (89%) and lower extremities (94%). The severely pruritic skin lesions included papules, pustules, lichenification and hyperpigmentation. Onchocercomata were found only in 28% of the patients and 56% had a positive skin snip for microfilaria (median 0.77 mf/mg). A topical Mazzotti test was positive in all cases. The ivermectin administration was associated only with minor and transient adverse events in the first 72 hours. The follow-up one month later revealed significant improvement of the itching and skin lesions. The parasitological tests turned out negative as well.*
***Conclusion:*** *Sowda is present in Ghana. A single oral dose of ivermectin results in significant clinical and parasitological improvements.*
***Keywords:*** *Onchocerciasis, hyperreactive onchodermatitis, sowda, treatment, ivermectin, Ghana*

## INTRODUCTION

A broad spectrum of skin lesions exists in onchocerciasis (1). The most widespread is the generalised form of onchodermatitis. Only a small percentage of patients exhibit the localized form of the disease. This is also known as hyperreactive onchodermatitis or sowda.

Sowda was first reported in Yemen in 1957 (2). Since then, several reports have been published on the occurrence of this particular type of onchodermatitis in a few other endemic areas (3-4). Sowda predominantly affects the lower extremities and gluteal regions, typically in an asymmetrical manner (5-7). The skin lesions include papules, pustules, hyperpigmentation and lichenification. Enlarged non-tender regional lymph nodes are part of the clinical features. The severe itching is a major cause of morbidity. In a study in Liberia, we demonstrated that the treatment of sowda with ivermectin could lead to a marked clinical improvement (8).

Onchocerciasis is endemic in Ghana but sowda has not been reported. Based on our experience in Liberia, we set out to actively search for patients with this disease in Ghana and recruited them for treatment with ivermectin. Further experience on ivermectin treatment in sowda patients is presented.

## METHODS

***Patient search:*** Colour photographs of typical skin lesions of sowda patients from Liberia were put together in an album. This was taken to different villages in the Hohoe district (Volta Region, Ghana), located near the Onchocerciasis Chemotherapy Research Centre (OCRC) in the town of Hohoe. The photo album was shown around inside the villages. Those having lesions similar to the ones depicted in the album were asked to come to the OCRC for clinical examination, diagnosis, and treatment .

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***Clinical examination:*** At the OCRC patients presenting themselves following the call were screened. Medical histories were taken. Dermatological examinations including searches for onchocercal nodules were conducted under good illumination. Grading of the skin lesions was undertaken in those patients having dermatological findings compatible with sowda.

The degree of skin lesions was classified as mild when only mild papular dermatitis without lichenification was present. Patients having more severe papular and pustular dermatitis and varying degrees of lichenification were graded as moderate or severe. Colour photographs were taken of all affected body regions. Blood was drawn for eosinophil count.

***Parasitological examination:*** Skin snips were taken from each patient using Holth punches from both sides of the pelvic girdle. The skin biopsies were weighed on a Sauter torsion balance (range 0.02-10 mg) and placed in the wells of microtiter plates filled with 0.4% collagenase solution (Boehringer Mannheim, Germany). The biopsies were digested for 72 hours at room temperature (modified from Schulz-Key (9). Finally, the suspension was transferred to a microscopic slide and examined for microfilariae at a magnification of 63x or 100x. The parasite load was calculated as the arithmetic mean of both pelvic skin biopsies. A topical Mazzotti test was performed on both thighs as described by Kilian (10). The result was read after 48 hours, and it was considered to be positive when new papules appeared.

***Ivermectin treatment****:* Ivermectin was administered as a single oral dose. The dosage was fixed according to body weight as follows - 30 kg or less: 3mg (½ tablet); 30 – 44 kg: 6mg (1 tablet); 45-64 kg: 9 mg (1½ tablets). For the purpose of monitoring any possible adverse event all patients were admitted to the OCRC for the first 3 days .

***Follow-up****:* One month after treatment all patients returned for follow-up. The clinical and parasitological examinations were repeated. Again photos were taken of all the body regions that had been initially affected. In addition, patients were questioned regarding any change of the itching and skin lesions.

***Scoring:*** The severity of the skin lesions on the pre- and post-treatment photographs was scored. To avoid any bias during the scoring procedure the photos of different patients were mixed and the information regarding treatment was concealed. The degree of papular, pustular, and lichenified dermatitis was graded separately as mild (=1), moderate (=2), severe (=3) and absence of dermatitis as zero. A total score of between 0 and 9 was obtained by adding up the score for each type of skin lesion. The extent of body surface area affected was determined using the "rule-of-nine" in a similar manner as used for cases of burn. The pre-and post treatment skin lesion scores and other findings were compared using the McNemar's test test.

***Ethical issues***: Ethical clearance was obtained from the OCRC and consent was obtained from each participant. In addition, the study was conducted in the research center and patients were admitted and received medical care for about 72 hours.

## RESULTS

Over a period of one month, a total of 18 patients from 16 different villages around Hohoe presented with skin lesions compatible to those shown in the photo album (Table 1). The group comprised of 12 (67%) female and 6 (33%) male patients. The mean age was 30 years with a range from 7 to 60 years. Those below the age of 14 were 5 (28%).

***Pre-treatment findings:*** Sixteen (89%) patients had moderate to severe onchodermatitis as typically found in sowda cases. Only 2 (11%) patients had the mild form of the disease and were consequently considered as having an intermediate form of sowda. Hyperpigmentation was a common dermatological feature. To the contrary, depigmented shin was found in only one patient. The lower extremities and gluteal regions were predominantly affected. The upper extremities and trunk were involved in only half of the cases. The skin lesions were asymmetrical in 17 (94%) patients. The mean body surface area affected was 44% (18% - 72%), and except one patient all had swollen femoral lymph nodes.

Onchocercal nodules were found in only 5 (28%) patients. One out of the six male patients had a hanging scrotum. All complained of itching; it was severe in 10, moderate in 5 and mild in 3 cases. Microfilariae of *O. volvulus* were detected in 10 (56%) patients. The median microfilarial density was 0.77 mf/mg. The topical Mazzotti test was positive in all patients. The mean eosinophil count was 25%.

Table 1. Clinical and parasitological findings in 18 patients from Ghana with chronic onchodermatitis prior to treatment.

| | Age group | | | |
|---|---|---|---|---|
| | 7-14 years | | >14 years | |
| | No | % | No | % |
| Male/female | 2/3 | 40/60 | 4/9 | 31/69 |
| Duration of skin lesion (mean, yr) | 5 | 4 | 13 | 12 |
| Itching | 5 | 100 | 13 | 100 |
| *Onchodermatitis:* | | | | |
| - Area of body affected (mean) | 5 | 27 | 13 | 39 |
| - Degree of severity: mild | 1 | 20 | 1 | 8 |
| Moderate | 2 | 40 | 5 | 38 |
| Sever | 1 | 20 | 8 | 62 |
| - Type of lesion: papules | 5 | 100 | 13 | 100 |
| Pustules | 2 | 40 | 5 | 38 |
| Lichenification | 1 | 20 | 9 | 69 |
| Hyperpigmentation | 5 | 100 | 12 | 92 |
| Depigmentation | 0 | | 1 | 8 |
| - Localization: trunk | 2 | 40 | 9 | 69 |
| Upper extremity | 2 | 40 | 7 | 53 |
| Gluteal region | 4 | 80 | 12 | 92 |
| Lower extremity | 5 | 100 | 12 | 92 |
| - Asymmetry | 5 | 100 | 12 | 92 |
| - Enlarged femoral lymph nodes | 5 | 100 | 12 | 9 |
| *Onchocercoma*: prevalence | 0 | | 5 | 38 |
| No./person (mean) | | | 1.4 | |
| Mf carriers: prevalence | 1 | 20 | 9 | 69 |
| Mf/mg (median) | (10.3) | | 13 | 0.27 |
| Topical Mazzotti test positive | 5 | 10 | 13 | 100 |
| Eosinophil count | 5 | 11 | 13 | 32 |

***Adverse events:*** The type and frequency of adverse events after ivermectin treatment are presented in Table 2. None of the patients were exempt from the transient adverse events. New papular rash was observed in 94 % of the patients being generalised in 44%. Three patients had oedema of the legs or arms. All complained of aggravated of the itching. The intensity of itching and rash reached its maximum in the first 24 to 36 hours subsiding after treatment; gradually thereafter. symptomatic therapy with analgesics was sufficient. No serious or life-threatening adverse events were recorded.

***Follow-up****:* One month after treatment, 10 patients reported to be free of itching (Table 3). In a further 7 patients the itching had decreased. Only one patient did not have any kind of relief from itching. Fifteen patients judged their skin lesions to have markedly improved.

Table2. Frequency of transient adverse events in the first 72 hrs after a single oral dose of ivermectin in 18 patients

| | Frequency | |
|---|---|---|
| | n | % |
| Pruritus increase | 18 | 100 |
| Papular rash: prevalence | 17 | 94 |
| Generalised | 8 | 44 |
| Fever | 5 | 28 |
| Headache | 4 | 22 |
| Myalgia | 3 | 17 |
| Joint pain | 1 | 6 |
| Oedema of arms or legs | 3 | 17 |
| Serious adverse effects | 0 | |

Table 3. Report of sowda patients on intensity of itching and severity of skin lesions one month after treatment with ivermectin (n=18).

| | | Frequency | |
|---|---|---|---|
| | | n | % |
| *Itching:* | increased | 0 | |
| | no change | 1 | 6 |
| | decreased | 7 | 39 |
| | no more itching | 10 | 56 |
| *Skin lesions:* | increased | 0 | |
| | no change | 1 | 6 |
| | mild improvement | 1 | 6 |
| | moderate improvement | 1 | 6 |
| | marked improvement | 15 | 83 |

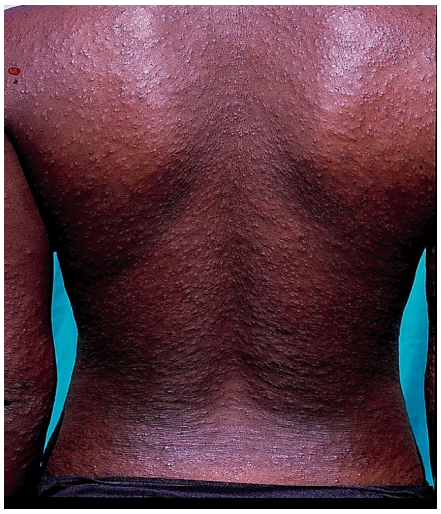
The effects of ivermectin on skin lesions, microfilariae prevalence, Mazzotti test reactions and eosinophil granulocytes are shown in Table 4. The difference between pre- and post-treatment results regarding the scores of skin lesions, the prevalence of microfilariae, and the results of the Mazzotti test reaction was significant ($p<0.0001$). Figures 1 and 2 demonstrate the marked improvement of the skin lesions after ivermectin therapy. No significant change of eosinophil count was detected within a month .

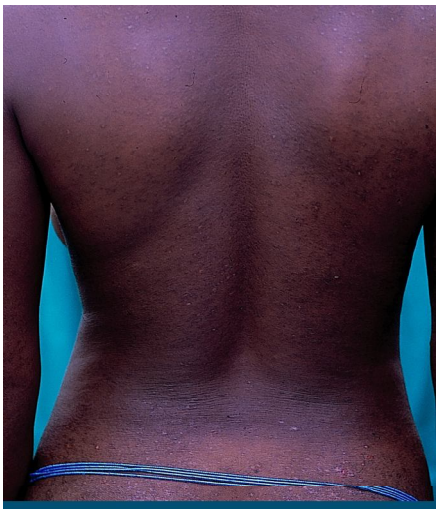
Table 4. Comparison of selected parameters before and after ivermectin treatment of 18 sowda patients.

| Parameter | Pre-ivermectin | Post-ivermectin | p-value |
|---|---|---|---|
| Skin lesions score* | 6 | 1 | $p<0.0001$ |
| Topical Mazzotti test positive | 18(100%) | 2(11%) | $p<0.0001$ |
| Eosinophil count | 25% | 22% | $p=0.4$ |

**Score: 0= no onchodermatitis; 1-9= severity of dermatitis*

(a)





(b)

Fig. 1. The severe papular reactive onchodermatitis localized to the trunk before (a) and after treatment (b).
**Note:** The severe papular reactive onchodermatitis localized to the trunk (a) has completely disappeared one month following ivermectin treatment leaving just slight skin discolouration (b).

(a)

(b)

Fig. 2**.** Lesion on lower extremities before and after treatment.
**Note:** Typical asymmetric distribution of onchodermatitis affecting only the right lower extremity (a). Marked hyperpigmentation and papules were found prior to treatment with ivermectin (a). One month later all the papules have disappeared and the hyperpigmentation is starting to decrease (b).

## DISCUSSION

The clinical features of sowda patients from Ghana are similar to those reported from other endemic areas (5-8). The strikingly asymmetric distribution of the skin lesions affecting predominantly the gluteal region and the lower extremities is similar to the sowda patients from Liberia, another West African country (5, 8). The skin lesions of sowda are not only characterized by the presence of papules but also by the hyperpigmentation of the affected body regions as encountered in almost all our patients.

There are reports that patients with sowda react severely following treatment with ivermectin (11-12). Sowda patients from Liberia had a marked swelling of the affected limbs associated with severe localised pruritus and tender regional lymph nodes following ivermectin administration (8). Similarly, the patients from Ghana suffered from one or more types of adverse events after taking ivermectin.

Severe symptomatic postural hypotension, as reported in a study comprising patients with generalized onchocerciasis, was not observed (13). Still, a close follow-up is warranted in the first days after treatment of sowda patients with ivermectin.

With a single dose of ivermectin, there was a significant clinical improvement and this is in concordance with the results reported by Pacque et al., Darge et al. and Baraka et al. (8, 12, 14). The absence of microfilariae and the negative local Mazzotti tests after treatment point out the good response to the ivermectin therapy, as well. The treatment outcome clearly demonstrates that patients with sowda profit from a single dose ivermectin treatment. In view of the fact that the sowda patients are relatively young females who not only suffer from the severe skin disease but also from the associated social stigmata, the improvement with just one dose of oral therapy of ivermectin has far reaching consequences. It has been recommended to repeat the ivermectin treatment in three month intervals (8).

In conclusion, the active search for patients with sowda in Ghana resulted in finding a significant number of cases over a very short period. A single oral dose of ivermectin was shown to cause a marked improvement of both the severe itching and skin lesions in the sowda patients.

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