

Chronic Urticaria in Returning Travellers: The Role of Anthelmintic Treatment

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Key Words

Helminthic infection · Albendazole · Eosinophilia

Abstract

Background: Chronic urticaria often poses a therapeutic challenge. The human immune response to helminths has a high degree of similarity to an allergic response in terms of skin manifestations, eosinophilia, and IgE elevation. Unfortunately, it is often complicated to diagnose such infections.

Objective: We sought to assess the effect of empirical anthelmintic treatment among returning travellers diagnosed with chronic urticaria, without clear proof of helminthic infection.

Methods: This is a retrospective case series of 19 returning travellers with chronic urticaria. All patients were treated with anthelmintic treatment given based on clinical suspicion only. A randomly selected control group of 20 patients with chronic urticaria, with no history of travel, was also enrolled.

Results: A positive clinical response was reported in 68.4% (13 patients) of the travellers' group within 3 months after treatment with anthelmintic therapy compared with 10% (2 patients) of chronic urticaria patients in the control group. No adverse effects from treatment were recorded. **Conclusion:** In patients with chronic urticaria, travel history to developing countries must be obtained. Empiric anthelmintic therapy might be beneficial, even in the absence of findings suggestive of helminthic infection.

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Introduction

Chronic urticaria is a frustrating condition for both patients and caregivers. An extensive work-up often does not uncover the aetiology, and many have a poor response to current therapy. Chronic urticaria has been reported to be associated with a number of infections, but these associations are not strong [1].

It is known that the human immune response to helminths has a high degree of similarity to an allergic response in terms of eosinophilia and IgE elevation [2]. Nevertheless, the mechanisms by which helminths could stimulate allergic cutaneous diseases are not fully understood. Travellers to developing countries are at higher risk of contracting helminthic infections. Unfortunately, the diagnosis of helminthic infection remains unsatisfactory owing to the lack of sufficient sensitivity and the high cost/inaccessibility of available tests.

The aim of this study was to determine the effectiveness of an empirical anthelmintic treatment among travellers returning from endemic countries who were diagnosed with chronic urticaria, even without proof of helminthic infection.

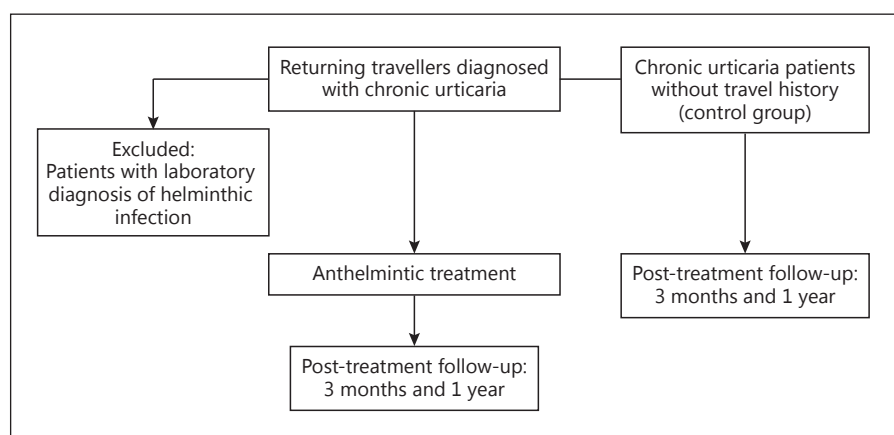
A.N. and S.B. contributed equally to this work.

Table 1. Patient characteristics

	Study group (n = 19)	Control (n = 20)	p
Mean age, years	33.2±13.7	39.7±18.1	0.212
Female gender	11 (58)	10 (50)	0.621
Country of birth (Israel)	17 (89)	18 (90)	0.957
Allergic background	6 (32)	8 (40)	0.584
Duration of symptoms, months	8.2±9.7	54.2±77.8	0.007
Eosinophilia ¹	7 (36.8)	1 (5)	0.02

Values are presented as means ± SD or n (%).

¹ Eosinophilia >6% or >500 eosinophils/μl.

**Fig. 1.** Flowchart of Materials and Methods.

Materials and Methods

For further details, see the online supplementary materials (see www.karger.com/doi/10.1159/000445715 for all online suppl. material) (fig. 1).

Results

The study group included 20 travellers with chronic urticaria; however, 1 patient was excluded because of insufficient data. Demographic and clinical data are presented in table 1. Six patients (32%) had a history of allergies (mostly allergic rhinitis and drug sensitivity). The average duration of chronic urticaria in the study group was 8.2 months.

Twelve patients (63%) reported having gastrointestinal symptoms such as abdominal discomfort, vomiting, or diarrhoea. Seven (37%) of the patients were found to have eosinophilia (>6% or >500 eosinophils/μl): 1,359 ± 604 eosinophils/μl (14.47 ± 6.84%); 5 out of 7 patients

who had tested for IgE had elevated levels: 243.2 ± 105.8 IU/ml (normal range, 4–188). All stool tests performed (16/19 patients) were negative. All patients were treated with albendazole, and 4 patients received additional drugs: ivermectin and/or praziquantel. The anthelmintic treatment was well tolerated, and no adverse effects were reported.

A positive clinical response was reported in 13 patients (68.4%). The majority, 11 patients (57.9%), had a complete response. However, no case of cure was reported in the control group ($p < 0.0001$; table 2). The clinical response was maintained at the 1-year follow-up. Furthermore, the proportion of patients with any response to treatment was also significantly higher among the study group compared with the control group (68.4 and 10%, respectively, $p = 0.00018$; table 2).

Patients in both groups were treated similarly – with antihistamines and/or steroid therapy – prior to our intervention. No significant association was found between factors suggestive of helminthic infection (eosinophilia, elevated IgE, or gastrointestinal complaints) and treat-

Table 2. Treatment outcomes

	Study group (n = 19)			Control group (n = 20)
	total (n = 19)	no allergic background (n = 13)	allergic background (n = 6)	
Complete response	11 (57.9)*	10 (77)**	1 (17)	0
Partial response	2 (10.5)	1 (8)	1 (17)	2 (10)
No response	6 (31.6)	2 (15)	4 (67)	18 (90)***

Values are presented as n (%). Data indicate response to treatment within 3 months. * $p < 0.0001$, comparison between the study and control groups; ** $p = 0.036$, comparison between patients with allergic background and those without; *** $p = 0.22$, comparison between patients with allergic background and control group.

ment outcome. Furthermore, no significant association was found between the duration of symptoms prior to the patient's arrival at the clinic or between travellers' trip characteristics and treatment outcome. However, patients in the study group with a history of allergic background had a significantly lower response rate to anthelmintic treatment. In fact, no significant difference was found between these patients and the control group with regard to response to treatment (table 2).

Comparing the epidemiological characteristics of the study group with the control group, no statistically significant differences were found (table 1). However, the average duration of symptoms in the control group was 54.2 months, whereas it was only 8.2 months in the study group ($p = 0.007$). Seven patients (36.8%) in the study group were noted to have eosinophilia, as opposed to only 1 patient (5%) in the control group ($p = 0.02$).

Discussion

Chronic urticaria has long been a puzzling clinical entity, and with current drug regimens many patients still remain a therapeutic challenge. An association between helminths and allergic cutaneous diseases such as urticaria, angioedema, and pruritus has been described [2]. Travellers to tropical destinations are at higher risk of acquiring such infections.

In our study the majority of the patients, 68.4%, had complete or partial response to the anthelmintic treat-

ment, while in the control group only 10% exhibited partial response to conventional treatment, and none were completely cured during the study period.

The duration of symptoms prior to arrival at a health care provider was significantly longer among the control group compared with the study group ($p = 0.007$). Hence, it is assumable that the higher response rate to treatment among the study group is the result of more successful treatment rather than the natural course of the disease.

A significantly higher rate of eosinophilia was observed among the study group compared with the control group ($p = 0.02$). This finding corresponds with published data regarding the presence of eosinophilia in patients with helminthic infection [3] and its absence in chronic urticaria patients [4]. It also supports the study hypothesis that travellers with chronic urticaria represent a unique subpopulation of chronic urticaria patients in whom the cause for urticaria is often infectious. Nonetheless, no significant association was found between the presence of eosinophilia and the response rate to anthelmintic treatment. Assuming that complete remission of urticaria following anthelmintic treatment is indicative of such an infection, we are reminded that the absence of eosinophilia does not exclude helminthic infection [3].

All stool samples examined were negative for ova and parasites. Stool testing is a complex process that, even under optimal conditions, has a low sensitivity [5, 6]. Twelve patients (63%) in the study group reported having gastrointestinal symptoms during their travels. However, there was no statistically significant association observed between the presence of gastrointestinal symptoms and the response rate to anthelmintic treatment. Indeed, as presented in the work of Humbert et al. [7], which deals with the cutaneous symptoms of toxocaral infection, dermal symptoms may be the sole manifestation of such infection.

Conclusion

Our findings emphasize the importance of obtaining an accurate travel history in chronic urticaria patients. In the presence of relevant history, an empiric anthelmintic treatment may be useful, even in the absence of supportive laboratory evidence of infection, and we would advocate considering this treatment in clinical practice.

Statement of Ethics

The study was approved by the ethics committee of the hospital.

Disclosure Statement

The authors have no conflicts of interest to declare.

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