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CORRESPONDENCE

Follow-Up of Treatment Response in Imported Acute Schistosomiasis

To the Editor-in-Chief:

We read with great interest the article by L. Praticò and colleagues in the *Journal of Travel Medicine*[1] and we would like to bring some additional comments to the readers' attention.

We agree that treatment of acute schistosomiasis in non-immune travelers remains challenging.[2–4]

Although infrequent, the observation that the course of the disease may be prolonged and recurrent is not new. In a case series of 23 consecutive travelers diagnosed with acute schistosomiasis, 5 (22%) experienced recurrence of symptoms and eosinophilia within the first 6 months after exposure despite praziquantel therapy and corticosteroids, and all of them required several courses of steroids and at least one additional course of praziquantel.[5]

Like others, we often observe a transient rising of the eosinophil count just after praziquantel therapy, and this is sometimes associated with clinical exacerbation (up to 50% of the cases if no steroids are co-administered). In such cases, normalization of the eosinophil count is sometimes slow. Provided that alternative etiology of eosinophilia such as strongyloidiasis has been reasonably excluded, such an evolution does not require additional measures beyond supportive treatment (in case of symptoms) and the usual recommended second course of praziquantel until clinical and parasitological cure (usually within a maximum of 6 months post-exposure/infection). Treatment failure with standard single dose praziquantel has been reported with variable frequency in travelers.[6–8] Distinction between failure to eradicate infection and worm burden reduction has not always been clearly stated in the different case series, and various diagnostic methods and case definition for failure have been used. Whether failure was a consequence of drug tolerance, acquired resistance or of suboptimal treatment was not always determined.[9]

Serological assays remain positive for prolonged periods following therapy and therefore have in our opinion no major role in post-treatment monitoring of patients, besides clinical assessment, eosinophil count, and egg detection. Whitty and colleagues observed variable enzyme-linked immunosorbent assay [ELISA] responses 3 to 5 months after treatment with a titer increase in 22% and absence of change in 32% of the cases.[10] In a cohort of 58 patients with schistosomiasis in Australia, 30 months after treatment, only 68% of travelers and 35% of immigrants ($p < 0.01$) achieved a fourfold antibody decline.[11] Our experience is similar. For several years now, we have been following up a cohort of 39 Belgian soldiers treated for *Schistosoma mansoni* infection.[12] Of the 24 participants with currently 5-year follow-up, serology [(ELISA) and/or indirect hemagglutination (IHA)] was still positive in most cases (16/24 for ELISA, 18/24 for IHA). Median eosinophilic counts stayed elevated after treatment in the first year but decreased after 5 years to lower levels [from 289,00/µL (before treatment) to 291,00/µL (1 year after treatment) to 195,50/µL (5 years after treatment) (p-value ≤ 0.003)]. Final results of the 39 treated study participants are expected at the end of the year.

We therefore find the authors' decision to administer artemisinin and multiple additional praziquantel treatments over months because of this so-called "serological non-response" rather questionable. In addition, artemisinin derivatives are indeed very effective on the larval stages within the first 28 days after infection (in a mouse model[13]), but the rationale for administering them thereafter is unclear to us.

Follow-up of treatment response in imported schistosomiasis needs in our opinion to be guided by active disease parameters, such as suggestive symptoms, raised eosinophil count, or parasitological/histological evidence of viable eggs, while raising or persisting serological titers have only marginal value. Rectal snips or sigmoidoscopy would be the preferable workout in these symptomatic patients after treatment.[14] The persisting symptoms, eosinophilia, and raising serology after treatment observed in these cases could have been caused by the triggered immuno-inflammatory reaction itself, and a tempering dose of corticosteroids might have been clinically more beneficial for the patients than retreatment with antimicrobials. Although combination therapy with praziquantel and artemisinin derivates for the treatment of acute schistosomiasis in travelers is probably more effective than praziquantel alone, no trial has been conducted in this population so far to support this hypothesis, in contrast with observations in endemic settings.[15,16] Multicentric well-designed prospective studies using artemisinin derivates in addition to praziquantel are required to redesign the therapeutic options of acute schistosomiasis where larval stages play a key pathogenic role.

In contrast with our concern of overtreatment, we wonder why treatment with (at least one course of) praziquantel has not been considered in the two other subjects (two out of six) with similar freshwater exposure in Lake Victoria, since attack rates are often high in similar situations, and absence of eosinophilia and serological response do not completely rule out infection with *Schistosoma*.

Finally, recently developed real-time polymerase chain reactions (PCRs) for the detection of *S. mansoni*

and *Schistosoma haematobium* in serum are very promising for the early diagnosis of acute schistosomiasis[17,18] and could be of help in the monitoring of treatment response as well, but once again this would require large prospective and systematic studies that are difficult to implement in single travel centers.

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