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Article in *Clinical Infectious Diseases* · September 2020

DOI: 10.1093/cid/ciaa1299

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Calcified neurocysticercosis: The knowledge gap remains

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Dear Editor,

We read the article by Coyle [1] entitled “New Insights into Calcified Neurocysticercosis: Closing the Knowledge Gap” with great interest. Coyle hints at new research that helps to close the knowledge gap regarding calcifications of neurocysticercosis (NCC). Surprisingly, recent studies that address just this question were not mentioned. [2, 3]

Coyle cites Bustos, et al. [4], who retrospectively examined studies of anthelmintic treatment (AHT) and found 38% of cysts resulted in residual calcifications at one year after AHT. Looking at the percentage of calcifications might be interesting, but the analysis of calcifications is more complex than that; it requires a different approach, such as to take into account the evolutionary phase of the parasites. Coyle points out that the rate of calcification had been well described for individuals with single degenerating cysts, a common presentation in India, [5, 6] but states that data on the rate of calcifications among individuals with multiple cysts is lacking. However, in their cyst-level analysis, Montgomery et al. [2] describe the number of active and degenerating cysts that calcified over a 2-year period. They also describe the number of calcifications that resolved during that time period overall and by ALB versus placebo. A recent paper by Carpio et al. [3] overlooked by Coyle also addresses this gap by depicting how the mean count of calcified cysts changed over time overall and by treatment.

Coyle also states that “studies to date have not focused on factors affecting the incidence of calcifications after treatment in individuals with multiple viable cysts (page 3)”. However, this very question was also addressed in the paper by Montgomery et al. By applying a multistate causal model, [7] the authors identified where in the trajectory ALB has the greatest impact. The authors found that ALB hastened the transition of active cysts to the degenerative stage and, subsequently, the majority of cysts resolved completely and did not calcify. That paper found that the impact of ALB on calcifications might be modified by patient characteristics (gender and age) and cyst burden. These findings suggest that ALB does not increase risk of calcification on average, although the impact may vary in subgroups. Previous studies carried out among patients with single cysts also found no

association between cyst calcification and ALB. [8]

Coyle also states “Early studies found albendazole... led to reduction in seizures.” However, the evidence complicated than this statement indicates. The Carpio et al. paper [3] explored the associations among ALB/placebo treatment, NCC cyst evolution, and seizure outcomes in 153 participants over 24-month follow-up using linear mixed effect models. The association between ALB treatment and seizure outcomes was nonlinear and changed over time. ALB was associated with a reduction in focal seizures in the short term, perhaps by hastening the resolution of the cysts; however, the effect was no longer discernible over the long term, because most cysts either calcify or resolve completely regardless of treatment. And even the two studies Coyle cites as indicating ALB decreases seizures [9,10] had mixed findings, with a significant reduction found in the number of generalized seizures but not partial seizures, which seems hard to explain.

Calcified NCC remains an enigma for practicing neurologists. Patients with severe refractory seizures may have only one calcified lesion, and patients with multiple calcifications may have no seizures. [11] Thus, questions remain about the rate of calcification, factors that influence this rate and the impact of calcified cysts on symptoms and more research is certainly needed, but recent publications have started to address some of these gaps in our knowledge.

None of the authors has any potential conflicts.

Accepted Manuscript

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