## **INVITED COMMENTARY**

## Albendazole for Neurocysticercosis in Children: How Long is Long Enough?

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he World Health Organization (WHO) recently provided guidelines for the diagnosis and treatment of viable parenchymal neurocysticercosis (VPN) [1]. A strong recommendation has been provided for anti-helminthic therapy for VPN, if lesions are not numerous or associated with raised intracranial pressure/hydrocephalus. This recommendation is associated with 'moderate'evidence for both cyst resolution and seizure control. For single enhancing lesions, the recommendation for anti-helminthic therapy has low evidence, and has been given a conditional recommendation by WHO. Guidelines for VPN have also been provided by the Infectious Diseases Society of America(IDSA)/ American Society of Tropical Medicine and Hygiene (ASTMH) [2]. Albendazole therapy alone for 10-14 days is recom-mended for 1-2 cysts, and combinational albendazole and praziquantel for 10-14 days for more than two cysts [2].

Recently, the Association of Child Neurology (AOCN) has also issued consensus guidelines for treatment of neurocysticercosis (NCC) in India [3]. As per these guidelines, albendazole therapy should be administered for 10-14 days for single viable lesion, and a combination of albendazole and praziquantel for 10-14 days for more than one ring-enhancing lesion.

In all these guidelines, the treatment recommen-dations for children are the same as for adults. However, extremely limited number of children have been enrolled in the randomized trials that form the evidence base for these recommendations. Moreover, the optimum duration of treatment with anti-helminthic drugs is stated as a 'research gap' in the WHO guidelines.

In face of the above information, the study by Singla, et al. [4] attempts to cover an important gap in the literature. In this open-label trial, the authors examined the efficacy of albendazole given for 14 days vs 28 days in children with newly diagnosed active NCC. The 14-days therapy was comparable to the 28-days therapy in achieving complete radiological resolution of the lesions at six months [6 (18.8%) vs 9 (27.3%); OR (95%CI) 0.61 (0.19 to 1.98); P=0.56]. Similar efficacy was also observed for proportion of children with seizure recurrence [5(15.6%) vs 2(6.1%);OR (95%CI): 2.87 (0.51-16.0); P=0.26] and calcification on follow-upimaging [26 (81.2%) vs 23(69.7%); OR (95%CI): 1.88 (0.59-5.99); P=0.39]. Several studies from India have previously attempted to assess optimal duration of anti-helminthic therapy. For 1-3 lesions, even shorter regimens of 7 days have been tried against 28 days, with comparable efficacy [5]. In a recent study by Johnson, et al. [6], 7-days regimen of albendazole vs 28-days regimen was compared for single-lesion NCC in children. Outcome measures including lesion resolution, seizure control and cognitive outcomes were found to be comparable between the two regimens.

In terms of combination therapy for NCC, for more than two cysts, combination of albendazole with prazi-quantel is given a strong recommendation by IDSA/ASTMH.The AOCN recommends combination therapy for more than one lesion. In the study by Singla, et al. [4], a small proportion of patients had more than one (2 to 3) lesions, and all were given albendazole monotherapy [4]. The role of combination therapy has been assessed in a recent study by Singh, et al. [7]. In this randomized, double blind, placebo-controlled trial, children with persistent NCC were assigned to receive either alben-dazole monotherapy, albendazole and praziquantel combination therapy, or placebo for 30 days. A higher proportion of children (62%) showed complete radio-logical lesion resolution at six months, compared to albendazole alone (26.3%) (*P*=0.02).

In the study by Singla, et al. [4], the overall rates of complete lesion resolution were very low (27.3%) compared to previous studies [5,8], with high rates of calcification (81.2%). This is an important consideration, as calcification of NCC predisposes to the recurrence of seizures. The limited recruitment sample in the study, attributable to convenience sampling, may have contri-buted to these

findings. Although seizure recurrence was comparable in the study by Singla, et al. [4], it would be interesting to observe this proportion in a longer follow-up as well as assess predisposing factors for calcification. Some of the predisposing factors that have been reported as determinants of calcification include larger size of lesions (>10 mm), presence of calcification on SWAN-MRI image [9], presence of edema, higher dose of albendazole, more than 24 months with seizures, lower dexamethasone dose, late antiparasitic treatment, and milder antibody response [10].

Despite a lack of robust high-quality evidence, there seems to be a shift in the guidelines towards recommendation of relatively shorter duration (10-14 days) of antihelminthic therapy for VPN. This regimen offers several advantages. Albendazole therapy for more than 14 days requires monitoring of liver function, which may be avoided with shorter regimens. Moreover, adherence is likely to be better. The study by Singla, et al. [4] adds strength to these recommendations. Several gap areas are also identified, including long-term outcomes following albendazole therapy, as well as need for retreatment, if any, of persistent active lesions. Certainly, there is urgent need for further robust, randomized trials for anti-helminthic therapy in children, addressing duration and, whether it may be further shortened, as well as for long-term outcomes including eventual seizure recurrence, cognition and quality of life-based outcomes that follow anti-helminthic therapy.

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