CURRENT LITERATURE

ANTIPARASITIC THERAPY FOR VIABLE CYSTS MAY HELP SEIZURE CONTROL IN PATIENTS WITH NEUROCYSTICERCOSIS

A Trial of Antiparasitic Treatment to Reduce the Rate of Seizures Due to Cerebral Cysticercosis

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BACKGROUND: Neurocysticercosis is the main cause of adult-onset seizures in the developing world. Whether therapy with antiparasitic agents results in improved seizure control has been questioned because of the lack of adequate, controlled studies.

METHODS: We conducted a double-blind, placebo-controlled trial in which 120 patients who had living cysticerci in the brain and seizures treated with antiepileptic drugs were randomly assigned to receive either 800 mg of albendazole per day and 6 mg of dexamethasone per day for 10 days (60 patients) or two placebos (60 patients). The patients were followed for 30 months or until they had been seizure-free for 6 months after the doses of the antiepileptic drugs had been tapered. The efficacy of treatment was measured as the decrease in the number of seizures after treatment.

RESULTS: In the albendazole group, there was a 46 percent reduction in the number of seizures (95 percent confidence interval, −74 to 83 percent) during months 2 to 30 after treatment. This reduction, which was not statistically significant, was composed of a nonsignificant reduction of 41 percent in the number of partial seizures (95 percent confidence interval, −124 to 84 percent) and a significant 67 percent reduction in the number of seizures with generalization (95 percent confidence interval, 20 to 86 percent). Most of the difference in the number of partial seizures was attributable to a few patients who had many seizures during follow-up. The proportions of patients who had partial seizures during follow-up were similar in the two groups (19 of 57 in the albendazole group and 16 of 59 in the placebo group), but the patients in the placebo group had a greater tendency to have seizures with generalization (22 of 59, vs. 13 of 57 in the albendazole group; risk ratio, 1.63; 95 percent confidence interval, 0.91 to 2.92). More of the intracranial cystic lesions resolved in the albendazole group than in the placebo group. With the sole exception of abdominal pain, side effects did not differ significantly between the two groups.

CONCLUSIONS: In patients with seizures due to viable parenchymal cysts, antiparasitic therapy decreases the burden of parasites and is safe and effective, at least in reducing the number of seizures with generalization.

COMMENTARY

As the leading cause of acquired epilepsy in the developing world, neurocysticercosis has only recently started to receive the attention it deserves in the epilepsy literature. Effective antiparasitic treatment has been available for 2 decades and its use seems intuitively logical. Yet, its benefit has been questioned because, aside from seizure occurrence, most patients are asymptomatic and those patients with seizures have only infrequent seizures that can be controlled with antiepileptic drugs. Open-label studies have not clearly supported a role for antiparasitic therapy, and some investigators proposed that the parasites eventually would be eliminated by natural processes. The study of Garcia and colleagues, thankfully, has ended the controversy by demonstrating the efficacy of a course of albendazole and dexamethasone in reducing seizures in patients with viable cysts—even though the seizure benefit was demonstrated only for generalized tonic–clonic seizures in a fraction of patients. The study also demonstrated that antiparasitic treatment significantly reduced the number of viable cysts. Treatment was associated with an increase in calcification in the cysts, suggesting that development of calcification is not as relevant to seizures as viable cysts. However, despite albendazole's clear efficacy against viable cysts, 41% of noninflamed and 21% of inflamed viable cysts were still present at follow-up. This may be one reason why there was not greater seizure improvement in the treatment group.

The findings of Garcia et al. generate new questions and provide incentive for new studies—some of which the authors

propose in the discussion. Would eradication of all viable cysts produce even greater seizure control? In a double-blind study, it has already been demonstrated that 28 days of treatment with albendazole is not superior to 7 days of treatment (1). An accompanying article suggested studying the effect of a second course of treatment (2). There may also be a place for other, more effective treatments that cross the blood brain barrier.

One paradoxical, but not totally unexpected, finding of the study was that in the first month after treatment, patients given albendazole had more seizures than the placebo group. This phenomenon likely is related to inflammation generated by dying cysts. Concern about this inflammatory reaction was one of the reasons that some clinicians advocated against antiparasitic treatment. Garcia et al. have demonstrated that the long-term benefits of treatment outweigh the short-term risks of increased seizures. The risk–benefit ratio may be improved even further if the inflammatory reaction can be better controlled with a higher dose of steroids, as suggested by the authors, or alternatively, by a longer course of steroids.

One potential criticism of this study is that antiepileptic drug changes were allowed during double-blind treatment. However, if this were to have any effect on the study findings, that effect would be to neutralize the difference between groups. In addition, not allowing antiepileptic drug changes for uncontrolled seizures would not be ethical in a long-term study. This study was thoughtfully designed, overall, and its results appear very valid.

Perhaps, in recognition of the importance of this paper, there was an accompanying editorial (3) and a perspective article (2) published. The editorial examined the evidence for and against antiparasitic treatment and supported expeditious elimination of parasites in all patients with active parenchymal neurocysticercosis (3). The perspective article indicated that neurocysticercosis is one of few potentially eradicable diseases and stressed the importance and feasibility of prevention of neurocysticercosis through multiple interventions, including treatment of human and animal carriers, improved hygiene and sanitation, improved pig-raising practices, and a variety of other public health measures. Investment of efforts and resources in the eradication of *Taenia solium*, the parasite that causes neurocysticercosis, will undoubtedly have the greatest return.

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References

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