Pharmacokinetic Optimisation of the Treatment of Neurocysticercosis

Julio Sotelo and Helgi Jung

Neuroimmunology and Neuropharmacology Departments, Instituto Nacional de Neurologia y Neurocirugia and Universidad Nacional Autonoma de Mexico, Mexico City, Mexico

Summary

Neurocysticercosis is the most important parasitic infection of the nervous system. It is common in communities living in conditions with poor hygiene. Until the last 2 decades, there was no specific pharmacological treatment: surgery and corticosteroids were the only medical alternatives. The recent introduction of anticysticercal drugs, an isoquinoline (praziquantel) and a benzimidazole (albendazole), has dramatically changed the medical management of neurocysticercosis.

Praziquantel is taken orally and undergoes extensive first pass hepatic transformation. Peak concentration in serum is reached after 1 to 2 hours and the elimination half-life is between 1 and 3 hours. Praziquantel permeates the blood-brain barrier, thus explaining its effectiveness on parenchymal brain cysticercosis. Plasma concentrations of the drug are increased when a high carbohydrate diet is administered. Cimetidine also increases the plasma concentration of prazi-
quantel by inhibition of cytochrome P450. Bioavailability of the drug is markedly reduced when given jointly with antiepileptics or corticosteroids, specially carbamazepine, phenytoin or dexamethasone. The current schedule for neurocysticercosis treatment lasts 2 weeks at daily doses of 50 mg/kg. Recently, a new therapeutic scheme has been proposed that considers the pharmacokinetics of the drug. This regime lasts only 1 day and includes 3 dosages of 25 mg/kg at 2-hour intervals. This increases the time that the parasite is exposed to high drug concentrations. This therapeutic scheme has produced similar results to longer schemes, with the additional advantages of cost, length of usual treatments and reduction in total dose received (being one-tenth of the total dosage).

Albendazole is considered by many as the drug of choice for treatment of neurocysticercosis. It is given orally and is rapidly and extensively metabolised to albendazole sulfoxide (ALBSO), which is considered to be the metabolite directly or indirectly responsible for both toxicity and efficacy outside the gastrointestinal tract. Concentrations of ALBSO are highly variable between individuals and it has a half-life of between 6 and 15 hours. It also crosses the blood-brain barrier. In patients with extrahepatic obstruction, the elimination process is prolonged and plasma concentration is increased. Fatty meals improve absorption. Concomitant administration of albendazole with dexamethasone or with praziquantel increases plasma concentration of ALBSO. Albendazole is administered in an 8 day course of 15 mg/kg per day in 2 divided doses 12 hours apart. This scheme, based on drug pharmacokinetics, has proven to be highly effective.

Inflammation is a common accompaniment of neurocysticercosis; in many cases it is the aetiopathogen responsible for histological damage. Corticosteroid therapy is useful for preventing further tissue injury. Long term corticosteroid therapy can be accomplished with 50mg of oral prednisone 3 times a week. Acute corticosteroid therapy includes brief courses with high dosages of intramuscular dexamethasone or intravenous methylprednisolone. Clinical decisions on cysticidal and anti-inflammatory treatments must be made with the information gathered by neuroimaging studies, either computed tomography or magnetic resonance, and by the analysis of cerebrospinal fluid.

1. Praziquantel

Praziquantel is a broad spectrum anthelmintic drug with activity against all species of schistosomes pathogenic to humans as well as against a wide variety of trematodes and cestodes. Single doses of praziquantel (10 mg/kg) eradicate intestinal taeniasis and regimens of 3 to 6 days (25 to 50 mg/kg/day) eradicate subcutaneous cysticerci.

Praziquantel has been used for human cysticercosis since 1980 when a beneficial response was observed. This report was followed by several uncontrolled studies and isolated case reports stressing the utility of praziquantel in neurocysticercos-