Considerations for the use of anthelminthic therapy for the treatment of neurocysticercosis

This document accompanies the WHO Guidelines on management of Taenia solium neurocysticercosis (WHO, 2021) and is intended for medical practitioners. It focuses on the two anthelminthic medicines used to treat neurocysticercosis: albendazole and praziquantel.

Introduction

• Neurocysticercosis is characterized by a great heterogeneity of clinical and radiological presentations, and randomized trials evaluating therapeutic schemes in all the scenarios are rare. As a result, in the latest treatment guidelines (IDSA/ASTMH, 2017; WHO, 2021), a high proportion of the evidence is of moderate/low quality and the strength of the recommendations is often weak/conditional.

• The two anthelminthic medicines used to treat neurocysticercosis are:
  - albendazole (ABZ), a broad-spectrum anthelminthic that is active against intestinal roundworms, lungworms and tapeworms (the study of ABZ for human medicine was initiated in 1979 and its effectivity against the disease was demonstrated in 1987); and
  - praziquantel (PZQ), a pyrazynoisoquinoline anthelminthic that has been used to treat human cysticercosis since 1979.

• Both medicines are effective against vesicular (viable) and colloid (degenerative) cysticerci, and the choice between them should primarily take into account their availability and cost in each country where the disease is endemic. The evidence of effectiveness is stronger for vesicular than for colloid cysts due to the heterogeneity among the studies in the latter case.

• Due to the inflammatory reaction around the cysts – a sign of parasitic degeneration caused by anthelminthics – use of anthelminthic medicines must always be combined with anti-inflammatory medicines (see below).

Doses

The location of the parasites is one of the main factors modulating the effectiveness of anthelmintics for neurocysticercosis. Parasites located in the parenchyma respond better to treatment than parasites located outside the parenchyma (mainly the ventricles and the subarachnoid space).

• Vesicular and colloidal parenchymal cysts
  ABZ is usually given at doses of 15 mg/kg per day, divided into two administrations, for 10 to 14 days. PZQ is administered at doses of 50 mg/kg per day, divided into three administrations, for 10 to 14 days. Shorter protocols for both medicines have also been claimed to be as effective. Recently, a study showed that the combination of ABZ + PZQ, at

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the same doses, is more effective than ALB alone in patients with more than two parenchymal cysts.

- **Vesicular and colloidal extraparenchymal cysts**
  Extraparenchymal cysts are less responsive than parenchymal cysts to anthelmintic treatment. To increase the effectiveness of the treatment, two strategies have so far been used: increasing the doses used (for example, with ABZ, 30 mg/kg/day for 10–14 days to be repeated 6 months later, in case of incomplete response); and increasing the duration of treatment (up to several months until a decrease of disease activity is evident).

### Practical considerations 1, 2, 3

- **Indications**
  - Before administering ABZ or PZQ, brain imaging (computerized tomography and/or magnetic resonance imaging) should be performed to assess the location, number and degenerative stage of the parasites, as well as the intensity of the inflammatory reaction.
  - The use of anthelmintics is recommended in case of vesicular (viable) and colloidal (degenerative) cysts. Their use is not recommended in the event of calcified (dead) parasites.

- **Contraindications due to the clinical/radiological characteristics**
  - Intracranial hypertension (main symptoms: progressive headache, nausea, vomiting, impaired visual acuity): independently of the cause (hydrocephalus or diffuse cerebral oedema), this life-threatening sign must be corrected (via surgery or anti-inflammatory treatment) before administering anthelmintic medicines.
  - Cysticercotic encephalitis (the presence of dozens of colloidal cysts) is a clear contraindication.
  - In the event of infection with multiple vesicular cysts, the possible use of anthelmintics should be undertaken with extreme caution, under expert supervision.

- **Administration**
  - The effectiveness of treatment depends on the plasma concentration of the medicine. This has been shown for ABZ used to treat parenchymal and extraparenchymal cysts. To increase the plasma concentration, both medicines should be administered with grapefruit juice and/or food, preferably with high-fat food for ABZ, and with high-carbohydrate food for PZQ.
  - Given the risk of the anthelmintic treatment, it is recommended, in the event of multiple parenchymal cysts or extraparenchymal localization, to administer anthelmintic treatments during hospitalization.

- **Anti-inflammatory treatment**
  - Symptoms (especially convulsions and headaches) may appear or worsen at the start of treatment. This is linked to the inflammatory reaction around the cysts, a prelude to the degeneration of the cysts.

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- To control the inflammatory response, anti-inflammatory medicines must be provided. Anti-inflammatory therapy should begin one or two days before anthelmintic treatment. It must continue throughout anthelmintic treatment, and should be reduced more or less quickly depending on the intensity of the inflammatory reaction.

- The most frequently used anti-inflammatories are corticosteroids (mainly dexamethasone and prednisone). The duration and doses of treatment will depend on the clinical condition of the patients and the characteristics of the parasites before treatment (number, location, stage and intensity of the inflammatory reaction).

- Doses will be higher for extraparenchymal localizations (generally up to 0.4mg/kg per day for dexamethasone and 1mg/kg per day for prednisone) because the inflammatory complications (arachnoiditis, vasculitis, intracranial hypertension) are potentially more severe.

- **Antiepileptic medicines**

  - As there is a risk of increased seizures during anthelmintic treatment, it is important to continue antiepileptic medicines during anthelmintic treatment. If the patient does not have a history of seizures and is not receiving antiepileptic medicines, the possible addition of such medicines should be discussed with an expert, as this will depend on the location and number of cysts.

  - There are no data to indicate the advantage of one antiepileptic medicine over another in epilepsy due to neurocysticercosis. The medicines and doses should be the same as those used in epilepsy due to other causes.

  - The recommended duration of treatment is at least 6 months after the last seizure in the event of complete disappearance of the parasites after anthelmintic treatment, and at least 2 years after the last attack if remnants of parasites persist (calcification, granuloma, gliosis).

- **Follow-up**

  - The effect of the anthelmintics (reduction or disappearance of cysts) must be evaluated by imaging 6 months after treatment.

  - If the cysts persist at this stage, the same management may be repeated, or a change of anthelmintic may also be chosen. Expert opinion should be obtained.

- **Specific cases**

  - **Pregnant women:** Since anthelmintic treatment is generally not an emergency, it is recommended to start treatment after childbirth.

  - **Children:** There are no data contraindicating anthelmintic medicines in children.