Adverse Effects of Chemotherapeutic Agents Used in Tropical Medicine

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Contents

Summary .......................................................... 31
1. Anthelmintics .................................................. 32
   1.1 The Benzimidazoles .................................... 32
   1.2 Praziquantel .......................................... 33
   1.3 Other Schistosomicidal Agents .................... 33
   1.4 Ivermectin ........................................... 33
   1.5 Diethylcarbamazine ................................. 34
   1.6 Other Anthelmintics ................................ 34
2. Antimalarial Agents ........................................ 35
   2.1 Chloroquine .......................................... 35
   2.2 Proguanil ............................................. 36
   2.3 Pyrimethamine plus Dapsone (‘Maloprim’) .... 36
   2.4 Quinine ................................................ 36
   2.5 Pyrimethamine plus Sulfadoxine (‘Fansidar’) 37
   2.6 Mefloquine .......................................... 37
   2.7 Halofantrine .......................................... 37
3. Antiprotozoan Agents (except Antimalarials) .... 38
   3.1 Metronidazole ........................................ 38
   3.2 Tinidazole ............................................ 38
   3.3 Ornidazole ............................................ 38
   3.4 Furazolidone ......................................... 38
   3.5 Diloxanide Furoate ................................ 38
   3.6 Efomithine (α-Difluoromethylornithine) ....... 39
   3.7 Benzimidazole ........................................ 39
   3.8 Nifurtimox ........................................... 39
   3.9 Pentamidine .......................................... 39
   3.10 Suramin .............................................. 40
   3.11 Sodium Stibogluconate ......................... 40
   3.12 Cotrimoxazole and Trimethoprim ............. 41
4. Drugs Used in the Chemotherapy of Leprosy ....... 41

Summary

Traditionally, many of the chemotherapeutic agents used in tropical medicine have possessed limited efficacy and serious adverse effects. This scenario has been revolutionised by the introduction into clinical parasitology of the benzimidazole compounds, praziquantel (and other schistosomicidal agents) and ivermectin for helminthiasis, and the 5-nitroimidazoles for protozoan infections. An effective armamentarium against Plasmodium spp. infections, especially P.
*Plasmodium falciparum*, is receding as widespread multiple drug resistance becomes commonplace. Although management of several more exotic parasitic infections, including trypanosomiasis, leishmaniasis and onchocerciasis remains unsatisfactory, several newer and relatively non-toxic preparations (including eflornithine and ivermectin) are now available, and offer optimism. However, there remains a very long way to go before a single preparation is available to combat all major protozoan and/or helminthic infections; such an agent would also need to be 100% effective when given as a single dose, safe not only in the healthy adult but also during pregnancy and lactation, stable at high ambient temperature and relatively low in cost.

Medicine as practised in tropical countries, i.e. those with a warm ambient environment, does not equate with the formal discipline of tropical medicine;\(^1\) the latter has traditionally been dominated by clinical parasitology, and covers protozoan and helminthic infections. Therefore, this review concentrates chiefly on chemotherapeutic agents used to combat infection with these 2 groups of organisms.\(^2-3\) Older compounds – which have in the main been overtaken by more recently introduced agents, most of them safer – receive lesser attention. Special problems arise in infancy, lactation and pregnancy.\(^4-7\)

### 1. Anthelmintics

#### 1.1 The Benzimidazoles

During the last 2 decades, chemotherapy of nematode infections has been dominated by the benzimidazole group of compounds.\(^2,3\) The best absorbed and most effective is *albendazole*; however, this agent is not without adverse effects, especially when administered at high dosage.\(^3\) When used for *Echinococcus granulosus* infection, elevated transaminase levels, leucopenia, gastrointestinal symptoms, allergic conditions and hair loss have been recorded;\(^2\) furthermore, in *E. multilocularis* infection, bone marrow depression was observed. Therefore, when used at high dosage (for systemic nematode infections), treatment should only be undertaken when constant medical supervision and monitoring of liver enzymes, leucocyte and platelet counts are possible. This agent should be avoided during pregnancy.\(^3\)

*Mebendazole* is, in contrast, poorly absorbed and its main use is in intestinal luminal nematode infections. Adverse effects relate mainly to the gastrointestinal tract (usually transient abdominal pain and diarrhoea),\(^3\) although at high dosage impaired hepatocellular function and bone marrow depression have been recorded;\(^2\) most of the adverse effects attributable to *albendazole* (see above) have been recorded with *mebendazole* when it has been administered at high dosage; therefore, haematological and biochemical monitoring is important.

The benzimidazole which has been used for the longest period (formerly used in veterinary practice) is *thiabendazole*. Like *albendazole*, it is well absorbed; however, it is more toxic than either *albendazole* or *mebendazole*.\(^2,3\) Dizziness and gastrointestinal disturbances (especially anorexia, nausea and vomiting) are common; other symptoms attributable to its use are pruritus, skin rashes, headache, fatigue, drowsiness, drying of mucous membranes, hyperglycaemia, visual disturbances (especially involving colour vision), leucopenia, tinnitus, cholestasis (and parenchymal liver damage), crystalluria, bradycardia and hypotension. Reports of Stevens-Johnson syndrome, toxic epidermal necrolysis, convulsions and mental disturbance(s) have also been recorded. Fevers, chills, angioedema and lymphadenopathy during administration are probably the result of an allergic response to dead parasites. A recent report documents photoaggravated allergic contact dermatitis following topically administered *thiabendazole*.\(^8\) *Thiabendazole* should be avoided in pregnancy.\(^3\)