

Nitazoxanide : Broad Spectrum Anti-Protozoal

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Intestinal parasitic infections rank amongst the most important causes of morbidity and mortality, especially so in the developing countries and tropics. In a high proportion of cases, protozoal and helminthic infections tend to coexist and have to be treated with antiprotozoal and anthelmintic drug given together. This makes such therapy less affordable to the majority of the sufferers, who are from the economically weaker sections of the society. Against this backdrop, availability of nitazoxanide offers a new ray of hope. It is the only agent that has broad coverage against both common intestinal parasitic protozoa and helminths. Nitazoxanide was originally discovered in 1980's by Jean Francois Rossignol at the Pasteur Institute. Initial studies demonstrated activity against tapeworms. In vitro studies demonstrated much broader activity. Rossignol subsequently led the preclinical and clinical development of albendazole and halofantrine. In 1994 it gained importance after its broad spectrum activity was recognized against common emerging and resistant intestinal protozoa and intestinal helminths (1-6).

Nitazoxanide, a 2 acetyloxy-N (5-nitro-2-thiazolyl) benzamide is well absorbed from the gut. It interferes with pyruvate ferredoxin oxidoreductase (PFOR) enzyme dependent electron transfer reaction which is important for anaerobic glucose energy metabolism. This results in cell swelling, membrane damage and vacuole injury of the trophozoites, resulting in dysfunction of the parasite. The drug is metabolized to the main active metabolite desacetyl nitazoxanide (tizoxanide). Excretion of the drug occurs in urine, bile and faeces (3,5). Nitazoxanide is active against protozoa such as giardia intestinalis, entamoeba histolytica and cryptosporidium parvum, helminths such as ascaris lumbricoides, ancylostoma duodenale, enterobius vermicularis, hymenolepis nana, trichuris trichura, strongyloides stercoralis, taenis saginata and

fasciola hepatica. It is also effective against bacteroides, helicobacter pylori and clostridium species (5-7).

In vitro studies reveal that nitazoxanide and its metabolite tizoxanide are 8 times and 1.5 times more active than metronidazole and other 5-nitroimidazole compounds against giardiasis and amoebiasis respectively. It resolves diarrhoea and associated symptoms within 7 days of initiation of therapy. It also eliminates cysts or trophozoites from the stools in the post treatment period (8-10). Not only this diarrhoea and enteritis associated with blastocystitis hominus also has been shown to resolve with nitazoxamide therapy (11).

Cryptosporidiosis occurs not only in AIDS patients but must also be looked for in immunologically competent children with diarrhoea. It is relatively difficult to treat this infection. A 3 day course of nitazoxanide has demonstrated unsurpassed efficacy and commendable safety in controlling diarrhoea in patients with normal immunity. It resolves diarrhoea and associated symptoms within 7 days of initiation of therapy. When given for several weeks, nitazoxanide appears promising for the treatment of cryptosporidial diarrhoea in immunocompromised patients. It has been shown to reduce cryptosporidial diarrhoea by approximately 50% in half of the HIV positive patients studied (8,9,12).

Nitazoxamide appears very promising for the treatment of ascariasis, enterobiasis, trichuriasis, hookworm infection, hymenolepiasis and strongyloidiasis. The results were closely comparable to broad spectrum anthelmintic drugs viz, albendazole, mebendazole, thiabendazole and praziquantel. Preclinical, in vitro studies have demonstrated that this drug has significant activity against Clostridium difficile, Campylobacter jejuni and Helicobacter pylori. Its therapeutic potential in anaerobic and microaerophilic bacterial infections is likely to undergo clinical evaluation.

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The recommended dosage in children is 15mg/kg/day divided in 2 doses orally for 3 days in most of the protozoal and helminthic infections. In cryptosporidiosis when given 100mg b.i.d and 200mg b.i.d in 1-4 years and 4-11 years old children respectively for 7 days, produces resolution of diarrhea in 80% and oocyst eradication in more than 95% cases (7). In HIV positive children with cryptosporidiosis, the duration of therapy is longer than 32 weeks (7,9,10,13).

The adverse effects reported are abdominal pain, diarrhoea, vomiting, headache, flatulence, fever, malaise, rhinitis, discoloration of urine, increased transaminases and increased creatinine levels. This drug should be prescribed with food to decrease the gastrointestinal effects (1-3).

Nitazoxanide is the only agent that has broad coverage against both common intestinal parasitic protozoa and helminths. This offers the convenience of single drug therapy of both type of infections. Considering the cost of repeated physician visits involved in the management of intestinal parasitic infections, the use of nitazoxanide is more cost effective than current treatment practices.

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