Nitazoxanide : A Broad Spectrum Antimicrobial

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Introduction

Intestinal parasitic infections are an important cause of morbidity and mortality worldwide. Nitazoxanide is a nitrothiazole benzamide compound with a broad spectrum of activity against a wide range of parasites, numerous gram positive and gram negative anaerobic bacteria and certain viruses.

Pharmacological Properties

Nitazoxanide, 2 acetyloxy *N* (5 nitro 2 thiazolyl) benzamide, is a new nitrothiazole benzamide compound. In humans, nitazoxanide is effective against a broad range of parasites, including *Giardia*, *Entamoeba*, *Cryptosporidium*, *Cyclospora*, *Trichomonas*, *Encephalitozoon intestinalis*, *Isospora belli*, *Blastocystis hominis*, *Balantidium coli*, *Ascaris*, *Trichuris trichura*, *Taenia saginata*, *Hymenolepis nana*, and *Fasciola hepatica* [1,2]. In vitro studies have also shown antimicrobial activity against numerous gram positive and gram negative anaerobic bacteria, specifically *Bacteroides* species, *Clostridium* species, and *Helicobacter pylori*, and aerobic gram positive bacteria.

In protozoa and anaerobic bacteria nitazoxanide inhibits the enzyme pyruvate ferredoxin oxidoreductase (PFOR) which is essential to anaerobic energy metabolism.

Pharmacokinetics

Nitazoxanide is moderately absorbed from the gastrointestinal tract, with 33% of the drug eliminated in the urine and 67% in the feces. After absorption nitazoxanide is rapidly hydrolyzed to its desacetyl derivative, tizoxanide, which is the active metabolite. Following oral administration, peak plasma concentration is achieved within 1-4 hour [3]. Tizoxanide is heavily protein bound in circulation (>99%), and its urinary elimination half life is 7.3 hour. On administration with

food, bioavailability of nitazoxanide is almost doubled. There are no adequate safety data for use of nitazoxanide in pregnant and lactating women.

Clinical Uses

1. Antiprotozoal
 - a. Cryptosporidiosis: It is the only US FDA approved drug for treatment of *Cryptosporidium* infection. A higher dose and/or extended duration of treatment may be required to achieve a sustained clinical and parasitological response in the immunocompromised population, especially those with CD4 count <50 cells/ mm³ [2].
 - b. Giardiasis: Nitazoxanide is approved for the treatment of infections due to *G. intestinalis* in patients >1 year of age. Nitazoxanide may have a role in treating metronidazole resistant giardiasis [1,4].
 - c. Other protozoal infections: It is effective in treatment of *E. histolytica*, *E. dispar*, *B. hominis* and *I. belli*.
2. Anthelmintic: In various studies Nitazoxanide has been found to be effective against *Ascariasis*, *lumbricoides*, *H.nana*, *T.trichura*, *T.saginata*, *Enterobius*, *Ankylostomata*, *Strongyloides* and *F. hepatica* [1,4]. Clinical studies in Mexico have shown parasite elimination rates ranging from 48% for heavy infection to 100% for light infections with *Ascariasis*. A three day course of nitazoxanide was demonstrated to have a higher cure rate and statistically significant egg reduction rate 21-30 days after treatment for trichuriasis in children aged 2-11 years, compared with a single 400mg dose of albendazole. Nitazoxanide has shown good activity against enterobiasis eradication (80-100%), ankylostomiasis (96%) and strongyloidiasis (94%) [1].

Nitazoxanide has been used as a single agent to

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treat mixed infections with intestinal parasites i.e. protozoas and helminths [5].

3. Rotavirus diarrhea: Two recent randomized trials in Cairo and Bolivia showed reduction in the duration of hospitalization and the duration of diarrhea in rotavirus diarrhea in children [6].
4. Antibacterial: Nitazoxanide is also effective in *Clostridium difficile* and *H. pylori* infections.
5. Chronic Hepatitis B and C infection: The antiviral activity of nitazoxanide was discovered in patients with AIDS who were treated for cryptosporidial diarrhea and had HBV or HCV co-infection. Nitazoxanide also increases sensitivity of alpha interferon 2b in the management of chronic HCV infection. Nitazoxanide and other thiazolides are promising new antiviral agents that may enhance current or future anti-hepatitis therapies [7].

Dosages

In Indian market it is available as tablet and oral suspension. The recommended dose is 100 mg q 12 hour for 1-3 years, 200 mg q 12 hour for 4-12 years and 500 mg q 12 hour for >12 years for three days [5]. It is recommended to be used for 36-48 weeks for chronic hepatitis as add on therapy to peginterferon with or without ribavirin.

Adverse Effects

It is a very safe drug to use across all age groups with no significant serious adverse effects reported in any study. The adverse effects reported were mainly affecting GIT such as nausea, diarrhea, abdominal discomfort and pruritus, pale yellow sclera, dizziness and harmless greenish discoloured urine [3]. No significant changes were noted in the ECG, vital signs and laboratory tests [8].

In conclusion, Nitazoxanide is a new nitrothiazole compound with broad spectrum activity against numerous intestinal protozoa, helminths, anaerobic bacteria, chronic hepatitis B and C viruses and few enteric viruses. The

drug has few side effects, requires a short course of treatment and has no significant drug interactions. Nitazoxanide and other newer thiazolides may represent a significant advancement in the treatment of intestinal parasitic infections, enteric viral infections, metronidazole resistant clostridial difficile infection and chronic hepatitis B and C infections.

Conflicts of Interest

None identified

References

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