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EDITORIAL COMMENTARY

Nitazoxanide: Jack of All, Master of None?

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Nitazoxanide (NTZ) is a first-in-class thiazolide discovered in 1984 [1]. Originally developed as a veterinary helminthic, it has been reported to be effective against a broad range of human pathogens [2]. Over the years it's spectrum has extended to include in vitro and/or clinical activity against enteric pathogens including *protozoa* (*Cryptosporidium parvum*, *Giardia lamblia*, Entamoeba, *Blastocystis hominis*, Cyclospora, Isospora *etc.*), *helminths* (*Taenia saginata. Hymenolepis nana*) and *bacteria* (Clostridium, Bacteroides, Helicobacter) [1, 3]. It was later discovered that NTZ was also effective against viruses [2]. It reduces symptom duration of viral gastroenteritis and rotaviral diarrhea [4]. It has been shown to have activity against Hepatitis B and Hepatitis C virus [1]. In in-vitro studies, it has also been found to be effective against the deadly Ebola virus [4].

In this issue of the IJP, Jinyi et al. have conducted a meta-analysis (13 RCTs, 768 cases) and found that there is a low level of evidence with regard to its efficacy and it is uncertain whether or not NTZ could improve the excretion rate of pathogens [5]. So does this mean that this "multifunctional" drug is simply a Jack of all but master of none?

Not quite. One has to delve deep inside to see why the authors arrived at these conclusions.

The first reason is that the relatively smaller number of trials that have been conducted on NTZ especially when compared to other drugs [1]. Even though it has been used off-label in 100 s of countries in millions of children, the number of publications on NTZ are relatively small [1, 3]. Secondly, the heterogenous nature of the trials have made it difficult to come up with meaningful results when clubbed together. Different NTZ doses, difference in study participants (differences in immune status and the pathogens that they carry), and variations in the outcomes studied have made it difficult to draw definite conclusions. The third reason is the difficulty to differentiate between non-response and re-infection. Re-infection rates are high especially in the tropics and is a confounder in studies with longer follow-up durations.

On the other hand, most of the large studies that have yielded positive results have been conducted by Romark laboratories which is owned by J.F. Rossignol who is the inventor of this drug. In this meta-analysis, one-third of the studies were funded by Romark and industry sponsored trials are always taken with a pinch of salt. So to sum it up, we do not have enough homogenous, unbiased data yet to draw meaningful inferences.

So what does the future hold for NTZ? Looking at its wide spectrum, good safety profile, short treatment course and the lack of resistance or any significant drug - interactions till date, NTZ holds a lot of promise for first-line therapy, empirical therapy as well as a fall-back option in resistant cases against a number of protozoal, bacterial and viral illnesses. It is administered orally and is heat stable making it suitable for use in remote and low resource settings. It also has a possible role as a drug for preventive chemotherapy with the Global Enteric Multicentre Study (22,568 children, 7 sites including India) finding that cryptosporidiosis is one of the most important causes of infectious diarrhea in children in developing countries [6]. But before embarking on that path we need more data. The need of the time is large properly conducted, industry-independent, homogenous studies with well-defined outcomes.

So is it a "Jack" or a "Master"? The Jury is still out on it. Wait and watch!

Compliance with Ethical Standards This article does not contain any studies with human or animal subjects performed by any of the authors.

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