

Antibiotics and Diarrhoea: A Reappraisal in a Nutshell

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Until early 1970s, antimicrobials occupied a pride of place in the therapy of pediatric diarrhoeal disease worldwide [1]. Then, a paradigm change in the concepts occurred. Rather than antimicrobials, increasing use of oral rehydration salts (ORS) turned out to be the principle therapy of diarrhoea [2]. Subsequently, the role of antibiotics in diarrhoea has squeezed to only limited indications such as bloody diarrhoea (presumptive shigellosis), severe diarrhea with fever/severe acute malnutrition, cholera, etc [3].

There is another aspect of diarrhoea vis-a-vis antimicrobials. Over the past some decades, availability of a multitude of antimicrobials has revolutionized the scenario of the infectious diseases with a welcome increase in man's lifespan [1]. However, here lies a paradox. The widespread use of antimicrobials, often irrational, tends to lead to appearance of multidrug-resistant (MDR) strains and emerging and re-emerging opportunistic infections [4-7].

Most antibiotics have the inherent property of provoking diarrhoea or diarrhoea-like manifestations, of varying intensity usually by interference with the normal gut flora, especially in infants and children. The pathogen *Cl. difficile*, is encountered in a large proportion of cases. Hence, such a diarrhoea is also termed "*Cl. difficile*-associated diarrhea" or "*Cl. difficile*-associated colitis". About 5 - 25% paediatric patients on antibiotics suffer from such a diarrhoea. Pseudomembranous colitis associated with *Cl. difficile* occurs in 10 to 20% of all AAD cases. In severe AAD, the incidence zooms up to as high as 60 - 90% [4].

Over the years, it stands fairly established that longer the duration of antibiotic therapy, more is the risk of AAD. Our consistent observation is that around one-half of the paediatric subjects on antibiotic(s) develop some sort of loose motions which may not strictly conform to the conventional definition of diarrhoea. Hike in frequency of loose motions severe enough to cause concern is rather infrequent. Likewise, bloody diarrhoea too is seen in a small proportion of cases.

Putting it in other words, AAD in most instances is mild. Mercifully, such a diarrhoea resolves without any treatment whatsoever. There is hardly any significant adverse effect on the health status of the child. Obviously, sheer conservative measures or a little reduction in the dose of the incriminating antibiotic may well suffice in obtaining relief.

In moderate AAD, the reduction in dose or discontinuation of the causative antibiotic usually resolves the problem. However, a small proportion of children suffering from AAD may develop fulminant and/or bloody diarrhoea. often refractory to discontinuation of the offending antibiotic and even additional therapeutic and supportive measures. This situation usually warrants a specific therapy (vide infra).

Even at the expense of repetition, let it be reemphasized that withdrawal of the offending antibiotic and offering supportive measures to maintain fluid and electrolyte balance and nutrition is the most important first aid measure in a large majority of the cases of AAD. Good food and water hygiene, meticulous hand-washing, and proper environmental are helpful. Incorporation of probiotics may have both a preventive and therapeutic role in AAD.

In cases suffering from severe AAD, metronidazole (preferably oral) should be considered the preferred drug. Tinidazole, ornidazole and nitazoxanide are the acceptable alternatives. Vancomycin, which is relatively quite expensive, is the superior option. In some cases, a combination of the two drugs may be given concurrently. A combination of vancomycin with rifampicin or cholestyramine has yielded promising results. In an occasional case that is still refractory, fidaxomicin has been found to be very effective. Today, this is by and large the best drug for *Cl. difficile*. However, its exorbitant cost is a limiting factor in its use in resource-poor countries

All said and done, rational antibiotic therapy and antibiotic stewardship are the most important preventive measure in AAD. Let us stop considering and using antibiotics as a "catchphrase" and "trump card".

Currently, a *Cl. difficile* vaccine is undergoing clinical trials [5-7].

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