

## Drug Update: Rifaximin

Rimjhim Shrivastava

### INTRODUCTION

Rifaximin is broad spectrum antibiotic with a unique property of being selective for gastrointestinal system. To add to its virtues, Rifaximin has a very good safety profile, low drug interaction and does not significantly affect the gastrointestinal microbiota.[1]

### PHARMACOKINETICS

Rifaximin is a semi-synthetic rifamycin derivative which acts by inhibiting bacterial protein synthesis as it binds to the beta-subunit of the bacterial DNA dependent RNA polymerase. It is also known to modify the pathogenicity of bacteria. It is very poorly absorbed in the gastrointestinal system thereby reducing its toxicity and enhancing the fecal concentration. Studies have observed almost undetectable levels of the drug in blood, urine, bile and breast milk. Almost 97% can be recovered unchanged in the stool. [1,2] The bactericidal action of Rifaximin works against a wide range of pathogens that includes gram positive, gram negative, aerobic and anaerobic bacteria. It also has enteric anti-protozoal activity as well. It has also been found useful in eradicating *Cryptosporidium parvum* and *Blastocystis hominis* gastroenteritis in HIV and AIDS patients.[3]

www.ispghan.org

### ADVERSE EFFECTS

With its lack of systemic absorption, rifaximin is a relatively safe medication and is associated with a low incidence of adverse events. In some placebo trials headache, flatulence, abdominal pain, constipation, nausea and vomiting have been observed. Skin rash and urticaria may be seen with long term use. [4,8]

### INTERACTION

As a virtually nonabsorbable antibiotic, drug interactions with rifaximin are uncommon. While rifaximin is capable of inducing the cytochrome P450 3A4 (CYP3A4) isoenzyme in vitro studies, clinical studies with rifaximin have shown no significant effect on drug metabolism by cytochrome P450 isoenzymes (6, 7). No dosage adjustments are required for hepatic dysfunction, even with liver failure and hepatic encephalopathy because systemic absorption is minimal (2).

### DOSAGE

The dose recommended for children above 12 years is 10-15mg/kg/day while the safety and efficacy has not been established in younger children. It should not be given for more than seven days.[8]

### CONTRAINDICATIONS

Rifaximin is contraindicated in children with intestinal obstruction or intestinal ulcerative lesions.[8]

### INDICATIONS

Rifaximin is mainly active in the small intestine owing to the high bile solubility but in colonic aqueous milieu it has low efficacy against the bacteria. Due to this property, it can preserve the gut microflora thus making it an ideal agent for gastrointestinal disorders.

1. Traveller's diarrhea: It a diarrheal disease caused mainly by *E coli*, but other bacteria as *Salmonella*, *Shigella*, viral and protozoal agents can also contribute, while travelling to an endemic area. Rifaximin was first approved for use in uncomplicated traveller's diarrhea in children more than 12 years of age. The dosage is 200mg three times a day for 3 days. It has also been shown to be effective in chemoprophylaxis of traveller's diarrhea.[6]
2. Infectious Diarrhea: Some uncontrolled clinical trials have suggested effectiveness of Rifaximin in treatment of infectious diarrhea unrelated to travel in adults. But there is limited similar data for children. Rifaximin is not approved for

Consultant Pediatric Gastroenterologist, Ekta Institute of Child Health, Raipur  
Swapnil Nursing Home, Raipur, Petals Children Hospital, Raipur  
Email: docrimjhim@gmail.com

children less than 12 years of age and infectious diarrhea is more commonly seen in this age group.

3. *Clostridium difficile* Infection in Children: Some adult studies have shown excellent activity of Rifaximin against *C. difficile*, but there are no pediatric study to support its use in children.
4. Small intestinal bacterial overgrowth syndrome (SIBO): It is a condition with increase in non-pathogenic bacterial population in the small intestine over  $10^5$  organisms in 1 millilitre, mostly due to motility disorders. It is characterised by diarrhoea, abdominal pain, and flatulence. Some pediatric studies suggest Rifaximin to be the antibiotic of choice for SIBO as it was found to be efficacious in 66% of cases and the efficacy increased when combined with partially hydrolysed guar gum. The dose used was 600mg/day for one week.[4]
5. Irritable bowel syndrome (IBS): is a common pediatric functional gastrointestinal disorder (FGID) characterised by abdominal pain and altered bowel habit. It is diagnosed clinically based on Rome IV criteria. The mainstay of treatment remains counselling, behavioural therapy and diet. Pharmacotherapy has been shown to have low efficacy. There is scarcity of studies to find out the role of Rifaximin in IBS in pediatric population. Rifaximin is effective in adult IBS associated with diarrhea. In pediatric population 65-91% of IBS have associated SIBO. Rifaximin has been shown to have good results in SIBO and IBS, with resolution of symptoms and fewer significant side effects. Rifaximin can be a good therapeutic option in IBS, though more data are required. [5,6]
6. Inflammatory Bowel Disease (IBD): There is limited data highlighting the utility of Rifaximin in pediatric IBD. One study observed that when treated with a higher dose of 1200 mg/day, 80% had improvement in their abdominal pain whereas few improvements were seen in lower doses. [7]
7. Hepatic encephalopathy (HE): It is a clinical entity resulting from liver insufficiency and manifesting as wide range of neuropsychiatric abnormalities. In many adult studies Rifaximin has been observed to be better than disaccharides as lactulose, and better or at par with neomycin for decreasing the serum ammonia levels and improving the neurological signs. The dose administered was 1200mg/day for three weeks. It was better tolerated with remarkable

safety profile as well. Pediatric studies are lacking for use of Rifaximin in pediatric HE.[9]

## CONCLUSION

Rifaximin is approved for travellers diarrhea in children more than 12 years of age. It has a broad-spectrum activity against gram negative and positive bacteria, and has very low systemic absorption. It has shown promising results in various other diseases but large scale pediatric data is warranted before its widespread use.

---

## FURTHER READING:

1. Koo HL, DuPont HL. Rifaximin: a unique gastrointestinal-selective antibiotic for enteric diseases. *Curr Opin Gastroenterol*. 2010 Jan;26(1):17-25. doi: 10.1097/MOG.0b013e328333dc8d. PMID: 19881343; PMCID: PMC4737517.
2. Javier A. Adachi, Herbert L. DuPont. Rifaximin: A Novel Non-absorbed Rifamycin for Gastrointestinal Disorders. *Clinical Infectious Diseases*, Volume 42, Issue 4, 15 February 2006, Pages 541–547, <https://doi.org/10.1086/499950>.
3. Gathe JC Jr, Mayberry C, Clemmons J, et al. Resolution of severe cryptosporidial diarrhea with rifaximin in patients with AIDS. *J Acquir Immune Defic Syndr*. 2008; 48:363–364. [PubMed: 18580340]
4. Avelar Rodriguez D, Ryan PM, Toro Monjaraz EM, Ramirez Mayans JA, Quigley EM. Small Intestinal Bacterial Overgrowth in Children: A State-Of-The-Art Review. *Front Pediatr*. 2019 Sep 4;7:363. doi: 10.3389/fped.2019.00363. PMID: 31552207; PMCID: PMC6737284.
5. Devanarayana NM, Rajindrajith S. Irritable bowel syndrome in children: Current knowledge, challenges and opportunities. *World J Gastroenterol* 2018; 24(21): 2211-2235 [PMID: 29881232 DOI: 10.3748/wjg.v24.i21.2211]
6. Bruzzese E, Pesce M, Sarnelli G, Guarino A. Pharmacokinetic drug evaluation of rifaximin for treatment of diarrhea-predominant irritable bowel syndrome. *Expert Opin Drug Metab Toxicol*. 2018 Jul;14(7):753-760. doi: 10.1080/17425255.2018.1488964. Epub 2018 Jun 22. PMID: 29897844.
7. Muniyappa P, Gulati R, Mohr F, Hupertz V. Use and safety of rifaximin in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2009 Oct;49(4):400-4. doi: 10.1097/MPG.0b013e3181a0d269. PMID: 19668011.
8. Scarpignato C, Pelosini I. Rifaximin, a poorly absorbed antibiotic: pharmacology and clinical potential. *Chemotherapy* 2005; 51 Suppl. 1: 36-66
9. Ladevaia MD, Prete AD, Cesaro C, Gaeta L, Zulli C, Loguercio C. Rifaximin in the treatment of hepatic encephalopathy. *Hepat Med*. 2011 Dec 22;3:109-17. doi: 10.2147/HMER.S11988. PMID: 24367227; PMCID: PMC3846583.