REVISTA DE GASTROENTEROLOGÍA DE MÉXICO
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EDITORIAL

Reflections on antibiotic resistance and what to do about it☆,☆☆

Reflexiones sobre la resistencia a antibióticos y qué hacer al respecto

The use and abuse of antibiotics may be considered an overly prevalent theme of discussion in a country such as Mexico, but unfortunately it is a practice that, despite past efforts, continues to have harmful and irreversible consequences. On May 27, 2010, the *Diario Oficial de la Federación* published a law stating that ''antibiotics can only be administered when prescribed by legally authorized health professionals in order to control their use and abuse, limiting the negative consequences of inadequate prescription and contributing to preserving the health of the Mexican population''.[1] Two of the many important reasons for passing this law are:

1. The increasing bacterial resistance in pathogens causing community-acquired and hospital-acquired infections in Mexico
2. To prevent self-medication and the creation of bacterial strains that are resistant to medication effectiveness

The indiscriminate and unjustified use of antibiotics has various consequences, but perhaps the most serious is resistance, which happens to be much higher in the developing countries.[2] How alarming is this situation for Mexico? Conclusions drawn from the following examples can help answer that question:[2]

1. The resistance of *S. pneumoniae* to penicillin is 70%.
2. The resistance of *Shigella spp* to ampicillin and cotrimoxazole is 81%.
3. More than 40% of the strains of *Pseudomona* are resistant to imipenem, ceftazidime, and levofloxacin.

In the current issue of our Journal, Novoa-Farías et al.[3] present an exceptional study on the susceptibility of enteropathogen bacteria isolated in Mexican patients with acute gastroenteritis to rifaximin and other antimicrobials. The present work stresses the fact that oral rehydration therapy is the standard treatment for acute gastroenteritis (as recommended in the Mexican Gastroenterological Association's ''Guidelines for the Diagnosis and Treatment of Diarrhea''[4]) and that antimicrobial agents are recommended only in severe or prolonged cases. In this context, there are 2 relevant aspects to understanding the susceptibility to antimicrobials of the gastroenteritis-causing bacteria: the attempt to initiate early therapeutic management and the epidemiologic surveillance of bacterial resistance. As shown by the authors through the analysis of bacterial sensitivity and stool samples obtained from 1,000 subjects in Mexico City with acute enteral infection, the susceptibility of the enteropathogenic bacteria (*E. coli, Shigella, Salmonella*, etc.) to antibiotics formerly considered first-line is lower than 70%: ciprofloxacin 67.3%, furazolidone 64.7%, trimethoprim-sulfamethoxazole 54.1%, and ampicillin 32.2%. In other words, today's patient with enteral symptoms receiving sulfas has a 50% probability of ineffective treatment.

Antibiotic resistance has recently been described as a situation related to genetic factors. For example, it has been suggested that drugs that are frequently used in Latin America, such as quinolones or tetracyclines, promote genes associated with antimicrobial resistance.[5,6] The observation in the study by Novoa-Farías et al. that close to 50% of the enteropathogen or enterotoxigenic *E. coli* strains are resistant to ciprofloxacin supports this concept.

Despite the discouraging epidemiologic results, the authors show that rifaximin at the recommended doses is efficacious against 99-100% of the bacteria identified as causing acute bacterial gastroenteritis in Mexico.

☆ Please cite this article as: Remes Troche JM. Reflexiones sobre la resistencia a antibióticos y qué hacer al respecto. Revista de Gastroenterología de México. 2016;81:1–2.

☆☆ See related content at doi: http://dx.doi.org/10.1016/j.rgmx.2015.07.003, Novoa-Farías O, Frati-Munari AC, Peredo MA, Flores-Juárez S, Novoa-García O, Galicia-Tapia J, et al. Susceptibilidad de las bacterias aisladas de infecciones gastrointestinales agudas a la rifaximina y otros agentes antimicrobianos en México. Rev Gastroenterol Méx. 2016;81(1):3–10.

Rifaximin, an analog of rifamycin, is a semi-synthetic antibiotic designed to have little gastrointestinal absorption. It inhibits the bacterial synthesis of RNA by binding to the β-subunit of the bacterial DNA-dependent polymerase RNA.[7] Its absorption is lower than 0.4%, making it an antibiotic that acts almost completely in the gut lumen, and most of it is secreted in the feces, unchanged. In addition, it has broad-spectrum activity against Gram-positive and Gram-negative, aerobic and anaerobic enteropathogens, and the probability of bacterial resistance is low.[7–9]

It has been demonstrated in the last few years that rifaximin at doses of 400 mg t.i.d. for 10 days or 550 mg t.i.d. for 14 days is superior to placebo in the adequate response of overall symptoms and bloating in patients with non-constipation irritable bowel syndrome (non-C IBS) (Level IB evidence, Grade A recommendation).[10] Even though the role of rifaximin in the microbiota is not clear, it has recently been described to reduce *Clostridium* concentrations and promote the growth of others, such as *Faecalibacterium prausnitzii*.[11] In a pilot study of 15 patients with non-C IBS, the administration of 550 mg of rifaximin t.i.d. for 14 days reduced the *Firmicutes*/*Bacteroidetes* ratio and contributed to intestinal biodiversity.[11] With respect to the effects of rifaximin on the microbiota, there are many still unresolved questions as to the interaction with factors related to the host and the synergism with probiotics that most certainly will be answered in the not-too-distant future.

Finally, it is worth mentioning that antimicrobial resistance is also related to factors not directly within the realm of medical knowledge, but just as real, such as antibiotic use in agriculture and livestock production, quality in the manufacturing of medications, and environmental instability. For all these reasons, I invite you to read the article by Novoa-Farías et al. and reflect upon their results.

Financial disclosure

No financial support was received in relation to this Editorial.

Conflict of interest

Dr. José María Remes-Troche is a Member of the Advisory Counsel of Takeda Pharmaceuticals, Sanfer, and Menarini and a Speaker for Takeda, Sanfer, Asofarma, Alfa-Wassermann, Almirall, and Astra-Zeneca.

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