



SCIENTIFIC LETTERS

Is azithromycin really a therapeutic option in intestinal salmonellosis?[☆]



¿Es realmente la azitromicina una opción terapéutica en la salmonelosis intestinal?

Dear Editor:

Acute gastroenteritis (AGE) is a common disease and a major cause of morbidity and mortality in children, and it is the most frequent reason for paediatric emergency room visits following respiratory infections. In Spain, the bacteria most frequently involved in AGE are *Campylobacter* and *Salmonella* species, which are also the most frequently involved in cases of foodborne illness in developed countries.¹ While antibiotic treatment is not always indicated, the growing resistance to antimicrobial drugs calls for the surveillance of in vitro susceptibility and for the periodical review of sensitivity data to update treatment guidelines.

The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the European Society for Paediatric Infectious Diseases (ESPID) recently published an update to the Guidelines for the Management of Acute Gastroenteritis in Children that featured azithromycin as an alternative treatment against non-typhoidal *Salmonella* (NTS) species.² Azithromycin is a semisynthetic macrolide antibiotic of the azalide class that acts by inhibiting bacterial protein synthesis, and has shown a similar or superior efficacy than third-generation cephalosporins and fluoroquinolones in the treatment of uncomplicated typhoid fever in several clinical trials.³ The scarceness of data on bacterial sensitivity to this antibiotic in Spain, and the lack of clinical breakpoints for interpreting minimum inhibitory concentration (MIC) values for azithromycin against *Salmonella* species mean that we have no information on the actual effectiveness of this antimicrobial agent in the treatment of salmonellosis. The

aim of our study was to assess the in vitro activity of azithromycin against clinical isolates of NTS.

We conducted a descriptive, prospective multicentre study with the participation of three hospitals of the Autonomous Community of Valencia. Each participating hospital was randomly selected and submitted NTS clinical isolates from patients with suspected AGE to the microbiology department of the Hospital Universitario de La Ribera in the first four months of 2014. The coordinating hospital confirmed the bacterial identification by means of NC52 panels for the MicroScan® WalkAway® system (Siemens, Germany). Then, antibiotic sensitivity was assessed by determining the MIC for azithromycin using E-test® strips (bioMérieux, Spain); the results were interpreted applying the epidemiological cut-off value established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for NTS (MIC ≤ 16 mg/L).⁴

We analysed a total of 136 NTS isolates (69 came from Alzira, 15 from Valencia and 52 from Castellón). The median age of patients was 7 years (range, 1–74), and 81% were male and 58% female. When tested for azithromycin sensitivity, 99% of isolates were found to be sensitive and only one isolate was resistant. The identified MICs ranged between 1.5 and 24 mg/L. The MIC₅₀ (concentration needed to inhibit 50% of the isolates) and the MIC₉₀ (concentration needed to inhibit 90% of the isolates) were 6 mg/L and 8 mg/L, respectively.

The results we obtained are consistent with several European studies that have described a distribution of MICs that ranges between 4 and 8 mg/L for most isolates.⁵ To date, the Clinical and Laboratory Standards Institute (CLSI) has not defined breakpoints for macrolides and *Enterobacteriaceae*⁶; in Europe, EUCAST has only established an epidemiological cut-off value for *Shigella* and *Salmonella typhi* according to which strains with a MIC of 16 mg/L or less are considered wild strains (with no resistance mechanisms) and thus susceptible to treatment with azithromycin.⁴

In light of these MIC results, azithromycin could be used for treatment of AGE caused by NTS, although it would be preferable if international committees were to establish clinical breakpoints for *Salmonella enterica* and azithromycin. If we only take into consideration the paediatric population, azithromycin covers the two main causes of bacterial AGE with an excellent sensitivity profile; also, its easy dosage (once a day) and good tolerability make it an

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interesting alternative for the first-line empirical treatment of bacterial AGE in cases in which there is a strong suspicion of a NTS aetiology and microbiological tests cannot be performed.

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- V. Pérez-Doñate^a, M. Borrás-Mañez^a, V. Domínguez-Márquez^b, D. Navalpotro-Rodríguez^c, J. Colomina-Rodríguez^{a,*}
- ^a Servicio de Microbiología, Hospital Universitario de la Ribera, Alzira, Valencia, Spain
^b Servicio de Microbiología, Hospital General Universitario de Castellón, Castellón, Spain
^c Servicio de Microbiología, Consorcio Hospital General Universitario de Valencia, Valencia, Spain
- *Corresponding author.
 E-mail address: jcolomina@hospital-ribera.com (J. Colomina-Rodríguez).

Focal nodular hyperplasia: A diagnosis to consider in a hepatic mass[☆]



Hiperplasia nodular focal: diagnóstico a considerar ante una masa hepática

Dear Editor:

Focal nodular hyperplasia (FNH) is a rare benign liver neoplasm that accounts for 8% of liver tumours in adults and less than 2% in children,^{1,2} although some authors report that its incidence has increased in the past five years. It is more prevalent in females (66% in the paediatric age group and 90% in adulthood) and in women of fertile age with a history of oral contraceptive use, although this association has yet to be confirmed.³

We present four cases of FNH in children aged 3–13 years diagnosed in our hospital, which are summarised in [Table 1](#) ([Fig. 1](#)).

It is widely believed that the pathogenic mechanism may be related to a hyperplastic response of hepatocytes to haemodynamic disturbances caused by local (vascular abnormalities or local venous thrombosis) or systemic factors (oral contraceptives and angiogenic molecules).⁴ Cases of FNH have also been described in children that have received chemotherapy, in whom the development

of FNH may be related to the vascular damage caused by this treatment, especially in patients that have undergone haematopoietic stem cell transplantation.³

The disease is usually asymptomatic, and it most commonly presents as a palpable abdominal mass or hepatomegaly found by chance or by an imaging test performed for a different reason. It occasionally presents with abdominal pain. In our series, three patients presented with self-limiting abdominal pain (spontaneous resolution), and a palpable mass was found only in case 2. In case 4, we did not find an association between the clinical manifestations and FNH, so we considered it a chance finding.

In typical cases, liver function is not impaired and alpha-fetoprotein levels are normal. Imaging tests may yield findings that guide the diagnosis. Magnetic resonance imaging (MRI) has shown the highest sensitivity and specificity for the diagnosis of FNH.⁵ The characteristic radiological findings are: solid mass, homogeneous, with well-defined margins, lobulated and vascularised in ultrasound imaging; in MRI, the lesion is isointense or hypointense compared to the rest of the liver parenchyma in T1-weighted sequences, and hyperintense or isointense in T2-weighted sequences, with rapid contrast uptake after infusion of gadolinium due to arterial inflow. The fibrous central scar is a typical feature but it is not constant (present in 30–60% of cases, depending on the study). None of these findings is pathognomonic. The most frequent localisation is the right hepatic lobe (only found in one of the cases in our series). Most cases have solitary lesions, but up to 8% may present with multiple nodules.²

Hepatocytes appear benign on histological examination; they are arranged in rope-like structures separated by fibrous septa with multiple arterial branches radiating from a large central artery. There are atypical forms of FNH, such

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