Et la fièvre typhoïde…

PLoS One. 2008 May 21;3(5):e2188. doi: 10.1371/journal.pone.0002188.

A multi-center randomised controlled trial of gatifloxacin versus azithromycin for the treatment of uncomplicated typhoid fever in children and adults in Vietnam.

Dolecek C, Tran TP, Nguyen NR, Le TP, Ha V, Phung QT, Doan CD, Nguyen TB, Duong TL, Luong BH, Nguyen TB, Nguyen TA, Pham ND, Mai NL, Phan VB, Vo AH, Nguyen VM, Tran TT, Tran TC, Schultsz C, Dunstan SJ, Stepniewska K, Campbell JI, To SD, Basnyat B, Nguyen VV, Nguyen VS, Nguyen TC, Tran TH, Farrar J.

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Abstract

BACKGROUND: Drug resistant **typhoid fever** is a major clinical problem globally. Many of the first line antibiotics, including the older generation fluoroquinolones, **ciprofloxacin** and ofloxacin, are failing.

OBJECTIVES: We performed a randomised controlled trial to compare the efficacy and safety of gatifloxacin (10 mg/kg/day) versus azithromycin (20 mg/kg/day) as a once daily oral dose for 7 days for the treatment of uncomplicated **typhoid fever** in children and adults in Vietnam.

METHODS: An open-label multi-centre randomised trial with pre-specified per protocol analysis and intention to treat analysis was conducted. The primary outcome was **fever** clearance time, the secondary outcome was overall treatment failure (clinical or microbiological failure, development of **typhoid fever**-related complications, relapse or faecal carriage of S. typhi).

PRINCIPAL FINDINGS: We enrolled 358 children and adults with suspected **typhoid fever**. There was no death in the study. 287 patients had blood culture confirmed **typhoid fever**, 145 patients received gatifloxacin and 142 patients received azithromycin. The median FCT was 106 hours in both treatment arms (95% Confidence Interval [CI]; 94-118 hours for gatifloxacin versus 88-112 hours for azithromycin), (logrank test p = 0.984, HR [95% CI] = 1.0 [0.80-1.26]). Overall treatment failure occurred in 13/145 (9%) patients in the gatifloxacin group and 13/140 (9.3%) patients in the azithromycin group, (logrank test p = 0.854, HR [95% CI] = 0.93 [0.43-2.0]). 96% (254/263) of the Salmonella enterica serovar Typhi isolates were resistant to nalidixic acid and 58% (153/263) were multidrug resistant.

CONCLUSIONS: Both antibiotics showed an excellent efficacy and safety profile. Both gatifloxacin and azithromycin can be recommended for the treatment of **typhoid fever** particularly in regions with high rates of multidrug and nalidixic acid resistance. The cost of a 7-day treatment course of gatifloxacin is approximately one third of the cost of azithromycin in Vietnam.

Et la fièvre typhoïde…

J Indian Med Assoc. 2007 Oct;105(10):582, 584, 586 passim.

Current pattern of enteric fever: a prospective clinical and microbiological study.

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Abstract

A prospective clinical and microbiological study was conducted in 145 blood culture positive cases of enteric **fever** below the age of 18 years over a period of eleven months (June 2004 to April 2005). It aimed to study the clinical profile, the relative magnitude of enteric **fever** in children, especially in those below the age of two years and to determine the current antibiotic sensitivity pattern of Salmonella typhi and S paratyphi. Enteric **fever** is a significant problem in the preschool years. Sixty-five per cent of cases were in the age group of 2 to 9 years, 27% in 0-5 years and 13% in age group 0-2 years. Ninety-two per cent of the cases were caused by S typhi. Paratyphoid **fever** is less common (8%), when occurs is caused by S paratyphi A. In-vitro sensitivity, using the Bauer-Kirby agar disc diffusion method, to ceftriaxone was 99%, cefixime-99%, cefotaxime-99%, cefpodoxime-72%, cefoperazone-93%, among quinolones, **ciprofloxacin**-95%, ofloxacin-83%, norfloxacin-79%. Sensitivity to the originally used antibiotics is reappearing: Ampicillin-87%, amoxicillin-89%, trimethoprim-sulfamethoxazole-76%, chloramphenicol-86%. Among other drugs, sensitivity to imepenam-100%, azithromycin-49%, aztreonam-65%, amikacin-98%. Nalidixic acid resistance is very high ie, 88%.

Et la fièvre typhoïde…

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Multidrug resistance in *Salmonella enterica serovar typhi* isolated from patients with typhoid fever complications in Lagos, Nigeria

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Et la fièvre typhoïde…

Table 1 Antimicrobial resistance of 41 strains of *Salmonella enterica serovar typhi* isolated from patients.

Antimicrobial agent	Average MIC (μg/ml)	Resistant strains (%)	Sensitive strains (%)
Ampicillin (A)	128	37 (90.2)	4 (9.8)
Chloramphenicol (C)	128	30 (73.2)	11 (26.8)
Streptomycin (S)	16	13 (31.7)	28 (68.3)
Tetracycline (T)	64	27 (65.9)	14 (34.1)
Gentamicin (G)	8	12 (29.3)	29 (70.7)
Cotrimoxazole (Co)	64	25 (61.0)	16 (39.0)
Cefotaxime (Ce)	16	21 (51.2)	20 (48.8)
Amoxicillin (Am)	2	7 (17.1)	34 (82.9)
Amoxacillin-clavulanic acid (Ac)	2	3 (7.3)	38 (92.7)
Ofloxacin (Ofl)	0.015	0 (0.0)	41 (100)
Ciprofloxacin (Cip)	0.015	0 (0.0)	41 (100)

Logos, Nigeria, 2005

Et la fièvre typhoïde…

Emergence of highly fluoroquinolone-resistant *Salmonella enterica* serovar Typhi in a community-based fever surveillance from Kolkata, India

Sir,

Typhoid fever caused by *Salmonella enterica* serovar *typhi* (*S.* Typhi) remains a major health problem in developing countries [1]. Traditional drugs such as chloramphenicol, ampicillin and co-trimoxazole were most effectively used as first-line drugs for the treatment of typhoid cases [1,2]. However, during the late 1980s and early 1990s the occurrence of multidrug-resistant *S.* Typhi strains, i.e. resistant to chloramphenicol, ampicillin and co-trimoxazole, led to the widespread use of fluoroquinolones (FQs) [1–3]. In recent years, nalidixic acid-resistant strains associated with reduced susceptibility to ciprofloxacin (minimum inhibitory concentration (MIC) $\geq 0.5\ \mu g/mL$) emerged and treatment failure with ciprofloxacin became a serious global concern [1,4]. Subsequently, isolation of highly FQ-resistant *S.* Typhi strains has been reported occasionally from other developing countries such as India and Bangladesh [5–7].

Letters to the Editor / International Journal of Antimicrobial Agents 31 (2008) 380–399

Et la fièvre typhoïde…

In this report, we document the isolation of two highly FQ-resistant (resistant to ciprofloxacin and ofloxacin) *S.* Typhi

The two patients, a 3-year-old male and a 5-year-old female, from whom the two FQ-resistant *S.* Typhi strains were isolated on 26 July 2004 belonged to the same family and presented with enteric fever. Both isolates showed high-level resistance to nalidixic acid (MIC > 256 μg/mL) as well as to FQs such as ciprofloxacin and ofloxacin (MICs of both drugs = 16 μg/mL). The isolates were also resistant to tetracycline and co-trimoxazole, but susceptible to traditional drugs such as chloramphenicol and ampicillin and newer drugs such as amoxicillin/clavulanic acid, ceftriaxone, aztreonam and amikacin.

Letters to the Editor / International Journal of Antimicrobial Agents 31 (2008) 380–399

Et *M. ulcerans…*

Antimicrob Agents Chemother. 2005 Aug;49(8):3182-6.

Efficacy of the combination rifampin-streptomycin in preventing growth of Mycobacterium ulcerans in early lesions of Buruli ulcer in humans.

Etuaful S, Carbonnelle B, Grosset J, Lucas S, Horsfield C, Phillips R, Evans M, Ofori-Adjei D, Klustse E, Owusu-Boateng J, Amedofu GK, Awuah P, Ampadu E, Amofah G, Asiedu K, Wansbrough-Jones M.

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Abstract

Mycobacterium ulcerans disease is common in some humid tropical areas, particularly in parts of West Africa, and current management is by surgical excision of skin lesions ranging from early nodules to extensive ulcers (Buruli ulcer). Antibiotic therapy would be more accessible to patients in areas of Buruli ulcer endemicity. We report a study of the efficacy of antibiotics in converting early lesions (nodules and plaques) from culture positive to culture negative. Lesions were excised either immediately or after treatment with rifampin orally at 10 mg/kg of body weight and streptomycin intramuscularly at 15 mg/kg of body weight daily for 2, 4, 8, or 12 weeks and examined by quantitative bacterial culture, PCR, and histopathology for M. ulcerans. Lesions were measured during treatment. Five lesions excised without antibiotic treatment and five lesions treated with antibiotics for 2 weeks were culture positive, whereas three lesions treated for 4 weeks, five treated for 8 weeks, and three treated for 12 weeks were culture negative. No lesions became enlarged during antibiotic treatment, and most became smaller. Treatment with rifampin and streptomycin for 4 weeks or more inhibited growth of M. ulcerans in human tissue, and it provides a basis for proceeding to a trial of antibiotic therapy as an alternative to surgery for early M. ulcerans disease.

Et *M. ulcerans…*

Antimicrob Agents Chemother. 2003 Apr;47(4):1228-32.

Isolation of three Mycobacterium ulcerans strains resistant to rifampin after experimental chemotherapy of mice.

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Abstract

By use of a murine model for Buruli ulcer, **Mycobacterium ulcerans** was found to be susceptible to **rifampin**, with the MIC being 0.5 to 1 micro g/ml. **Three** mutants were isolated **after rifampin** monotherapy. Two were **resistant** to **rifampin** at 8 micro g/ml, and one was **resistant** to **rifampin** at 32 micro g/ml. The mutants harbored Ser416Phe mutations and His420Tyr mutations in the rpoB gene, and these mutations have also been found to be responsible for **rifampin** resistance in the leprosy and tubercle bacilli. The results indicate that while **rifampin** may be active against M. **ulcerans**, it should never be used as monotherapy in humans.

Curr Opin Infect Dis. 2010 Oct;23(5):445-55. doi: 10.1097/QCO.0b013e32833c2209.

Recent advances in leprosy and Buruli ulcer (Mycobacterium ulcerans infection).

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Abstract

PURPOSE OF REVIEW: After tuberculosis, leprosy (Mycobacterium leprae) and Buruli ulcer (M. ulcerans infection) are the second and third most common mycobacterial infections in humankind, respectively. Recent advances in both diseases are summarized.

RECENT FINDINGS: Leprosy remains a public health problem in some countries, and new case detections indicate active transmission. Newly identified M. lepromatosis, closely related to M. leprae, may cause disseminated leprosy in some regions. In genome-wide screening in China, leprosy **susceptibility** associates with polymorphisms in seven genes, many involved with innate immunity. World Health Organization multiple drug therapy administered for 1 or 2 years effectively arrests disseminated leprosy but disability remains a public health concern. Relapse is infrequent, often associated with higher pretreatment M. leprae burdens. M. ulcerans, a re-emerging environmental organism, arose from M. marinum and acquired a virulence plasmid coding for mycolactone, a necrotizing, immunosuppressive toxin. Geographically, there are multiple strains of M. ulcerans, with variable pathogenicity and immunogenicity. Molecular epidemiology is describing M. ulcerans evolution and genotypic variants. First-line therapy for Buruli ulcer is **rifampin** + streptomycin, sometimes with surgery, but improved regimens are needed.

SUMMARY: Leprosy and Buruli ulcer are important infections with significant public health implications. Modern research is providing new insights into molecular epidemiology and pathogenesis, boding well for improved control strategies.

Et *M. ulcerans*…