Travel Medicine and Infectious Disease (2009) 7, 40—43

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevierhealth.com/journals/tmid

An outbreak of peritonitis caused by multidrug-resistant *Salmonella Typhi* in Kinshasa, Democratic Republic of Congo

J.J. Muyembe-Tamfum [a,b], J. Veyi [c], M. Kaswa [a], O. Lunguya [a], J. Verhaegen [d,*], M. Boelaert [e]

[a] *National Institute for Biomedical Research, Kinshasa*
[b] *Department of Microbiology, University of Kinshasa Medical School, The Democratic Republic of Congo*
[c] *Department of Surgery, Kinshasa General Hospital, The Democratic Republic of the Congo*
[d] *Department of Microbiology, Laboratory Medicine (Microbiology), University Hospital Leuven, Herestraat 49, 3000 Leuven, Belgium*
[e] *Department of Epidemiology, Institute of Tropical Medicine, Antwerp, Belgium*

Received 25 March 2008; received in revised form 15 December 2008; accepted 16 December 2008

KEYWORDS
Salmonella Typhi;
Peritonitis;
Multidrug-resistant;
Democratic Republic of Congo

Summary Between October 2004 and January 2005, 144 patients with peritonitis were admitted to the surgical wards of Kinshasa General Hospital and a few private city clinics. 63 patients (44%) underwent surgical intervention because of intestinal perforation consistent with typhoid fever; the case fatality rate was 53%. The majority of patients had received a course of first-line antibiotics such as chloramphenicol, ampicillin or co-trimoxazole before admission.

On bacteriological investigation, *Salmonella Typhi* was isolated from the blood of 11 patients with peritonitis. The isolates were all resistant to ampicillin, chloramphenicol, tetracycline and co-trimoxazole, but sensitive to third-generation cephalosporins, quinolone (nalidixic acid, ciprofloxacine) and amoxicillin-clavulanic acid.

Several factors contributed to the poor outcome of this disease including a) the use of inappropriate antibiotics, b) long delay in diagnosis, c) difficult access to health facilities.

This is the first documented outbreak of typhoid fever caused by a multidrug-resistant *S. Typhi* in Kinshasa.

* Corresponding author. Tel.: +32 16 34 70 73; fax +32 16 34 79 31.
E-mail address: jan.verhaegen@uzleuven.be (J. Verhaegen).

1477-8939/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tmaid.2008.12.006

Introduction

Typhoid fever is a severe Serotype clinical syndrome caused by *Salmonella enterica serotype Typhi* and characterised by persistent high fever, headache, abdominal pain, constipation and/or diarrhoea. If not treated appropriately, the disease can involve life-threatening complications such as gastro-intestinal bleeding and ileal perforation. Each year, an estimated 16 millions cases of typhoid fever with 600,000 deaths occur all over the world, mostly in Africa.[1]

Kinshasa, the capital city of the Democratic Republic of Congo (DRC), is an endemic area for typhoid fever.

Salmonella Paratyphi C, *Salmonella Enteritidis* and *Salmonella Typhimurium* are the most common non-typhoidal Salmonella in Kinshasa. More than 60% of the Salmonella isolated from 1994 to 2000, were resistant to ampicillin, tetracycline, chloramphenicol and co-trimoxazole. In contrast, all four antibiotics were still effective against the majority of *Salmonella Typhi* strains isolated during the same time period.[2] Therefore, these antibiotics were prescribed until recently empirically as the first-line therapy for patients with typhoid fever in Kinshasa. Between October and November 2004, an unusual outbreak of peritonitis occurred in Kinshasa with a high rate of intestinal perforation and mortality among young adults and school children. The location of the intestinal perforation was consistent with typhoid fever.

Materials and methods

All available epidemiological information was collected on patients admitted with peritonitis in the General Reference Kinshasa Hospital, General Ndjili Hospital, Roi Baudoin hospital and the University Hospital UNIKIN between October 2004 and January 2005. Patient registers and individual patient records were checked, data were recorded on standardized forms and entered into an EXCEL format. A confirmed case of typhoid fever was considered as a case of peritonitis for which laboratory confirmation was obtained by culture.

In November 2004, venous blood samples were collected from 16 patients with fever and peritonitis hospitalized in General Ndjili Hospital, Roi Baudoin hospital and the University Hospital UNIKIN. Blood cultures were inoculated in brain-heart infusion broth.

The antibiotic susceptibility testing of the isolates was performed using the Kirby-Bauer disk diffusion method on Mueller Hinton agar with Neo-sensitabs Rosco disks. The following ten antibiotics were tested: ampicillin (A,33 μg), tetracycline (T,80 μg), chloramphenicol (C,100 μg), kanamycin (K,100 μg), gentamicin (G,40 μg), streptomycin (S,100 μg), nalidixic acid (NA,130 μg), co-trimoxazole (Co,5,2 and 240 μg) amoxicillin-clavulanic acid (AC, 20 + 10 μg) and ciprofloxacine (Ci,10 μg).

Minimal Inhibitory Concentrations (MICs) of these antibiotics were determined by the E-test method (AB Biodisks, Solna, Sweden) in the laboratory of the University Hospital Leuven Department Medical Microbiology.

Results

Fig. 1 shows the epidemic curve of 144 cases of peritonitis admitted to different hospitals in Kinshasa between October 2004 and January 2005. Cases were reported from 18 out of the 24 communes of Kinshasa, but the majority (53%) resided in the suburb of Kimbanseke, one of the most densely populated areas with poor sanitation and crowded living conditions. The median age of patients was 14 years (IQR 20) and 58% were male. Before admission to hospital, most of the patients were treated with antimalarial drugs, and/or antibiotics (ampicillin, chloramphenicol, co-trimoxazole) without success. Fourty-one (41) of the 144 patients underwent surgical intervention because of symptoms of peritonitis. Twenty-three (56%) were children and 18 were adults. Sixty-four of the 144 patients admitted to hospital died (Case Fatality Rate 44.4%). 58 of the 103 patients (56.4%) without surgical intervention died and among them 51.7% were children. Case fatality rate among patients with surgical intervention was much lower (9.3%).

S. typhi was isolated from 11 patients out of 16 for whom blood culture was attempted. All the 11 strains of *S. Typhi* were resistant to ampicillin, chloramphenicol, tetracycline and co-trimoxazole (Table 1).

MICs were determined for all 11 strains and showed resistance to ampicillin (>256 mg/L) and co-trimoxazole (>32 mg/L) but susceptibility to gentamicin (range 0.5—1.5 mg/L)

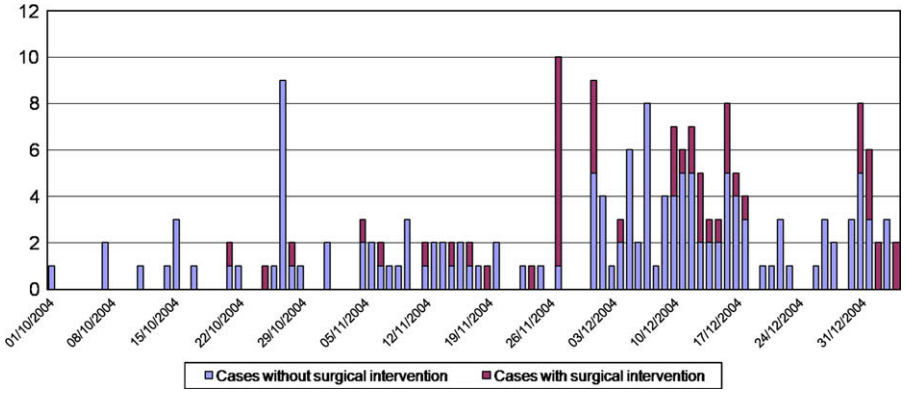

Figure 1 Epidemic curve of peritonitis cases.

Table 1 The determination of the Minimum Inhibitory Concentration (mg/L) of different antibiotics against 11 strains of *Salmonella enterica serotype Typhi* isolated in Kinshasa.

Labid	Ampicilline	Ofloxacine	Ciprofloxacine	Gentamicin	Co-trimoxazol	Cefotaxime
008/05	>256	0.12	0.023	1	>32	0.12
012/05	>256	0.064	0.012	0.5	>32	0.19
013/05	>256	0.094	0.023	0.5	>32	0.19
86/04	>256	0.064	0.016	0.75	>32	0.12
87/04	>256	0.12	0.016	1.5	>32	0.12
89/04	>256	0.094	0.016	0.5	>32	0.12
3773	>256	0.094	0.016	0.5	>32	0.25
3493	>256	0.12	0.032	1	>32	0.25
3454	>256	0.094	0.023	0.5	>32	0.25
3091	>256	0.064	0.016	0.5	>32	0.12
3714	>256	0.094	0.016	0.5	>32	0.25

cefotaxime (range 0.12—0.25 mg/L) and ciprofloxacine (range 0.012—0.032 mg/L).

Discussion

A large and severe outbreak of typhoid fever is described with multidrug-resistant *Salmonella enterica serotype Typhi* in Kinshasa.

On December 15, 2004 WHO reported a continuing outbreak of typhoid fever in Kinshsasa. The cases occurred in the suburbs of Kikimi, Kimbaseke, Masina and Ndjili.

According to WHO a total of 13,400 cases was reported, 615 severe cases of peritonitis, with or without perforation, including 134 deaths have occurred.[3]

Our data probably describe only the ''tip of the iceberg'' of the true number of cases, as emphasis was placed on the unusual increase in peritonitis cases observed in the city's hospitals. The case fatality rate among those patients was very high, over 40% mainly among children. The emergence of multidrug-resistant *S. typhi* was already documented in Africa, notably in Egypt,[4] in Kenya, in 1997—1999[1,5] and South Africa in 1992.[6] Until recently, chloramphenicol was for a long time, the antibiotic of choice for the treatment of typhoid fever in Kinshasa, because it was effective and cheap. The alternative antibiotics were ampicillin or co-trimoxazole. The current emergence of multidrug-resistant *S. Typhi* strains in Kinshasa is an important public health concern. Physicians were recommended to replace chloramphenicol by ciprofloxacine for the treatment of adult patients and amoxicillin-clavulanic acid for the treatment of typhoid fever infected children.

Typhoid fever is a waterborne disease with a predominant person-to-person transmission. There was a strong presumption that the water supply system in the affected suburbs was the potential source of infection. Most households had no access to safe, clean water and good sanitation. The commonest water supply system in the suburbs of Kinshasa is by self-made water tanks (Fig. 2a). Exceptionally, some people were cutting off the water tube in order to fill the tank with water during the night because the water pressure is not enough to pump up during the day (Fig. 2b).

Figure 2 Two examples of domestic water tank/reservoirs.

Early recognition of cases, treatment with appropriate antibiotics and provision of clean water are the classic recommendations for typhoid case management during the epidemics. The dire situation of the water supply in urban Kinshasa warrants urgent intervention to prevent similar outbreaks.

Conflicts of interest

The authors have no conflicts of interest concerning all the aspects of the present work reported in this paper.

Acknowledgements

This study was carried out in collaboration with the Kinshasa general hospital, Kinshasa University Hospital UNIKIN, the Institute of tropical medicine in Antwerp/Belgium and the Laboratory of Microbiology of the University Hospital Leuven, Belgium.

We are grateful to every patient who participated in this study, their relatives and nurses who cared for them. Our special thanks are addressed to the doctors in the different infection wards who were in charge of infected patients.

References

1. Kariuki S, Gilks C, Revachi G, Hart CA. Genotypic analysis of multidrug-resistant *Salmonella enterica Serovar Typhi*, Kenya. *Emerg Infect Dis* 2000;**6**:649—51.
2. Lunguya O, Asuni M, Mumba D, Mabwa L, Nsungu M, Manienga J, et al. Sérotypes et pharmacorésistance des Salmonella et Shigella à Kinshasa (1994—1999). *Congo Médical* 2005;**IV**(3): 227—33.
3. WHO. Weekly Epidemiological Record No 1; January 7, 2005.
4. Mikhail I, Girgis NI, Woody JN. Antibiotic-multiresistant *Salmonella Typhi* in Egypt. *Trans R Soc Trop Med Hyg* 1989;**83**:120.
5. Kariuki S, Gilks C, Corkill J, Kimari J, Banea A, Waiyaki P, et al. Multidrug-resistant non-typhi Salmonellae in Kenya. *J Antimicrob Chemother* 1996;**38**:425—34.
6. Coovadia YM, Gathiram V, Bhamjee A, Garratt RM, Musana K, Pillay N, et al. An outbreak of multiresistant *Salmonella typhi* in South Africa. *Q J Med* 1992;**82**:91—100.