Antibiotic Sensitivity of Endemic Shigella in Mbarara, Uganda.

East African Medical Journal Vol. 75 No. 3 March 1998
ANTIBIOTIC SENSITIVITY OF ENDEMIC SHIGELLA IN MBARARA, UGANDA
D. Legros, MD, MPH, Epicentre, P.O. Box 2362, Kampala, Uganda, D. Ochola, MD, MPH, Ministry of Health, P.O. Box 8, Entebbe, Uganda, N. Lwanga, Lab technologist, Mbarara University, P.O. Box 1410, Mbarara and G. Guma, Senior Lab technologist, Ministry of Health, P.O. Box 8, Entebbe, Uganda.

Request for reprints to: Dr. D. Legros, Epicentre, P.O. Box 2362, Kampala, Uganda.

ANTIBIOTIC SENSITIVITY OF ENDEMIC SHIGELLA IN MBARARA, UGANDA

D. LEGROS, D. OCHOLA, N. LWANGA and G. GUMA

SUMMARY

We analysed the chimio-sensitivity to antibiotics of endemic strains of *Shigella* isolated in Mbarara district, southwest Uganda. Twenty four strains were isolated, of which none was sensitive to cotrimoxazole and eight (33.4%, 95% CI [15.6 - 55.3]) to ampicillin, the two antibiotics recommended to treat dysentery during non epidemic periods in Uganda. Two isolates were resistant to nalidixic acid and none was resistant to the fluoroquinolones (Ciprofloxacin®, Norfloxacin®). It is concluded that the results of this survey could be used to facilitate the elaboration of a new treatment protocol to treat endemic dysentery cases in Uganda.

INTRODUCTION

Epidemics of dysentery caused by multiresistant *Shigella dysenteriae* type 1 (Sd1) are one of the greatest problems affecting Eastern and Central Africa(1,2). In addition, there are other strains of *Shigella* causing non-watery (often bloody) diarrhoea isolated during non-epidemic periods: *Shigella flexneri, Shigella sonnei* and *Shigella bodydii.*

In 1993, a Sd1 sensitivity survey conducted in Uganda showed that most of the isolated strains were resistant to cotrimoxazole and ampicillin(3). Nalidixic acid was therefore introduced as the first line treatment for use in epidemic situations, cotrimoxazole and ampicillin remaining the drugs of choice for use during non-epidemic periods.

Since non-epidemic *Shigella* resistant to usual antibiotics has already been reported from other parts of the world(4), we decided to test the sensitivity of these strains in Uganda in order to update national treatment policies.

MATERIALS AND METHODS

A cross-sectional survey was conducted among patients presenting with bloody diarrhoea to health facilities in Mbarara district, a district located southwest of the country where dysentery is endemic. Two hospitals (OPD) and four health centres participated to the study.

Patients suffering from bloody diarrhoea for four days or less, visually checked by the health personnel, who did not take antibiotics during the week prior to consultation, and willing to participate, were included into the study.

For each of the study patient, stools sample was obtained, put in Portagerm (BioMériux) transport medium and brought to Mbarara University laboratory for culture and identification. Stools from patients recruited from Mbarara hospital were directly inoculated from containers.

Laboratory procedures were carried out according to WHO guidelines for *Shigella* isolation(5). Samples were cultured using Mac Conkey agar (non-specific) and XLD (more specific for *Shigella* isolation) media. Kigler medium and polyvalent antisera against *Shigella dysenteriae* A_1 A_2, *Shigella flexneri, Shigella sonnei,* and *Shigella boydii* C_1 C_2 C_3 were used for identification procedures , as well as a monovalent antisera against *Shigella dysenteriae* type 1. Antibiotics susceptibility testing was performed using Mueller Hinton medium (BioMerieux). The following antibiotics were tested: ampicillin, Ciprofloxacin®, nalidixic acid, Norfloxacin®, mecillinam and cotrimoxazole. The diffusion test procedure was used to measure the antibiotic sensitivity of the isolates, using the comparative method. A sample of isolated strains was taken to the Central Public Health laboratory in Kampala and to Pasteur Institute in Paris for quality control purposes.

Since our sample size was less than 30, we used the exact binomial formulas to calculate the 95% confidence interval around the observed proportions.

RESULTS

Sixty nine stool samples were collected between November 1996 and April 1997 from six selected sites in Mbarara district. Twenty four *Shigella* strains were isolated from these 69 samples (isolation rate: 34.8%): 15 *Shigella flexneri,* five *Shigella sonnei,* two Sd1, one *Shigella dysenteriae* A_2 (for example, a non Sd1 strain of *Shigella dysenteriae*) and 1 *Shigella boydii* C1. The quality control measures were done on eight strains. The results were identical to those of Mbarara, both in Kampala and in Paris.

The sex ratio M/F among *Shigella* patients was 2.0 (16/8). Age ranged from nine months to 50 years (median 22.5 years).

Table 1

Sensitivity pattern of the Shigella strains (n=24) with 95% confidence interval for each antibiotic tested, Mbarara district, Uganda, 1996 - 1997

	Sensitive	Intermediate	Resistant
Ampicillin	33.4% [15.6 - 55.3]	8.3% [1.0 - 27.0]	58.3% [36.6 - 79.9]
Ciprofloxacin®	50.0% [29.1 - 70.9]	50.0% [29.1 - 70.9]	0.0%
Nalidixic acid	70.8% [48.9 - 87.4]	20.8% [7.1 - 42.2]	8.4% [1.0 - 27.0]
Norfloxacin®	54.2% [32.8 - 74.4]	45.8% [25.6 - 67.2]	0.0%
Mecillinam	37.5% [18.8 - 59.4]	12.5% [2.7 - 32.4]	50.0% [29.1 - 70.9]
Cotrimoxazole	0.0%	8.3% [1.0 - 27.0]	91.7% [73.0 - 99.0]

None of the strains that we isolated was sensitive to cotrimoxazole, and eight (33.4%) were sensitive to ampicillin (Table 1). Two isolates (one *Shigella flexneri* and one *Shigella boydii*) were resistant to nalidixic acid. No strain resistant to fluoroquinolones was found in our sample.

DISCUSSION

This study was carried out on a limited number of stools samples. However, because of the duration of the recruitment and because samples were obtained from six facilities covering the entire district, we believe that our findings are applicable to the endemic strains of *Shigella* circulating in Mbarara district, if not in all southwest Uganda.

We did not isolate any strain sensitive to cotrimoxazole and only one third of sample was sensitive to ampicillin, the two recommended drugs for use in Uganda during non-epidemic periods. Given the proportions observed, it seems very unlikely that a bigger sample size would have provided opposite results. For the same reason, the level of resistance to nalidixic acid can be assumed to remain low for endemic strains of *Shigella* in that part of the country. The relatively recent introduction of this drug in Uganda, when compared to the neighbouring countries, might probably explain this finding. The use of nalidixic acid as first line treatment against dysentery during both endemic and epidemic periods should be considered.

In our sample, fluoroquinolones, unlike mecillinam, proved to be effective *in vitro* against endemic strains of *Shigella.* Although these drugs could be the next line of antibiotics against dysentery (after nalidixic acid), the cost of the five-day treatment which is recommended today would not allow their use on a large scale in a country such as Uganda.

ACKNOWLEDGEMENTS

This study was conducted by the CDD/ARI programme of the Ministry of Health and Epicentre, with financial support from UNICEF and Médecins sans Frontières. We thank the personnel of all the health facilities who participated to the study

REFERENCES

1. Cobra, C and Sack, D.A. Strategic response to epidemic dysentery in Africa. Department of International Health, School of Hygiene and of Public Health, John Hopkins University, Baltimore, USA. 1994; 74p.
2. Keush, G.T. and Bennish, M.L. Shigellosis: recent progress, persisting problems and research issues. *Paediat. Infect. Dis. J.* 1989; **8**:713-719.
3. Review of the dysentery situation in Uganda. Control of Diarrhoeal Disease Programme. Ministry of Health, Entebbe, Uganda, February, 1995.
4. Bennish, M.L., Salam, M.A., Haider, R. Barza, M. Therapy for Shigellosis. II. Randomised, double blind comparison of ciprofloxacin and ampicillin. *J. Infect. Dis.* 1990; **162**:711-716.
5. WHO Guidelines for the control of epidemics due to *Shigella dysenteriae* type 1. WHO. Geneva, 1988; publication n°. SER/88.12.