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Case Reports

Shigellosis non responsive to "sensitive" antibiotics

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Introduction

Shigellosis is the commonest cause of blood and mucus diarrhoea among children[1]. In Sri Lanka Shigella flexneri is the predominant serotype isolated and S. dysenteriae takes the third place[1,2].

Worldwide there is an evolving antibiotic resistance[3]. In common practice furazolidone still remains the drug of choice at the first presentation and gentamicin is reserved for severe infections.

Case report

A two-year-old girl was admitted to Colombo South Teaching Hospital with a one day history of blood and mucus diarrhoea. Following initial assessment, treatment with furazolidone was commenced after obtaining stools for culture and antibiotic sensitivity testing (ABST).The sample was sent to the Medical Research Institute (MRI).

Few hours after admission child developed two generalized convulsions. The second convulsion was prolonged and did not respond to rectal diazepam and required intramuscular paraldehyde to achieve control .The temperature was recorded as 39^{o}C and the child's sensorium was depressed. There were about twenty bowel openings within 6 hours.

All these clinical features pointed towards a virulent organism that prompted us to change the antimicrobial to intravenous (IV) gentamicin (2.5mg/kg per dose 8 hourly).

On the 3rd day of IV gentamicin the general condition of the child remained the same. The frequency and consistency of stools remained unchanged, high fever spikes continued.; IV cefuroxime was added on best guess basis at this point, as the ABST was not available.

The culture of the 1st stool sample isolated Shigella dysentriae type II that was sensitive to nalidixic acid and gentamicin and intermediately sensitive to furazolidone.

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On completion of 5 days IV cefuroxime and 7 days of IV gentamicin the fever spikes continued, the stool frequency reduced but macroscopic blood and mucus persisted.

A second sample of stools was sent for culture at this stage with a detailed clinical history and a special request to check sensitivity to 2nd line drugs.

On day 10 of IV gentamicin and day 7 of IV cefuroxime the result of the 2nd sample was available. In spite of treatment for 7 days with IV gentamicin which was sensitive to the causative organism isolated in the 1st sample, the second sample yielded the same organism. It remained sensitive to gentamicin and in addition was sensitive to cefotaxime, ceftriaxone and cefuroxime showed intermediate sensitivity.

As the dysentery persisted and the child remained ill all antibiotics were omitted. A fresh course of treatment with IV cefotaxime was commenced after consultation with the microbiologist at enteric bacteriology unit, MRI.

Clinical condition of the child showed marked improvement with this. She was discharged after 5 days of treatment with IV cefotaxime and a total hospital stay of 16 days.

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Discussion

The sensitivity pattern of Shigella species isolated at MRI during the last quarter of year 2000 shows 100% sensitivity to gentamicin.

The resistant diarrhoea of our child to the sensitive antibiotic, which is considered as a gold standard of therapy in severe dysentery, is an important issue.
The reasons for poor response in spite of correct dosing may be due to inaccurate sensitivity testing, pharmacokinetic properties of the drug or the substandard quality of drugs administered to the child.

Discrepancy between in vitro sensitivity testing and in vivo therapeutic response to the drug may be due

to variations in laboratory conditions or variations in pharmacokinetic properties of the drug.

Variations in laboratory conditions are observed due to varying potencies of antibiotic disks, density of the organism, type of medium and pH, incubation conditions and subjective errors in reading. Antibiotic sensitivity testing at the MRI uses WHO recommended standard methods since January 2001. Daily quality control studies are carried out to eliminate variations and assess accuracy of tests.

Pharmacokinetic properties of gentamicin show marked variations in vitro and in vivo conditions[4]. The in vivo drug concentration depends on clearance, age, volume of distribution, and haematocrit. Gentamicin does not penetrate into cells. There is wide variation in peak concentrations and t/2 of the drug under hypercapnic conditions and febrile illnesses.

The peak concentration reached in children up to 5 years is half that of adults with age related doses. It correlates best with doses calculated according to surface area. Ideally gentamicin doses should be titrated on an individual basis with monitoring of drug concentration in blood to prevent administration of sub therapeutic or toxic doses of the drug; i.e. loading dose of 3mg/kg and maintenance dose of 2.5 mg/kg, measure levels with the 3rd dose, trough <2mcg/ml, peak (1hour post dose) 5-10mcg/ml if levels are within peak and trough range to repeat every 3rd day. We are yet to have this facility available in Sri Lanka.

In contrast cefotaxime has better intracellular penetration and stable pharmacokinetic properties.

Every institution needs to adopt its own policy to evaluate the quality of drugs on a regular basis to prevent administration of drugs of sub standard quality. Evaluation of quality of drugs is available at the state sector on request.

The only available criteria to treat a case of severe bacillary dysentery in our country is a reliable ABST. If the pertinent drug, which shows repeated sensitivity to the isolated organism, is not responsive, the clinician faces a dilemma. If similar scenarios recurrently take place it is necessary to evaluate the quality of drugs available and reassess their pharmacokinetic properties. The fast emerging problem of drug resistance will be established by using 2nd line drugs such as cephalosporins when the organism still remains sensitive to a cheap safe and effective drug as gentamicin.

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