RETALIATION OF SALMONELLA

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SUMMARY

Typhoid fever is endemic in developing countries because of the non-availability of clean drinking water. Blood cultures on pyrexial patients were done. Of the 25 blood cultures, 24 yielded growth of Salmonella typhi and one paratyphi A. The isolates were sensitive to quinolones (100%), 3rd generation cephalosporins (95%), aztreonam (76%), amoxycillin and chloramphenicol (20%) and SMZ-TMP (0%). From eighty to hundred percent patients improved with quinolones, 50% with 13 chloramphenicol, 20% with Ceftriaxone and none with amoycillin. With the rising resistance of Salmonella to the currently available new toxic and expensive drugs we should adopt basic hygienic principles rather than spend time and money on drugs.

INTRODUCTION

There are nearly 2000 Salmonella serotypes most of which reside in animals, the exception being Salmonella typhi which invariably has human source.[1] These organisms cause enteric fevers which range from self-limited gastroenteritis to typhoid fever, a potentially life threatening illness. Typhoid fever results in high mortality and morbidity. It is water born and is endemic in developing countries where there is scarcity of potable water.[1]

The R-factor-mediated multiple resistance noted since 1972-73 has influenced not only the cost of the treatment but also the toxicity of various newly administered drugs.[2] One of such single large size 98 MDa plasmid has been isolated. It encodes resistance to chloramphenicol, ampicillin, tetracycline, streptomycin, Sulphamethoxazole-Trimethoprim (SMZ-TMP) but shows sensitivity to naldixic acid, quinolones and 3rd generation cephalosporings.

MATERIAL AND METHODS

All those patients from OPD or casualty who were running a temperature of 101 F^0 or above were admitted in Medical A ward of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, from January 1993 to January 1995. A proforma was prepared which included symptoms, signs and various investigations. Blood cultures were taken and only those positive for Salmonella were included in the study. Moreover, the drug responses were also recorded.

RESULTS

Most of the patients belonged to Peshawar and their ages ranged from 12 to 55 years. The minimum duration of hospital stay was three days and the maximum 16 days.

Blood culture yielded growth of Salmonella typhi in 24 patients and paratyphi A in only one. Sensitivity test showed that all 25 (100%) isolates were sensitive to quinolones, 24 (95%) to 3rd generation cephalosporins, 19 (75%) to aztreonam (Azactam), 15 (60%) to aminoglycosides, 13 (52%) to Ist generation cephalosporins, 2 (20%) each to amoxycillin and choraphenicol and none to SMZ-TMP.

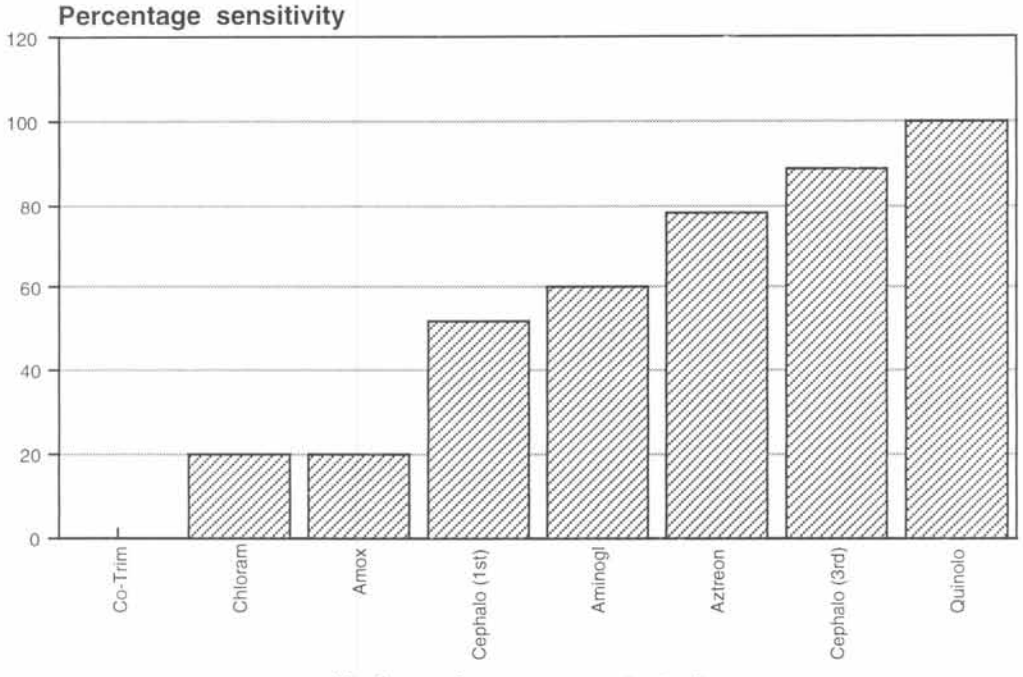
(Table–I) The sensitivity of Salmonella to various drugs in different antibiotic groups is shown in Table–II. Various quinolones were given to 21 patients and 20 of them improved. Ciprofloxacin was effective in all 8 patients (100%). Eight (80%) out of 10 patients responded to ofloxacin and 4 (805) out of 5 patients responded to pefloxacin. The two patients who did not respond to ofloxacin and pefloxacin in 5 days, improved with ciprofloxacin and were included in that sub-group.

One patient clinically diagnosed as respiratory tract infection was started on cephazoline before culture was available and improved with the same antibiotic. Ceftrixone was effective in only one (20%) of the five patients who received this drugs. Of the six patients who received Chloromycetin only three (50%) responded. None of the three patients responded to amoxycillin. SMZ-TMP and aztreonam were not used in this study.

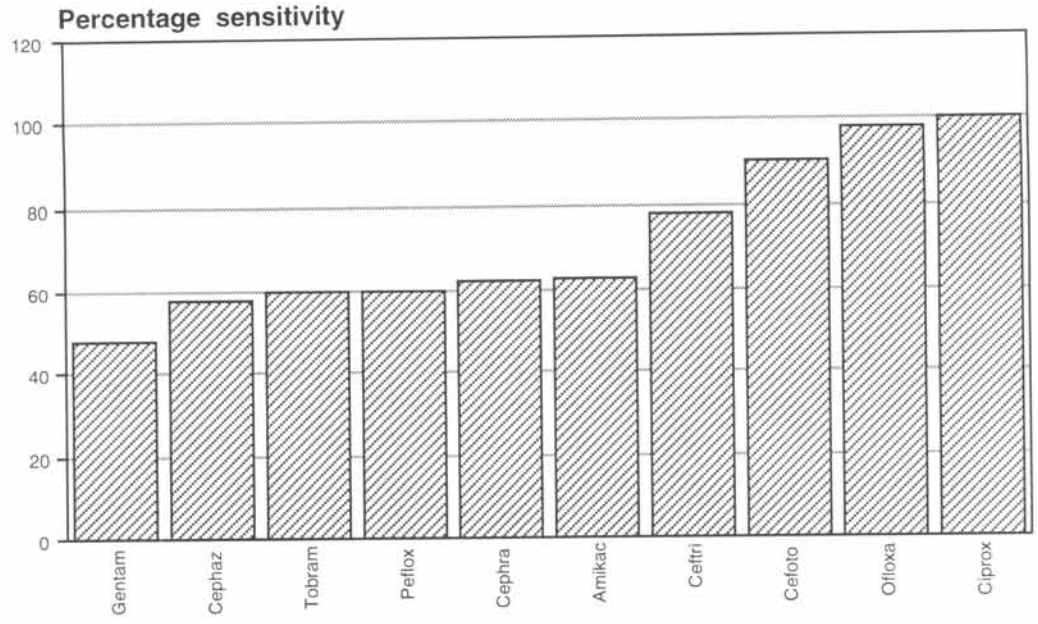
DISCUSSION

In several parts of the world where typhoid fever is endemic there is serious concern about the emerging patterns of Salmonella species that are resistant to the currently and antibiotics.[3] These organisms cause significant morbidity and mortality. Since the first report of its successful use in 1948, chloramphenical has been the mainstay of therapy for long and is still the drug of first choice in many parts of the world i.e. India, China, USSR.[4-7] More recent studies have shown SMZ-TMP, ampicillin and amoxycillin to be effective in cases caused by chloramphenicol-susceptible and chloramphenicol-resistant organisms. However, as has previously been noted, a number of cases due to chloramphenicol-resistant and ampicillin-resistant strains were seen in 1970 in Mexico and the United States and there were several deaths.[5] Strains of Salmonella typhi resistant to chloramphenicol, ampicillin and

TABLE–I



TABLE–II



Sensitivity to various drugs tested

SMZ-TMP have been reported from Pakistan, India, Vietnam, California, North Eastern United States and Spain. This resistance has increased in some series from 16% to 80% in India.[5,6,8]

In our patients the invitro resistance of Salmonella to SMZ-TMO wa 100% and that to chloramphenicol and amoxycilline 80%. Resistance to aminoglycosides was from 36 to 65%. However in our clinical practice none of the three patients responded to amoxycillin (0%) inspite of the positive culture and sensitivity report from the laboratory i.e. invitro study. A similar change was observed for chloramphenicol where the clinical outcome showed animprovement in 50% of the cases inspite of the recorded 20% sensitivity by the laboratory results.

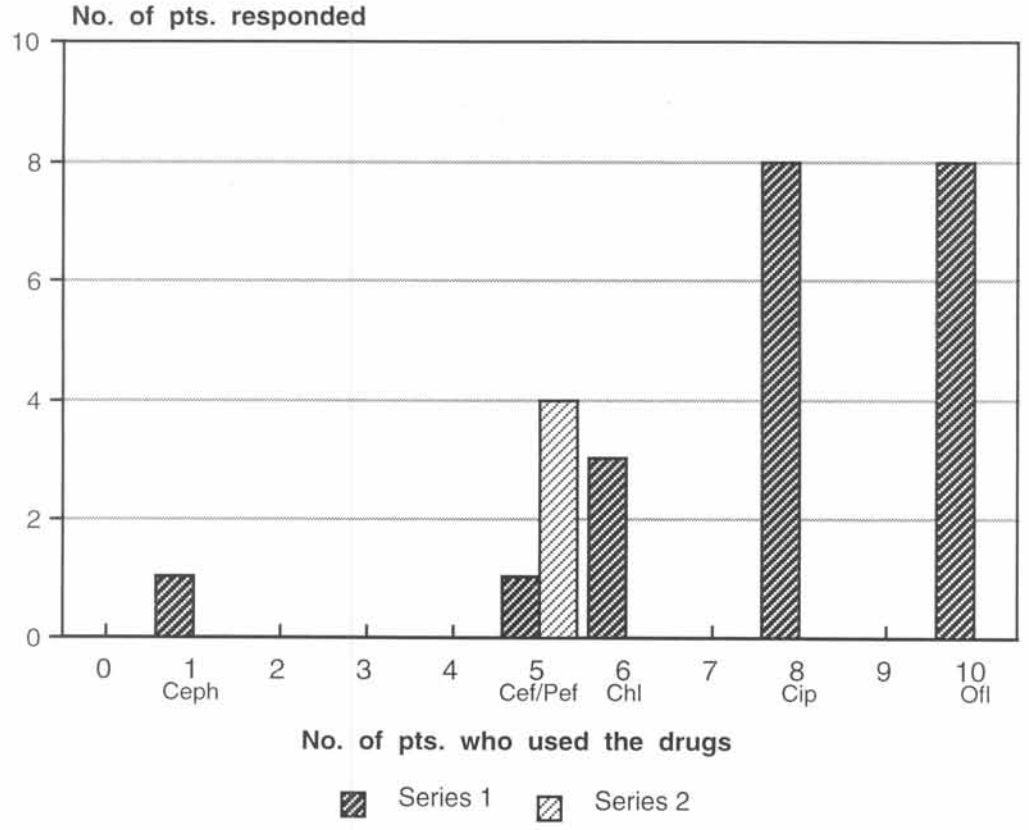
Resistance to these commonly used drugs mentioned above needs a change in therapeutic approach to typhoid fever. In this search cephalosporins have been studied and both cephaloridine and cephradine were effectivel used in small series of patients. Paradelis (1980) also found the multi-resistant strains very sensitive to cephradine and treated 10 such patients succesfully with it.[9] The signly patients in our series in whom it was used responded well and the use of these drugs needs further clinical evaluation.

Third generation cephalosporins have good tissue penetration and prolonged antibacterial activity. Girgis (1993) reported cefixime to be a very effective oral drug.[10] Cefomandal is successful only when it is used as a continuous infusion for 10-15 days. There are many randomized comparative studies of the efficacy of ceftriaxone.[2]

In our study the invitro sensitivity of 3rd generation cephalosporins was 96%. Cefotaxime (88%) was better than cefrriaxone (77%) in the patients tested. In clinical practice ceftriaxone was administered to 5 patients of whom only one (20%) responded. These results show the same discrepancies between in-vitro studies and

TABLE–III

CLINICAL RESPONSE OF PATIENTS TO VARIOUS DRUGS



clinical effectiveness. Inspite of the cost of the drug, exceedingly large doses i.e. 2gm BD and the intravenous route which necessarily requires hospital admission, the results were disappointing.

Ciprofloxacin has excellent activity against the enterobacteriaceae, including the majority of organisms resistant to currently available penicillins, cephalosporins and aminoglycosides. The drug was 100% effective in clinical set up.[5,11] Ofloxacin and fleroxacin were also 100% effective and the clinical cure rate with pefloxacin was above 90%.[12-14] The minimum inhibitory concentration of rufloxacin against S.typhi is reported to be 4-16 times higher than the above mentioned quinolones.[15]

In our patients the in-vitro activity of quinolones was 100%. Ciprofloxacin was 100% effective as compared with ofloxcin (96%) and pefloxacin (60%). The clinical efficacy of ciprofloxacin was 100% in eight patients. However of all the 10, only 8 (80%) responded to ofloxacin. Clinical efficacy of pefloxacin was also 80%. As before, discrepancies persist between clinical responses and the laboratory data. Inspite of 96% sensitivity to oflocacin from the laboratory clinical improvement was observed in only 80%. however the results for ciprofloxacin remained consistent.

Salmonella has shown a gradual increase in its resistance over the years to the newly introduced quinolones, thus posing a major threat to the community and forcing

us to search for alternative means and antibiotics to combat this threat.[16] In our series 76% of the patients were sensitive to Aztreonam. Farid and Girgis (1987) used this drugs in eleven patients all of whom were cured.[10] The oral monobactam e.g. Tigenim has been reported to inhibit 90% of strains of E-coli, Klebsiella and Salmonella. Carbape-nems (biapenem, imipenem, meropenem) in-vitro inhibit 90% of isolates of entero-bacteriaceae and Salmonella typhi. Ist use in children eradicated Salmonella spp.[17,18] The in-vitro activity of azithromycin has been found to be very high against enteric pathogens including Salmonella typhi, Gradello Me (1993) has suggested its use in such infections.[19] The results of the use of Timocillin in enteric fever were very promi-sing in Thailand.[20] The new parenteral oxime-type cephalosporin, FK-037, inhibits 90% isolates of Salmonella typhi.[21] The antibiotic susceptibility of Salmonella is en-hanced many folds to cefuroxime, ciproflo-xacin, chloramphenicol and rifampicin when lactoferrin is combined with these drugs.[22]

As is obvious from the rising resistance to various antibiotics, nature is one the side of the bacteria. The dwindling list of drugs leads us to consider other means of control. Some of these may be as followed:

1. Education in the basic principles of hygiene.
2. The supply of clean drinking water to every household and frequent inspections by the water authorities.
3. Patient isolation and facilities for the disposal of excrement.
4. Immunization

Where sophisticated and expensive drugs have failed commonsense may succeed. An old English proverb says, "an ounce of prevention is better than a pound of cure:." What the third world needs is better living conditions. It may be more sensible to funnel funds into improving these rather than develop new drugs to combat established disease.

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