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Original Article

Clinical profile and antibiotics response in typhoid fever

Bajracharya BL[1], Baral MR[2], Shakya S[3], Tuladhar P[4], Paudel M[5], Acharya B[6]
[1]Consultant, [2]Professor, [3,5,6]Former MOs, [4]MO, Department of Paediatrics, Kathmandu Medical College, Sinamangal, Kathmandu, Nepal

Abstract
Objective: The objective of this study is to evaluate the clinical profile and drug response in typhoid fever.
Methods: This is a retrospective analysis of paediatric patients suffering from typhoid fever who were admitted at Kathmandu Medical College Teaching Hospital, Sinamangal during the period of two years and nine months.
Results: Total numbers of 100 cases of typhoid were studied. Diagnosis of Typhoid fever was based on clinical features, Widal test and blood culture. The sensitivity pattern of drugs in blood culture was recorded. The mode of presentation, treatment history, laboratory investigations reports, antibiotics administered and response to therapy were recorded.
Conclusion: Quinolone is still the highly sensitive drug and most widely used for *Salmonella typhi*. Because of the indiscriminate use of these drugs, resistant to ciprofloxacin has been quite high and the duration of the defeverscence period has also been prolonged. But Ofloxacin is still showed highly effective and widely used with good response.

Key words: clinical profile, antibiotics response, typhoid fever.

Typhoid fever is the systemic disease with significant morbidity almost throughout the year and more especially during the rainy season during that time water contamination is very high. Though the incidence has decreased markedly in the developed country it is still high in incidence in the developing countries. Improved standard of public health have resulted in a marked decline in the incidence of typhoid fever in developed countries. Ingestion of food or water contaminated with human faeces is common mode of transmission. Water borne out break due to poor sanitation and direct feco-oral spread due to poor personal hygiene are encountered most often. The first major epidemic of multidrug resistant *S. typhi* was reported in 1972 in Mexico. The emergence of many strains of S. *typhi* that are resistant to multiple antibiotics has imposed a serious problem in the public health. Chloramphenicol was considered the gold standard antimicrobial agent for the treatment of typhoid till 1948[1]. But there has been increase in the resistance of strains of *S. typhi* to chloramphenicol in the last two decades. *S.Typhi* resistant to chloramphenical was first reported from Britain in 1950[2] and from India in 1972[3].Since then, an increasing frequency of antibiotic resistance has been reported from all parts of the world, but more so from the developing countries[4]. The uses of gold standard anti microbial drug like chloramphenicol, ampicillin and co-trimoxazole have become infrequent and quinolones have become the first line of treatment of typhoid fever. However over the last few years there has been increase in the defervescence period in patients treated with quinolone. The causative organism *S. typhi* and *paratyphi* are abundant in the water especially if it is contaminated with sewage.

Material and methods

100 patients with the clinical suspicion of typhoid fever proven either by blood culture or by Widal test with single titre have been enrolled. Study period was 2 years and 9 months and patient aged from 11 months to 17 years with male 34 and female 66. As the Kathmandu Medical College is an upcoming hospital and was initially running in a different location prior to this study, the numbers of patient admitted were small. The number seemed even smaller because only positive either by blood culture or by widal without seeing rising titre were taken into account. Some patient came already with blood culture done from outside the hospital and other had tests done in the hospital.

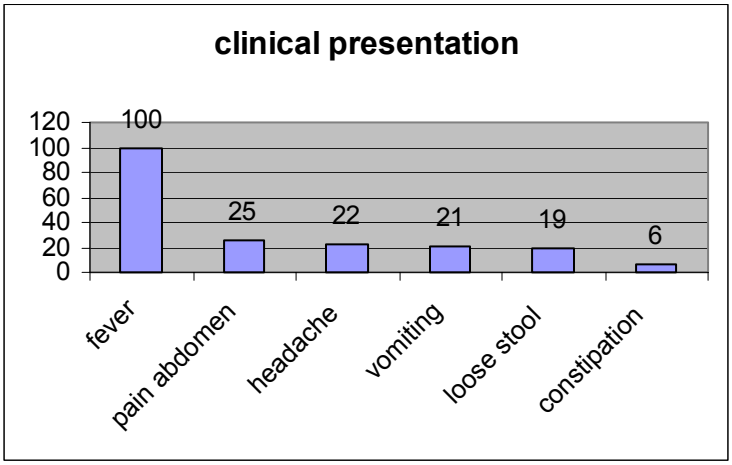
Correspondence
Dr. B. L. Bajracharya
Kathmandu Medical College Teaching Hospital
Sinamangal, Kathmandu, Nepal.
E-mail: blbajracharya@mail.com.np

Those with blood culture were pending and already started on antibiotics, the widal test was sought. Those who were already on antibiotics before blood test of any nature they were sought for widal tests in the hospital. Those whose clinical suspicion was high for typhoid fever were tested for blood culture.

Result

Total numbers of 100 cases were studied. Males were 34, and female 66. Average age of presentations was 8.4 years. Fever was present in all 100% cases, Pain abdomen in 25%, headache in 22%, vomiting in 21% and loose stools in 19%, and constipation in 6% cases. Among the clinical findings hepatomegaly was present in 60% ranging from just palpable to 7.5 cm below costal margin; splenomegaly 45%. In 5% of the cases liver and spleen were not palpable.

Table 1: Clinical presentation of the patients showing different symptoms among them fever was present in all the cases

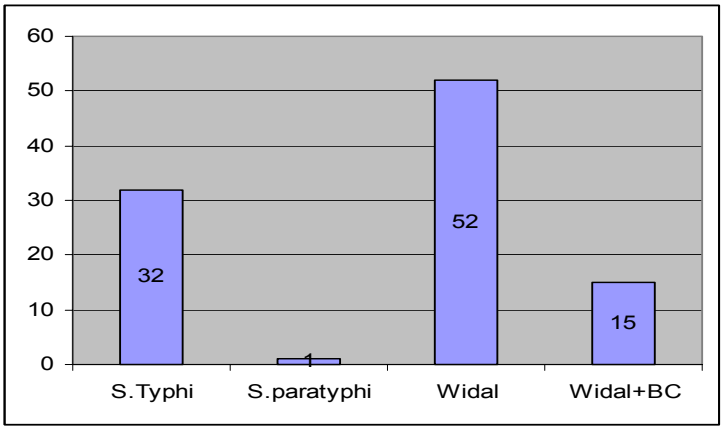


Blood culture for *S. typhi* was positive in 32 and for *S.paratyphi* 1. Widal test was being widely used as many patients came to the hospital already taking antibiotics either for typhoid fever or for other reason. 52% had single widal test titre160 or more which was considered significant for *S. typhi* or *S.paratyphi*. Among the widal positive cases 15 of them also had positive blood culture.

Table 2: Titre of 160 or more was taken into consideration as positive for *S.Typhi* or *S.Paratyphi*

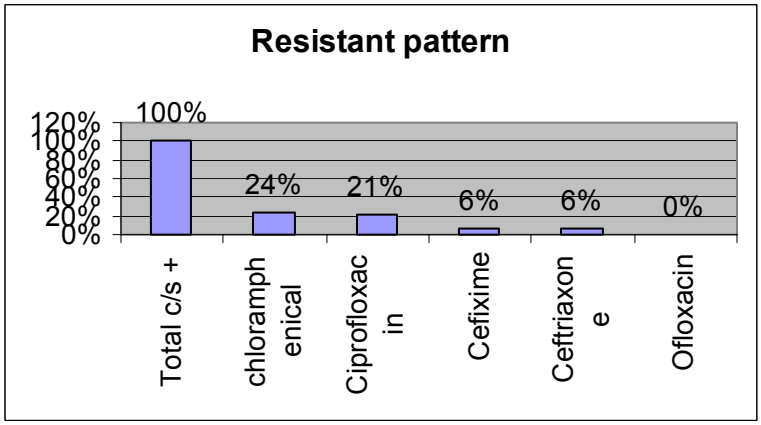
Type	*160*	*320*	*640*
O	29	20	-
H	-	31	20
AH	-	-	1

Table 3: Diagnosis of Typhoid fever was made with blood culture or widal test significant in a single reading



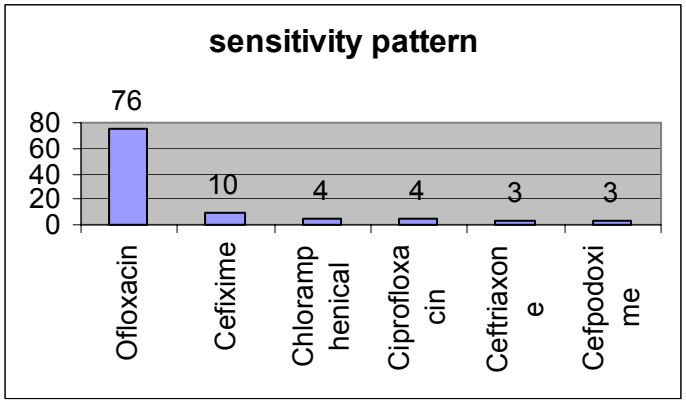
Resistant to the drug was regarded as drug resistant to the *S.typhi* as well as not responded to that drug for the period of the expected defeverscent period which was taken up to 6 days for any treating drug. Second line therapy was sought if the defeverscent period has been more than 6 days of the treatment. Resistant to *S. typhi* observed in the blood culture was as follows; Chloramphenicol 8 (24%), Ciprofloxacin 7 (21%), Cefixime 2 (6%), Ceftriaxone 2 (6%), which required change of the second line therapy where ofloxacin was regarded as second line therapy.

Table 4: Resistant to various drug but not to ofloxacin



Ofloxacin was the most commonly used antibiotic in our study (76 patients). All 33 positive cases were sensitive to the Ofloxacin (100%), 3 (9%) were treated with Chloramphenicol, 4 (12%) were treated Ciprofloxacin. Third generation oral cephalosporins alone were used, Cefixime in 11(33%), Ceftrioxone in 3 (9%) and Cefpodoxime in 3 (9%) cases. 2 (6%) cefixime, 1(3%) ceftriaxone needed second line therapy as the defeverscent period was more than 6 days.

Table 5: Sensitivity patterns of drugs



Discussion

Since the introduction of chloramphenicol in 1948, it has been the drug of choice in the treatment of typhoid fever in most parts of the world. But the indiscriminate use of the drug and acquisition of plasmid mediated R factor has led to the development of resistance to *S. typhi* against this drug[5]. The emergence of chloramphenicol resistant has imposed a big problem regarding the treatment of patients with typhoid fever. Alternative drugs suggested included co-trimoxazole, ampicillin and amoxycillin. In our study, incidence of chloramphenicol resistant was found to be 24%. Resistant to ciprofloxacin, cefixime and ceftriaxone was also present in significant number of patients though both of the resistant to ceftriaxone have responded clinically. The defervescent period for ciprofloxacin is about 3-5 days according to the literature and for third generation cephalosporin is about three days. In one study[6] ciprofloxacin was used as second line drug where they also found significant number of chloramphenicol resistant. They also observed the duration of defeverscent period was up to eight days for ciprofloxacin and for chloramphenicol was up to 10 days. We did not wait more than six days of defeverscent period and we did not give ciprofloxacin as a second line drug because resistant to this drug in up to 21%. Though quinolone group of drugs emerged as useful drug for the treatment of multiple drug resistant cases of *S. typhi* unfortunately, ciprofloxacin resistant has emerged high. The resistant to quinolone is not plasmid coded but due to an altered DNA gyrase subunit, which is also being reported both from the Indian subcontinent and West[7,8]. In the present study we have observed that the defervescent period was comparatively longer, about 6 days for quinolone group. Indiscriminate use of drugs is one of the important factors leading to drug resistant and in case of ciprofloxacin, low cost, advantage of oral route, tolerability, convenient twice a day dosage schedule have contributed towards its indiscriminate use. In our study, resistant to third generation oral cephalosporins were only 2%, which required second line drug like ofloxacin.

Conclusion

Quinolone is the good first line therapy for typhoid fever. Though the resistant to ciprofloxacin was high and defevercent period was prolonged it is still used with prolonged duration of therapy up to 14 days and higher dose of 30 milligram per kilogram body weight with good response. But ofloxacin can be used as first line therapy as the there has not shown any resistant to this drug in our study.

Recommendation

Clinical suspicion for the diagnosis of enteric fever is good diagnostic tool where there is an insidious onset of fever along with headache, malaise, abdominal pain or discomfort. The indiscriminate use of drugs in typhoid fever should be discouraged. Appropriate antibiotic indicated by sensitivity tests should be employed to prevent the development of resistant strains of *S.typhi.* Ofloxacin has shown to respond to all the typhoid fever cases treated with this drug. None of them were needed to replace with the second line drug. Because of the low cost, convenient twice a day dose, easy oral route ofloxacin could be a good first line drug of choice for the treatment of typhoid fever.

Acknowledgement

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