Spectrum of in vitro drug sensitivity of Salmonella bacilli and clinical profile of typhoid patients presenting at a hospital in Srinagar, India.

Syed Arshad Hussain, Parvaiz Ahmad Koul, Shamila Hamid, Imran Khan, Ab Wahid* Javid Iqbal Wani

MD int.medicine,Ex Senior Resident Skims Soura, Presently Consultant/B-Grade in Health Deprt.kashmir
MD Comm medicine, Senior Resident
PHD Statistics, Asst. Processor, SKUAST
MD Int medicine,professor medicine former Head
MD int medicine,Assoc professor medicine
Department(s) and institution(s)
* Dept int medicine SKIMS SOURA SGR KASHMIR
** Dept.Comm.med, SKIMS, Srinagar  INDIA
*** SKUAST, Srinagar,INDIA

ABSTRACT

Background: Enteric fever (typhoid) is the commonest ailment for which the medical treatment is sought in developing countries including India. The emergence of drug resistance to multiple drugs along with the varied clinical profile is a matter of high concern. Objective: The objective of this study was to assess the pattern of in vitro drug sensitivity of Salmonella typhi as also to assess clinical profile in enteric same patients. Design: It was an observational study carried over a period of 3 years in a tertiary hospital in culture positive salmonella typhi patients who were admitted in hospital for diagnosis and treatment. Material and methods: A total of 52 culture positive patients were recruited in first phase of study to assess the drug sensitivity pattern but in second phase clinical profile of only 36 patients out of 52 were studied. Sixteen were excluded in this phase as they were having additional medical problems like CRF, Liver diseases, malabsorption states leading to mix up of clinical features. Results: All the patients were found to be resistant to chloramphenicol and cloxacillin and sensitive to ceftriaxone, ciprofloxacin and nitrofurantoin. Pyrexia was the most common presentation in all the 36 patients (100%), Splenomegaly in 30 patients (80%). Least common symptom were headache and abdominal pain (5.5%).Conclusion: The occurrence of multidrug resistant enteric fever is very common now. There is drug resistance to those drugs which were previously called “Gold standard”. Ceftriaxone/nitrofurantoin /ciprofloxacin have taken the first place in management. The clinical features were almost similar but bleeding tendencies with variable gut signs and symptoms was noteworthy in some patients.

Introduction

Enteric fever is the most common febrile illness for which patients seek treatment in developing countries, including India.1 With improvements in sanitation, food storage, processing and handling though burden of disease has reduced markedly yet Enteric fever continues to occur in all parts of the world, especially in central Asia, south Asian subcontinent and middle east Africa.4 The incidence is highest in south central /south Asian region, medium in the rest of Asia, Africa, latin America and lowest in other parts of the world.1,2,3 The disease occurs due to substandard drinking water with poor sanitation along with poor hygiene.2 Risk factors include contaminated water, food and drinks purchased from street vendors, as well as raw fruits and vegetables.1,2,3,4 “That is why disease is more prevalent in developing countries as compared to developed countries”. Typhoid is a challenging problems in our medical OPDs as this infection is a significant cause of morbidity and mortality. However many reports from developing countries show that clinical presentation and treatment has changed significantly over years.5,6 In affected population a major concern is the occurrence of multi drug resistant strains which have been reported
The emergence of antimicrobial resistance has been reported from Indian subcontinent as well. In India such resistance has been reported from Calcutta, Calicut and Nagpur. Multidrug resistance has also been reported from Srinagar & Kashmir. The variation in clinical features may include gut disturbances, bleeding tendencies along with higher function involvement besides fever.4,5,6

**OBJECTIVE:** The study was done to assess

a) The pattern of drug sensitivity in culture positive (for *Salmonella typhi*) patients.

b) Clinical Profile of culture positive patients.

**MATERIAL AND METHODS:** This was a hospital based study carried over a period of 3 years. The study was done in two phases.

**Phase I:** The patients who presented with the febrile illness lasting for few days were subjected to Blood Culture/Sensitivity and widal antibody titres besides other routine investigations like complete hemogram, urine analysis and biochemical profile. Antibiotic in vitro sensitivity was performed by the Disc diffusion method of stokes, using Mueller-Hinton medium. A total of 52 culture positive patients were recruited in first phase of study to assess the drug sensitivity pattern.

In vitro testing for drug sensitivity/culture was done for following antibiotics: Amoxicillin, cotrimoxazole, cloxacillin, chloramphenicol, gentamycin and amikacin. The other drugs included were ciprofloxacin (quinolone) and ceftrixaone (4th generation cephalosporin) besides nitrofurantoin. The data was thoroughly scrutinized in all the positive patients prior to documentation.

**Phase II:** In the second phase clinical profile of only 36 patients was documented and analysed. The 16 patients were excluded in the 2nd phase due to additional medical problems responsible for clinical features of the patients like CRF, Liver diseases and malabsorption disorders.

**RESULTS, BIOSTATISTICAL ANALYSIS AND OBSERVATIONS:**

A total of 52 patients turned to be blood culture positive for *Salmonella typhi*. The organism was found sensitive to ceftrixaone, ciprofloxacin and nitrofurantoin in the entire 52 patients (100%). The culture sensitivity pattern to Aminoglycosides was variable. Almost half the patients were sensitive to gentamycin and amikacin and remaining were resistant. Resistance was found to multiple drugs like ampicillin in n=46 patients (88.9%) and cotrimoxazole resistance in n=50 patients (96.9%). All the patients n=52 (100%) were resistant to chloramphenicol and cloxacillin.

The Ciprofloxacin, Ceftrixone and Nitrofurantoin was used as single reference group as all of them were having 100 percent sensitivity and all other antibiotics were compared with this reference. It was found that all other antibiotic drugs had statistically significant resistance as compared to the reference antibiotics i.e., (Ciprofloxacin, Ceftrixone and Nitrofurantoin) see Table 1. The Amikacin and Gentamycin are found to be least resistant, i.e., 50 percent each, followed by Amoxicillin (88.9%) and Cotrimoxazole (96.9%) while as, Chloramphenicol and Cloxacillin are found to be 100 percent resistant. The data was analyzed by R-software using Fisher’s Exact test and p-value <0.05 was considered to be statistically significant.

<table>
<thead>
<tr>
<th>Table 1: Comparison of antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Resistant</strong></td>
</tr>
<tr>
<td>(Cipro, Ceftri, Nitrofurantoin)</td>
</tr>
<tr>
<td>Amikacin</td>
</tr>
<tr>
<td>Gentamycin</td>
</tr>
<tr>
<td>Ampicillin</td>
</tr>
<tr>
<td>Co trimoxazole</td>
</tr>
<tr>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>Cloxacillin</td>
</tr>
</tbody>
</table>

The data was analyzed by R-software using Fisher’s Exact test and p-value <0.05 was considered to be statistically significant.

**DISCUSSION**

Enteric fever continues to be one of the commonest causes of febrile illness in the developing world. Enteric fever is a major health problem for which medical treatment is sought in the South Asia. It correlates with the poor sanitation and lack of access to clean drinking water. WHO estimated the annual global incidence of typhoid fever is 0.3% to 12, 3, 4. The South Asian countries like Nepal, Pakistan and India continue to have the frequent outbreaks of the typhoid fever, 6, 7, 8, 9. In India it is endemic with morbidity ranging from 102 to 2219 per lac population. Chloramphenicol was once considered the golden standard of treatment for typhoid fever after its introduction in 1948 and for this reason it continued to be prescribed right and left for typhoid patients. The other drugs which were also considered as the primary drugs included Amoxicillin and co-trimoxazole. 2,3,4,5,6,8 However, in last 2 decades there has been a dramatic increase in the resistance of *S.* typhi to traditionally used chloramphenicol which was first reported in Britain 1950. Later from many areas of the world drug resistance was reported to Chloramphenicol in addition to
Ampicillin and Co-trimoxazole. Drug resistant enteric fever was reported from Nepal, Pakistan and India a well. In India the drug resistant enteric fever was reported from Calcutta, Nagpur, Chandigarh and Jammu and Kashmir. In our study, Salmonella strains were seen to be almost 100% resistant to chloramphenicol. Ampicillin and cotrimoxazole as depicted in table 1, which is compatible with the results of many studies conducted in different parts of the world including India, Nepal Bangladesh and Pakistan. Moreover in this particular study the typhoid strains were seen significantly sensitive (100%) to second line drugs such as Ciprofloxacin and Cephalsporins like Ceftriaxone which is again compatible with several studies done across globe and in South Asia including India. This shows the drug treatment of salmonella has shifted from traditional first line to second line of drugs in South Asia and other regions of world. One more important thing that we observed in our study is that sensitivity of Salmonella to nitrofurantion is 100%, Thus nitrofurantion has got a place in the treatment of the Typhoid which is totally unique as it was not being previously used for this purpose. However there are no related studies available to compare and hence needs more research.

Other group of drugs like Aminoglycosides were seems partially sensitive to typhoid so it is not recommended for treatment of typhoid. In our study we did put patients on second line of drugs like ciprofloxacin and ceftriaxone and the patients respond nicely 10-18d

As for as clinical profile (Phase II of Study) of patients with the drug resistant enteric fever is concerned, fever continues to be the main symptom of the disease for which patient seek treatment. Fever was present in all the 32 patients (100%) as depicted in bar chart which is in accordance to the basic literature and the recent studies.Organomagaly such as splenomegaly was observed in 30 patients (83%) which is again in concordance with the majority of studies and the previous literature available. Other usual common symptoms like headache, loose-motion, cough, abdominal pain, pallor were also seen in cases in our study. However different studies show different frequency of these features. Two important note worthy uncommon features were observed in drug resistant enteric fever cases including clinical bleeding in 11(30%) and altered sensorium in 4(11%), which was definitely higher than reported in the other studies 15, 18. In this study though the predominance of pyrexia in almost all patients and splenomegaly almost in 2/3 pts is consistent with the basic literature of the typhoid/enteric8,15,16 fever but higher frequency of bleeding tendencies is the novel association of multidrug resistant enteric fever which has emerged in last one decade. This finding needs to be further evaluated in depth by research.

REFERENCES

Copyright 2010 BioMedSciDirect Publications IJBM - ISSN: 0976:6685. All rights reserved.