The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/18.4103

ORIGINAL PROF-4103

TYPHOID FEVER;

TO DETERMINE THE OUTCOME OF COMBINATION VERSUS MONO ANTI-BIOTIC THERAPY IN TYPHOID FEVER.

Abid Naeem[1], Subtain-Ul-Hassan Abid[2], Muhammad Huzaifa Abid[3]

1. MBBS, MCPS, FCPS (Medicine)
   MCPS (Pulmology)
   MCPS (Family Medicine)
   Associate Professor Medicine
   MIMC-Medical College Mirpur AJK.
2. MBBS, FCPS (Resident)
   Department of Medicine
   CMH, Jhelum, Pakistan.
3. MBBS (Final year)
   Chandka Medical College
   Larkana, Sindh, Pakistan.

Correspondence Address:
Dr. Abid Naeem
MBBS, MCPS, FCPS (Medicine)
MCPS (Pulmology)
MCPS (Family Medicine)
Associate Professor Medicine
MIMC-Medical College Mirpur AJK.
abidnaeem56@yahoo.com

Article received on:
08/07/2017
Accepted for publication:
20/10/2017
Received after proof reading:
02/01/2018

ABSTRACT… Typhoid fever caused by Salmonella Typhi, is the most common gastrointestinal infectious disease affecting all over the world particularly in Asia where more than 13 millions peoples are affected. Six hundred thousand (600.0000) death occur annually all over the world.[1] Nearly eighty percent (80%) occur in Asia. The main source of infection is contaminated food, water and poor hygiene. Monotherapy, emerging drug resistance and long duration drug treatment is further complicating the problem.[2] Approach to combination antibiotic therapy and shortest duration of treatment is needed. **Period:** January 2016 to June 2016. **Objectives:** To determine the outcome of combination versus mono anti-biotic therapy in typhoid fever. **Study Design:** A prospective descriptive study. **Place of Study:** Mohi-Ud-Din Teaching Hospital Mirpur AJK. **Results:** Among 138 patients, the relapse rate was high in patients treated with monotherapy as compared combination therapy. **Conclusion:** Relapse is more common in ciprofloxacin and ceftriaxone groups. Among combination therapy, (ciprofloxacin and ceftriaxone,) relapse was less common. When relapsed patients were retreated with combination therapy, the patients were completely cured.

Key words: Salmonella Typhi, Blood Culture, Widal Test, Typhidot, Ciprofloxacin, Ceftriaxone.

Article Citation: Nadeem A, Abid S, Abid MH. Typhoid fever; to determine the outcome of combination versus mono anti-biotic therapy in typhoid fever. Professional Med J 2018;25(1):39-44. **DOI:**10.29309/TPMJ/18.4103

INTRODUCTION

Typhoid fever is caused by salmonella typhi organism, gram-negative bacilli. A less severe form is caused by Salmonella paratyphi.[3] Typhoid fever is a life threatening infection frequently found in Asian sub-continent, particularly Pakistan and India. The main source of infection is contaminated food and water and poor hygiene.[5]

More than 13 million peoples are affected in Asia. During acute infection, S.typhi multiplies in neutrophil phagocytic cells before being released into the blood stream. After ingestion of contaminated food and water, the typhoid organism reach small intestine, rapidly penetrate the mucosal epithelium and reach the intestinal lymphoid system.[6] The bacilli are drained to mesenteric lymphoid node, after which they enter the circulation through thoracic duct.[7] The incubation period is 8-14 days in reticulo-endothelial system i.e. liver, spleen and bone marrow.

The clinical presentation of acute non complicated typhoid varies from mid to low grade fever and abdominal discomfort. Acute fever is characterized by fever, constipation, headache, malaise, constipation, headache, and anorexia.[9] In complicated fever intestinal perforation occur in 3% of cases. Abdominal discomfort is often restricted to right lower quadrant but may be diffuse. Altered mental status has been associated with high fatality rate. Other serious complications are associated with typhoid fever include hemorrhage, hepatitis, myocarditis, pneumonia, disseminated intravascular coagulation (DIC) and, thrombocytopenia.[11]

Globally 17 million cases are recorded and about 600,000 deaths associated with typhoid fever. Definite diagnosis of typhoid fever depends on the isolation of S. typhi from blood and bone marrow.[15] Blood culture is the mainstay of diagnosis of the disease.

Salmonella is characterized by somatic (O) and flagellar (H) antigen. Widal test and typhidot are commonly used. Typhidot specifically detect IgM and IgG antibodies. Typhidot M has 100% sensivity, specificity and to define positive and negative culture. Blood culture blood is the Gold standard but it takes 1-2 weeks for the culture to become positive.[16] In our study typhidot was used as diagnostic tool witch become positive within 2-3 days after infection, while latest test typhidot M is positive within three hour.[17] Our study is based on the diagnosis and treatment of typhoid fever with combined versus monotherapy to shorten the duration of treatment. The patients were admitted patients in Mohi-Ud-Din Teaching Hospital Mirpur AJK from January 2016- June 2016.

AIMS & OBJECTIVES

The objective of this study is to find out the outcome of combined versus monotherapy in the treatment of typhoid fever.

MATERIAL AND METHODS

A study was conducted at Mohi-Ud-Teaching Hospital Mirpur AJK from January 2016-june 2016. A total of 138 patients were included in this study. All the patients were admitted through medical OPD. The patients were divided in 02 age groups. Group A=(age-15-25 years) =105 patients. Group B=(age-26-35 years) =33 patients. Typhidot serological test was the main diagnostic tool used in this study. Widal test is less sensitive than typhidot. Blood culture is the confirmatory test but it was not included in this study as the test report is delayed from one to two weeks.

Inclusion Criteria

Typhoid patients

Exclusion Criteria

1. Brucellosis
2. Leukemia
3. Lymphoma
4. Malaria
5. Viral infections
6. Inflammatory bowel disease
7. Malignancy

Study Design

A prospective descriptive study.

Data Analysis

Age group (years)	Male=96	Female=42	Total patients
A=15-25	76	29	105
B=26-35	20	13	33
			138

Table-I. Age wise distribution total number of patients=138

Table-I Shows age wise distribution of 138 patients which include both male and female patients ranging from young to middle age patients. Group A (age=15-25 years) which include 76 male and 29 female, a total of 105 patients. Group B (age=26-35 years) which include 20 male and 13 female, a total of 33 patients. Some total of 96 male and 42 female patients was 138.

Male =96	Ciprofloxacin dose=500 mg(BD)	Ceftriaxone= Ceftriaxone dose=1G(BD)	Combination= Ciprofloxacin500 mg(BD) + Ceftriaxone1G(BD)	Duration of treatment= 05days	Cured patients= 61	Partially cured patients= 35
A=32	32			5	18(29.50%)	14(40.00%)
B=32		32		5	15(24.59%)	17(48.57%)
C=32			32	5	28(45.90%)	4(11.28%)

Table-II (a). Outcome of drug treatment for 05 days in96 male patients.

Table-II (a) shows outcome of drug treatment in 96 male patients. Ninety six patients were equally divided into group A, B, and C groups. Each groups, contain 32 patients.

Group A (32 patients) treated with Ciprofloxacin dose=500mg (BD).

Group B (32 patients) Treated with Ceftriaxone dose=1G (BD).

Group C patients treated with

Combination=Ciprofloxacin 500mg (BD) + Ceftriaxone1G (BD).
Each group was treated with for 05 days.
Sixty one (61) patients completely and 35 patients partially cured.
Among cured 61patients the 18 (29.50%) belong to Group A (32 patients) who were cured with Ciprofloxacin dose=500 mg (BD) after 05 days treatment.
Among cured (61patients) the 15(24.59%) belong to Group B (32 patients) who were cured with Ceftriaxone= 1G (BD) after 05 days treatment.
Among cured (61patients) the 28(45.90%) belong to Group C (32 patients) who were cured with Combination= Ciprofloxacin 500mg (BD) + Ceftriaxone1G (BD) after 05 days treatment
Among partially cured patients (35patients) 14(40.00%), 17(48.57%), 4(11.28%) belongs to Group A, Group B, Group C 4(11.28%) 4(11.28%), respectively.

Table-II (b) shows that relapse rate noted in 15 patients among 61 cured patients. Relapse was found in 6(40.00%), 7(46.66%), 2(13.33%) who were treated with Ciprofloxacin dose=500mg (BD, Ceftriaxone dose=1G (BD), Combination=Ciprofloxacin) dose=500 mg (BD)+ Ceftriaxone dose=1G(BD)for 05 days respectively.

Table-II (c) shows that cured patients were nine (09), 4(44.44%), 5(55.55%), 2(22.22%), cured by Ciprofloxacin dose=500 mg (BD, Ceftriaxone dose=1G (BD, Combination=Ciprofloxacin) dose=500 mg (BD)+ Ceftriaxone dose=1G(BD) respectively. Among, Non responsive patients=4, 2(25%), 2(75.00%), 0(0%) ciprofloxacin, ceftriaxone, and combination (ciprofloxacin+ ceftriaxone) respectively. Hundred percent cured by combination therapy.

Table-III (a) shows outcome of drug treatment in 42 female patients. Forty two patients were equally divided into group A, B, and C groups each groups, each contains 14 patients.
Group A (14 patients) treated with Ciprofloxacin dose=500mg (BD).
Group B (14 patients) Treated with Ceftriaxone dose=1G (BD).
Group C (14patients) treated with Combination=Ciprofloxacin 500mg (BD) + Ceftriaxone1G (BD).
Each group was treated for 05 days.
Twenty nine (29) patients completely and 13 patients partially cured.

Table-III (b) shows that relapse noted in 11 patients among 29 cured patients. Relapse found in 3(27.27%),5(45.45%),3(27.27%) who were treated with Ciprofloxacin dose=500mg(BD, Ceftriaxone dose=1G(BD), Combination=Ciprofloxacin) dose=500 mg(BD)+ Ceftriaxone dose=1G(BD) for 05 days respectively.

Table-III (c) shows that cured patients were eight (08). 2(33.33%), 3(50.00%), 3(50.00%) cured by Ciprofloxacin dose=500 mg (BD, Ceftriaxone dose=1G (BD, Combination=Ciprofloxacin) dose=500 mg (BD)+ Ceftriaxone dose=1G(BD) respectively. Among, Non responsive patients=3, 1(50.00%), 2(50.00%), 0(0%) ciprofloxacin, ceftriaxone, and combination (ciprofloxacin+ ceftriaxone) respectively. Hundred percent patients cured by combination therapy.

Cured patients= 61	Ciprofloxacin dose=500 mg (BD)	Ceftriaxone dose=1G (BD)	Combination= Ciprofloxacin) dose=500 mg(BD)+ Ceftriaxone dose=1G(BD)	Total relapsed patients=15
18	6			6(40.00%)
15		7		7(46.66%)
28			2	2(13.33%)
				15

Table-II (b). Relapse after 02 weeks among 61 cured patients.

Relapsed patients= 15	Ciprofloxacin dose=500 mg(BD)	Ceftriaxone dose=1G (BD)	Combination= Ciprofloxacin) dose =500 mg(BD)+ Ceftriaxone dose=1G(BD)	Duration of treatment= 05days	Total relapse patients=15	Cured patients=9	Non responsive patients= 4
6	6			5	6(40.00%)	4(44.44%)	2(25%)
7		7		5	7(46.66%)	5(55.55%)	2(75.00%)
2			2	5	2(13.33%)	2(22.22%)	0(0%)

Table-II (c). Outcome of treatment for 05 days of 15 relapse patients.

Female=42	Ciprofloxacin dose=500 mg(BD)	Ceftriaxone dose=1G(BD)	Combination= Ciprofloxacin dose=500 mg(BD + Ceftriaxone dose=1G(BD)	Duration of treatment= 05days	Cured patients= 29	Partially cured patients= 13
A=14	14			5	9(31.03%)	5(38.46%)
B=14		14		5	8(27.58%)	6(46.15%)
B=14			14	5	12(41.37%)	2(15.38%)

Table-III (a). Outcome of drug treatment for 05 days in 42 female patients.

Cured patients=29	Ciprofloxacin dose=500 mg (BD)	Ceftriaxone dose=1G (BD)	Combination= Ciprofloxacin) dose=500 mg(BD)+ Ceftriaxone dose=1G(BD)	Total relapsed patients=11
9	3			3(27.27%)
8		5		5(45.45%)
12			3	3(27.27%)
				11

Table-III (b). Relapse after 02 weeks among 29 cured patients

Relapse patients 11	Ciprofloxacin dose=500 mg(BD	Ceftriaxone dose=1G (BD)	Duration of treatment= 05days	Combination= Ciprofloxacin) dose=500 mg(BD)+ Ceftriaxone dose=1G(BD)	Total relapse patients=11	Cured patients=8	Non responsive patients=3
3	3		5		3(27.27%)	2(33.33%)	1(50.00%)
5		5	5		5(45.45%)	3(50.00%)	2(50.00%)
3			5	3	3(27.27%)	3(50.00)	0(0%)

Table-III (c). Outcome of treatment for 05 days of relapse 11 patients.

RESULTS

The relapse rate was high in patients treated with monotherapy as compared combination therapy.

DISCUSSION

Typhoid fever is global problems particularly in developing countries.[18] The main Culprit organism is salmonella typhi .Contaminated food, water and poor hygiene is the main source of infection. About 13-17 million people are affected all over the world, resulting in 600,000 death every year. Eight (80%) deaths occurred alone in Asia. Salmonella is resist ant to first line drugs, chloremphinicole, ampicillne, and co-trimoxazole.[19] Ten among the second line drugs Fluoroquinolones, Ciprofloxacin dose=500 mg (BD, Ceftriaxone dose=1G(BD), has proven the most effective drugs in the treatment of typhoid fever. Ciprofloxacin and Ceftriaxone is are given for 7-14 days. ceftriaxone is well tolerated; however we have to keep in mind the tolerability of Ciprofloxacin, like CNS excitation, allergic rashes and photosensivity.[21] Emerging resistance to ciprofloxacin is another problem which is particularly common in Pakistan where ciproflaxcin is Indiscriminately used without checking the drug indications and its side effects.[23] The purpose of our study was to confirm and shorten the duration of treatment typhoid fever by giving combination therapy as compared to monotherapy.[25]

CONCLUSION

Relapse is more common in ciprofloxacin and ceftriaxone groups. Among combination therapy, (ciprofloxacin and ceftriaxone,) relapse was less common. When relapsed patients were retreated with combination therapy, the patients were completely cure.

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Great minds have purpose;
others have wishes.

– Washington Irving –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Abid Naeem	1st Author	
2	Subtain-Ul-Hassan Abid	Data collection	
3	M. Huzaifa Abid	Data collection	