SPONTANEOUS BACTERIAL PERITONITIS
COMPARISON OF TREATMENT WITH CIPROFLOXACIN AND CEFTRIAXONE IN PATIENTS WITH CIRRHOSIS LIVER AND ASCITES

ORIGINAL
PROF-1926

DR. INAMULLAH KHAN
MBBS, MRCP
Senior Registrar Medical C Unit
Khyber Teaching Hospital, Peshawar

DR. FAZLE SUBHAN
MBBS, FCPS
Registrar Medical "D" Unit
Khyber Teaching Hospital, Peshawar

DR. ZAHIDULLAH KHAN
MBBS, MCPS, FCPS
Registrar Medical "A" Unit
Khyber Teaching Hospital, Peshawar

ABSTRACT... Objective: To compare the efficacy of ciprofloxacin with ceftriaxone in the treatment of spontaneous bacterial peritonitis in patients with cirrhosis liver and ascites. **Design:** This hospital based quasi-experimental study. **Setting:** Department of Medicine, Khyber Teaching Hospital Peshawar. **Period:** October, 2009 to April, 2010. **Material and Methods:** A total of 200 patients were selected by non-probability purposive sampling method after obtaining an informed consent. Sample size was calculated through WHO statistical calculator. All the selected patients had clinical and biochemical evidence of cirrhosis liver and spontaneous bacterial peritonitis. Both sexes were included in the study. They were randomly divided into two groups; group I was treated with ciprofloxacin and group II was treated with ceftriaxone. **Results:** 200 patients including 124 males and 76 females with spontaneous bacterial peritonitis were included in the study. 100 patients each were treated with ciprofloxacin and ceftriaxone in the two groups. 82% responded favourably to 5 days course of I/V 200mg ciprofloxacin and 91% were cured with 5 days therapy of I/V 2gm ceftriaxone. **Conclusions:** Both ceftriaxone and ciprofloxacin are equally effective in the treatment of spontaneous bacterial peritonitis.

Key words: Cirrhosis, Spontaneous bacterial peritonitis, Ciprofloxacin, Ceftriaxone.

INTRODUCTION

Hepatic cirrhosis represents the tenth major cause of death in the USA. 1 Among the major complications of cirrhosis ascites seems to be the most frequent one and is associated with increased susceptibility to infections and poor long-term outcome[1,2]. Spontaneous bacterial peritonitis (SBP) is characterized by spontaneous infection of ascitic fluid in the absence of intra-abdominal source of infection[3,4]. The prevalence of SBP in cirrhotic patients with ascites has been estimated at 10 to 30%[5-7] and has a recurrence rate of 70 percent in 1 year[3,4]. SBP is related to altered host defenses, overgrowth of microorganisms and bacterial translocation from intestinal lumen to mesenteric lymph nodes[8]. The risk of developing SBP is greater in those with a coexistent gastrointestinal bleed, high serum bilirubin, a previous episode of SBP and low ascitic fluid protein concentration (less than 1gm/dl)[9,10].

The clinical presentation of SBP is highly variable. Presenting signs and symptoms include fever, changes in mental status, abdominal tenderness, gastrointestinal (GI) bleeding, chills, nausea and vomiting. In 30% of patients it is asymptomatic[15,16].

For the diagnosis of SBP, the number of polymorphonuclear leucocytes (PMN) from the ascitic fluid obtained by paracentesis must exceed 250 cells/mm3 and from bacteriological cultures only one germ must be isolated[11-13]. Since SBP is in most cases a monomicrobial infection, the presence of more microorganisms in the culture (>1) must raise the suspicion of secondary peritonitis[14].

In 2000 The International Ascites Club published a consensus document on the diagnosis, management, and prophylaxis of SBP[17]. The guidelines suggested several antibiotics that might be used for empirical treatment such as cefotaxime, cefonicid, ceftriaxone, ceftazidime, and amoxicillin–clavulanic acid. In some studies these antibiotics showed similar rates of efficacy-ranging from 77% to 93%.

The duration of therapy should be a minimum of five days. This recommendation is derived from a trial showing that a 5-day course of cefotaxime was as effective as a 10-day course of therapy[18].

Little has changed in the antibiotic recommendations for

SBP since the publication of the guidelines in 2000. Indeed, the antibiotic regimen of cefotaxime 2 g every 12 hours, continues to be advocated as a regimen of first choice[19]. However, the availability of generic formulations of several cephalosporins suggests that clinicians have other options at their disposal.

Many studies have shown the efficacy of ciprofloxacin and ceftriaxone in the treatment of spontaneous bacterial peritonitis and they are approved as first line drugs in the treatment of spontaneous bacterial peritonitis[20,21].

Present study is an attempt to identify the antibiotic of choice in the treatment spontaneous bacterial peritonitis and concerns regarding the use of ceftriaxone as an empirical therapy in our set up.

PATIENTS AND METHODS

This hospital based quasi-experimental, one center study was carried out in Department of Medicine, Khyber Teaching Hospital Peshawar from October, 2009 to April, 2010. A total of 200 patients above age 25 years and who were diagnosed as case of spontaneous bacterial peritonitis after ascitic fluid paracentesis were included in the study after taking informed consent. The sample size was calculated through WHO statistical calculator according to the prevalence of disease with absolute precision of 10 %. The diagnosis of SBP was established according to the following criteria: ascitic fluid with a polymorphonuclear differential count of more than 250 cells/mm3 and the absence of clinical, biological, or radiological findings suggestive of secondary peritonitis. Patients who had cirrhosis due to other causes like heamochromatosis, Bud-Chiari Syndrome or primary billiary cirrhosis were excluded from study. Moreover, patients with ascites due to hepatoma or other malignancy or due to cardiac, pericardial or renal disease were also excluded from the study.

A detailed history and examination was performed and each patient was thoroughly investigated (e.g. Hemoglobin and Total Leucocyte count, liver function tests, PT, APTT, Urea, Creatinine, blood sugar etc) according to special proforma devised for the purpose of study. The diagnosis of cirrhosis with ascites was verified by clinical, biochemical, and ultrasonographic findings. Applying full protocol of aseptic techniques, 10ml of ascitic fluid was obtained for routine biochemical and cytological tests after taking written consent. Patients who qualified the above criteria for SBP were randomly divided into 2 groups (Ciprofloxacin Vs Ceftriaxone) by using random number table. Patients in group I were treated with 200 mg of intravenous (I/V) Ciprofloxacin (Ciproxin®). The patients in group II were treated with 2gm of Ceftriaxone (Rocehpin®). The duration of treatment was 5 days.

After 5 days of treatment, 10 ml of ascitic fluid was again analysed. The infection was considered to have resolved when all signs of infection disappeared and the ascitic fluid PMN count was below 250 cells/ mL.

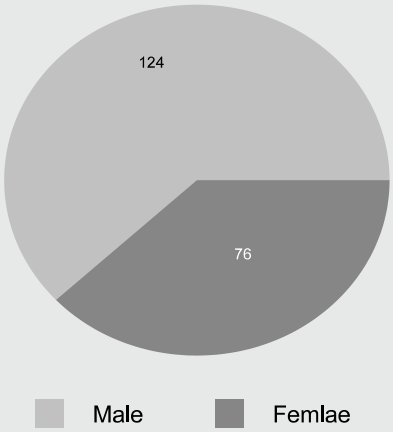
The data was analyzed using SPSS version 11.0.The data was tabulated. Mean, mode, median, percentages and ratios were recorded where necessary.

RESULTS

This study was conducted in the department of medicine at Khyber Teaching Hospital, Peshawar.

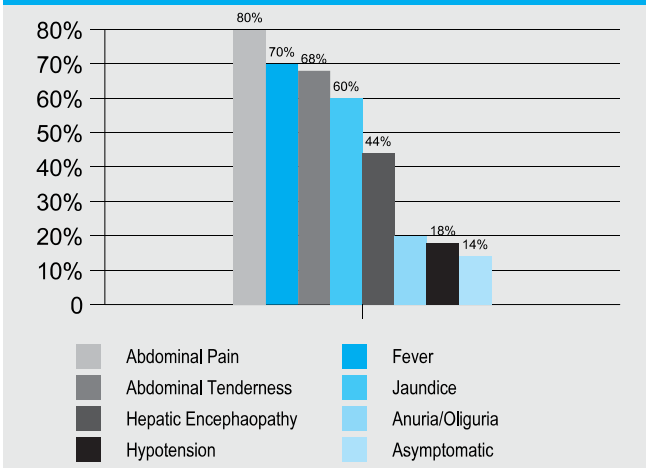
A total of 200 patients having spontaneous bacterial peritonitis were included in the study. 124 were male and 76 were female with a ratio of 1.6:1 as shown in fig 1. Majority of the patients in the study were in the age range of 46 and 55 years as shown in table I. Mean age was 48 years and median age was 51.5 with mode age 49 years.

Fig-1. Sex distribution of patients



The clinical presentation of patients with spontaneous bacterial peritonitis was variable. The most common presentation was abdominal pain followed by fever. Other symptoms included abdominal tenderness, jaundice, hepatic encephalopathy, hypotension while few were asymptomatic. The details are shown in Fig 2.

Fig-2. Clinical features in patinets with SPB



100 patients each with spontaneous bacterial peritonitis were put on I/V ciprofloxacin and ceftriaxone. In ciprofloxacin group, 82% of patients responded favorably while 18% did not respond. In ceftriaxone group, 91% of patients cured while 9% showed no response. The above results are summarized in table II and III respectively.

DISCUSSION

Spontaneous bacterial peritonitis is the spontaneous bacterial infection of the previously sterile ascitic fluid in cirrhosis liver without any apparent surgically treatable intra abdominal source of infection[22]. It is a common and potentially fatal complication of cirrhosis with ascites[23]. Its mortality has been decreased from 80 to 30 % due to prompt diagnosis and early initiation of adequate treatment[24].

In view of the heterogeneous clinical presentation, a high index of suspicion is required to establish the early diagnosis and start empirical antibiotic therapy to avoid serious sequale.

The present study is designed to determine the antibiotic

Table-I. Age distribution in study

Age range (years)	Total no. of Patients	%age
25-35	14	7%
36-45	36	18%
46-55	80	40%
56-65	50	25%
66-75	20	10%

Table-II. Ciprfloxacin responsive vs non responsive patients

Response	Total no. of patients	%age
Responsive	82	82%
Non Responsive	18	18%

Table-III. Ceftriaxone responsive vs non responsive patients

Response	Total no. of patients	%age
Responsive	91	91%
Non Responsive	09	09%

of choice in the treatment of spontaneous bacterial peritonitis and whether a short course of days is sufficient to resolve SBP in cirrhotic patients.

The antibiotic regimen of cefotaxime 2 g every 12 hours continues to be advocated as a regimen of first choice[19]. Ceftriaxone is a third-generation cephalosporin with similar effectiveness and does not have renal toxicity. Our data confirm the efficacy of ceftriaxone for the treatment of SBP.

In our study males outnumbered females. This may be because preference is given to male for hospitalization and treatment as compared to females in our society. This fact is also proved by national and international studies as well[5,21,25]. Study conducted by Muhammad D, et al showed an equal distribution of sex[29].

The most common presenting symptoms were abdominal pain (80%) and fever (70%). Other

symptoms/ signs in the descending order were abdominal tenderness (68%), Jaundice (60%), hepatic encephalopathy (44%), anuria/ oliguria (20%), hypotension (18%) and 14% patients were asymptomatic. Nearly the same percentage is also observed in another local study[30]. Memon AQ, el al showed different presenting symptoms and signs from the present study[31].

Many studies have been conducted on the efficacy of ciprofloxacin and ceftriaxone in the treatment of spontaneous bacterial peritonitis and these are approved as first line drugs in the treatment of spontaneous bacterial peritonitis[20,21].

In our study a short course of 5 days of treatment with ceftriaxone resolved SBP in 91% of our patients. A local study conducted by Javid G et al, showed that ceftriaxone was effective in 95% of patient after treatment for 5 days[26]. This result is comparable with our study. A study conducted by Gomes et al, found that ceftriaxone was effective in 100% of patient in resolving the infection. This percentage is quite high as compared to our study but his sample size was small (n=30) which may have resulted in high percentage[25]. Franca et al, found in his study that SBP resolved in 73% of patients after five days short course of ceftriaxone[21]. Tuncer I, et al found that ceftriaxone was effective in 83% of patients in his small study conducted in Turkey which nearly correlates with our study[27].

Regarding the response of spontaneous bacterial peritonitis to 5 days I/V Ciprofloxacin (Ciproxin®) therapy, 82% patients responded favorably and 18% patients did not show any improvement in the present study. A small study (15 patients in Ciprofloxacin Arm) conducted in Turkey by Tuncer I, et al showed the response rate of 80% which correlates well with our study[27]. A multicenter study from abroad conducted by Terg R, et al showed that SBP resolved in 76.3 % of patients after 5 days treatment with I/V Ciprofloxacin[28]. Angelini and colleagues evaluated the efficacy of ciprofloxacin in 116 patients. Infection resolved in 82% after 5 days of treatment[20].

The results obtained from above mentioned studies clearly indicate that the frequency of Spontaneous Bacterial Peritonitis in cirrhotic patients with ascites is quite high in general population. More over, Spontaneous Bacterial Peritonitis responds quite favorably to 5 days I/V ceftriaxone and ciprofloxacin therapy.

CONCLUSION

Spontaneous bacterial peritonitis is a common and major complication of liver cirrhosis with ascites. Early diagnosis and prompt treatment is mandatory. Both ceftriaxone and ciprofloxacin are equally effective and can reduce the morbidity and mortality in patients with chronic liver disease.

REFERENCES

1. Runyon BA. Practice Guidelines Committee, American association for the Study of Liver Diseases (AASLD). **Management of adult patients with ascites due to cirrhosis.** Hepatology 2004; 39:841-56.

2. Gines P, Fernandez-Esparrach G. **Prognosis of cirrhosis with ascites.** In: Arroyo V, Gines P, Rodes J, Schrier RW, eds. Ascites and renal dysfunction in liver disease: pathogenesis, diagnosis, and treatment. Malden, Mass: Blackwell Science, 1999:431-41.

3. Rimola A, Garcia-Tsao G, Navasa M. **Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document.** J Hepatol 2000; 32:142-53.

4. Coral G, de Mattos AA, Damo DF, Viegas AC. **Prevalence and prognosis of spontaneous bacterial peritonitis.** Experience in patients from a general hospital in Porto Alegre, RS, Brazil (1991-2000). Arq Gastroenterol 2002; 39(3):158-62.

5. Imran M, Hashmi SN, Altaf A, Rasheed H, Hussain T. **Spontaneous bacterial peritonitis.** Professional Med J 2006; 13(2): 201-5.

6. Evans, LT, Kim, R, Poterucha, JJ, Kamath, PS. **Spontaneous bacterial peritonitis in asymptomatic outpatients with cirrhotic ascites.** Hepatology 2003; 37: 897.

7. Van Erpecum KJ. **Ascites and spontaneous bacterial peritonitis in patients with liver cirrhosis.** Scand J Gastroenterol Suppl 2006; 243: 79-84.

8. Strauss E, Caly WR. **Spontaneous bacterial peritonitis:** Rev Soc Bras Med Trop 2003;36:711-7.

9. Caly WR, Strauss E. **A prospective study of bacterial infections in patients with cirrhosis.** J Hepatol 1993; 18: 353-8.

10. Bac D-J, Siersema PD, Mulder PGH, DeMarie S, Wilson JHP. **Spontaneous bacterial peritonitis: outcome and predictive factors.** Eur J Gastroenterol Hepatol 1993; 15: 635-40.

11. Berg RD. **Mechanisms promoting bacterial translocation from the gastrointestinal tract.** Adv Exp Med Biol 1999; 473: 11-30.

12. Guarner C, Soriano G. **Bacterial translocation and its consequences in patients with cirrhosis.** Eur J GastroenterolHepatol 2005; 17: 27-31.

13. Moore K. **Spontaneous bacterial peritonitis (SBP).** In Warrel DA et al. Oxford Textbook of Medicine, 4th Edition, Oxford University Press 2003, Vol 2, sections 11-17, 739-741.

14. Levison ME, Bush LM. **Peritonitis and intraperitoneal abcesses.** In Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases. 6th Edition, Elsevier, Churchill Livingstone, Philadelphia, 2005, Vol 1, 927- 951.

15. Carey WD, Boayke A, Leatherman J. **Spontaneous bacterial peritonitis: Clinical and laboratory features with reference to hospital-acquired cases.** Am J Gastroenterol. 1986; 81: 1156–1161.

16. Bandy SM, Tuttle A. **Spontaneous bacterial peritonitis E-medicine from Web MD.** Updated July 16, 2008.

17. Rimola A, Garcia-Tsao G, Navasa M, et al. **Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: A consensus document.** J Hepatol. 2000; 32: 142–53.

18. Runyon BA, McHutchinson JG, Antillon MR, et al. **Short course vs. long course antibiotic treatment of spontaneous bacterial peritonitis: A randomized controlled trial of 100 patients.** Gastroenterology. 1991; 100: 1737–42.

19. Ghassemi H, Garcia-Tsao G. **Prevention and treatment of infections in patients with cirrhosis.** Best Pract Res Clin Gastroenterol. 2007; 21: 77–93.

20. Angeloni S, Leboffe C, Parente A, et al. **Efficacy of current guidelines for the treatment of spontaneous bacterial peritonitis in the clinical practice.** World J Gastroenterol. 2008; 14: 2757–62.

21. Franca AVC, Giordano HM, Seva-Pereira T, Soares EC. **Five days of ceftriaxone to treat spontaneous bacterial peritonitis in cirrhotic patients.** J Gastroenterol. 2002; 37: 119–22.

22. Strauss E, Caly WR. **Spontaneous bacterial peritonitis.** Rev Soc Med Trop. 2003, 36(6): 711-17.

23. Ascites In: Sherlock S, Dooley J. **Diseases of the liver and biliary system.** 11 ed. Oxford, England: Blackwell Science, 2002: 127 – 46.

24. Caly WR, Strauss E. **A prospective study of bacterial infections in patients with cirrhosis.** J Hepatol 1993; 18: 353-8.

25. Gomez-Jimenez J, Ribera E, Gasser I, Artaza MA, Del Valle O, Pahissa A, Martinez-Vazquez JM. **Randomized Trial Comparing Ceftriaxone with Cefonicid for Treatment of Spontaneous Bacterial Peritonitis in Cirrhotic Patients.** Antimicrob. Agents Chemother 1993;37:1587-1592.

26. Javid G, Khan BA, Shah AH, Gulzar GM, Khan MA. **Short-course ceftriaxone therapy in spontaneous bacterial peritonitis.** Postgrad Med J 1998; 74: 592-595.

27. Tuncer I, Topcu N, Durmus A, Turkdogan MK. **Oral ciprofloxacin versus intravenous cefotaxime and ceftriaxone in the treatment of spontaneous bacterial peritonitis.** Hepatogastroenterology. 2003; 50(53):1426-30.

28. Terg R, Cobas S, Fassio E, Landeira G, Ríos B, Vasen W, et al. **Oral ciprofloxacin after a short course of intravenous ciprofloxacin in the treatment of spontaneous bacterial peritonitis: results of a multicenter, randomized study.** J Hepatol. 2000; 33(4): 564-569.

29. Muhammad D, Javed M, Iqbal MN, Husain A, Qayyum A. **Bacteriology of spontaneous bacterial peritonitis.** Professional Med J 2007; 14(4): 551-555.

30. Iqbal S, Iman N, Alam N, Rahman S. **Incidence of Spontaneous Bacterial Peritonitis in liver cirrhosis, the causative organisms and antibiotic sensitivity.** JPMI 2004; 18:614-9.

31. Memon AQ, Memon G, Khaskheli A. **Spontaneous Bacterial Peritonitis in Cirrhosis with Ascites - An Experience at PMCH Nawabshah.** Med Channel 1999; 5(1): 31-4.

Article received on: 13/02/2012 Accepted for Publication: 23/06/2012 Received after proof reading: 00/00/0000

Correspondence Address:
Dr. Inamullah Khan
H.No. 42, St. 1/A
Army Housing Scheme (ASKARI-III)
Defence Officer Colony
Khyber Road, Peshawar Cantt.
inamullah76@hotmail.com

Article Citation:
Khan I, Khan Z, Subhan F. Comparison of tretament with ciprofloxacin and ceftriaxone in spontaneous bacterial peritonitis in patients with cirrhosis liver and ascities. Professional Med J Aug 2012;19(4):482-487.