World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v16.i38.4871

World J Gastroenterol 2010 October 14; 16(38): 4871-4875
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
© 2010 Baishideng. All rights reserved.

BRIEF ARTICLE

Clinical significance of C-reactive protein values in antibiotic treatment for pyogenic liver abscess

Hai-Nv Gao, Wen-Xia Yuan, Mei-Fang Yang, Hong Zhao, Jian-Hua Hu, Xuan Zhang, Jun Fan, Wei-Hang Ma

Hai-Nv Gao, Wen-Xia Yuan, Mei-Fang Yang, Hong Zhao, Jian-Hua Hu, Xuan Zhang, Jun Fan, Wei-Hang Ma, State Key Laboratory of Diagnosis and Treatment of Infectious Diseases, the First Affiliated Hospital of Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Author contributions: Yuan WX, Yang MF and Zhao H collected all the clinical data; Hu JH and Zhang X were involved in statistical data analysis; Fan J provided financial support for this work and was also involved in editing the manuscript; Ma WH and Gao HN designed the study and wrote the manuscript.

Correspondence to: Wei-Hang Ma, MD, State Key Laboratory of Diagnosis and Treatment of Infectious Diseases, the First Affiliated Hospital of Zhejiang University, No. 79 Qingchun Road, Hangzhou 310003, Zhejiang Province, China. yinzihan@yahoo.com.cn

Telephone: +86-571-87236721 Fax: +86-571-87236755
Received: May 17, 2010 Revised: July 5, 2010
Accepted: July 12, 2010
Published online: October 14, 2010

Abstract

AIM: To investigate the clinical significance of C-reactive protein (CRP) values in determining the endpoint of antibiotic treatment for liver abscess after drainage.

METHODS: The endpoints of antibiotic treatment in 46 patients with pyogenic liver abscess after complete percutaneous drainage were assessed by performing a retrospective study. After complete percutaneous drainage, normal CRP values were considered as the endpoint in 18 patients (experimental group), and normal body temperature for at least 2 wk were considered as the endpoints in the other 28 patients (control group).

RESULTS: The duration of antibiotic treatment after complete percutaneous drainage was 15.83 ± 6.45 d and 24.25 ± 8.18 d for the experimental and the control groups, respectively (P = 0.001), being significantly shorter in the experimental group than in the control group. The recurrence rate was 0% for both groups. However, we could not obtain the follow-up data about 3 patients in the control group.

CONCLUSION: CRP values can be considered as an independent factor to determine the duration of the antibiotic treatment for pyogenic liver abscess after complete percutaneous drainage.

© 2010 Baishideng. All rights reserved.

Key words: Liver abscess; C-reactive protein; Antibiotic treatment; Drainage; Retrospective studies

Peer reviewer: Guangcun Huang, MD, PhD, The Research Institute at Nationwide Children's Hospital, 700 Childrens Drive, Columbus, OH 43205, United States

Gao HN, Yuan WX, Yang MF, Zhao H, Hu JH, Zhang X, Fan J, Ma WH. Clinical significance of C-reactive protein values in antibiotic treatment for pyogenic liver abscess. *World J Gastroenterol* 2010; 16(38): 4871-4875 Available from: URL: http://www.wjgnet.com/1007-9327/full/v16/i38/4871.htm DOI: http://dx.doi.org/10.3748/wjg.v16.i38.4871

INTRODUCTION

Over the past two decades, complete percutaneous drainage combined with antibiotics has been considered as the routine treatment for liver abscess. This combined approach is clinically effective and has significantly reduced the death rate associated with liver abscess[1]. However, the duration and the protocol for the antibiotic treatment after percutaneous drainage is a matter of debate. Conventionally, the duration of antibiotic treatment is determined by the overall health condition after percutaneous abscess drainage[2-4] or by the white blood cell count[5]. The duration of antibiotic treatment was usually prolonged as much as possible[6]. However, assessments performed by considering the overall health condition as the end-point

of antibiotic treatment tend to be subjective. Moreover, standardized criteria for different patients cannot be developed easily. The white blood cell count can be affected by various factors such as physiological situations that may not truly reflect the clinical condition[7]. Prolonged antibiotic treatment has various disadvantages such as pyogenic antibiotic resistance and double infection. To decrease the incidence of antibiotic-resistant bacteria, reduce medical expenses, and increase patient compliance, a more sensitive parameter is required to determine the optimum duration of antibiotic treatment after percutaneous abscess drainage. C-reactive protein (CRP) is an acute-phase protein that is synthesized by liver endothelial cells, which is considered as the most valuable indicator of inflammation, and is a useful marker to determine the usage of antibiotics and assess the efficacy of the antibiotics[8-11]. However, there is no clinical report on the validity of using CRP values to determine the endpoint of liver abscess treatment. We analyzed the CRP values of the patients who were admitted to our hospital between June 2007 and February 2010. The investigation report is as follows.

MATERIALS AND METHODS

Subjects

We performed a retrospective study on 46 patients with liver abscess who were admitted to our hospital between June 2007 and February 2010. The diagnosis was based on typical clinical symptoms such as fever and upper abdominal pain along with the results of liver examination by ultrasonic and computed tomography. There were 32 male and 14 female patients; 8 patients had an abscess on their left liver lobe and 38 had an abscess on their right liver lobe. Ten patients had diabetes and 9 had cholecystitis. Among the 46 cases, 11 had positive culture results, including 4 from blood culture and 6 from abscess culture, and 1 from both; 8 (73%) of 11 patients showed *K. pneumoniae* infection. All the patients received effective antibiotic treatment and underwent percutaneous drainage of the liver abscess when the fluid was identified during ultrasonography.

Study methods

Inclusion criteria: The patients fulfilling the following criteria were included: (1) those undergoing effective antibiotic treatment; and (2) those who had undergone percutaneous abscess drainage when the fluid was identified during ultrasonography.

Exclusion criteria: The patients fulfilling any of the following criteria were excluded: (1) those who had undergone surgery; (2) those who had discontinued hospitalization before the treatment ended or continued medication out of the hospital. The duration of antibiotic treatment could not be determined for these patients; (3) those who had not chosen the right antibiotics and had prolonged hospitalizations; and (4) those who had not undergone percutaneous drainage.

Endpoints of the treatment: (1) Normal CRP values or (2) normal body temperature for at least 2 wk.

Experimental group: Normal CRP values were considered as the endpoint of antibiotic treatment in those patients.

Control group: Normal body temperature for at least 2 wk was considered as the endpoint of antibiotic treatment in those patients.

Mode and duration of follow-up: Visits were continued until March 2010 after hospitalization was ended.

Major endpoints: Duration of antibiotic treatment and recurrence rate.

CRP and white blood cell counts: CRP and white blood cell counts were determined every 3-5 d for the patients with normal CRP values were considered as the endpoint. Antibiotic treatment was stopped when the CRP values returned to normal. CRP and blood tests were not regularly performed for the control group, and the major criteria for discontinuing antibiotic treatment was normalization of body temperature for at least 2 wk.

Statistical analysis

The mean ± SD values were used for quantification. SPSS13.0 software was used for statistical analysis. *T*-test was used to compare the quantitative data. Chi-square analysis was used to compare the measurement data. P values < 0.05 were considered to be statistically significant.

RESULTS

Comparison of the known criteria

Normal CRP values were considered as the endpoint of antibiotic treatment in 18 patients (experimental group), and normal body temperature for at least 2 wk were considered as the endpoint in other 28 patients (control group). The gender, age, size of liver abscess before and after percutaneous drainage, duration of antibiotic treatment before the percutaneous drainage and the time of follow-up were comparable between the two groups (P > 0.05). In both groups, none of the patients showed recurrence of pyogenic liver abscess. We could not obtain follow-up information of 3 patients in the control group, in the intention-to-treat analysis, these patients would be considered as treatment failure.

Comparison of antibiotic treatment

The duration of antibiotic treatment after complete percutaneous drainage for the experimental and the control groups were 15.83 ± 6.45 and 24.25 ± 8.18 d, respectively (P = 0.001). The total duration of antibiotic treatment was 23.06 ± 7.36 d for the experimental group and 31.11 ± 7.30 d for the control group (P = 0.001) (Table 1).

Table 1 Data of liver abscess patients and duration of antibiotic treatment (mean ± SD)

	Experimental group	Control group	*P* value
Age (yr)	57.72 ± 10.39	58.68 ± 11.73	0.779
Women, *n* (%)	5 (28)	9 (32)	0.754
Size of abscess before therapy (diameter)	7.22 ± 1.44	8.01 ± 2.63	0.291
Size of abscess after therapy (diameter)	3.64 ± 0.89	4.02 ± 1.77	0.484
Antibiotic treatment before percutaneous drainage (d)	7.22 ± 5.39	6.82 ± 4.59	0.788
Antibiotic treatment after percutaneous drainage (d)	15.83 ± 6.45	24.25 ± 8.18	0.001[1]
Duration of follow-up (mo)	9.25 ± 5.67	9.24 ± 4.94	0.995
Recurrence rate	0%	11% (follow-up information for 3 individuals was not obtained)	0.151
Total duration of antibiotic treatment (d)	23.06 ± 7.36	31.11 ± 7.30	0.001[1]

[1]Statistical difference between the two groups of data.

Comparison of CRP values and white blood cell counts

The overall average time required for the white blood cell count and the percentage of neutrophils to normalize after the initiation of antibiotic treatment was 17.95 ± 8.00 d. The average time taken for the CRP values to normalize was found to be 21.44 ± 7.06 d for these 46 patients. There was significant difference ($P = 0.045$) between the two durations. The white blood cell count and the percentage of neutrophils had normalized before the CRP values returned to normal. In 5 patients, it was normal even before the percutaneous liver abscess drainage.

DISCUSSION

Liver abscess is a rare disease, with an incidence of 1.0-17.59 cases per 1 000 000 people[12,13]. The death rate for untreated cases is 100%. Currently, the major therapies for liver abscess are antibiotic treatment, percutaneous drainage combined with antibiotics, and surgery. Usually, antibiotics can be used alone for single liver abscess smaller than 3 cm in size. Percutaneous drainage combined with antibiotics is performed for liver abscesses larger than 3 cm. Surgery has to be performed in the cases of multiple abscesses[14]. Due to the effectiveness of these treatments, the death rate of the patients with liver abscess has decreased gradually over the last 20 years; the current death rate is only 6%-14%[1,15].

However, the optimum duration of antibiotic treatment is still a matter of debate. The current treatment protocols are all based on clinical experience, and there is no medical evidence to validate these protocols. Two representative treatment procedures have been suggested: (1) administration of antibiotics alone, for at least 6 wk; after successful percutaneous drainage, antibiotics are continued for another 7 d until all the symptoms disappear[2,3]; and (2) after complete percutaneous drainage, antibiotics are intravenously administered for at least 3 wk, which is followed by oral administration for 1 or 2 mo to prevent recurrence[4]. Furthermore, a study in the United States recommended prolonged antibiotic treatment in the cases of liver abscess[4]. Therefore, antibiotic treatment for liver abscess is considered to be a prolonged procedure. The referred endpoint indicators are non-specific. There are no exact markers to determine the endpoint of antibiotic treatment for liver abscess.

In China, there is no established guideline for the duration of antibiotic treatment after percutaneous drainage. In 45 diabetic patients with pyogenic liver abscess, treatment was not stopped after normalization of body temperature and physical condition; instead, the treatment was continued for 12 wk even after recovery from the abscess[16]. Another study reported that combined use of antibiotic treatment and percutaneous drainage for 4-6 wk was an extremely effective approach[17]. However, the appropriate treatment procedures and the endpoint of antibiotic treatment recommended in these studies required further investigations.

In recent years, Rahimian *et al*[18] reported that antibiotic treatment for liver abscess should not be prolonged. They also reported that short-term antibiotic treatment did not increase the death rate. They had treated 73 patients with liver abscess with intravenous antibiotic administration for 17.5 d, and the associated death rate was 2.5%. However, they did not mention the process of determination of the endpoint of antibiotic treatment. In 2009, the continuing education website of John Hopkins University reported that that after effective percutaneous drainage, the duration of the antibiotic treatment should be determined on the basis of the normalization of the white blood cell count and body temperature, and the treatment should be continued for 14-42 d[5] (unpublished data).

The total white blood cell count and the percentage of neutrophils have been used as standard indicators for the detection of infection, since the measurement methods for these parameters are simple, cheap, and of great clinical utility. These indicators are widely employed in most hospitals, especially in general hospitals. However, the use of the white blood cell count and the percentage of neutrophils as the endpoint of the treatment do not completely reflect the clinical condition. White blood cell count can vary due to various pathological conditions, and they may be influenced by physiological and various other factors such as postprandial intense exercise, cold temperature, pain, and fear. In a retrospective study in China, among 28 patients with thoracic abscess, 4 had normal white blood cell count and significantly elevated

CRP levels[19]. This finding indicates that some patients, especially some elderly patients had lower response to infection. Moreover, among children with lower respiratory system infection, there is no significant difference between the white blood cell counts of patients with pyogenic infection and those with virus infection[20]. Elevated white blood cell count has been traditionally considered as a diagnostic criterion even for patients with appendicitis; however, a prospective study indicated that the sensitivity and specificity of the elevated white blood cell count for diagnosing appendicitis were only 76% and 52%, respectively. The receiver operating characteristic (ROC) curve also indicated that elevated white blood cell count was not clinically relevant for diagnosing appendicitis[7]. ROC curve, is a graphical plot of the sensitivity, or true positives, or false positives, also known as a relative operating characteristic curve, because it is a comparison of two operating characteristics as the criterion changes. So ROC analysis provides tools to select possibly optimal models and to discard suboptimal ones independently. In our data, the white blood cell count and the percentage of neutrophils of some patients were normal even in the initial stage of the disease or before percutaneous drainage. Therefore, white blood cell count did not completely reflect their condition; consequently, it cannot be used as a criterion for medication.

After the onset of inflammation, CRP synthesis increases within 4-6 h, doubling every 8 h. The CRP level reaches the peak value (around 150-350 mg/L) within 36-50 h after infection. The high levels persist through the inflammation period. Therefore, when the infection is controlled, the CRP levels decrease quickly, and the decrease is strongly correlated with the relief from symptoms and with the duration of the treatment. However, the CRP level is not affected by factors such as gender, age, anemia, hyperglobulinemia, and pregnancy[21]. Clinically, the CRP levels have been used to determine whether antibiotic treatment should be started and to judge the effectiveness of the antibiotics. However, very few studies have considered the CRP value as a criterion for determining the endpoint of antibiotic treatment. In 1995, a report suggested that when both CRP and white blood cell counts are normal, antibiotic treatment for the abscess should be discontinued. The accuracy of using CRP values for the assessment of the abscess was as high as 99%, and there were no reports of negative results from the blood culture[9]. However, there have been no further studies on these findings. We realized that CRP value could be considered as an endpoint criterion for liver abscess treatment. In our data, the duration of the shortest treatment was only 11 d, the longest treatment period was not more than 4 wk, and the recurrence rate had not increased.

In summary, the CRP level could be used as an independent factor for determining the duration of the antibiotic treatment in the management of pyogenic liver abscess after complete percutaneous abscess drainage. It can be widely used in clinics. However, for further evaluation of the viability of CRP assessments, studies using more samples and random control trials should be performed.

COMMENTS

Background

Complete percutaneous drainage combined with antibiotics has significantly reduced the death rate associated with pyogenic liver abscess. However, the duration and the protocol for the antibiotic treatment after percutaneous drainage is a matter of debate in those patients. The referred endpoint indicators are non-specific. There are no exact markers to determine the endpoint of antibiotic treatment for liver abscess.

Research frontiers

Antibiotic treatment for liver abscess was considered to be a prolonged procedure. In recent years, it has been reported that antibiotic therapy for treating liver abscess should not be prolonged as short-term antibiotic treatment did not increase the death rate of the patients. However, the process of determination of the endpoint of antibiotic treatment was not mentioned. In 2009, the continuing education website of John Hopkins University reported that that after effective percutaneous drainage, the duration of the antibiotic treatment should be determined on the basis of the normalization of the white blood cell count and body temperature of the patients.

Innovations and breakthroughs

There are no exact markers to determine the endpoint of antibiotic treatment for pyogenic liver abscess at present. C-reactive protein (CRP) is considered as a useful marker to determine the usage of antibiotics and assess the efficacy of the antibiotic. However, there is no clinical report on the validity of using CRP values to determine the endpoint of liver abscess therapy. The authors proposed that the CRP value can be considered as an independent factor to determine the duration of the antibiotic treatment for pyogenic liver abscess after complete percutaneous drainage. In this study, normal CRP values were considered as the endpoint of antibiotic treatment.

Applications

Using CRP value as the endpoint of antibiotic treatment can decrease the duration of antibiotic treatment, thus decreasing the incidence of antibiotic-resistant bacteria, reducing medical expenses, and increasing patient compliance.

Terminology

CRP is an acute-phase protein that is synthesized by liver endothelial cells, which is considered as the most valuable indicator of inflammation. Percutaneous abscess drainage is a procedure performed to remove or drain a contained collection of infected fluid (abscess) from an area of the body such as the chest, abdomen, or pelvis.

Peer review

This manuscript is about a retrospective study to investigate the possibility of using CRP to determine the endpoint of antibiotic treatment along with percutaneous drainage for pyogenic liver abscess patients, and the data indicate that CRP value can be considered as an independent factor to determine the duration of the combination of antibiotic administration and percutaneous drainage. The manuscript is innovative and of putative interest for the readers.

REFERENCES

1 **Yu SC**, Ho SS, Lau WY, Yeung DT, Yuen EH, Lee PS, Metreweli C. Treatment of pyogenic liver abscess: prospective randomized comparison of catheter drainage and needle aspiration. *Hepatology* 2004; **39**: 932-938

2 **Gyorffy EJ**, Frey CF, Silva J Jr, McGahan J. Pyogenic liver abscess. Diagnostic and therapeutic strategies. *Ann Surg* 1987; **206**: 699-705

3 **Perera MR**, Kirk A, Noone P. Presentation, diagnosis and management of liver abscess. *Lancet* 1980; **2**: 629-632

4 **Wang JH**, Liu YC, Lee SS, Yen MY, Chen YS, Wang JH, Wann SR, Lin HH. Primary liver abscess due to Klebsiella pneumoniae in Taiwan. *Clin Infect Dis* 1998; **26**: 1434-1438

5 **Carpenter CF**, Swami A. Hepatic Abscess. Available from: URL: http://prod.hopkins-abxguide.org/diagnosis/surgical_infections/hepatic_abscess.html?contentInstanceId=255357

6 **Seeto RK**, Rockey DC. Pyogenic liver abscess. Changes in etiology, management, and outcome. *Medicine* (Baltimore) 1996; **75**: 99-113

7 **Cardall T**, Glasser J, Guss DA. Clinical value of the total white blood cell count and temperature in the evaluation of patients with suspected appendicitis. *Acad Emerg Med* 2004; **11**: 1021-1027

8 **Bjerrum L**, Gahrn-Hansen B, Munck AP. C-reactive protein measurement in general practice may lead to lower antibiotic prescribing for sinusitis. *Br J Gen Pract* 2004; **54**: 659-662

9 **Berger C**, Uehlinger J, Ghelfi D, Blau N, Fanconi S. Comparison of C-reactive protein and white blood cell count with differential in neonates at risk for septicaemia. *Eur J Pediatr* 1995; **154**: 138-144

10 **Khan MH**, Smith PN, Rao N, Donaldson WF. Serum C-reactive protein levels correlate with clinical response in patients treated with antibiotics for wound infections after spinal surgery. *Spine J* 2006; **6**: 311-315

11 **Melbye H**, Bjørkheim MK, Leinan T. Daily reduction in C-reactive protein values, symptoms, signs and temperature in group-A streptococcal pharyngitis treated with antibiotics. *Scand J Clin Lab Invest* 2002; **62**: 521-525

12 **Jepsen P**, Vilstrup H, Schønheyder HC, Sørensen HT. A nationwide study of the incidence and 30-day mortality rate of pyogenic liver abscess in Denmark, 1977-2002. *Aliment Pharmacol Ther* 2005; **21**: 1185-1188

13 **Tsai FC**, Huang YT, Chang LY, Wang JT. Pyogenic liver abscess as endemic disease, Taiwan. *Emerg Infect Dis* 2008; **14**: 1592-1600

14 **Hope WW**, Vrochides DV, Newcomb WL, Mayo-Smith WW, Iannitti DA. Optimal treatment of hepatic abscess. *Am Surg* 2008; **74**: 178-182

15 **Chan KS**, Chen CM, Cheng KC, Hou CC, Lin HJ, Yu WL. Pyogenic liver abscess: a retrospective analysis of 107 patients during a 3-year period. *Jpn J Infect Dis* 2005; **58**: 366-368

16 **Kong LB**, Wang XH, Qian JM, Zhang F. Diabetes mellitus with bacteriogenic liver abscesses: clinical analysis of 45 cases. *Zhongguo Shiyong Waike Zazhi* 2002; **22**: 414-415

17 **Liu J**, Yu N, Wan JH. Cefminox used to treat bacterial liver abscess:its clinical efficacy. *Zhonghua Yiyuan Ganranxue Zazhi* 2006; **16**: 1408-1409

18 **Rahimian J**, Wilson T, Oram V, Holzman RS. Pyogenic liver abscess: recent trends in etiology and mortality. *Clin Infect Dis* 2004; **39**: 1654-1659

19 **Chen YN**, Qin HM, Wan N, Liu S, Wang L. Clinical value of C-reactive protein, erythrocyte sedimentation rate and white blood cell count in patients with empyema. *Shiyong Yiji Zazhi* 2004; **11**: 726-727

20 **Prat C**, Domínguez J, Rodrigo C, Giménez M, Azuara M, Jiménez O, Galí N, Ausina V. Procalcitonin, C-reactive protein and leukocyte count in children with lower respiratory tract infection. *Pediatr Infect Dis J* 2003; **22**: 963-968

21 **Jaye DL**, Waites KB. Clinical applications of C-reactive protein in pediatrics. *Pediatr Infect Dis J* 1997; **16**: 735-746; quiz 746-747

S- Editor Wang YR **L- Editor** Ma JY **E- Editor** Lin YP