Biomedical Research 2017; 28 (22): 10043-10047 *ISSN 0970-938X*
www.biomedres.info

Survey of chronic hepatitis B of community and early liver cancer screening for these specific population in follow-up.

Jin-long Ma[1*], Fan Yang[2]

[1]Department of Hygiene Monitor, Xi'an Center for Disease Control and Prevention, Xi'an 710054, Shanxi Province, PR China

[2]Department of Infectious Disease Control and Prevention, Xi'an Center for Disease Control and Prevention, Xi'an 710054, Shanxi Province, PR China

Abstract

Objective: To explore the establishment, follow-up and early intervention effect of community-based specific population of chronic hepatitis B (CHB) and to provide references for the prevention and treatment of early liver cancer.

Methods: Residents of a total of 12 communities in our city, 39603 cases were screened to analyze the incidence and epidemiological characteristics of CHB. A specific population of CHB was selected for the study and a specific population was set up. The specific population was followed up and the related indexes were detected, to observe the prognosis of liver disease and the incidence of the situation.

Results: Totally 39603 cases were screened and 1495 patients with CHB were enrolled in the specific population. In the first follow-up, 1362 cases were included, the B ultrasound displayed abnormalities in 401 cases, the detection rate of liver cancer was 0.51%. In the second screening, there were 309 cases of ALT abnormality, the AFP positive was found in 34 cases, the abnormalities of B ultrasound were in 432 cases, the detection rate of liver cancer was 2.41%. In the third screening, the ALT abnormality are 357 cases, the AFP positive was found in 41 cases, the abnormalities of B ultrasound were in 466 cases, the detection rate of liver cancer was 2.71%.

Conclusion: It is possible to improve the early detection rate of early liver cancer by establishing a specific population of CHB in the community and carrying out the follow-up, which can provide references for the screening and the secondary prevention of early liver cancer.

Keywords: Chronic hepatitis B, Community, Early liver cancer, Screening.

Accepted on October 24, 2017

Introduction

Chronic hepatitis B (CHB) is a worldwide public health problem, and China is one of the areas with high incidence of CHB. With the long-term implementation of control measures for hepatitis B, new patients showed a downward trend [1]. The World Health Organization reported that about 2 billion people worldwide infected with hepatitis B virus, of which about 300 million people as chronic hepatitis B virus carriers. In China, there are about 100 million hepatitis B virus carriers, accounting for about 7%, and the incidence of CHB is about 2%. Different regions have different situations, and each year 2% to 3% of patients with hepatitis B are processing to cancer [2,3]. Hepatocellular carcinoma is a common clinical malignant tumor of digestive system, taking the second place in China's cancer mortality. There is a variety of factors to induce it, such as viral infections, cirrhosis, alcohol, chemical carcinogens, drinking water pollution and genetic. Hepatitis B virus infection is one of the main incentives [4,5]. CHB is easy to progress to cirrhosis, and thus lead to the formation of liver cancer, hepatitis B cirrhosis-related liver cancer accounted for a higher proportion of liver cancer. Once the liver cancer is discovered, which most of the cases already have entered the late stage, so improvement the early diagnosis of liver cancer is particularly important [6,7]. In the 1980s, China began to pay attention to the regular screening of liver cancer and its effect evaluation study, the results showed that screening can reduce the mortality of patients with liver cancer and extend its survival. The main content of the secondary prevention (early detection, early diagnosis and early treatment) in the implementation of screening for CHB patients is a key link to improve the prognosis of patients with liver cancer and reduce the mortality of liver cancer [8,9]. In this study, we established a community-specific population of CHB and conducted regular screening follow-up. The results were analyzed as follows.

Materials and Methods

Inclusion and exclusion criteria

The objects were 39603 residents from 12 communities in our city from July 2015 to December 2016. After screening, the average age of patients diagnosed with CHB was 40.92 ± 9.63 years old, and the course of disease was 7 months to 16 years. Inclusion criteria : 1) patients with previous history of hepatitis B or HBsAg positive>6 months, remained positive HBsAg or HBVDNA [10]; 2) patients with informed consent, willing to follow the observation, age ≥ 20 years old; 3) with or without fear, fatigue, abdominal distension, nausea and liver pain and other chronic hepatitis manifestations. Exclusion criteria: 1) severe liver cirrhosis, chemical liver injury, other types of viral hepatitis patients; 2) patients has developed to be typical cirrhosis or liver cancer; 3) combined with psychosis, severe underlying diseases.

Cohort establishment method

According to the multi-stage stratification random sampling principle, the survey population was determined from the 12 communities. Before the implementation, the community doctors accepted relevant training for on-site work of the community supervision and inspection and extraction of some respondents to review. Through the releasing of health leaflets about hepatitis B and liver cancer and provision of free medical examinations, residents can actively participate in this study. The respondents informed consent, and take part in the research voluntarily. The participant data was recorded into the excel table, blood samples was taken, which was used for the establishment of community population chronic of hepatitis B. They were followed up every six months. Through the telephone, WeChat and e-mail, etc. These communities of specific population of CHB were informed of the time and place of review, patients lost to follow-up caused by migration, out and other reasons was controlled in the effective range, and the lost rate was no more than 10%, to improve the follow-up compliance.

Screening methods and indicators

The screening indicators included two pairs of hepatitis B and liver function (Toshiba TBA-40FR Automatic biochemical analyzer, Japan), alpha fetal protein (Beckman Coulter UniCel DxI800, America) and liver B-ultrasonography. 4 ml venous blood of the subject was extracted for blood biochemical examination. The blood specimens were marked and the data registration form was registered. B-ultrasound check and analysis for the subjects was performed by the hospital or cooperative community hospital ultrasound imaging physician.

Follow-up tracking and evaluation methods

The follow-up information was recorded and the incidence and death of liver cancer were recorded, reduce the omission and misappropriation, and the subjects would interviewed at any time and the situations of patients who were diagnosed with hepatocellular carcinoma were followed. Standardized incidence ratios (SIR) of specific CHB-specific population in the community: take the incidence of annual cancer in China's hepatitis B population as a standard, and 2.5% was used to estimate the number of theoretical liver cancer yearly CHB specific population of this study in this study, which is the expected number of patients. Based on the formula SIR=actual incident number/expected incident number to calculate the SIR of annual hepatocellular carcinoma in community-specific CHB population.

Statistical method

The data were analyzed by SPSS19.0, the counting data was presented as percentage (%). χ^2 test was used for the statistical difference, $P<0.05$ means differences were statistically significant.

Results

Establishment results of community CHB specific population

In 39603 community residents, 1495 cases have CHB patients, and the prevalence of hepatitis B was 3.64%, including 1135 male and 360 female, the difference was statistically significant ($P<0.05$); The proportions of people in different age were 34.11% (510/1495) for the 40 to 49-year-old population, 26.49% for the 50 to 59-year-old population (396/1495), 24.95% for the 30 to 39-year-old population (373/1495), 10.84% for the over 60 years old population (162/1495), 20-29 years old population of 3.61% (54/1495); 40 to 49 years old and 50 to 59 years old group were high-incidence groups, 20 to 29 years old was the low population. In male population, 40 to 49 years old is the high-risk group, while in female population, 30 to 39 years old is high-risk group (Table 1).

Table 1. *Gender distribution of patients of CHB specific population in different age groups (n, %).*

Age	Cases	Male (1135)	Female (360)	χ^2	P
20~29 years old	54	50 (4.41)	4 (1.11)	8.52	0.00
30~39 years old	373	242 (21.32)	131 (36.39)	33.14	<0.001
40~49 years old	510	418 (36.83)	92 (25.56)	15.45	<0.001
50~59 years old	396	320 (28.19)	76 (21.11)	7.04	0.01
60 years old~	162	105 (9.25)	57 (1.94)	12.26	<0.001
Total	1495	1135 (75.92)	360 (24.08)	803.51	<0.001

Results of first screening follow-up

In the 1495 cases of CHB specific population, 1362 cases participated in the follow-up, including 1005 male and 357 female, total compliance rate was up to 91.15%. In male patients, there were 203 cases (20.20%) of ALT abnormalities, 22 cases of AFP positive (2.28%), and 326 of B-

ultrasonography abnormality (32.44%), while in female, 56 cases of abnormal ALT (15.69%), 4 cases of AFP (1.12%), 75 cases of B-ultrasonography abnormality (21.00%). 10 cases of patients were HBsAg negative, 5 cases of HBcAb negative, 3 cases of liver cirrhosis, 5 cases of hepatic fibrosis and 7 cases of early liver cancer, liver cancer detection rate was 0.51%. AFP positive difference in male and female showed not statistically significance (P>0.05), but there is significant difference in ALT abnormality and B-abnormal abnormality rate between male and female (P<0.05) (Table 2).

Table 2. Results of first screening follow-up (n/%).

Age	Cases	Male (1005)	Female (357)	χ^2	P
ALT abnormality	260	203 (20.20)	56 (15.69)	3.48	0.06
AFP positive	26	22 (2.20)	4 (1.12)	1.606	0.21
B-ultrasonography abnormality	401	326 (32.44)	75 (21.00)	16.57	<0.001

Results of second screening follow-up

In the 1495 cases of CHB specific population, 1413 patients participated in the review including 1042 male and 371 female, and the total compliance rate was 94.51%. In male patients, there were 251 cases (24.09%) of ALT abnormality, 29 cases of AFP positive (2.78%), and 346 of B-ultrasonography abnormality (33.20%), while in female, 58 cases of abnormal ALT (15.63%), 6 cases of AFP (1.35%), 86 cases of B-ultrasonography abnormality (23.18%). 16 cases of patients were HBsAg negative, 6 cases of HBcAb negative, 6 cases of liver cirrhosis, 6 cases of hepatic fibrosis and 34 cases of early liver cancer, liver cancer detection rate was 2.41%. AFP positive difference in male and female was not statistically significant (P>0.05), but there is significant difference in ALT abnormality and B-abnormal abnormality rate between male and female (P<0.05) (Table 3).

Table 3. Results of second screening follow-up (n/%).

Age	cases	Male (1089)	Female (374)	χ^2	P
ALT abnormality	309	251 (24.09%)	58 (15.63%)	11.45	0.00
AFP positive	34	29 (2.78%)	5 (1.35%)	2.40	0.12
B-ultrasonography abnormality	432	346 (33.20%)	86 (23.18%)	12.95	<0.001

Results of third screening follow-up

In the 1495 cases of CHB specific population, 1463 patients participated in the review including 1089 male and 374 female, and the total compliance rate was 97.86%. In male patients, there were 297 cases (27.27%) of ALT abnormality, 35 cases of AFP positive (3.21%), and 367 of B-ultrasonography abnormality (33.70%), while in female, 60 cases of abnormal ALT (16.04%), 6 cases of AFP (1.60%), 96 cases of B-ultrasonography abnormality (25.67%). 18 cases of patients were HBsAg negative, 7 cases of HBcAb negative, 9 cases of liver cirrhosis, 7 cases of hepatic fibrosis and 39 cases of early liver cancer, liver cancer detection rate was 2.67%. AFP positive difference in male and female was not statistically significant (P>0.05), but difference in ALT abnormality and B-abnormal abnormality rate showed statistical significance between male and female (P<0.05) (Table 4).

Table 4. Results of third screening follow-up (n/%).

Age	cases	Male (1089)	Female (374)	χ^2	P
ALT abnormality	357	297 (27.27)	60 (16.04)	19.03	<0.001
AFP positive	41	35 (3.21)	6 (1.60)	2.65	0. 10
B-ultrasonography abnormality	466	374 (34.34)	92 (24.60)	12.18	<0.001

The results of liver cancer detection in follow-up

Through screening a specific population 3 times a year, the actual number of newly diagnosed hepatocellular carcinoma was 39 in 1495 community CHB specific population, and the annual incidence rate was 2.71%. The annual SIR was 1.07, that is the community of CHB specific population of liver cancer risk for the general hepatitis B population of 1.07 times in this study.

Discussion

China is the one of the countries with highest incidence of liver cancer and the highest number of deaths. The global cancer report shows that new cancer cases and the number of deaths in China is the first place in the world. In recent years the incidence of liver cancer in China is about 26.39/100 thousand [11]. The infection rate of hepatitis B in China is up to 7%, about 1 person per 14 person is a hepatitis B virus carrier. Approximately 90% of liver cancer is closely related to hepatitis B, and the cancer risk of hepatitis B is 100 to 150 times than the ordinary people, which is significantly higher in men than that in women [12]. Liver cancer has the characteristics of concealment, rapid progress, high degree of malignancy and high recurrence rate [13,14]. The prognosis of liver cancer is poor, if not treated, usually the survival of patients is shorter. Once the symptoms of liver cancer occurred, it often has been advanced, therefore early diagnosis and timely treatment is the key to extend the survival time of patients. The current diagnosis rate of liver cancer is still low [15,16]. Most clinicians attach more importance to the treatment of patients who already with hepatocellular carcinoma, and have less attention to early detection and early intervention of liver cancer. Therefore, it is necessary to establish a prospective study of high risk population of liver cancer.

In this study, 1495 prospective patients with CHB were enrolled in a survey of 39603 residents in 12 communities. The screening results were analyzed by three follow-ups in a year.

In order to reduce the impact of bias, most of the data in the study were analyzed by general descriptive analysis. The research group provided services such as training and technical consultation to the participating community medical personnel, and regularly supervised and examined the screening work. In the course of the study, the community of CHB specific population were supported by related knowledge and medical counseling and other services to improve their health consciousness, and actively cooperate with the screening and follow-up. A few young people went out to school and work, so the response rate of these people was relatively low. The compliance of other people was higher, the total compliance rates of the three follow-ups were 91.15%, 94.51% and 97.86% respectively, which controlled the bias of loss to follow-up within the effective range to improve the quality of the study.

This study was completed in three phases, the first stage is to carry out the initial screening: the examination of HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb and liver function for the community population; the second phase is to establish a specific population, propose the screening concept for the specific population for liver cancer, and the population with CHB were included in the study; the third stage is to establish the screening model and to track: the community of CHB specific population were treated with periodic screening (every four month), and evaluate and analyze the early screened indicators, including HBsAg, HBcAb and AFP of the positive situation, liver function and B ultrasound, especially for the patients with clinical manifestations of fear, fatigue, abdominal distension, nausea and liver pain, and give active treatment and follow-up to patients diagnosed as liver cancer.

The results of this study show that in 39603 residents of communities, 1495 cases have CHB, and the hepatitis B prevalence rate is 3.64%, higher than the low-incidence areas in China and lower than the high-incidence areas, which was similar to the national average hepatitis B situation in general [17]. The reasons may be that the population were sampled mostly from the area with higher economic level by multi-stage stratification method. With the acceleration of urbanization in our country, the rural population in the community has increased, their low health consciousness and the crowded living environment resulted in difficult management of hepatitis B, so the risk of transmission is higher, and the incidence is higher with it [18,19]. The results of cohort establishment indicated that male patients with CHB were significantly more than female, and middle-aged population had high incidence, the three screening follow-up results showed that male abnormalities of ALT and B-ultrasound were significantly higher than female [(χ^2=19.03, P<0.001), (χ^2=12.18, P<0.001)], which may be related to the male population, especially middle age, had not pay attention to food hygiene, long-term to stay up late, work pressure, frequent entertainment and other factors. The specific reasons require further investigation and study.

Alpha-fetoprotein (AFP) is considered to be a diagnostic marker of liver cancer with good accuracy and economy, which is beneficial to community use and promotion [20]. In the technical options of this study, on the premise that ensuring the screening technology with high sensitivity, B-ultrasound was considered more appropriate community, so five indexes of hepatitis B, liver function, AFP qualitative and liver B-ultrasound screening were employed to enhance testing quality management. When the test results are doubtful or relatively special, the timely re-examination and guidance from the professionals on the entire process ensured the effectiveness and scientific of this study should be taken. Relevant research results show that the incidence of liver cancer in China in recent years had been 26.39/100 thousand [11], the results of this study suggested that liver cancer incidence of 1495 cases of community-specific hepatitis B specific population was 39 cases, the detection incidence was 2.67%, the annual SIR was 1.07, and the tracking follow-up of specific population improved the detection rate of early liver cancer to a certain extent. But the time of follow-up may be a disadvantage. We will improve it in the future study.

In summary, this study based on the principle of people-oriented respected and protected the privacy of the population, eliminated the ideological concerns of the population, thereby improved the early detection rate of liver cancer, 5-year survival rate of liver cancer patients and quality of life, to reduce mortality and increased the role of secondary prevention (early detection, early diagnosis, early treatment) of liver cancer, which has a certain social benefits and provides referential basis for early screening and intervention of hepatitis B-related liver cancer patients in other areas.

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***Correspondence to**

Jin-long Ma

Department of Hygiene Monitor

Xi'an Center for Disease Control and Prevention

PR China