



Liver Biopsy Experience

Karaciğer Biyopsisi Deneyimi

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ABSTRACT

Objective: To investigate the frequency of complications and insufficient material rates of liver biopsies and association with experience in liver biopsies that made for diagnosis of chronic viral hepatitis.

Materials and Methods: We retrospectively reviewed our four years liver biopsy experience between 2008-2011. The records of patients were investigated retrospectively. In our clinic, the number of doctors perform a liver biopsy and doctors with experience were recorded. Tabulation was performed and student's t-test and X2 test was used for statistical method. P<0.05 was considered statistically significant.

Results: Data of 305 liver biopsy has been reached in the study period. Biopsy-related complication rate was found 3.1% (serious complication 0.3%, non-serious complication 2.8%). Receiving rate of insufficient material was decreased with experience and was found to be 25%, 17%, 8%, 5.4% in 2008-2011, respectively (p<0.05). The rate of insufficient material by increased experience, in 2011 dropped to 5.4%. Of all the cases called for biopsy, it was detected that 33 cases (9.7%) refused liver biopsy.

Conclusion: Cory liver biopsy complication rate is low and can be safely applied to patients for the diagnosis of chronic hepatitis. Receiving rate insufficient material and development of complications related to experience of who perform the biopsy. This negativity can be reduced by increased experience. (*Viral Hepatitis Journal* 2012; 18(3): 115-9)

Key words: Percutaneous liver biopsy, tru-cut biopsy, complications, experience

ÖZET

Amaç: Kronik viral hepatit tanısı amacıyla yapılan karaciğer biyopsilerinde, komplikasyon ve yetersiz materyal alma nedenleri ve sıklığını ve deneyimle ilişkisini araştırmak amaçlanmıştır.

Gereç ve Yöntemler: 2008-2011 yılları arasındaki dört yıllık dönemde karaciğer biyopsi deneyimlerimizi retrospektif olarak değerlendirdik. Hastalarımıza ait kayıtlar retrospektif olarak araştırıldı. Kliniğimizde yıllara göre karaciğer biyopsisi yapan hekim ile hekimlerin yıllara göre tecrübe oranları kaydedildi. Veriler tabule edilerek student's t-test ve χ^2 testi ile değerlendirildi. P<0,05 anlamlı kabul edildi.

Bulgular: Çalışma döneminde 305 karaciğer biyopsi verisine ulaşıldı. Biyopsiye bağlı komplikasyon oranı %3,1 idi (ciddi komplikasyon %0,3, ciddi olmayan komplikasyon %2,8). Yetersiz materyal alma oranı deneyimle azaldı. Yetersiz materyal alma oranı 2008 ile 2011 arasında sırasıyla %25, %17, %8, %5,4 idi (p<0,05). Artan tecrübe ile yetersiz materyal alma oranımız 2011 yılında %5,4'a düştü. Çalışmada biyopsi randevusu verilenlerin 33 (%9,7)'ünün biyopsiyi reddettiği saptandı.

Sonuç: Kör yapılan karaciğer biyopsisinin komplikasyon oranı düşüktür ve kronik hepatit tanısı için hastalara güvenle uygulanabilir. Biyopside materyal yetersizliği ve komplikasyon riski, işlemi uygulayan personelin tecrübesiyle ilişkilidir. Artan tecrübeyle bu olumsuzluk azaltılabilir. (*Viral Hepatit Dergisi* 2012; 18(3): 115-9)

Anahtar Kelimeler: Perkutan karaciğer biyopsisi, tru cut biyopsi, komplikasyonlar, deneyim

Introduction

Percutaneous liver biopsy has been used for years(1). The first percutaneous liver biopsy was performed in 1883. Today, liver biopsy is needed mostly in the diagnosis of chronic liver diseases, determination of treatment indications and assesment of treatment responses at histopathological level. Also, it is necessary for unexplained liver function abnormalities, space occupying lesions in the liver and the involvement of the liver in systemic diseases (2). Liver biopsy is the gold standard for staging fibrosis. Inflammation, necrosis, steatosis, hepatic iron and other parameters can be determined by liver biopsy (3).

There are several methods used to obtain liver tissue (4). These are percutan, transjugular, laparoscopic and plugged biopsies. Percutaneous fine-needle biopsy of the liver (PFNB) is a simple method. Needles used for PFNB were classified in three groups.; a) Suction needles (Menghini-type needle, Klatskin-type needle, Jamshid-type needle type) b) Cutting needles (Vim-Silverman needle, Tru-Cut needle) c) Spring-loaded cutting needles that have triggering mechanisms. Each of them has some advantages and disadvantages. Meaningful difference was not detected among the needles in terms of obtaining appropriate specimens. In diffuse liver lesions except fibrosis, diagnostic success is largely independent of the used needle.

Diagnosis of liver cirrhosis with tru-cut needle is easier, because fibrotic liver tissue can be destroyed with vacuum-type needles (5). Hopper et al.(6) detected in their experimental animal study that the success of obtaining the specimen and the specimen quality were more satisfying with automatic tru-cut needles compared with vacuum-type needles. De Man et al. (7) described that longer specimens were obtained with automated needles compared with manual needles. Although liver is rich in vascular structures, liver biopsy-related complications are rare. 60 % of complications are seen in the first two hours after the procedure, 96% may be seen within one day. Hospitalization due to complications, especially with tru-cut needles was required in 1-3 % of the patients.

The most frequent complications in hospitalized patients were pain and hypotension due to vasovagal reflex(4)

We aimed to investigate complication rates of our liver biopsies and insufficient materials in association with biopsy experience.

Material and Methods

The data of this study were obtained by the retrospective analysis of liver biopsies performed in Sakarya Education and Research Hospital at the Department of Infectious Diseases and Clinical Microbiology between 2008-2011.

In 2008, Sakarya State Hospital was transformed into education and research hospital. The specialist doctors (N.T., A.O., M.Y.) at the hospital did not experience a liver biopsy. On the second half of 2008, professor with experience in a liver biopsy (O.K.) began to work in hospital and to teach liver biopsy. Four specialist doctors, three young fellows and a professor doctor performed liver biopsy at this centre and 10% of liver biopsy has performed by young fellows in the study. In our clinic, young fellow doctors began to study in 2010.

Biopsy method: Percutaneous liver biopsy was performed to Chronic Hepatitis B and Chronic Hepatitis C patients with tru-cut biopsy method. 16-18 G semi-automatic tru-cut biopsy gun (ASCUT, Grand Theft Auto Medical Product and Service, in Italy) was used in the biopsies.

Pre-biopsy Testing

Before the biopsy; patients were investigated for chronic hepatitis B and C. HBsAg, HBeAg, anti-HBe, anti HCV, HBV-DNA, HCV RNA, ALT, AST, complete blood count, prothrombin time, bleeding-clotting time and the entire abdominal ultrasonography were performed.

Biopsy was not performed to patients who carry contraindication (prolonged prothrombin time, hemangioma, infection in that area and mass in the right lobe). Before the biopsy, all patients were informed about the procedure and written consents were received.

Localization of patient's liver was determined in the supine position by percussion. Dullness area was marked at the intersection of midclavicular line and intercostal space. Firstly, skin antisepsis with povidone-iodine was applied to the region. Secondly, local anesthesia with 2cc.lidocaine was applied to biopsy region. Then, we said the patients to expire deeply and hold their breath. Biopsy specimens were obtained with disposable 16-18G tru-cut needles. Obtained specimens were sent to pathology laboratory in formalin.

Complete blood count (CBC) was performed for bleeding disorders before the biopsy (trombocytopenia, idiopathic

Table 1. Complications and insufficient specimens by years

Years	n	The number of doctors applying biopsy procedure /The number of doctors with experience n/n (%)	The number of inadequate specimen n (%)	p value	Complication n (%)	p value	The number of patients who did not come to appointment n (%)
2008	8	3/1 (33.3)	2 (25)	<0.026	0 (0)	>0.05	3 (37.5)
2009	94	3/1 (33.3)	16 (17)		3 (3,1)		13 (12.1)
2010	112	4/4 (100)	9 (8)		2 (1,7)		7 (5.9)
2011	91	7/4 (57.1)	5 (5.4)		5 (5.4)		10 (9.9)

Table 2. Distribution of complication

Patient number	Age/ /gender	Reason of biopsy	Time complication was detected	Date	Complication	Conclusion
1	50/F	CHC	>2 days	2011	Hematoma in liver	She was observed for three days, followed by ultrasonography. When the size began to reduce was seen, she was discharged.
2	38/M	CHB	< 2 hours	2011	Subcutaneous hematoma	No intervention was done. It was resorbed spontaneously.
3	60/M	CHC	>2 days	2011	Liver abscess/Pain shock	Antibiotic treatment was started. The abscess was drained.
4	45/M	CHB	< 2 hours	2010	Hypertension/Pain shock	Followed in intensive care unit. Blood pressure regulation was arranged. Pain was managed with opioid analgesics.
5	40/M	CHB	< 2 hours	2011	Panic disorder	Sudden sencop experienced. He came to himself after 2-3 minutes.
6	27/M	CHC	< 2 hours	2009	Pain shock	Anesthesiologist consulted. Pain was managed with opioid analgesics.
7	21/M	CHB	< 2 hours	2009	Pain shock	Anesthesiologist consulted. Pain was managed with opioid analgesics.
8	34/M	CHB	< 2 hours	2009	Pain shock	Anesthesiologist consulted. Pain was managed with opioid analgesics.
9	45/F	CHB	< 2 hours	2010	Pain shock	Anesthesiologist consulted. Pain was managed with opioid analgesics.
10	60/F	CHC	< 2 hours	2011	Allergic reaction	Given the very low amount of the local anesthetic agent, allergic reaction was observed. Biopsy was canceled.

trombocytopenic purpura etc) and CBC was also obtained to check of bleeding complication after the biopsy (8).

Insufficient material criteria: If a biopsy specimen includes less than four portal spaces, it is accepted as insufficient material. For the statistical tests, student's t-test, χ^2 test was used and a p value of less than 0.05 was accepted significant.

Results

Between 2008-2011, 338 patients were called for liver biopsy. But a total of 33 patients (9.7%) denied liver biopsy. As a result, liver needle biopsy was done to 305 patients. Of the patients, 185 were (60.6%) male and 120 (39.4%) were female. Liver biopsy was performed to 256 (84%) chronic hepatitis B(CHB) patients and 49 (16%) chronic hepatitis C(CHC) patients.

Insufficient liver biopsy tissue was taken from 32 patients (10.5%). Inadequate specimen rates according to years were shown in Table 1. Insufficient specimen rate was 17% in 2009. However this rate decreased to 5.4% in 2011 (p=0.026).

There was no fatality as a consequence of our needle biopsy practices. Our complication rate was 3.2% (n=10). Serious complications such as massive bleeding, organ perforation and hemoperitoneum did not occur. The most important complication was liver abscess developed in one patient (0.3%). In this patient

ultrasonography showed fluid collection in the lower lobe of the liver. Antibiotic therapy was initiated (piperacillin /tazobactam 2.25 g 3x1). In the following days, the patient was followed by ultrasonography. On the seventh day, liver abscess was determined by magnetic resonance imaging. Ultrasound-guided abscess drainage was performed. The patient recovered completely and subsequently discharged.

The most common complication was excessive pain (1.9%). Pain was in the right upper quadrant in 5 patients (1.6%) and in the right lower quadrant in one patient (0.3%). Pleural and peritoneal irritation was suspected in these patients. Chest X-ray and abdominal ultrasonography were in normal limits. The pain did not response to non-steroidal anti-inflammatory analgesics. The pain was managed with opioid analgesics. These patients were subsequently discharged.

Serious bleeding was not observed in any patient. Minimal sized liver hematoma was detected in a patient by ultrasonography. In this patient, hemoglobin values remained normal. Hematoma resolved without the need of intervention. Hematoma was not detected in repeat ultrasonography. One patient developed a subcutaneous hematoma. Liver was normal in abdominal ultrasonography. Hemoglobin values did not decrease during follow-up. One patient was extremely worried and experienced a panic attack, despite no pain. Syncope was

observed in a short duration. Two patients required to be followed in intensive care unit. One of these patients suffered hypertensive episode due to pain shock. Although, this patient had no previous history of hypertension, blood pressures increased to 220/110 mmHg. After blood pressures were regulated, the patient recovered completely and subsequently discharged. Following the other patient in intensive care unit was due to pain shock and liver abscess. One patient developed allergic reaction to local anesthetic agent given before the biopsy. Given the very few amount of the local anesthetic agent, common hyperemia was observed in the skin and biopsy was canceled. Complications were seen in only two patients two days after biopsy. Remainder complications were seen in less than two hours after biopsy.

Discussion

Liver biopsy has an important role in determining the severity of chronic liver diseases (4). Liver tissue sampling with appropriate size is necessary for a valid pathological report. The number of portal spaces is important and 6-8 spaces in the specimen are usually sufficient. The number of the portal space is directly proportional to the size of the biopsy. Specimen of 1.5 cm is usually enough for the diagnosis of diffuse liver diseases (4). In our inpatient clinic, biopsy attempts were done to 305 patients and insufficient specimens were taken from 32 of them (10.4%). The main reason for the failure was attributed to lack of experience. Rate of getting insufficient material was 17% in 2009, however it was declined to 5.4% in 2011. These findings pointed that more experience is related with more successful biopsy.

Due to physical and mental discomfort, patients may refuse the biopsy and this can lead to delay in the diagnosis and treatment (9). Of all the patients in our study, 33 patients (9.7%) did not come to their appointment. This rate may be related with biopsy phobia. Some of the patients get worried about the biopsy procedure, live serious anxiety and run away from this procedure. The benefits, contraindications and potential risks of the biopsy should be told to patients in detail and a sense of confidence should be provided. In a similar study, including 1177 patients with chronic hepatitis C, it was reported that 59% of the patients refused the biopsy due to anxiety (10). The reason of this phobia may be either insufficient information or misinformation.

The most important disadvantages are being invasive and causing complications (11). Despite being invasive, liver biopsy is still a significant and a safe procedure with low complication rate. Informing patients about the complication rates and the results would prevent them from escaping the procedure. Patients should be informed in detail about the biopsy procedure for the prevention of insufficient information and misinformation.

There was no statistically significant difference in terms of complication rates with respect to years ($p > 0.05$). Within years, complication rate did not improve. Factors associated with this condition may result from these: Our hospital is education and research hospital, fellows learn how to make the biopsy and sometimes unexperienced fellows perform the biopsy first time in their practices.

In a study, there was no relation between the frequency of pain or bleeding and the experience or speciality of the operator (12).

Complications of percutaneous liver biopsy are classified as minor and major complications. Minor complications are pain requiring analgesia and temporary hypotension. Pain is the most common complication of percutaneous liver biopsy and affects 84% of the patients.

Major complication is very rare in liver biopsies (13). In a study including 4275 biopsies performed by Myers RP and et al. that thirty-two patients had significant biopsy-related complications (0.75%) (14). In our study, the rate of major complication was only 0.3% and the most frequent complication was pain shock (1.9%). The majority of patients developing pain shock were men while it is more likely expected in women (M/F:7/1). Death was not seen in any patient in our series. Mortality of percutaneous liver biopsy is 1/10.000-12.000. Mortality is usually associated with hemorrhage. Severe bleeding usually occurs in the first 2-4 hours, late bleeding may occur within one week after the biopsy. Bleeding may manifest itself as intrahepatic or extrahepatic bleeding. It is usually detected by ultrasonography (13). In the study of Piccinino and et al., 68 276 percutaneous liver biopsies were performed from 1973 to 1983. Rate of death was 9/100000 and it was always due to haemoperitoneum (15).

Chemical peritonitis was reported in 0.43% and hemato-bilia was reported 0.07% in a large series (16). Bleeding requiring transfusion or intervention occurs in approximately 1/500 biopsy. Small intrahepatic and subcapsular hematomas after liver biopsy are usually asymptomatic. Pain, tachycardia, hypotension, and decreased hemoglobin level can be seen in large hematomas (17).

In our study, millimetric sized intrahepatic bleeding was detected in a patient by ultrasonography (0.3%). This patient was observed for a period of three days and followed by ultrasonography. When it was seen that the hematoma size began to reduce, the patient was discharged.

Among our cases, liver abscess was the most serious complication. In that patient, biliary tree was injured during the biopsy. Puncture of the gall bladder is a complication that should be avoided. This may either stay locally or even progress to biliary peritonitis. To avoid this complication, emptying of the gall bladder thereby making its volume less before the biopsy is important (18,19). Other rare complications of liver biopsy are pneumothorax, hemothorax, hemobilia, perforations of visceral organs, bacteriemia, sepsis, emphysema, breakage of biopsy needle, anaphylaxis due to rupture of cyst hydatid and subphrenic abscesses (19). These rare complications were not seen in this study.

As a result, complication rate attributed to liver biopsy was very low in our series. Moreover, any death was not occurred. To our knowledge, liver biopsy should be safely performed, if the diagnosis of liver disease is needed. Insufficient material rate will decrease with increasing experience. As a result, our complication rate is very low. But experience is very important to achieve least complication rate. The frequency of complications in liver biopsy depends on the center's and the practitioner's experience.

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