The Evaluation of Hepatocyte Function After ESWL with Hepatobiliary Scintigraphy

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Özet: *ESWL'DEN SONRA HEPATOBİLİYER SİNTİGRAFİ İLE HEPATOSİT FONKSİYONLARININ DEĞERLENDİRİLMESİ*

Son yıllarda safra taşlarının tedavisinde cerrahi dışında birçok tedavi yaklaşımı ortaya çıkmıştır. Bunlar arasında extracorporeal shock wave lithotripsy (ESWL) en etkili ve umut veren yöntemlerden birisidir. Bu prospektif çalışmada ESWL'nin hepatoselüler fonksiyon üzerine olan etkileri kantitatif hepatobiliyer sintigrafi ile incelendi. Safra taşları ultrasonografi ile ortaya konan 12 hasta (2 erkek, 10 bayan) ile 10 kontrol (5 erkek, 5 bayan) çalışmaya alındı. Hepatik ekskresyon fraksiyonu (HEF) ve ortalama transit süresi (OTS) hesaplandı, normal sınırlar kontrollerden elde edildi. Bütün hastaların Pre-ESWL-HEF ve OTS değerleri normal sınırlar içinde idi. Tüm hastalarda OTS'de Post-ESWL olarak değişiklik görülmezken, HEF değerleri ESWL sonrasında 12 hastanın beşinde belirgin derecede düştü.

Sonuç olarak ESWL'yi takiben hepatoselüler disfonksiyon ortaya çıkabilmektedir.

Anahtar kelimeler: ESWL, hepatobiliyer sintigrafi.

Summary: *Several non-surgical approaches have recently become available for the therapy of patients having gallstones. Among these, extra corporeal shock wave lithotripsy (ESWL) is the most promising and effective therapy mode.*

This prospective study is conducted to investigate the effects of ESWL on hepatocellular function, using quantitative hepatobiliary scintigraphy. Twelve patients (2 male, 10 female) with ultrasonographically documented gallstones and 10 controls (5 male, 5 female) were included in the study. Hepatic extraction fraction (HEF) and mean transit time (MTT) values were calculated and normal ranges were established from the control group.

The pre-ESWL MTT and HEF values of all patients were within normal range. Although no change was observed between the control and post-ESWL MTT values of all patients; the post ESWL HEF values decreased significantly in 5 of the 12 patients.

We concluded that; hepatocellular dysfunction may arise following ESWL.

Key words: ESWL, hepatobiliary scintigraphy.

Several nonsurgical approaches have recently been introduced for the therapy of patients having gallstones. These new modalities are increasingly more popular alternative to open cholecystectomy, especially in patients refusing operation or having operative risks. Among these, extracorporeal shock wave lithotripsy (ESWL) has been available in gallstone fragmentation since 1985(1).

Several experimental and mostly morphologic studies have been reported about the effects of ESWL on surrounding tissues (2,3). Some clinical studies in which liver functions investigated by amino transferases (ALT, AST) have revealed that after ESWL these tests rises minimally (4).

In this study, to determine the acute changes in hepatocyte functions after ESWL, we calculated the hepatocyte extraction fraction (HEF) and the hepatic mean transit time (MTT) by using quantitative hepatobiliary scintigraphy.

SUBJECTS AND METHODS

ESWL PROCEDURE

A second-generation lithotriptor (Lithostar Plus; Siemens, Erlangen, Germany) was used. It integrates equipment for the electromagnetic

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Table I: Results.

	PATIENTS													CONTROLS
	1	2	3	4	5	6	7	8	9	10	11	12	MEAN±SD	MEAN±SD
Pre-ESWL														
HEF	92	100	100	100	98	100	100	90.7	100	100	100	100	98.3±3.3	97.8±2.2
(%)		12	9.1	9.9	11	8.7	16.2	15.7	12.9	11.8	10.9	13	11.9±2.3	11.5±1.9
MTT	12.2													
(min.)														
Post-ESWL														
HEF	99	100	100	40	67	100	100	100	100	70	80	79	86.2±19.4	-
(%)														
MTT	13	11.7	10.4	9.6	15.2	12.5	11.6	11.6	8.4	9.8	11.3	10.7	11.3±1.7	-
(min.)														

generation and focusing of shock waves with a ultrasound targeting system in an over-table module. Nine selectable power settings progress from about 30% (setting 1) to 100% (setting 9) of the maximum focus pressure (5). Twelve patients (2 male, 10 female) with ultrasonographically documented gallstones and ten controls (5 male, 5 female) were included in the study. Patients were selected according to following criteria. Inclusion criteria were: 1) history of biliary colic; 2) solitary radiolucent gallbladder stone up to 30 mm in diameter or up to three radiolucent stones with a similar total stone mass; 3) gallbladder visualization on an oral cholecytogram; 4) identification of the stones and gallbladder by ultrasound and succesful positioning of the stone in the shock wave focus; and 5) shock wave path that avoids lungs and bone. Exclusion criteria were: 1) acute cholecystitis, cholangitis, biliary obstruction, or known bile duct stones; 2) gastroduodenal ulcers; 3) acute pancreatitis; 4) coagulopathy, current use of anticoagulants, aspirin, or nonsteroidal anti-inflammatory agents; 5) vascular aneurysms or cysts in the shock wave path; and 6) pregnancy (6). Before ESWL patients received ursodeoxycholic acid (UDCA) at 7.5 mg/kg/day dose for three months. The number of shock waves administered varied from 500 to 3000 for a given session (mean duration 60 min.). Patients were positioned in supine and targeted by subcostal route. No analgesia or anesthesia was needed. Patients and controls underwent quantitative hepatobiliary scintigraphy before ESWL and 24 hours after ESWL. Simultaneously liver function tests were measured in patients and control subjects serum. Liver function tests were consisted of aspartate aminotransferase (AST), alanintransferase (ALT), alkaline phosphatase (ALP), amylase and direct (DB) and indirect bilirubine (IDB) levels.

SCINTIGRAPHIC PROCEDURE

All patients received an intravenous injection of 6 mci of Tc-99m EHIDA, a member of the iminodiacetic acid class of tracers. Patients were imaged from anterior projection with GE-400 AC/T gamma-camera-computer system. Dynamic images were obtained at 60 seconds per frame, beginning at least 1 minute to tracer injection and continuing for 60 minutes (7). The calculations were performed according to previously reported techniques (4,8,9,10). In brief, regions of interests were manually drawn for the cardiac blood pool and the liver on the images. Care was taken to ensure that the liver region of interest did not include the right kidney, large bile ducts, or regions of possible scatter from adjacent cardiac structures. The time-activity curves for the cardiac blood pool and liver was generated from these regions. Deconvolutional analysis of the cardiac and hepatic curves was performed with Fourier transform technique resulting liver retention function curve (LRFC). The hepatocyte extraction fraction (HEF) was calculated from the LRFC using following formula:

$$\text{HEF} = \frac{\text{Y intercept exponential fit liver response curve}}{\text{Y-MAX data value liver response curve}}$$

The hepatic mean transit time of traces was then analysed by integrating the area under liver retention function curve and dividing by the maximum height of the curve (11).

RESULTS

The pre-ESWL MTT and HEF values of all patients were within the normal range. Although no change was observed between the control and post-ESWL, MTT values, HEF values decreased significantly in 5 of the 12 patients when compared with the control values (Table I). A direct correlation was also observed between the number of shocks applied and impairment of HEF values. All of the pre-ESWL values of ALT, AST, ALP, amylase, DB and IDB were within the normal range Post-ESWL AST and ALT levels of 9 patients revealed subtle increment when compared to the pre-ESWL values but remained in the laboratory normals. Post-ESWL ALP levels increased minimally in 5 patients and amylase levels in only one patient. Post-ESWL DB and IDB values did not show any change.

DISCUSSION

Measurement of liver enzymes such as AST, ALT and ALP reflect liver cell damage and memrane permeability, and do not directly reflect hepatocyte function. Although liver biopsy samples may reveal fine detail of structure, they reflect hepatocellular function at best only indirectly. Measurement of hepatic uptake of the HIDA family of tracers may provide a useful marker for hepatocellular function. Visual analysis of the images may be clinically helpful but is subjective and provides no quantitative data. In the other hand quantitative analysis is valuable in enabling detection of subtle changes in pathophysiology and in comparision of sequential studies. Deconvolutional analysis technique is a safe and objective method. It can be used for seperating primary hepatocellular disease from biliary disease (4). It also previously demonstrated that HEF measurements correlate with hepatocellular function in the setting of hepatic ischemia and transplantation (9).

In 5 of twelve patients whom received higher shock wave discharges, HEF values decreased. The reduced HEF values indicate that hepatic function may be impaired by ESWL. No change in MTT suggests that this impairment was limited to uptake phase of tracer by hepatocytes and biliary excretion of tracer was not affected.

We concluded that; hepatocellular dysfunction may arise following ESWL, and calculation of the HEF by means of deconvolution analysis should be useful to dedect and monitor this dysfunction. Further wide population studies which included following-up of patients at time intervals, are required to make decision.

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