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STUDY OF THE ELECTRIC ACTIVITY OF THE CIRRHOTIC LIVER WITH IDENTIFICATION OF AN ELECTROHEPATOGRAM

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1. ABSTRACT

In a recent study we could characterize an electrohepatogram (EHG) for the normal liver which consisted of regular monophasic, positively deflected slow waves or pacesetter potentials (PPs). We proposed that the EHG might act as an investigative tool in the diagnosis of liver diseases. In this communication, we studied the electric activity of the liver in hepatic cirrhosis. 42 patients with liver cirrhosis (30 men, 12 women, mean age 41.2 ± 14.3 years) and 20 healthy volunteers (14 men, 6 women, mean age 42.2 ± 13.1), who acted as controls, were enrolled in the study. Three silver-silver chloride electrodes were applied, 3-4 cm apart, to the abdominal skin parallel to and 1.5-2 cm below the right costal margin. Two 20-minute recording sessions were performed for each subject. In contrast to the regular reproducible PPs recorded in the healthy volunteers, the PPs of the cirrhotic patients had irregular rhythm, frequency and amplitude with occasional silent (no PPs) areas. The registered waves were identical from the 3 electrodes in the same subject in the healthy controls, while differed from one electrode to the other in the cirrhotic patients. The "hepatoarrhythmic" pattern encountered in the cirrhotic liver was consistent and reproducible. An EHG could be identified for the cirrhotic liver. It exhibited a "hepatoarrhythmic pattern" due probably to loss of the lobular architecture of the liver and its replacement with regeneration nodules and fibrosis.

2. INTRODUCTION

The liver is the center of the body's metabolic activity and is important for the carbohydrate, protein and fat metabolism (1). It secretes bile, stores vitamins and iron, degrades hormones and hemoglobin and inactivates drugs and toxins (1). The liver may be involved in various pathologic conditions such as infections, tumors, cysts and others. The diagnostic tools for the liver are numerous and comprise sonography, CT scanning, scintiscanning, positron emission tomography, nuclear magnetic resonance, needle biopsy and others.

Electric activity, in the form of slow waves or pacesetter potentials (PPs) and fast activity spikes or action potentials could be recorded from various organs including the stomach, small intestine, sigmoid colon, rectum and gall bladder (2-24). The waves were recorded either transluminally or percutaneously (5,18,19,23). Wave abnormalities were detected in the electrogram of the aforementioned organs when they were diseased (5,6,12,13,16,17,24,25).

In preceding studies, we could identify an electrohepatogram for the normal liver in a canine model (26) and in humans (27). It consisted of PPs which were monophasic with a positive deflection (figure 1). The waves had identical amplitude and frequency from the 3 electrodes which were sutured to the liver capsule. They were reproducible when the recordings were repeated in the same animal or subject. In the canine model, liver insult by temporary hepatic artery and portal vein ligation, produced a "dysrhythmic EHG"; the waves showed irregular frequency and amplitude (26). Liver irradiation effected 2 EHG patterns: dysrhythmic and silent in which no signals were recorded (26).

It has been postulated in the previous publications (26,27) that the EHG might act as an investigative tool in the diagnosis of liver diseases. This assumption prompted the author to study the electric activity of the liver in cirrhosis aiming at the identification of a specific EHG pattern for this condition.

3. MATERIAL AND METHODS

3.1. Subjects

The study comprised 62 subjects: 42 patients with liver cirrhosis and 20 healthy volunteers who matched the patients in age and sex and acted as controls. The clinical data of the subjects are shown in table 1. All cirrhotic patients had a history of viral hepatitis B and C

Table 1. Clinical data of the 62 studied subjects

Diagnosis	No	Sex		Age (years)		Duration (months of disease)	
		M	F	mean	range	mean	range
Healthy volunteers	20	14	6	42.2 ±13.1	34-62	-	-
Liver cirrhosis	42	30	12	41.2 ±14.3	32-58	16.6. ±3.1	14-21

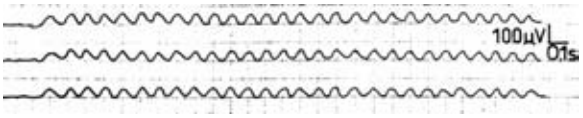

Figure 1. Electrohepatogram showing the pacesetter potentials exhibiting the same frequency and amplitude from the 3 electrodes applied to the liver. (from Shafik[27])

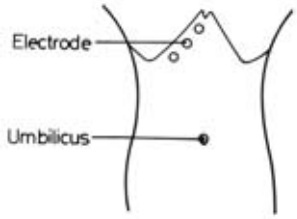

Figure 2. Sites of electrodes on the skin.

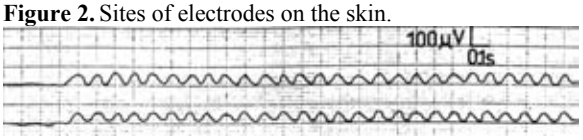

Figure 3. Percutaneous electrohepatogram in healthy volunteers showing the pacesetter potentials exhibiting a regular rhythm with the same frequency and amplitude from the 3 electrodes applied to the skin.

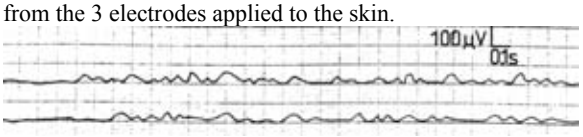

Figure 4. Percutaneous electrohepatogram of a patient with liver cirrhosis showing that the PPs have an irregular rhythm, frequency and amplitude from the 3 electrodes in the same patient, a picture of "hepato-arrhythmia".

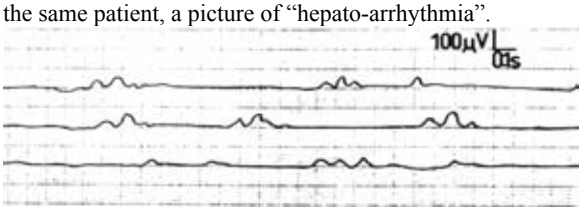

Figure 5. Percutaneous electrohepatogram of a patient with liver cirrhosis showing a silent area between the arrhythmic pattern of the PPs.

which was followed by liver cirrhosis. Subjects with ascites were excluded from the study. The patients had an enlarged spleen. Investigations showed moderate impairment of the liver functions. Sonographic and liver biopsy studies revealed that the liver cirrhosis was of the mixed micro- and macronodular type. The healthy volunteers had no history of liver troubles in the past or at the time of presentation. Liver function tests and sonography showed normal results.

3.2. Technique of electrohepatographic recording

The technique was already described (27) and will be mentioned in brief. The subject was instructed to fast for 12 hours prior to the recording session. He or she lay supine and uncovered from above the level of the nipples to below the umbilicus. Three silver-silver chloride electrodes (SmithKline-Beckman, Los Angeles, CA, USA) were fixed by gel to the skin at the sites shown in figure 2. The 3 electrodes were placed on a transverse line parallel to and below the right costal margin. One electrode was sited 2.5-4 cm below and lateral to the xiphoid process and the other 2 electrodes were placed 1.5-2 cm below the costal margin and 3-4 cm apart. A reference electrode was applied to one of the lower limbs. The electrodes were connected to a Beckman R611 recorder (Sensor Medico, Anaheim, CA, USA) with a time constant of 10 s, high-frequency cutoff of 0.08 Hz, and a paper speed of 1mm/s. A 20-minute recording was performed for each subject at each of minimally 2 recording sessions.

The reproducibility of the results was ensured by the repetitions of the recordings in the individual subject. The results were analyzed statistically using the Student's t-test. Differences assumed significance at $p<0.05$, and values were given as mean ± standard deviation (SD).

4. RESULTS AND DISCUSSION

No adverse effects were met with during or after the recording sessions and all the subjects were evaluated. The procedure was well accepted by the individuals.

4.1. Normal subjects

PPs were recorded from the 3 electrodes of each subject (figure 3). The configuration of the wave was characteristic and constant in all the recordings: it was monophasic with a large positive deflection (figure 3). The PPs in the individual subject exhibited the same frequency, amplitude and regular rhythm by the 3 electrodes. The frequency recorded a mean of 9.2 ± 1.4 cycle/s (range 7 – 12) and amplitude of 49.8 ± 12.6 µV (range 40 – 62). Bursts of fast activity spikes or action potentials were not encountered in any subject. Likewise, no abnormal recordings, such as of waves with different morphological character or of those propagating in a retrograde fashion, were registered from the liver. The electric pattern in the individual subject was reproducible on all test days.

4.2. Liver cirrhosis

The PPs recorded from cirrhotic patients had irregular rhythm, frequency and amplitude (figure 4). In the same recording, some PPs had a higher amplitude than the others, and an inconsistent frequency. The waves registered from each of the 3 electrodes in the individual subject had a frequency and an amplitude which differed from one electrode to the other. This "hepato-arrhythmic pattern" was consistent when the recordings were repeated in the same patient. In some recordings of the same subject we obtained 'silent' areas in which no electric waves were recorded (figure 5); those silent areas were followed by electric activity of the hepato-arrhythmic pattern. We did not encounter a patient in whom no electric activity was registered throughout the whole recording session.

The current study demonstrated that the cirrhotic liver has an arrhythmic pattern which seems to be due to loss of the regular architecture of the liver lobules. In liver cirrhosis degeneration of liver cells occurs and is followed by the formation of regeneration nodules, fibrosis and loss of lobular architecture of the liver (28,29).

Hepatic cells in the regeneration nodules appear to generate electric waves, but these waves, as is demonstrated in the current study, had an irregular rhythm, frequency and amplitude probably due to the irregular arrangement and functional impairment of the hepatocytes. The different rhythms from the 3 electrodes of the same individual may also be due to the variable patterns of hepatocyte arrangement and activity in the nodules. This appears to explain the difference in frequency and amplitude registered from each electrode in the same subject. The recorded silent areas could result from the presence of excess fibrosis between the regeneration nodules. It seems that the fibrous tissue does not generate electric activity.

The overall EHG picture demonstrated irregular electric hepatic activity, which corresponds to the impaired function of the liver in hepatic cirrhosis. We did not study the correlation between the electric activity and the degree of liver cirrhosis. The current study evaluates liver cirrhosis in patients with moderate liver functions and no ascites. The EHG in more advanced stages of liver cirrhosis needs further studies.

In conclusion, an EHG could be identified for the cirrhotic liver. It demonstrated an "hepato-arrhythmic" pattern due probably to loss of the lobular architecture of the liver and its replacement with regeneration nodules and fibrosis.

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