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Research Article

Monoethylglycinexylidide extraction level as a measure of hepatic detoxification and excretion functions in cirrhotics undergoing laparoscopic cholecystectomy under general anesthesia

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KEYWORDS

Cirrhotic patients;
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MEGX

Abstract *Objectives:* To estimate plasma monoethylglycinexylidide (MEGX) level at 15 and 30 min after intravenous injection of lidocaine as a measure for detoxification and excretory function of the liver in cirrhotic patients in comparison with non-cirrhotic patients assigned for laparoscopic cholecystectomy (LC).

Patients and methods: The study included 50 cirrhotic and 10 non-cirrhotic patients assigned for LC. Only Child-Pugh (CP) class A or B patients with adjusted liver functions were included in the study. Both patients and controls received anesthesia using a similar protocol. Intravenous lidocaine (1 mg/kg) was injected over 1 min, and blood samples were obtained immediately before lidocaine injection (S_0) to assure absence of MEGX in plasma and 15 min (S_{15}) and 30 min (S_{30}) after lidocaine administration. MEGX values > 90 ng/ml are considered normal. The extent of MEGX extraction was calculated as plasma MEGX level at S_{30} minus S_{15}.

Results: Mean operative and anesthesia times were 59.3 ± 10.4 and 73.9 ± 12.2 min, respectively. Mean sevoflurane 18.1 ± 2.4 ml/h. Operative and anesthetic data showed non-significant difference between patients categorized according to CP class and in comparison with controls. Estimated plasma MEGX levels at 15-min and 30-min after lidocaine injection were significantly higher in controls compared to patients and in patients of CP class A compared to those of class B. The

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extent of extraction was significantly lower in patients of CP class B compared both to controls and patients of class A with non-significantly lower extraction level in patients of class A compared to controls.

Conclusion: Laparoscopic cholecystectomy is safe and feasible in cirrhotic patients and MEGX test as a measure of detoxification and excretory function of the liver is a reliable test that showed a relationship to the extent of hepatic derangement.

1. Introduction

Cirrhosis causes a hyperdynamic circulation with increased cardiac output and decreased systemic vascular resistance; however, it endangers hepatic circulation in the form of decreased venous perfusion secondary to reduced portal blood flow as a consequence of portal hypertension. Also, hepatic arterial blood flow can be decreased because of impaired autoregulation [1,2].

The burden of operative risk on the liver is dependent on both the underlying liver disease, type of surgery, operative approach, and duration. Anesthetics increase the burden on hepatic blood flow in the form of reduced hepatic blood flow by 30–50%, but agents such as isoflurane, desflurane, sevoflurane, and propofol cause less perturbation in hepatic arterial blood flow than other inhaled anesthetic agents and so are preferred for patients with liver disease. Traction on abdominal viscera may cause reflex dilatation of splanchnic veins and thereby lower hepatic blood flow [3–5].

Dynamic tests are related to the ability of the liver to metabolize or eliminate defined substances in a given time. Thus, dynamic tests have the advantage of quantifying the functional status at the time point of assessment. Historically, the bromosulfophthalein and indocyanine green tests have been used as dynamic function tests. Unfortunately, these tests are no longer used because of lack of commercial availability of bromosulophthalein and high cost of indocyanine green [6,7].

Lignocaine is a compound with a high hepatic extraction and an oxidative metabolic pathway catalyzed by the hepatic P450 IIIA4 cytochrome yielding monoethylglycinexylidide (MEGX). Estimation of plasma MEGX levels after intravenous injection of lignocaine constitutes a simple dynamic liver function test. The idea behind this test is to detect reduced clearance of lidocaine in cases of liver diseases or reduced hepatic blood flow by measurement of plasma MEGX. Reduced liver function or hepatic blood flow results in reduced formation of MEGX in humans. This test has the advantage that it is easy to do [7,8].

The current prospective study aimed to estimate plasma MEGX level at 15 and 30 min after intravenous injection of lidocaine as a measure for detoxification and excretory function of the liver in cirrhotic patients in comparison with control non-cirrhotic patients assigned for laparoscopic cholecystectomy.

2. Patients and methods

The current prospective comparative study was conducted at Anesthesia Department, Kasr Al-Eini University Hospital since Jan 2009 till June 2012. After approval of the study protocol by the Local Ethical Committee and obtaining fully informed written patients' consent, 50 cirrhotic patients assigned for laparoscopic cholecystectomy (LC) were enrolled in the study. For comparative purposes, 10 non-cirrhotic, age-, and sex-matched controls assigned for LC were enrolled in the study.

Inclusion criteria included cirrhotic patients whose hospital files included the required preoperative data especially liver function tests, abdominal ultrasonography, and their baseline Child-Pugh (CP) class. Only patients with adjusted liver functions and were CP class A or B were included in the study. Patients with clinically detectable ascites or had history of or defined obstructive jaundice or recent attack of gastrointestinal bleeding were excluded from the study. Both study and control groups received anesthesia using a similar protocol. Atropine 0.2 mg and midazolam 0.03 mg/kg were administered IV before induction of anesthesia. Anesthesia was induced with fentanyl 1–2 μg/kg and propofol 2 mg/kg Endotracheal intubation was facilitated by IV atracurium 0.5 mg/kg. Anesthesia was maintained with sevoflurane in oxygen 3 l/min. Ventilation was controlled to keep PaCO2 between 30 and 40 mmHg. Atracurium was used as a muscle relaxant during surgery. Non-invasive intraoperative monitoring included heart rate (HR), systolic, and diastolic blood pressure (SBP & DBP). After surgery, all patients were extubated and were followed in ICU for 24 h and thereafter in the surgical ward. At ICU, heart rate, blood pressure, and oxygen saturation were monitored continuously with a non-invasive method.

2.1. Estimation of serum MEGX

All samples were taken from a plastic cannula on the contralateral arm to that used for the administration of lidocaine. The cannula was kept patent with a trocar. Blood samples were drawn into EDTA; plasma was separated within 30 min and stored at −40 °C until analysis. Concentrations of monoethylglycinexylidide (MEGX) were analyzed with gas chromatography using etidocaine as an internal standard [9].

Intravenous lidocaine was injected in a sub-therapeutic dose (1 mg/kg) over 1 min after transfer to ICU. Blood samples were obtained immediately before lidocaine injection (S_0) to assure absence of MEGX in plasma and 15 min (S_{15}) and 30 min (S_{30}) after lidocaine administration. MEGX values > 90 ng/ml are considered normal, whereas values below 50 ng/ml reflect impaired liver function and values ranged between 50 and 90 ng/ml reflect affected liver function [9]. The extent of MEGX produced as a measure for detoxification and excretion functions of the liver was calculated as plasma MEGX level at S_{30} minus S_{15}.

2.2. Statistical analysis

Results were presented as mean ± SD, ranges, numbers, percentages, and ratios. Data were analyzed using Chi-square test