



Randomized Open Label Clinical Study on Assessment of Effect of Liquid and Solid Meal Intake in Cirrhotic Patients

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Abstract

Portal hypertension is almost unavoidable complication of cirrhosis. The physiological stimuli like food intake will affect the splanchnic circulation in cirrhotic patients. Hence the present study has been designed to measure the portal blood flow pressure after ingestion of solid and liquid meal in normal and cirrhotic patients. It is a randomized open label clinical study. The study included 32 male healthy volunteers (52 to 74 years) and 10 clinically proven cirrhotic patients (54-76years). The portal blood flow velocity was measured by Doppler method. The portal flow velocity in the fasting and in post prandial period was measured at the time interval of 15,30,45,60 and 90 minutes after either solid or liquid meal ingestion. Solid meals include 4 idli's each weighing 50 gms with dhal and chutney. The liquid meal includes Ensure healthy mix in 270ml of water. Both the liquid and solid meals' calorific value is 405. The results indicate that, the basal blood flow velocity in cirrhotic patients is on higher side in comparison to normal subjects. Intake of solid as well as liquid meals increased the portal velocity in both normal as well as cirrhotic patients and it was found to be high at 45 minutes. In cirrhotic patients the liquid meal itself is able to increase the portal pressure in comparison to normal volunteers. The study can be concluded that being cirrhotic patients are more susceptible to vein puncture through increase in blood flow velocity low food load or liquid food might help them to control the velocity induced blood vessel rupturing. The observation has direct clinical implications and first time we are reporting with such a study in Indian population.

Keywords- Liver, hepatic circulation, pathogenesis, food, color Dopplers, clinical research.

Introduction

The post prandial drowsiness is a common and important physiological phenomenon felt after the meal ingestion in the post prandial period. This is due to diversion of blood from the systemic circulation from inactive tissues like skin, muscles and brain, to splanchnic circulation. These

physiological stimuli like food intake also affect the deregulated splanchnic circulation in cases of cirrhosis with portal hypertension and lead to a dangerous complication of ruptured esophageal variceal bleeding. The Post prandial increment of portal blood flow is detrimental for rupture esophageal varices due to sudden increase in

portal venous pressure (Ozdoganetal., 2008; Vorobioff et al., 1984; Grossmann 1993; Yin et al., 2001).

Malaysian study by Lau siengchuo showed that there is a significant change in portal hemodynamics after the liquid meal post prandially with no significant in gender (Peristic et al., 2005). Portal hypertension is almost unavoidable complication of cirrhosis and unfortunately portal hypertension caused by cirrhosis generally persist and progressive despite development of even an extensive collateral circulation, this includes gastro esophageal varices which are responsible for the main complication of portal hypertension (Schiedermaier et al., 2006). The prevalence of varices at the time of diagnosis of cirrhosis is widely variable and ranges from 0% to 80 % in 93 progressive studies published from 1980 to 2003. The recent prospective cohort studies showed that the incident of esophageal varices in patients with newly diagnosed cirrhosis is nearly 5% per year (Sidery et al., 1994).

Hence from the available literature it has been clear the presence of portal blood flow velocity will be a crucial one for the cirrhotic patients. These patients already been exhibiting higher blood pressure and obstruction even slight change in the blood flow velocity might end up in blood vessel injury. Hence the present study has been designed to the measure the portal blood flow pressure after effect ingestion of solid and liquid meal.

Materials and Methods

Study design and Patient selection

This study included 32 healthy volunteers from the age group of 52 to 74 years (62-63) males are selected. They are examined clinically and had no known gastrointestinal disorder and no diabetics or peripheral vascular disease and they were not taking any kind of medication. Another group of 10 patients from the age group of 54-76 (65-66) who were all clinically, biochemically, endoscopically and ultrasonographically proven cases of cirrhosis with portal hypertension were

selected for this study. They were not having any cardiac disease or any other known systemic disease other than cirrhosis. All participants gave written informed consent to take part in the study, which was approved by the ethical committee (CMC/PHY/04/2013).

The entire healthy subject abstained from eating the night before ultrasonographic study. The cirrhotic patients also fasted overnight before the examination and the medications which are altering the hemodynamic parameters have been stopped at least three days before the study. The healthy volunteers were divided into two groups each of 16 in numbers. One group was studied portal flow velocity in the fasting and also in the post prandial period of 15,30,45,60 and 90 minutes intervals after eating the solid meal, which contain 450 kilo calories of energy (4 idli's each having 50 gms of weight with dhal and chutney).

Another group of healthy volunteers were ingested 270ml of a standardized liquid meal (Ensure plus powder) after a basal period. The meal contained 16.7 % protein, 30% fat and 53.3% carbohydrate giving a total caloric value of 405 k cal (equivalent to 1648 kJ). Then they were involved in the Doppler study in serial time interval of 15, 30, 45, 60 and 90 minutes after the basal recording in the fasting state.

The cirrhotic patients who were selected in the study are divided into two groups. One group was given the same calorie solid meal as like healthy volunteers in group one and another group of cirrhotic patients were ingested Ensure plus powder of same calorie and studied the portal flow velocity in different time interval period in each group after recording a basal measurement

Measurement of portal blood flow velocity

(Hansen et al., 1998)

Each subject was examined after overnight fasting in supine position after a rest of 15 minutes so as to avoid any influence of food, posture and exercise. Overall assessment of the hepato- biliary system by B mode was made before Doppler examination. Then portal vein was identified near

the bifurcation of hepatic artery. The whole length hepatic vein was traced and the middle of the hepatic vein selected by an appropriate anatomic window in the angle of not less than 60 degree. The flow direction was identified by color hue which is used to encode the greater frequency shift. The axial size of sample volume was adjusted to encompass the portal vein lumen in its entirely middle third. The time averaged mean flow velocity of portal vein was calculated automatically by the instrument after tracing of the spectral display (single cardiac cycle), where as maximum and minimum velocity were calculated manually.

Measurement of time averaged maximum velocity of the portal flows were done at least twice for each side and the average were used for the further studies. These measurements were also repeated in 30, 45, 60 and 90 minutes intervals with the same patient and the observations were recorded. In each group the measurement of portal flow velocity also recorded in the same manner.

Statistics

Data were expressed as mean \pm SD. Statistical significance between cirrhotic and normal subjects were analyzed by student 't' testsun paired using GraphPad Prism, 4.03 (San Diego, US). Statistical significance at $P < 0.05$ was considered as statistical significance.

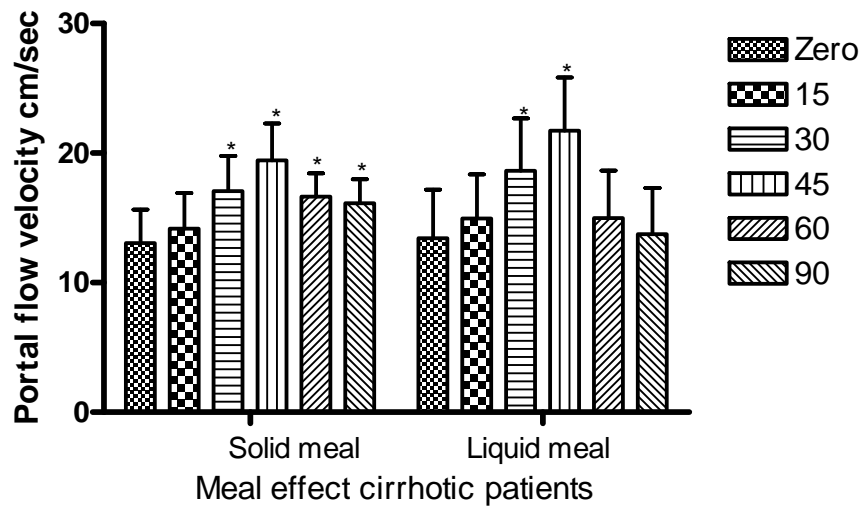
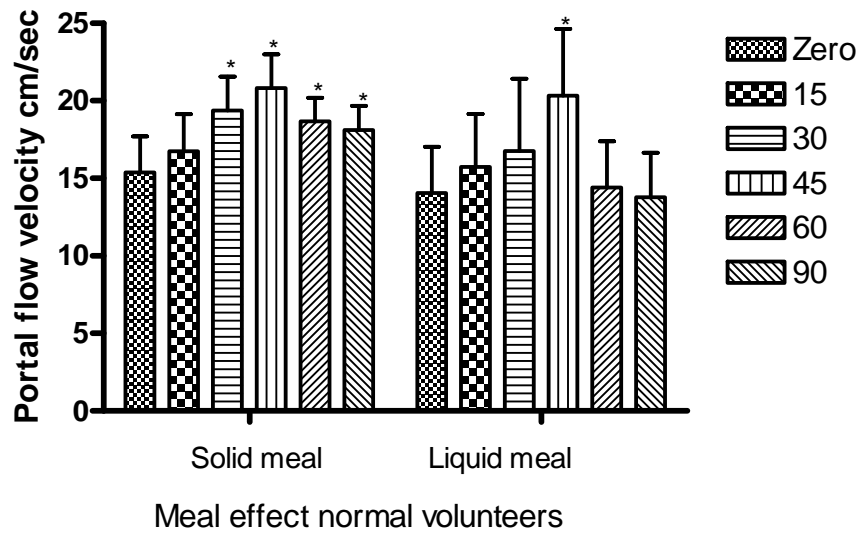
Results

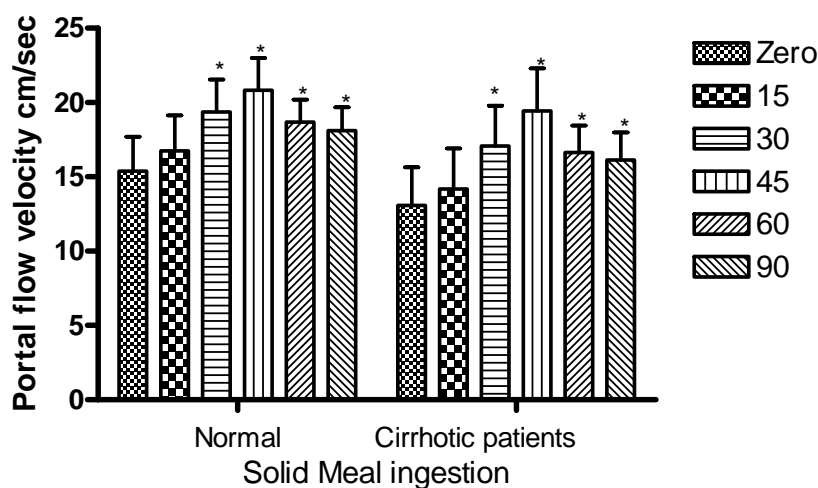
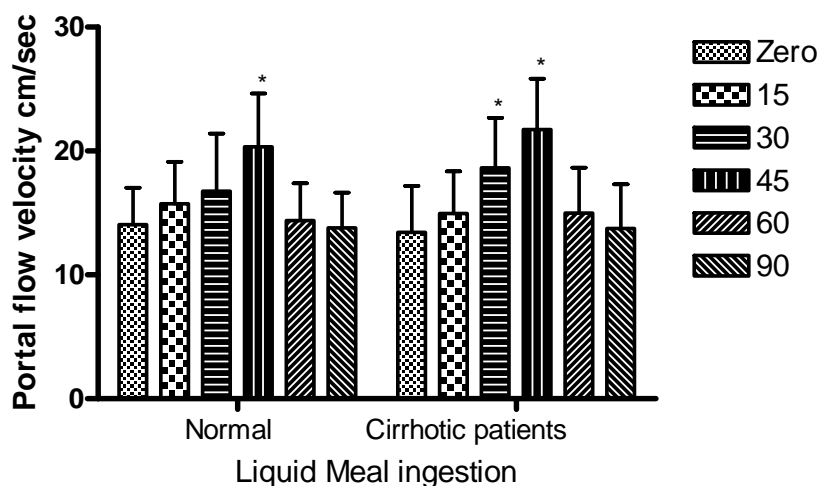
Effect of liquid and solid meal ingestion in normal and cirrhotic patient

The portal blood flow velocity across the patient was found to be lower in cirrhotic patient in comparison to the normal volunteers. Administration of liquid meal significantly increased the portal blood flow velocity in cirrhotic patient at 30th minute in comparison to the normal volunteers. The other time points measured did not alter the blood flow velocity across the group. The proportionate increase in the blood flow velocity after food intake was found to be gradual

between the groups and the peak increase in the blood flow velocity was observed at 45th minute. In comparison to the zero minute the fold increase in blood flow velocity was found to be 62% with liquid meal and 49% in solid meal intake in cirrhotic patient. Whereas, at 45th minute the percent fold increase in blood flow in normal volunteer was found to be 45% and 35% with solid and liquid meal respectively, which is much lower than the cirrhotic patients.

In the normal volunteers the blood flow to the liver has been maintained and above the base value with the solid meal administration in both cirrhotic and normal volunteers up to 90 minutes of the measurement. The blood flow has been reduced after 45 minute of liquid meal administration in both normal and cirrhotic patients. In comparison to the solid meal, administration of liquid meal has controlled blood flow velocity. Both liquid and solid meal has shown peak portal blood flow velocity at 45th minute.





Discussion

In the present study portal vein the mean portal vein velocity are significantly increased from the baseline value of 15.38cm\sec to a maximum value of 20.83 at 45 min after a solid meal and also had a significant increase in velocity compared with baseline value. Findings of this study are comparable with studies by Chuo et-al (2005) in healthy Malaysian adult population. It has been shown that, increment on total volume flow, velocity and diameter 15 minutes after meal ingestion. Differences on increment of portal vein velocity after meal ingestion mainly are due to dynamics variability of gastric emptying (Sabba et al., 1990).

The increase in the gastrointestinal blood flow in post prandial state depends on either an increased

cardiac output, a shunting of blood from less active tissue to the gastrointestinal tract or combination of two (Vorobioff et al., 1984). Traditionally it is believed that the majority of this response is due to the chemical stimuli from components of the hydrolyzed food such as glucose and fatty acid as well as gastrointestinal secretions. Few studies have considered the importance of mechanical distension of stomach and intestine in regulation of gut blood flow in mammals (Vorobioff et al., 1984).The initial lack of increase in PFV might be due to less distension of stomach by liquid meal and by single exponential emptying of gastric contents into the duodenum. The marked increase in PFV after 45 minutes might be due to chemical stimulation by the constituent of liquid meal to facilitate

digestion and absorption in the small intestine. The decrease in PV in 60 min is due to clearance of vasodilators released as by product on food and metabolic activity of gut is cleared by normally functioning liver. The further decrease in PFV at 90mins might be buffering action of hepatic arterial blood flow which is required for supply of oxygen to the liver for its metabolic activity. The meal test with post meal PFV measurement is generally accepted as a reproducible non-invasive test to evaluate the severity of portal hypertension. Zardi EM *et al* conformed that post meal PFV increases in the both healthy individuals and patient with chronic hepatitis, while in cirrhotic patient no significant changes occurs(Hansen et al., 1998).

It has been strongly suggested that portal flow velocity is not related to the degree of endoscopic abnormalities in patients with liver cirrhosis and that it has no value in identification of cirrhosis at risk of upper gastrointestinal bleeding (Cioni et al., 1996). Similarly Sabaa *et al.* (1990 and 1991) showed a significant increase in portable blood flow in normal healthy individuals after 30 minutes to 150 minutes but the cirrhotic patient showed a blunted hyperemia. In our study we have observed sustained flow velocity in solid meal and decreased blood flow with liquid meal taken patients. Assessment of patients with the significant increase in postprandial allows the use of several treatment option. It was recently observed that administration of low dose isosorbide mononitrate attenuate post prandial hyperemia. By contrast, propranolol is ineffective in blunting post prandial hyperemia but has some effects in reducing post prandial portal blood flow.

The study can be concluded that the cirrhotic patients are more susceptible to vein puncture through increase in blood flow velocity. Hence giving low load of food or liquid food might help them to control the velocity induced blood vessel rupturing. The observation has direct clinical implications and first time we are reporting with such a study.

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