Potential Precipitating Factors of Esophageal Variceal Bleeding

Thesis

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Abstract

Potential Precipitating factors of esophageal variceal bleeding

Back ground The incidence of variceal bleeding ranges between 8 and 32 % at 2 years from first diagnosis of esophageal varices (EV) . Although high-risk varices (i.e., large size, red color) are vulnerable to rupture, predicting when these varices will rupture is challenging. The Valsalva maneuver causes an abrupt increase in variceal pressure which can induce EV bleeding.

Objectives Valsalva maneuver-associated activities such as straining during defecation, vomiting, and cough are believed to cause abrupt increase in variceal pressure. Whether these actions can precipitate rupture of esophageal varices (EV) is unknown. The association of EV bleeding with these activities and other potential risk factors such as ingestion of non-steroidal anti-inflammatory drugs,alcohol will be investigated.

Methods This study will use a standard questionnaire to assess Valsalva maneuver-related activities including constipation , vomiting , and cough , and also assess the use of NSAID,alcohol in the week preceding inclusion in the study on 150 patients 75 group A presented with hematemsis and 75 group B as control.

Conclusion The study showed significant differences between the cases and the control in cough, border line significant in vomiting and non-significant results in cough and carring heavy objects Also significant differences in both groups regarding NSAIDs intake as one of the predisposing factor and hepato-cellular dysfunction (demonstrated by CHILD'S classification).

Keywords : Esophageal varices - Portal hypertension - Hematemsis

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List of Abbreviations

AKT1	Aktivated kinase 1
Cav-1	caveolin-1
EGD	Esophago-gastro-dudonoscopy
EVL	Esophageal variceal ligation
ET	Endothelin
ET-1	Endothelin-1
EV	Esophageal varices
FHVP	Free hepatic vein pressure
$_{e}$ NOS	Endothelial nitric oxide synthase
HSC	Hepatic stellate cell
HVPG	Hepatic venous pressure gradient
ILCP	Italian liver cirrhosis project
$_{i}$NOS	Inducible nitric oxide synthase
KPa	KiloPascals
LES	Lower esophageal sphincter
$_{n}$NOS	Neuronal nitric oxide synthase
NSAIDs	Non steroidal anti- inflammatory drugs
PPG	Portal pressure gradient
PDGF	Platelet derived growth factor
SBP	Spontaneous bacterial peritonitis

SEC	Sinusoidal endothelial cells
TIPS	Transjagular intrahepatic portosystemic shunt
TGF-b	Transforming growth factor beta
VEGF	Vascular endothelial growth factor
WHVP	Wedged hepatic vein pressure

INTRODUCTION

INTRODUCTION

Over the past several years, there has been a noticeable progress in the field of portal hypertension especially in its management. Such progress has also benefited the overall management of esophageal varices especially during its episodes of bleeding. Esophageal varices (EV) are one of the most serious complications of portal hypertension, causing 70% of all gastro intestinal bleeding episodes in patients with liver cirrhosis. Standardizations in supportive and new therapeutic treatments have reduced the bleeding related mortality within the last 30 years from about 50% to 15-20 % (**D'Amico and de Franchis, 2003**).

The majority of patients with cirrhosis will develop varices during their lifetime. At least one-third of these patients will bleed from their varices (**De Franchis and Primignani, 2001).**

Although high-risk varices (i.e., large size and red color) are vulnerable to rupture, predicting when these varices will rupture is challenging **(Bernard et al., 1997).**

In addition to pharmacological and endoscopic prevention, means to identify and avoid precipitating factors is the next step in improving the outcomes of patients with high-risk EV and EV bleeding. Portal and variceal pressure is a major determinant of EV rupture. Valsalva maneuver causes an abrupt increase in variceal pressure, which can induce EV bleeding **(Staritz et al., 1985).**

Increase in intra-abdominal pressure markedly increase azygous blood flow, an index of gastro-esophageal collateral blood flow, and markedly increase variceal pressure and tension. Large volume paracentesis demonstrates the beneficial effect

of relieving high intra-abdominal pressure and reducing variceal pressure, which suggests that transient increase in intra-abdominal pressure could have a harmful effect on EV bleeding **(Escorell et al., 2002).**

Isometric exercise and carrying heavy objects reportedly increase portal pressure **(Bandi et al., 1998)**.

More over ingestion of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) is also associated with EV bleeding **(De ledinghen et al., 1999).**

Although patho-physiological studies demonstrate the harmful hemodynamic effect of these activities and behaviors (valsalva manueuver: e.g. constipation, cough, vomiting, carrying heavy objects). The association between these activities and behaviors and EV bleeding should be well studied.

The aim of the present study is to evaluate the association between potential precipitating factors and EV bleeding through a meticulously designed questionnaire.

REVIEW OF LITERATURE

Portal hypertension

Portal hypertention is defined as a persistent pressure elevation of >12 mmHg in the portal vein circulation, dilation of the portal vein to >13 mm or portal venous pressure gradient (difference between the pressure of the portal vein and that of the inferior vena cava) exceeding 5 mm Hg **(Garcia-Pagan et al., 2005).**

Hepatic portal system

Embryologically, the portal system is a unique, as it develops from the extra-embryonic vitelline and umbilical veins draining from the yolk sac and the placenta, in contrast to the systemic which develops from the intra-embryonic anterior and posterior cardinal veins. Thus, any umbilical infection or intervention could affect the portal venous system **(GRAY, 1918).**

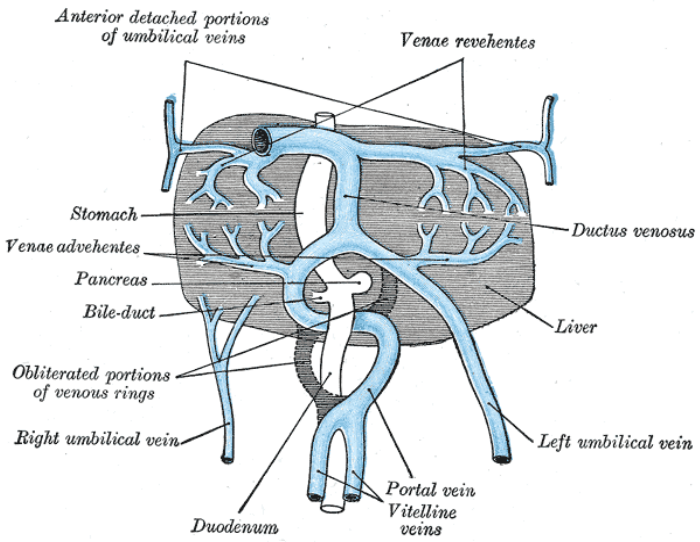

Fig. (1): Development of the Portal vien **(www. The Bartleby.com)**

Anatomy of the portal vien

The liver receives a dual blood supply, from the oxygen-rich hepatic artery and the nutrient-rich portal vein. Approximately 75% of blood reaching the liver is supplied by the portal vein, with the balance delivered via the hepatic artery. In total, hepatic blood flow comprises nearly 30% of total cardiac output (**Shah et al., 2002).**

The portal system includes all the veins which drain the blood from the abdominal part of the digestive tube (with the exception of the lower part of the rectum) and from the spleen, pancreas, and gall-bladder. From these viscera the blood is conveyed to the liver by the portal vein. In the liver this vein ramifies like an artery and ends in capillary-like vessels termed sinusoids, from which the blood is conveyed to the inferior vena cava by the hepatic veins. From this it will be seen that the blood of the portal system passes through two sets of minute vessels: (*a*) the capillaries of the digestive tube, spleen, pancreas, and gall-bladder and (*b*) the sinusoids of the liver. In adults the portal vein and its tributaries are destitute of valves. In the fetus and for a short time after birth valves can be demonstrated in the tributaries of the portal vein; as a rule they soon atrophy and disappear, but in some subjects they persist in a degenerate form.

The portal vein (vena portæ) is about 8 cm in length, and is formed at the level of the second lumbar vertebra by the junction of the superior mesenteric and lienal veins, the union of these veins taking place in front of the inferior vena cava and behind the neck of the pancreas. It passes upward behind the superior part of the duodenum and then ascends in the right border of the lesser omentum to the right extremity of the porta hepatis, where it divides into a right and a left branch, which accompany the corresponding branches of the hepatic artery into the substance of