ORIGINAL ARTICLES

Comparison of Gastric Mucosal Blood Flow in Normal Subjects and in Patients with Portal Hypertension Using Endoscopic Laser-Doppler Velocimetry

PRABHA SAWANT, RAJESH BHATIA, P M KULHALLI, S S MAHAJANI, S A NANIVADEKAR

Department of Gastroenterology, Loknaya Tilak Municipal Medical College & Hospital, Sion, Bombay 400 022
and Division of Human Pharmacology, R & D Laboratories, Zandu Pharmaceutical Works Ltd, 70, Gokhale Road (S), Dadar, Bombay 400 025

Abstract

Objective: To compare gastric mucosal blood flow (GMBF) in normal subjects with that in patients with portal hypertension with or without portal hypertensive gastropathy (PHG).

Methods: GMBF was measured by endoscopic laser-Doppler velocimetry in 20 gastroscopically normal subjects and 30 patients with portal hypertension with or without PHG. The effects of breath-holding (vasomotor reflex), submucosal epinephrine and sublingual isosorbide dinitrate were also studied.

Results: In normal subjects, GMBF on the greater curvature was (mean ± SD) 9.5 ± 1.3 V and on the lesser curvature, 9.1 ± 1.9 V. Breath-holding caused a reduction in GMBF by 57.1 ± 13.7%, submucosal epinephrine reduced it by 41.5 ± 21.5% and sublingual isosorbide caused a rise of 24.8 ± 15.2%. The GMBF on the greater and lesser curvature respectively in patients with mild PHG (7.7 ± 1.2 V and 7.4 ± 0.8 V) and those with severe PHG (6.5 ± 3.5 V and 6.0 ± 2.2 V), was significantly less than that in normal subjects (p < 0.05 and p < 0.001 respectively). Vasomotor reflex was blunted in patients with mild and severe PHG (21.9% ± 0.3 and 23.1% ± 17.7 respectively, p < 0.001). Responses to submucosal epinephrine and sublingual isosorbide were similar to those recorded in normal subjects.

Conclusions: Patients with portal hypertension have significantly reduced GMBF and significantly attenuated vasomotor reflex in the gastric vascular bed as compared to normal subjects.

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Key words: Portal hypertensive gastropathy, breath-holding, epinephrine, isosorbide dinitrate.

Introduction

Laser-Doppler velocimetry (LDV) is a reliable and reproducible non-invasive technique for measurement of tissue blood flow in experimental animals and in human subjects. It has been validated against invasive techniques such as radioactive tracer disappearance studies, microsphere technique, thermodilution method and electromagnetic flow measurements.1,5

Gastro-intestinal mucosal blood flow has been reliably measured by endoscopic LDV.6-9 The technique has been used to study gastric mucosal blood flow (GMBF) in patients with portal hypertension and resultant portal hypertensive gastropathy (PHG) and the influence of pharmacological agents and endoscopic sclerotherapy on it.10,11 However, LDV has not been extensively employed to assess hemodynamic parameters such as vasomotor reflex in these patients. We undertook endoscopic measurement of GMBF employing LDV in normal human subjects and in patients with portal hypertension; we measured the response of GMBF to breath-holding, submucosal injection of epinephrine and sublingual administration of isosorbide dinitrate.

Methods

Twenty subjects (12 men, 8 women; aged 23 and 60 years) with a clinical diagnosis of non-ulcer dyspepsia and referred for diagnostic gastroscopy were recruited for this study as gastroscopically normal subjects. None of them had received any drug for at least one week before the study and all were non-smokers and non-alcoholics.

Thirty patients (24 men, 6 women; aged 25 to 60 years) with portal hypertension due to cirrhosis of liver were also studied. They were divided into three groups based on endoscopic findings: i) no gastropathy, ii) mild gastropathy (erythema or mosaic appearance of gastric mucosa), and iii) severe gastropathy (sherry-red spots or erosions, diffuse hemorrhagic gastriis). Portal hypertensive gastropathy was confirmed by histology and capillary
<table>
<thead>
<tr>
<th>Subjects (n)</th>
<th>Normals (20)</th>
<th>PH with no</th>
<th>PH with mild</th>
<th>PH with severe</th>
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<tbody>
<tr>
<td>GMBF</td>
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<tr>
<td>Lesser curvature (V)</td>
<td>9.1 ± 1.9</td>
<td>8.5 ± 2.1</td>
<td>7.7 ± 0.8*</td>
<td>6.3 ± 2.2**</td>
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<tr>
<td>Greater curvature (V)</td>
<td>9.5 ± 1.3</td>
<td>8.1 ± 2.5</td>
<td>7.7 ± 1.2*</td>
<td>6.5 ± 3.5**</td>
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<td>Response to breath-holding (% reduction in GMBF)</td>
<td>57.1 ± 13.7</td>
<td>35.6 ± 10.0</td>
<td>23.3 ± 20.2**</td>
<td>23.1 ± 17.2**</td>
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<tr>
<td>Response to submucosal epinephrine (% increase in GMBF)</td>
<td>41.5 ± 21.5</td>
<td>36.8 ± 29.8</td>
<td>38.9 ± 25.2</td>
<td>41.0 ± 23.7</td>
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<tr>
<td>Response to sublingual isosorbide</td>
<td>25.8 ± 15.2</td>
<td>27.6 ± 34.9</td>
<td>18.0 ± 14.9</td>
<td>50.1 ± 40.3</td>
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**Table: Gastric mucosal blood flow (GMBF) and its modulation recorded in normal subjects and patients with portal hypertension**

morphometry. The etiology of cirrhosis was: alcoholic-16, posthepatic-8 and cryptogenic-6 patients. Their Child-Pugh's classification was as follows: class A—10, B—13 and C—7. The study protocol was approved by the Institutional Review Committee and the procedures followed conformed to the Declaration of Helsinki for Human Experimentation. All subjects signed an informed consent.

**Laser-Doppler velocimetry**

GMBF was measured through an endoscope as previously described with minor modifications. We used a laser-Doppler perfusion monitor (Perilux PP-3, Perimed, Stockholm, Sweden) with an endoscopic fiberoptic probe (2.5 mm diameter). The flowmeter output was recorded on a strip-chart recorder (BBC, Goerz Metrawatt, 120-SE). Recordings were obtained with 0.2 time constant, band width of 12 kHz, artifact filter switch ‘on’ and wide-band switch ‘off’ (0.5 inch deflection for 1 volt output, chart speed of 6 cm/min). All recordings were obtained by the same person throughout the study. All measurements were made at the same time of the day to avoid diurnal variation if any, and at a room temperature of 24 ± 1°C in a temperature-controlled blood flow laboratory.

**Endoscopic procedure**

After overnight fast, each subject received intravenous butylphocapamine bromide (20 mg), 10 min prior to the procedure. Lidocaine jelly (2%, 10 mL) was used for pharyngeal topical anesthesia. Esophagogastrododenal endoscopic examination was performed (Olympus IT-20) for mucosal pathology. The LDV endoscopic probe was then passed through the biopsy channel and positioned against a flat area of the mucosal surface, at an angle of ± 30° from the perpendicular to the mucosal surface. The pressure applied on the probe was such that a distinct glow of laser light was visible on the mucosal surface while recording the blood flow. All recordings were made with the probe under vision. The endoscopist was blind to the recordings obtained.

The GMBF recordings were obtained at two sites on the lesser curvature at least 5 cm apart (one in mid-body and the other below the cardia) and two sites on the greater curvature directly opposite these. At one of the above sites, the response to breath-holding (10 sec, in inspiration) was studied in duplicate.

Epinephrine was then injected submucosally (1 mL of 1:10,000 solution) using endoscopic injector (23 G, 2 mm length). The LDV probe was then positioned on the blanched area of the mucosa, avoiding the injection tract, within 60 sec of the injection. The effect of isosorbide dinitrate (10 mg) placed sublingually was studied by obtaining a record of GMBF up to 10 min after administration. The tablet was gently pushed in place from the side of the mouth gag.

**Statistical analysis**

The mean GMBF values and the various responses obtained in the three study groups at corresponding sites were compared to those in normal subjects by applying Student's t test. The GMBF values are expressed as signal output in volts. All values are presented as mean ± SD.

**Results**

The GMBF values recorded at different sites on both the lesser and greater curvatures (9.1V ± 1.9 and 9.5V ± 1.3 respectively) in the 20 normal subjects were similar (Fig). Repeat measurements after an interval of one week in 10 normal subjects showed only minor variation (lesser curvature 8.4V ± 2.0 and 9.0V ± 2.6; greater curvature 8.7V ± 1.1 and 8.9V ± 3.0), confirming the
reproducibility of the technique. A mean reduction of 41.5% ± 21.5% in GMBF was observed after submucosal epinephrine injection. Breath-holding caused a reduction of 57.1% ± 13.7% in GMBF, whereas isosorbide dinitrate caused a mean increase in GMBF of 25.8% ± 15.2%. In subjects with portal hypertension but no PHG, the GMBF was similar to that in normals as were vasodilator response to epinephrine and vasodilator response to isosorbide. However, the decrease in GMBF following breath-holding was found to be significantly reduced (35.6% ± 10.0%, p<0.05) (Table). Patients with mild and severe PHG showed a decrease in GMBF as compared with normals. Further, the vasodilator response to breath-holding was significantly reduced (p<0.001) (Table). Patients with severe PHG showed an increased response to isosorbide, but this was not statistically significant.

Sample recordings from subjects in different groups are presented in the Fig. A single intravenous injection of butylscopolamine bromide (20 mg) was sufficient to reduce peristaltic activity and allow undisturbed recording of GMBF in all subjects.

Measurement of GMBF and other procedures of the protocol could be completed within a period of 30 min in each subject without any difficulty or undesirable signs and symptoms.

**Discussion**

The present study provides information on hemodynamic status of normal gastric mucosa and an insight into the pathobiology of gastropathy associated with portal hypertension. LDV measurement of blood flow at different sites in man and the various induced responses have been shown to be fairly reproducible. Our observations in 10 normal subjects also substantiate the reproducibility of these measurements. Our findings of decreased GMBF in patients with severe PHG are in conformity with those of others. However, Panes et al reported increased GMBF in cirrhotic patients with PHG.

Our observation on the induced changes in GMBF (selective attenuation of only vasomotor reflex) may support the 'passive congestion' theory proposed by Iwao et al. This vasomotor reflex response, in addition to visual endoscopic assessment, may serve as an indicator of severity of PHG. The vasomotor tone in the gastric mucosa may be altered, depending on the extent of portal venous hypertension and local capillary pooling. The vasodilator response is possibly opposed by such a compromised vasomotor tone.

In this context, it is interesting to note that Belcaro et al observed a similar attenuation of the venous vasomotor reflex in the perimalleolar skin in patients with
lower limb venous hypertension.

Prolonged therapy with Centella asiatica, an Indian medicinal herb was found to improve the venous vasomotor reflex. It would be interesting to study the effect of therapy with propranolol or venodynamic agents like Centella on the GMBF and the vasomotor reflex in patients with portal hypertension and PHTG.

References