SHORT REPORTS

Effect of Sublingual Isosorbide Dinitrate on Wedged Hepatic Venous Pressure in Cirrhotics with Portal Hypertension

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Abstract
Sublingual isosorbide dinitrate (5 mg) was given to six cirrhotics with portal hypertension to see its effect on wedged hepatic venous pressure (WHVP). The WHVP was determined using Selddinger's technique and an end-hole 7F or 8F catheter. WHVP values fell in four of six patients and rose minimally in two. Mean WHVP decreased from 24±58 mmHg to 18±50 mmHg (mean fall 25%), and this effect lasted for 20 min.

Key words: Cirrhosis, isosorbide dinitrate, portal hypertension, wedged hepatic venous pressure.

Introduction
Portal venous pressure depends upon the amount of blood flow and the vascular resistance in portal venous tributaries. The volume of blood flow can be reduced by lowering the cardiac output with beta-adrenergic blockers, and vascular resistance can be reduced by vasodilators.

The efficacy of propranolol in lowering portal venous pressure and thereby preventing recurrent oesophageal variceal bleeding is well established. Results of the efficacy of isosorbide dinitrate in lowering portal venous pressure (PVP) have, however, been controversial. In two studies, this drug lowered PVP efficiently by oral, sublingual and parenteral routes, while in one it showed no effect on PVP when instilled intravenously. Similarly, sublingual nitroglycerine was not effective in lowering PVP while its oral administration significantly reduced PVP in cirrhosis.

A preliminary study was therefore done on biopsy proven cirrhotics to see the effect of sublingual isosorbide dinitrate on portal pressure. As wedged hepatic venous pressure (WHVP) is often representative of PVP, this parameter was used in the evaluation.

Material and Methods
Six patients with biopsy proven post-necrotic cirrhosis (3 males, 3 females; aged 20–50 years) were studied. All had portal hypertension and had bled from oesophageal varices in the past. At the time of the study the patients were hemodynamically stable, and had no active bleeding or ascites. Following Child's criteria, two were in A, three in B and one in C grade. Prothrombin time was normal in all the cases.

Measurements of Hepatic Venous Pressures
All patients were studied in the supine position in a basal postabsorptive state after overnight fasting. A mild parenteral sedative (pentazocine 50 mg and promethazine 25 mg intramuscularly) was given prior to the procedure and the right femoral vein was catheterized by the Selddinger technique under local anesthesia. An end-hole 7F or 8F catheter was used. All right heart pressures were recorded and blood O2 saturations measured. Free and wedged hepatic venous pressures were recorded. The patients were then given isosorbide dinitrate 5 mg sublingually and WHVP was monitored every 5 min for 20 minutes. Before removal of the catheter from the wedged position, a small amount of radiographic dye was injected to confirm the wedged position of the catheter and a short run of 35 mm cine film taken for record. The catheter was then moved back and all right heart pressures and blood O2 saturations were measured again.

Results
Following sublingual isosorbide dinitrate mean WHVP in six cirrhotic patients with portal hypertension fell from 24±58 mmHg to 18±50 mmHg, a fall of 25% (Fig). Two of six patients showed a slight rise in WHVP, but the other four showed a fall. Except for a transient fall in the systemic blood pressure, no other side effect was noted. Two patients complained of mild headache during the procedure.

Discussion
A prompt fall in WHVP occurred after sublingual administration of isosorbide dinitrate in four of six patients with cirrhosis and portal hypertension.

The drug has been used orally, sublingually and intravenously in many studies to lower portal venous pressure, and the response varied from nil to significant fall in PVP. Freeman et al. noted 35% reduction in PVP with intravenous and 44% with oral administration of isosorbide dinitrate, while Hallemans et al. found 21% reduction in PVP with intravenous and oral use of the drug. Intravenous instillation of 5 mg isosorbide dinitrate produced no effect on PVP in another study. The mechanism of such differential effects of isosorbide dinitrate on PVP may lie in differing drug pharmacokinetics following oral, sublingual
times a day seems to be a suitable alternate route of administration. Further studies are needed to ensure that the phenomenon of tachyphylaxis does not counteract its hypotensive effect.

References

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