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Acute variceal bleeding: Pharmacological treatment and primary/secondary prophylaxis

A. Dell'Era MD
Assistant Professor of Medicine (Gastroenterology)

R. de Franchis* MD
Professor of Medicine, Director (Gastroenterology)

F. Iannuzzi MD
GI Fellow

Department of Medical Sciences, University of Milano, and Gastroenterology 3 Unit, IRCCS Ospedale Maggiore Policlinico, Mangiagalli and Regina Elena Foundation, Via Pace 9, 20122 Milano, Italy

Variceal bleeding is one of the most severe complications of portal hypertension related to liver cirrhosis. Primary prophylaxis is considered mandatory in patients with cirrhosis and high-risk oesophageal varices, and once varices have bled, every effort should be made to arrest the haemorrhage and prevent further bleeding episodes. In acute variceal bleeding, vasoactive drugs that lower portal pressure should be started even before endoscopy, and should be maintained for up to 5 days. The choice of vasoactive drug should be made according to local resources. Terlipressin, somatostatin and octreotide can be used; vasopressin plus transdermal nitroglycerin may be used if no other drug is available. In variceal bleeding, antibiotic therapy is also mandatory. In primary and secondary prophylaxis, beta-blockers are the mainstay of therapy. In secondary prophylaxis (but not in primary prophylaxis) these drugs can be combined with organic nitrates.

Key words: liver cirrhosis; therapy; prophylaxis; variceal bleeding.

Variceal bleeding is one of the most severe complications of portal hypertension associated with liver cirrhosis, carrying a mortality within 6 weeks in the order of 11–20%.

* Corresponding author. Tel.: +39 02 5503 5331/2; Fax: +39 02 5032 0747.
E-mail address: roberto.defranchis@unimi.it (R. de Franchis).

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Primary prophylaxis is therefore considered mandatory in patients with cirrhosis and oesophageal varices, and once varices have bled every effort should be made to arrest the haemorrhage and prevent further bleeding episodes.

Oesophageal variceal bleeding occurs only when there is a clinically significant portal hypertension, defined as hepatic vein pressure gradient (HVPG) >12 mmHg.[1,2] Pathophysiologically, portal pressure depends on blood inflow and on resistance in the portal system. Therefore, to reduce portal pressure we can act on reducing portal blood flow by using splanchnic vasoconstrictors, and on the resistance in the portal system by using vasodilators. Some drugs (e.g. vasopressin and somatostatin) are short-acting, and therefore they are used in the setting of acute bleeding; others (e.g. non-selective beta-blockers) are long-acting and are used in primary and secondary prophylaxis.

In this chapter we will review the drugs used in the setting of acute haemorrhage and for primary and secondary prophylaxis of variceal bleeding.

ACUTE VARICEAL BLEEDING

The pharmacological treatment of acute bleeding aims at arresting the haemorrhage, preventing rebleeding, and reducing mortality. In cirrhotic patients, clinical studies[3,4] and a meta-analysis[5] have confirmed the beneficial effect of vasoactive drugs for variceal haemorrhage (Figure 1). Current guidelines[6] recommend starting pharmacological therapy with vasoactive drugs as soon as possible – even during transfer to the hospital,[3] since almost a quarter of deaths happen early[7] – and maintaining it for up to 5 days, since this is the time frame in which early rebleeding is most frequent.[6] Diagnostic and eventually therapeutic endoscopy is facilitated by the use of vasoactive drugs, and should be performed as soon as possible after admission.

Several drugs are available to treat acute variceal haemorrhage, and the choice should be made according to local resources, bearing in mind that the only drug shown

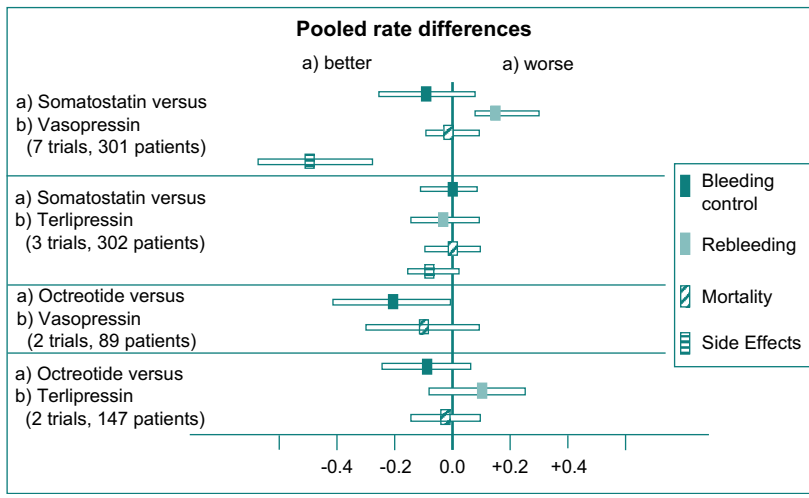

Figure 1. Comparison of vasoactive drug treatments for variceal bleeding in cirrhosis: a meta-analysis. From D'Amico et al (*Seminars in Liver Disease* 1999; **19:** 475–505) with permission.