Interplay of portal pressure, portal perfusion and hepatic arterial inflow in modulating expression of hepatic encephalopathy in patients with spontaneous or artificially created portosystemic shunts

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The major theme of this discussion is how portal pressure after portosystemic shunt procedures may modulate the expression of hepatic encephalopathy. Decades of emphasis on the paramount importance of maintaining portal venous perfusion after shunt procedures is now being re-examined. In countries where non-cirrhotic portal hypertension is common, physicians have long recognized that hepatic encephalopathy is rare even with total portosystemic shunting. However, once decompressive shunts are created, hepatic encephalopathy becomes a clinical problem. Why this occurs needs to be better understood. In the meantime, there has been virtual abandonment of surgical shunts in favor of endoscopic variceal ablation treatment. This is despite the fact that surgical shunts that only partially decompress the portal hypertension are associated with excellent long-term control of variceal bleeding and low rates of hepatic encephalopathy. The time has come to once again examine the key relationship between portal pressure, portal perfusion with hepatic arterial inflow in inducing hepatic encephalopathy after creation of portosystemic shunts. [Indian J Gastroenterol 2003;22(Suppl 2):S25-S27]

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However, most hepatologists recognized that encephalopathy was rare in the absence of clear-cut reduction of liver function even when large portosystemic collateral vessels were present. Hence, adoption of the term hepatic encephalopathy. Nonetheless, recognizing that encephalopathy could occur in patients with large portosystemic shunts without significant liver disease, it was agreed that Type B (for portosystemic bypass) HE should be included in the classification of hepato-cerebral syndromes associated with liver dysfunction.

HE is unusual in patients with non-cirrhotic portal hypertension (NCPH) even after large variceal bleeding episodes. This is true even in patients with total portosystemic shunting from birth. Only when superimposed liver disease occurs or when a surgical shunt is performed is HE a clinical issue. The degree of portosystemic shunting of splanchnic blood could not be increased by the shunt procedure. Also, essentially little or no portal venous hepatic perfusion could have been lost since by definition there is virtually none if there is 100% shunting. Therefore, reduction in portal pressure must be in some way responsible for the appearance of HE after shunt procedures.

Traditionally, modifications of portosystemic shunts to reduce the incidence of postoperative HE and worsening liver function were centered around trying to preserve residual portal venous hepatic perfusion. There is evidence to support the lower frequency of HE with these modifications, but significant data exist to suggest that this is independent of portal venous hepatic perfusion. Indeed, these data suggest that preservation of portal pressure is the key factor in reducing the frequency of HE following surgical shunt.

Similar experience has been gained in performing portal decompression with the transjugular intrahepatic portosystemic shunt (TIPS). Based on a portosystemic pressure gradient of 12 mmHg being the cut-off point above which variceal bleeding occurred, initial patients had very aggressive portal decompression. Frequency of HE as high as 25% of cases after TIPS was reported. This led to a proposal by Rossie and colleagues to achieve a 50% reduction in pressure gradient; this resulted in control of variceal bleeding and low rates of
HE. In some cases, embolization of specific vessels was performed in addition to TIPS. While these observations are not as pure as those with surgical shunts for NCPH, they lead to the same conclusion. Excessive reduction in portal pressure leads to increased risk of HE in patients with portosystemic shunts.

How could preserved portal pressure in patients with portosystemic shunts 'protect' patients from HE? Prikker suggested that excessive decompression may lead to enhanced absorption of toxins (e.g., ammonia) from the gut. This may relate not only to absorption but also to a greater splanchnic venous flow rate with complete decompression of portal hypertension. In other words, even if ammonia absorption was not enhanced, greater flow rates of ammonia-containing blood could overwhelm the capacity of the patient to handle the systemic delivery of this toxin. Excellent studies in the portacaval shunt rat model support this concept.12,13

Another mechanism proposed is that portal pressure modulates compensatory changes in hepatic arterial inflow. Studies in dogs indicate that hepatic arterial inflow is greater with residual portal hypertension after shunt procedures.7 Surgeons with experience with patients with NCPH who rarely exhibit HE comment on the very large size of the hepatic artery, which supports this concept. The presumed neurohumoral mechanism for hepatic arterial compensation after reduction or loss of portal venous hepatic perfusion is poorly understood, but could be mediated by adenosine.14

Using ammonia as an example, we can construct the following perspective. Patients who have total portosystemic shunts and normal liver status deliver substantial quantities of ammonia into the systemic circulation. Portal hypertension may limit absorption of ammonia, but ultimately the second pass through the liver via the hepatic artery clears ammonia efficiently; the greater the hepatic blood flow, the better the ammonia clearance. It should be noted that muscle and other organs also participate in limiting the systemic accumulation of ammonia. These mechanisms may be indirectly maintained by the liver (e.g., muscle wasting is seen in advanced liver disease).

If portal pressure is reduced, ammonia absorption is increased and splanchnic venous flow increases. Moreover, compensatory increase in hepatic arterial inflow may fail to occur, thereby reducing ammonia clearance. In addition, other crucial aspects of liver function may be compromised. Comparison of the increment in hepatic arterial blood flow in patients with low (say <5 mmHg) versus preserved or high (say >10 mmHg) portal pressure after standardized shunt procedures could be evaluated in studies.

Before dismissing a role for loss of portal venous perfusion of the liver as a factor in post-shunt HE, some points should be made. In patients exhibiting no HE but have 100% shunting (e.g., portal vein thrombosis) small collateral vessels may re-establish some degree of portal venous perfusion of the liver. In theory, a complete portal venous decompression could inhibit flow through these small feeding vessels. The impressive ability for collateral vessel formation in the portal hypertension circulation is well described.15 Therefore one cannot dismiss the possibility that neocollateral vessels bridging the splanchnic venous bed and the hepatic circulation could be a mechanism preventing HE in patients with long-standing NCPH.

Recently, Rossle and Piotrowski10 re-emphasized the issue of diversion or short-circuiting hepatic arterial inflow in a retrograde fashion after creation of a low-pressure outlet upstream from the liver. Unlike in end-to-side shunts where essentially all hepatic arterial inflow is driven through the sinusoids, side-to-side surgical shunts or TIPS can steal this important component of total hepatic blood flow. Depending on the relative contact time of hepatic arterial blood with hepatocytes, the reversed blood flow upstream to the decompression shunt may have variable clearance of toxins. Essentially, what may arise is not only a reduced compensatory hepatic arterial blood flow with excessively lowered portal pressure, but also a steal of this blood flow away from sinusoidal perfusion. This illustrates the complexity of trying to establish the relative importance of hepatic perfusion and portal pressure in the genesis of HE after decompression procedures.

Some other approaches to increasing hepatic blood flow have been reported with portosystemic shunts. One was to anastomose an abdominal artery to the transected portal vein stump.16 After an initial bout of enthusiasm, this procedure was quietly abandoned. There was some evidence that the procedure attenuated portosystemic shunt sequelae17 but over-arterialization due to the very high perfusion pressures led to fibrosis and eventual loss of effective blood flow. Another interesting approach in the rat was transposition of the portal vein and inferior vena cava. All portal blood drained into the inferior vena cava while inferior vena cava blood perfused the liver. This has not been done in humans despite an apparent major reduction of shunt sequelae.18 Both these approaches support the concept that effective hepatic perfusion and not just portal venous perfusion is capable of sustaining liver function after portosystemic anastomosis.

It remains to be established whether a small-stoma end-to-side portacaval shunt will be the best approach to portosystemic decompression. Pharmacologic measures to increase hepatic arterial flow, possibly even by pump infusion, also merit consideration. In countries where large numbers of patients experience variceal bleeding due to NCPH, variceal banding or sclerotherapy...
Expression of encephalopathy in presence of portosystemic shunts

Table 1: Factors Influencing HE after portosystemic shunts

1. Portal hepatic perfusion
2. Hepatic arterial inflow
3. Contact of total hepatic blood flow with hepatocytes
4. Portal pressure
5. Functional status / mass of hepatocytes
6. Severity of precipitating factors

Table 2: Reasons why portal pressure needs to be preserved

1. Preserve portal hepatic perfusion
2. Permit optimum hepatic arterial compensation
3. Reduce limit ammonia absorption
4. Limit increase in splanchnic venous flow
5. Decrease hepatic arterial steal phenomenon

Table 3: Reasons why major portal decompression may be bad

1. Enhanced absorption of ammonia
2. Anoxia due to toxins - loss of muscle mass
3. Disordered amino acid metabolism - loss of muscle mass
4. Poor hepatic arterial inflow - reduced hepatic mass
5. Reduced ammonia clearance by liver
6. Decreased testosterone - loss of muscle mass

Table 4: The optimum shunt?

1. Sufficient drop in pressure to prevent variceal bleeding
2. Resolution or no aggravation of ascites
3. Low incidence of HE
4. Preservation of hepatic function
5. End-to-side to maintain arterial perfusion?
6. Small stoma
7. Easy operation
8. No stenosis over time

is currently the mainstay of therapy.

A simple partial decompression procedure may be safe in many patients. Either an end-to-side anastomosis with a carefully calibrated stoma or the small-caliber H-graft side-to-side technique should be explored further. The potential for reversal of flow with the latter procedure along with the hepatic arterial steal phenomenon make it less attractive on a theoretical basis.

In Tables 1-4, the concepts outlined in this discussion are summarized. There may be strong reasons to examine why we are so reluctant to perform surgical shunt procedures. It appears to be fear of reproducing the unsatisfactory results in the latter half of the last century, even though newer surgical techniques appear to have improved outcomes. We need to more rigorously examine the complex interrelationship between portal pressure, portal venous and hepatic arterial perfusion after creation of portosystemic shunts.

References


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