Editorial

TIPS and refractory ascites. Lessons from the recent history of ascites therapy

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Refractory ascites, a term introduced during the 1950's to define the ascites not responding to sodium restriction and diuretics, was an extremely frequent condition prior to the 1960's, when the medical treatment of ascites consisted of the administration of mercurial or thiazide diuretics. These agents have a poor natriuretic effect in patients with marked hyperaldosteronism, who represent approximately 50% of the patients with cirrhosis admitted to hospital with tense ascites. These patients were then treated by large-volume paracentesis.

Loop diuretics and spironolactone were introduced in clinical practice in 1960, and this represented a major step forward. Spironolactone was found to be effective in most cases not responding to thiazides (1). On the other hand, the association of spironolactone and furosemide or ethacrynic acid potentiated the natriuretic effect of each drug while reducing their side effects on potassium metabolism (2). Using these modern diuretics the prevalence of refractory ascites was decreased to less than 10%. Refractory ascites, however, continued to be a major problem in clinical practice since at that time large-volume paracentesis was suggested as a precipitating factor of hepatorenal syndrome (3) and, therefore, it was no longer used as a specific treatment of patients with cirrhosis and ascites.

Sporadic reports on the potential usefulness of side-to-side portacaval shunt in the treatment of refractory ascites have appeared since 1955 (4). However, it has never gained general acceptance due to the significant early postoperative mortality and high incidence of chronic incapacitating encephalopathy associated with this procedure (5). Another treatment of refractory ascites with a transient popularity was the Rhodioascit apparatus which extracted and concentrated the ascitic fluid and reinfused it into the general circulation (6). These procedures were introduced and abandoned without the support of randomized controlled trials.

In 1974, LeVeen introduced peritoneovenous shunting for the treatment of ascites (7). His original idea – if the ascitic fluid derives from plasma, most problems related to ascites formation could be solved by returning it to the intravascular compartment – was subsequently proved to be correct. Numerous studies performed during the 1980's showed that peritoneovenous shunting in cirrhosis with refractory ascites was associated with a marked suppression of renin, aldosterone, norepinephrine and antidiuretic hormone, indicating an improvement of circulatory dysfunction, an amelioration of renal function and an increased response to diuretic treatment (8). An outstanding feature is that whereas the LeVeen shunt has been investigated very carefully in a pathophysiological context (i.e. exploring the mechanisms by which it improves renal and circulatory function), it has been very poorly assessed from a therapeutic point of view. Although there were numerous reports describing the early and late complications that may follow the insertion of the prosthesis, very few studies aiming to assess the efficacy of the procedure in different subsets of patients in order to improve the indications of the shunt have been performed. Few attempts have also been made to prevent the most important problem of the LeVeen shunt: early obstruction of the prosthesis. The Denver shunt with a single valve, which was specifically designed to prevent shunt obstruction, was not effective in reducing this problem (9). A second Denver shunt with a double valve was then introduced, but no comparative studies between this prosthesis and the LeVeen shunt have been performed. Finally, it is interesting to note that well-executed randomized controlled trials compar-
The transjugular intrahepatic portosystemic shunt (TIPS) is a nonsurgical portacaval anastomosis which behaves as a side-to-side portacaval shunt (16). TIPS is currently used with increasing frequency as a treatment of variceal bleeding in cirrhosis. Its main advantage over the traditional surgical shunts is the lack of postoperative complications related to the surgical procedure. However, as expected, TIPS may also impair hepatic function and induce severe hepatic encephalopathy (16). TIPS has the additional problem of a high rate of shunt malfunction due to stenosis of the stent lumen or the hepatic vein segment connecting with the prosthesis (17). During the past 3 years five pilot studies assessing TIPS in more than 80 patients with refractory ascites have been published (18–22). More than 10 other investigations have been reported in abstract form. All the studies show similar results. TIPS is associated with a marked suppression of renin, aldosterone and norepinephrine and an improvement in renal function and the renal response to diuretics. A significant number of patients remain free of ascites with minimal or no diuretic therapy during follow-up. The incidence of hepatic encephalopathy after TIPS is high (ranging between 50% and 75%). However, since hepatic encephalopathy was satisfactorily managed by standard treatment in most cases, TIPS is proposed as a useful treatment of refractory ascites in cirrhosis.

In this issue of the Journal of Hepatology, Lebrec et al. report a randomized controlled trial comparing TIPS versus therapeutic paracentesis in patients with refractory ascites (23). This investigation is important for various reasons. Firstly, it is the first randomized study comparing TIPS with an alternative effective treatment of refractory ascites. Secondly, it confirms that TIPS is highly effective in the control of refractory ascites. Finally, it suggests that TIPS in patients with refractory ascites is associated with a significant reduction in survival.

The recent history of therapy in hepatology, particularly in the field of portal hypertension and ascites, has been characterized by an excessive number of swings in attitudes. New treatments are rapidly introduced, sometimes with little background research into indications, complications and effects on the natural history of the disease and survival; these treatments are then abandoned, occasionally with little justification, as soon as new therapies are developed. Surgical portacaval shunts are clear examples of this attitude. They were widely used for the management of patients with variceal bleeding for many years but are now rarely performed. The principal reason for this change is that, whereas surgical shunts are very effective in controlling the hemorrhage, they increase the incidence of hepatic encephalopathy and do not improve survival. However, this ignores the fact that surgical shunts also have beneficial effects on other frequent complications related to portal hypertension, such as ascites, spontaneous bacterial peritonitis and hepatorenal syndrome, and may improve the quality of life of the patients (24). Peritoneovenous shunting is another example. It would be an excellent therapy for refractory ascites provided the rate of shunt obstruction was reduced. Therefore, research into this procedure should have been directed to preventing shunt obstruction (i.e. using materials with less thrombogenic properties). The clearest example, however, is the paracentesis pendulum. Paracentesis was the commonest treatment of ascites prior to the 1960's; it was subsequently abandoned; but now it is the treatment of choice for tense ascites in cirrhosis in many centers.

TIPS, if not properly assessed, could be another example of a pendulum swing. It is an effective treatment of refractory ascites and very attractive from a pathophysiological point of view, but it also has significant problems. The rate of shunt obstruction is higher than that observed with the LeVeen shunt. Moreover, it increases the incidence of hepatic encephalopathy and does not improve, in fact it may reduce, survival. Therefore, TIPS has the disadvantages of both the LeVeen prosthesis and the surgical portacaval shunts. To avoid the possibility of a TIPS pendulum, it should not be considered as a regular treatment of refractory ascites at present. Multicenter randomized controlled trials in large series of patients should determine whether TIPS improves the results obtained with paracentesis or peritoneovenous shunting in terms of quality of life and survival. These trials should take into account the facts that patients with refractory ascites do not constitute a homogenous population, and that TIPS may be useful in some patients.
and harmful in others. The identification of these subgroups of patients may be the principal aim of these trials, since this would allow individual treatment according to the characteristics of each patient.

References


