Refractory ascites and ascitic fluid filtration and concentrate infusion

Ascites is the most common problem encountered by hepatologists involved in the care of patients with chronic liver disease. It occurs almost twice as frequently as variceal bleeding, and occurs in 50% of patients within 10 years of a diagnosis of compensated cirrhosis. From the era of Celsius to the late 1940s, repeated paracentesis was the only form of treatment that could be offered to these hapless patients. The introduction of diuretics in the early 1950s had a revolutionary impact on the management of cirrhosis. Medical treatment in the form of salt and fluid restriction and diuretics is safe and efficacious for the control of ascites in the vast majority of cirrhotics.

However, up to 20% may prove refractory to this approach, and this may adversely affect both quality of life and long-term survival. Depending on the existence of other complications, the 1-year survival of patients with refractory ascites varies from 20%-50%. Such patients are thus appropriate candidates for more invasive forms of treatment such as large-volume paracentesis (LVP), ultrafiltration with ascites reinfusion, peritoneovenous shunting, TIPS, or orthotopic liver transplantation (OLT). The choice of a particular procedure has to be made after careful consideration, weighing the efficacy, safety, cost-effectiveness, and influence on survival.

LVP with plasma expansion has resurfaced as the most frequently used modality for management of tense ascites. This is especially true in the Indian scenario, the options of TIPS and OLT being largely unavailable. Numerous studies, some of them comparing LVP with diuretics, have shown a high efficacy (more than 90% vs 70% for diuretics) of this procedure in eliminating ascites. Other significant advantages of LVP have been a far lower complication rate (16% vs 60%) and shorter hospital stay, though no survival advantage was demonstrated. A major disadvantage of repeated paracentesis is that it can lead to protein depletion and exacerbate malnutrition in these patients whose capacity to synthesize proteins is already decreased.

In an attempt to conserve body protein while selectively removing sodium, water, and other substances, Adler and Katz, in 1958, was probably the first to filter ascitic fluid, and reinfuse the protein concentrate into the peritoneal cavity. This ushered in an era during which paracentesis with reinfusion of unmodified or partly concentrated ascitic fluid was commonly used for managing ascites. In the 1970s, Levy et al designed the Rhodioascent machine which ultrafiltered low-molecular-weight substances less than 45,000 daltons from ascitic fluid and concentrated its protein content 2-4 fold before reinfusing it intravenously.

The machine fell into disrepute after an initial enthusiasm, due to several reasons: the need for CVP monitoring, patient discomfort because of long duration (up to 12 hours) of the procedure, and the occurrence of serious complications like pulmonary edema, disseminated intravascular coagulation and variceal hemorrhage in up to 8% of patients. Several modifications ensued in an attempt to overcome these shortcomings. It was suggested that a partial instead of total removal of ascitic fluid by the Rhodioascent would avoid serious complications because of smaller volumes returned intravenously, while decreasing the dose of diuretics required.

Hariprasad et al described a new technique of extracorporeal dialylic ultrafiltration of ascitic fluid with intraperitoneal reinfusion, in a patient in uremia and intractable ascites. Since it conserved protein and allowed removal of large fluid volumes at a fast rate (average 3-5 hours) without adverse hemodynamic effects, he suggested its use in non-uremic patients using only a pump and dialyzer (to provide ultrafiltration), while excluding the dialysis machine. This was promptly put into practice in a number of centers, with gratifying results. Double ultrafiltration, which further reduces the time of the technique (2 hours) and separate ultrafiltration, which considerably decreases patient discomfort, are additional modifications of Hariprasad’s technique which have been employed.

This issue of the Journal carries a report by Mehta et al comparing the cost, efficacy and safety of TVP with plasma expansion to that of ascitic ultrafiltration and intravenous reinfusion (AFI) in the management of tense or intractable ascites. The technique described by Landini et al has been modified by the authors, using a hemodialyzer instead of a hemofilter. Both TVP and AFI were found to be equally effective in removing ascites, causing a similar degree of weight loss.

Previous studies have reported a significant immediate, though transitory, rise in ascitic fluid albumin with AFI. This is said to improve the opsonic activity of ascitic fluid. An improvement in serum albumin over longer follow up has also been shown; this could be secondary to transfer of protein from the peritoneum or, as suggested by some, improved liver function, the cause of which could be multifactorial. Beneficial hemodynamic effects due to increase in atrial natriuretic factor and decrease in plasma renin activity have also been reported.

Akin to available literature comparing the two techniques, both procedures were well tolerated in the current study, with no evidence of clinical DIC, worsening of renal function or hyponatremia. The percentage of minor
febrile reactions at 70% was however considerably higher than the 10%-50% incidence reported earlier. The time taken for AFI (median 12 hours) was not only significantly more than that of TVP, but also much longer as compared to all recent reports of this technique. This could detract considerably from the charm of the procedure, by increasing patient discomfort as well as increasing the probability of infective complications like bacterial peritonitis. This may translate into prolonged hospital stay and higher cost of treatment in the long run.

By withholding diuretics after TVP/AFI the authors may have tried to show that slower reaccumulation of ascites. However, only a marginal trend towards slower weight gain could be documented, confirmation of which would require larger numbers of patients matched for Child’s status to be included in each group. In actuality, salt and fluid restriction as well as diuretics must continue after either TVP or AFI to accrue the maximal clinical benefit to the patient.

The real benefit highlighted by Mehta et al was a 33% reduction in cost with AFI. However, this too needs to be taken with a pinch of salt since it is at the expense of considerable prolongation of procedural time (12 hours vs 3-5 hours in studies using hemofilters), reuse of the hemodialyzer (admittedly not an uncommon practice) and inclusion of a week’s cost of diuretics in the TVP group — this certainly cannot be generalized to the individual patient.

The role of TIPS and OLT in refractory ascites cannot be ignored. After successful placement of an intrahepatic portosystemic shunt, complete response of ascites was found in 74% and partial response in 18%, at 3 months. Higher survival at 1 year after TIPS was associated with complete response. Child’s status, cause of liver disease and hepatic encephalopathy did not contribute to survival outcome. TIPS thus is a useful procedure for control of refractory ascites, especially while the patient is awaiting OLT. Improvement of functional renal failure with TIPS is an added advantage, whereas other forms of treatment like LVP and peritoneovenous shunting may aggravate it.

A note of caution has been added by the finding that response of ascites after TIPS may be delayed up to a month and occurs in the presence of aggravated systemic vasodilation. TIPS may not thus be a panacea for all patients with ascites. Careful attention to cardiac and renal status needs to be given prior to the procedure, keeping in mind that sodium excretion is not immediate or complete. Continued sodium and water restriction is mandatory after the procedure.

Considering the shortened survival of patients with refractory ascites, and the current 1-2 year survival after OLT exceeding 75% in the West, OLT remains the treatment of choice. One has only to wait for it to become technically and economically feasible in our set-up!

In conclusion, AFI conserves body protein, making it a far more physiologic option than TVP for the relief of ascites; its other benefits include low cost (when compared to the cost of albumin). Intraperitoneal instead of intravenous infusion could further avoid serious infective or hematologic complications. However, TVP with volume expansion is also a time-tested procedure and larger trials confirming the superiority of AFI are required, before relegating TVP to history once more.

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**BOOK REVIEW**

*Gastroenterology Scene in India: Past and Present, Landmarks and Milestones.* Edited and Published by Dhananjaya Sharma. Jabalpur, 1997. 188 pages

My first reaction on seeing this book was “It was about time someone did it.” Most students of gastroenterology in India can hold out on the world history of this subject, especially in the field of endoscopy. Very few know about our own record in this century, except what they learnt by word of mouth. And how sadly fleeting this can be is obvious when we read the chapter on History of Gastroenterology in India by the late Professor N Madanagopal. If this book was conceived a year later, we would never again have access to Prof Madanagopal’s treasure trove.

Other such pearls in this book are the chapters on Gastroenterology in India by Prof F P Antia, Gastroenterology in Calcutta by Prof D N Guha Mazumder, Portal Hypertension in India — Historical Aspects by Prof S K Mathur and Prof A N Supe, History of Surgical Gastroenterology Departments in India by Prof N Rangabashyam, On the Threshold of Liver Transplantation by Prof Rajan Saxena, and The Development of Gastroenterology: As AIIMS Faculty Member by Prof B N Tandon.

Some chapters lay down the unique circumstances and problems encountered in setting up the speciality in corners of India, e.g., Dr Philip Augustine in Kerala, Dr S P Misra in Allahabad, Dr S V Mukewar in Nagpur, Dr S S Prasad in Patna. Some others deal with the experience in individual institutions, and a few with individuals’ experiences.

Overall, Dr Sharma deserves credit for this venture. It must have been an effort, sitting in Jabalpur, to mobilize these chapters from so many authorities with so little time on their hands (maybe Dr Sharma can consider a chapter on this experience in the next edition!). Having said this, I must confess that, to me, some of the chapters seem out of place (an occasional ego trip included), dwelling curiously on history; some focus more on the world and very little on India. The editing is less than desirable, and the printing style has scope for improvement. Dr Sharma wanted the articles to “bear the stamp of their author’s style,” but this need not have resulted in a warts-and-all outcome. Still, a giant step!

Finally, no price is printed on this book. I presume Dr Sharma wants to make this a priceless collection for the truly interested. There should be a lot of takers.

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