TREATMENT OF CIRRHOTIC ASCITES BY PERFUSION OF AUTOGENOUS ASCITIC FLUID*

A PROVISIONAL REPORT

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The intravenous use of ascitic fluid as a form of therapy has been known for several decades. Davis and Blalock[3] noted that the transfer of human ascitic fluid in group compatible animals and human recipients was practicable. In 1941 Davis[2] in a clinical and experimental study used ascitic fluid from cirrhotic and cardiopathic patients in the treatment of shock, and found it a useful plasma expander.

A similar study was carried out in 1947 by Molina *et al.*,[10] with comparable results. Furthermore the authors noted that injection of small amounts of autogenous ascitic fluid into a cirrhotic patient produced no untoward effect.

Since then several groups of workers have practised infusion of ascitic fluid into cirrhotic patients.[4-6,8,14] Emmrich and Fliege[4] have used it as a therapeutic measure in the management of decompensated liver cirrhosis. Kaiser *et al.*[6] have found that it improved renal function and helped to control ascites. Lempke *et al.*[7] submitted that it was a valuable aid in preparing the cirrhotic patient for surgery, supporting him during the operation. The procedure was well tolerated.

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Britton[1] infused autogenous ascitic fluid, the salt and water content of which had been reduced by dialysis. It was considered a procedure of value especially in the preparation of patients for major surgery although there were some minor side-effects.

Yamahiro and Reynolds[14] used autogenous ascitic fluid as a rapid plasma expander to observe the effect on renal blood flow and glomerular filtration rate. They used it in combination with a mercurial diuretic, and noted that sodium excretion was much higher than after a diuretic alone. Similar results were obtained by Papper and Saxon[11] using saline infusions as the plasma expander. Yamahiro and Reynolds[14] infused volumes varying from 1,800 to 5,400 ml., noted the absence of venous congestion, and concluded rightly that a large proportion of the fluid infused had diffused back into the peritoneal cavity.

Attempts have been made to drain the ascitic fluid into the inferior vena cava by bringing the long saphenous vein into the peritoneal cavity, or by means of a Spitz-Holter valve mechanism.[13] Unfortunately the general experience is that the effluent inevitably becomes blocked and ascites accumulates again.

The rationale of infusion of autogenous and unaltered ascitic fluid is, firstly, to preserve its protein content and use it to augment the plasma-colloid level, secondly, to increase the effective circulating blood volume and correct the hypovolaemia in the peripheral flow. This, in turn, will increase renal blood flow and the glomerular filtration rate and a diuresis is thus induced, which may be increased by administration of a diuretic, such as a mercurial, which is rapid in action and effective. The diuresis induced is accompanied by increased passage of sodium in the urine and in effect the water and salt components of the ascitic fluid are evacuated.

By this method, paracentesis is safely accomplished without the risk of hypovolaemic shock to the patient. The relief from abdominal distension is achieved much more rapidly than would be the case following the use of diuretics.

Finally, and not of least importance, the period of hospitalization of these patients is considerably reduced as they need stay only for the procedure and are subsequently allowed to go home. There is less need to maintain them on a low-salt diet or an oral diuretic.

With the modern management of the cirrhotic with ascites by means of dietary and diuretic control, most forms of the disease can be adequately treated. There are nevertheless a number of cases which remain resistant to most forms of medical regime. Furthermore, even those cases which respond to diuretics may require maintenance therapy for a prolonged period. At Baragwanath Hospital there is a high incidence of cirrhotics with ascites, which is 'refractory'. It is difficult to maintain our Bantu patients on a prolonged diuretic course, as the outpatient follow-up is unsatisfactory. A number of these patients come to hospital in a late stage of cirrhosis, when diuretic therapy is unsatisfactory and one needs recourse to periodic paracentesis.

It is for the above reasons that a therapeutic trial of infusion of autogenous ascitic fluid was started some 18 months ago at Baragwanath Hospital.

MATERIAL AND METHOD

Twenty-three patients received a total of 119 infusions. Although they do not represent an actual selection of patients, they were all referred to me by physician colleagues because of some degree of resistance to the accepted forms of medical treatment. Patients taken over for therapy had been previously investigated so as to exclude either inflammatory lesions of the abdomen or malignancy. A routine liver biopsy was carried out to confirm the presence of cirrhosis.

The basic procedure follows a set routine. The abdominal skin is prepared for paracentesis. Ascitic fluid is collected in an empty and sterile plastic container of the Fenwal type of 600 ml. capacity. (This type of bag is commonly used for collecting and transfusing blood. It has a built-in tube extension with needle attachment to collect fluid and a sealed connecting piece to which an ordinary giving set may be attached.) When the bag is full of ascitic fluid the tube is clamped, a filtered infusion set is attached to it and the contents of the bag gravitated into a forearm vein. The procedure is demonstrated to a nurse, who remains in attendance and carries out the subsequent manoeuvres, that is, when the infusion is through, the giving set is clamped, the bag lowered and allowed to fill anew from the ascitic pool. Thus the procedure is carried out by alternately filling the bag and infusing its contents into the venous stream.

The perfusion takes place at all times through a closed circuit; no air can enter it, as the plastic container collapses on emptying. The fluid is allowed to run in rapidly, in order to get rapid plasma expansion: the time taken for collecting and infusing 600 ml. of ascitic fluid varies between 30 and 45 minutes and a close watch is kept for any evidence of overload. A chart is kept of the patient's pulse rate, temperature and general well-being. If there is an undue rise in the pulse rate or temperature the rate of infusion is reduced. When 1,200 - 1,800 ml. of ascitic fluid has been infused a diuretic is given to the patient parenterally. The whole procedure takes 8 - 48 hours before completion, which is taken to be when the ascites is considerably reduced or when drainage has stopped. Throughout the procedure a careful check is kept on the fluid intake and output, which is recorded.

After each procedure the patient is allowed to go home if his general state of health permits it. He is advised to report back as soon as his abdomen again becomes distended. Our experience is that the majority of those who return still require a further infusion but they need to come back at increasingly longer intervals, commensurate with a decreasing rate of formation of ascites. Eventually some of them do not require any further treatment. Apart from the diuretic received by all the patients during the infusion, some, with a marked tendency to re-accumulate ascites, have received in addition short-term maintenance therapy with thiazide, aldosterone antagonist and potassium supplements.

Few patients have complained of any discomfort during the infusion, and I have gradually been able to increase the total volume of fluid infused, as it soon appeared evident that these patients are remarkably tolerant of large volumes of fluid being given intravenously, provided that the abdomen is being decompressed at the same time. The actual volume of ascitic fluid which the patient has received by the end of the infusion varies from one individual to another. It is seldom less than 8 l. over 8 - 10 hours and often much more. The largest amount infused into one patient has been 74,400 ml. over a period of 51 hours. During this period the pulse rate rose from 82 to 104 beats per minute, with no clinically detectable rise in central venous pressure.

RESULTS

In order to obtain a better appreciation of the results the patients have been grouped into 2 categories:

A. Those with moderately advanced cirrhosis but without gross decompensation.

B. Those with very advanced cirrhosis, or with cirrhosis complicated by other diseases.

The results of treatment are shown in Table I.

TABLE I. RESULTS OF TREATMENT OF 23 PATIENTS WITH ASCITES

	Case No.	*Age*	*No. of infusions*	*Results*
Group A	1	22	4	Not followed up
	2	33	1	Not followed up
	3	38	9	Improved; no further paracentesis
	5	35	4	Improved; no further paracentesis
	6	46	14	Improved; occasional paracentesis only
	8	38	1	Not followed up
	10	30	14	Improved; no further paracentesis
	11	48	1	Not followed up
	12	52	1	Not followed up
	13	48	5	Not followed up
	15	45	2	Not followed up
	17	40	4	Improved; no further paracentesis
	19	38	6	Improved; occasional paracentesis only
	22	35	4	Progress satisfactory; still require paracentesis, but at longer intervals
	23	53	2	
Group B	4	50	14	Initial improvement; died suddenly 18 months later after an infusion
	7	34	10	Not improved; died eventually of liver failure
	9	5	1	Died of unrelated cause some time later
	14	63	12	Not improved
	16	56	4	Not improved; died eventually of liver failure
	18	45	2	Advanced cirrhosis; died shortly afterwards of liver failure
	20	62	3	Advanced cirrhosis; died shortly afterwards of liver failure
	21	28	3	Advanced; not improving

Group A

Fifteen patients were treated in this group. Seven patients who received an average of 2 paracenteses were not followed

up, i.e. they did not report back for a check and if need be, further treatment. The result obtained here, therefore, cannot be assessed. Case 13, however, after receiving 5 infusions returned to his home village, and we heard subsequently from a mission hospital that he was still suffering from ascites.

Cases 3, 5, 6, 10, 17, and 19 have shown definite improvement as measured by the patients' general well-being, the decrease in the formation of ascites, and the progressively longer intervals at which paracentesis and infusion of ascitic fluid has been needed. Four of them do not require further treatment. Cases 6 and 19 still need infusions occasionally. These patients are not maintained on any diuretic and although they have been advised to use salt sparingly in their food, it is doubtful if this advice is ever heeded.

The above 8 patients who responded favourably to this form of therapy, received an average of 7 infusions each, the highest number being 14 and the lowest 4.

Group B

There were 8 patients in this group and they received an average of 6 infusions each.

Case 4 died rather unexpectedly following an infusion. This patient had been under treatment for 15 months, during which time he received ascitic fluid infusions on 13 occasions. He had been an invalid, but had improved to the extent that he was needing paracentesis at 2-monthly intervals, and could carry out light duties. He had reported again with the complaint of generalized weakness and abdominal distension. On this occasion the infusion was carried out at a more leisurely rate, but after a few hours, although the urinary output had been normal, he began complaining of nausea and listlessness. The procedure was then discontinued, as the jugular venous pressure had increased, and he was digitalized. Three hours later his condition suddenly deteriorated and he died.

At autopsy there was pulmonary congestion, due undoubtedly to hypervolaemia, and bilateral pyelonephritis. This was an unexpected finding, and one wondered if the renal pathology was responsible for the unusual physiological phenomena.

Case 9, a child of five, had additional pathology. He was perfused once only, and died during his period of hospitalization from an unrelated cause.

Four patients, cases 7, 16, 18 and 20, had advanced liver cirrhosis, evidenced by high bilirubinaemia, mental confusion (case 18), flapping tremor (case 20), and azotaemia with renal impairment. Only small perfusions could be carried out which did not alter their progress, and they died eventually of liver failure.

Case 21, with advanced liver disease, was making no satisfactory progress, and in view of our experience with the above cases, was given no further ascitic fluid infusions.

Case 14, the only White patient in this series, had a post-necrotic cirrhosis, and in addition was suffering from obesity, diabetes and mild cardiac failure. She received infusions of ascitic fluid on 12 occasions, and, although after each infusion she had had a good diuresis and appeared better, her long-term response was not sufficiently encouraging to justify a more extensive trial.

The results in group B were on the whole poor. It is perhaps a fair assumption to say that, had case 4 not developed secondary pathology, he would have maintained a satisfactory progress. Again one can suggest that case 14 might have fared better, had her cirrhosis not been complicated by other pathology. Lastly, the advanced cirrhotics failed to derive any real benefit from perfusion. The diuresis obtained was not considerable and though there was no evidence of increased central venous pressure it appeared that the fluid diffused back into the peritoneal cavity only too readily. There was little subjective improvement and no impression made on the ascites.

The biochemical data followed on the whole a regular pattern. The haemoglobin, packed cell volume and serum proteins were at a lower level generally, immediately after perfusion, due evidently to increased dilution. But in those who benefited from the treatment there was a steady rise in the level of the haemoglobin and serum proteins.

The electrolyte contents of the plasma and ascites was usually identical, and the pre- and post-infusion picture showed no significant differences. In one patient at least (case 10), there was marked hypokalaemia at the beginning of treatment, but with improvement in her general condition, the serum potassium reached a normal level.

Diuresis was obtained in most cases, the specific gravity of the urine dropping to about 1004 - 1005. During perfusion, the excretory ratio of sodium to potassium in the urine rose remarkably. The degree of diuresis, however, bore no constant relationship to the amount of fluid infused. In at least one instance, in case 5, the diuresis induced exceeded the amount infused.

Similarly to the findings of other workers,[6,14] I have found that a fair proportion of the infused ascitic fluid diffused back into the peritoneal cavity. Thus in 1 patient, case 19, on 1 occasion, 14,400 ml. of ascitic fluid was infused during 22 hours. The amount of urine passed during that period was 4,790 ml. Estimation of the actual volume of ascites by isotope dilution technique, using ^{131}I-tagged albumin, showed the volume of ascitic fluid at the beginning to be 7,509 ml. and at the end 1,607 ml., thus the amount of ascites actually displaced had been only 5,902 ml. although 3 times that amount had been circulated into the blood stream. In fact after subtracting the amount excreted in the urine, it is found that only about 1,100 ml. of fluid have gone to expand the vascular and interstitial compartments. This explains why it is generally possible to infuse large volumes of autogenous ascitic fluid with relative safety.

The commonest side-effect of the procedure was a rise in temperature and pulse rate. It happened in almost every case, and appeared to be due to a slight reaction. When of greater severity it was accompanied by rigors, but this was rare and if the rate of perfusion was slowed down the condition returned to normal.

Cardiovascular and respiratory embarrassment were most uncommon, and a rise in jugular venous pressure with pulmonary congestion occurred in only 1 case as described above.

One would expect this form of treatment to increase the portal hypertension, as the augmented peripheral circulation must also determine an increase in the splanchnic circulation. Theoretically, at least, there is a danger of bleeding from varices or from the portal bed. In case 20, bleeding into the abdominal cavity occurred during infusion. This patient, however, also had a low prothrombin index, marked liver dysfunction and a flapping tremor. He was given a transfusion of fresh blood and the bleeding appeared to cease.

Sepsis has not been a complication of note. Case 7 developed abdominal tenderness and some peritonism after an infusion. She was treated with antibiotics and it settled down readily. Case 21 had some wound sepsis for a week after one procedure.

There was little discomfort associated with the infusion of ascitic fluid, and it was only when it was allowed to progress for a long time that some patients complained of being ill at ease.

DISCUSSION

The infusion of unaltered and autogenous ascitic fluid in cirrhotic patients is a simple procedure, and although Britton's method of infusing dialysed ascitic fluid is more effective, and highly commendable, it is felt that the above technique, by its very simplicity and ease of operability, may find wider application. Other workers,[5,6,8] have similarly infused unaltered ascitic fluid, and noted the improvement in the patient's condition, with the inducement of a sodium diuresis and a decrease in the ascites. Yamahiro and Reynolds[14] submit that the rapid plasma expansion decreases the production of aldosterone and thus induces diuresis. There is also no doubt that the improved renal flow and glomerular filtration rate are potent factors in achieving diuresis.

Like Kaiser and his co-workers,[6] I have infused large amounts of ascitic fluid and have found no deleterious

effects on the patients. I have also not been deterred by the presence of oedema, which in the cases in this series was largely due to hypoproteinaemia. In the presence of cardiac insufficiency it would be inadvisable to proceed with the infusion, and the cardiac condition should receive primary attention.

As mentioned above, the tolerance of the cirrhotic patient to the infusion of large volumes of intravenous fluid is largely due to the diuresis obtained and especially to the easy diffusibility of fluid back into the peritoneal cavity. The latter does not detract from the merits of the procedure, as it is known that the protein content does not diffuse back readily.[9,12]

This then leads to a rise in serum proteins, which will help to correct any hypoproteinaemic oedema, when present, as was observed in 1 patient (case 17). Further, the rise in serum proteins and the concomitant fall in ascitic proteins will tend to retard the formation of ascites. This might explain why patients responding to this form of treatment do not form ascites again so readily.

In this series most patients who responded to ascitic fluid perfusions did not show lasting results until the procedure had been repeated on several occasions, sometimes as many as 14 times. These patients improve both subjectively and objectively; however the basic pathology in the liver remains unaltered, and therefore re-accumulation of fluid is the rule. The fact that gradual decrease in the formation does take place suggests that the patient may be tided over a period of decompensation. Provided that there is no hepatotoxic agent operating, it is perhaps the regeneration of liver tissue or decrease in the level of the portal hypertension which is eventually responsible for the long-term improvement.

The infusion of ascitic fluid in the advanced cirrhotic patient with gross decompensation has given disappointing results, and has not altered the prognosis favourably. Although the procedure is therefore not recommended for this type of case, as it does not *per se* aggravate the condition, it is reasonable to allow a trial period. The only absolute contraindication is marked azotaemia and renal failure.

On the other hand in the moderately severe cirrhotic, with peripheral hypovolaemia but good renal function, it is a procedure of merit which is a useful adjuvant to medical therapy and may even at times replace it with advantage.

SUMMARY

Twenty-three patients with cirrhosis of the liver have received infusions of unaltered and autogenous ascitic fluid on a number of occasions. The procedure used was a simple one and may be easily undertaken. Few complications were observed. Most patients derived an immediate benefit. In the cirrhotic with gross decompensation the prognosis remained unaltered, but in the moderately severe case good results were obtained.

It is offered as a good adjuvant to medical treatment, and one that may provide a successful response when the latter has failed.

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REFERENCES

1. Britton, R. C. (1961): Arch. Surg., **83**, 364.
2. Davis, H. A. (1941): *Ibid.*, **42**, 453.
3. Davis, H. A. and Blalock, J. F. (1939): J. Clin. Invest., **18**, 219.
4. Emmrich, R. and Fliege, H. J. (1951): Med. Welt. (Berl.), **20**, 931.
5. Girard, M., Fraisse, H. and Chabanon, R. (1949): Arch. Mal. Appar. dig., **38**, 910.
6. Kaiser, G. C., Lempke, R. E., King, R. D. and King, H. (1962): Arch. Surg., **85**, 763.
7. Lempke, R. E., Kaiser, G. C., King, R. D. and King, H. (1963): J. Amer. Med. Assoc., **183**, 347.
8. Longo, T. and Forti, D. (1964): Minerva med., **55**, 1887.
9. McKee, F. W., Wilt, W. G. jnr., Hyatt, R. E. and Whipple, G. H. (1950): J. Exp. Med., **91**, 115.
10. Molina, R. D., Santos, H. A. and Alimuring, M. M. (1947): Amer. J. Med. Sci., **213**, 435.
11. Papper, S. and Saxon, L. (1956): J. Clin. Invest., **35**, 728.
12. Prentice, T. C., Siri, W. and Joiner, E. E. (1952): Amer. J. Med., **13**, 668.
13. Smith, A. N. (1962): Lancet, **1**, 671.
14. Yamahiro, H. S. and Reynolds, T. B. (1961): Gastroenterology, **40**, 497.