

CONTENT

**Clinical Trail Report: WLFHY-500 WeiLi Computerlized Ascites Dialytic
Ultrafiltration & Reinfusion System (The Earth Temple Hospital, Beijing)**

.....Page 1

**Clinical Trail Report: WLFHY-500 WeiLi Computerlized Ascites Dialytic
Ultrafiltration & Reinfusion System (No. 302 Hospital of PLA)**

.....Page 7

Clinical Trail Report: WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion System

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Ascites is one of the common symptoms in internal medicine and bring patients great pains. It is a sort of difficult in clinical practice to eliminate completely the factors that lead to production of ascites. Over a long period of time physicians have been trying to look for methods to manage refractory ascites. As a common complication of cirrhosis, ascites in some patients response poorly to traditional treatments including limited intake of sodium and water and administration of diuretics. This kind of refractory ascites affects significantly the function of heart and lung, and it will also result to dangerous complications including infection in abdominal cavity and hepato-renal syndrome.

Ultrafiltration of ascites and peritoneal reinfusion could control ascites caused by various factors. It will relieve dyspnoea immediately and improve symptoms significantly. As to reports of related studies, the effective rate is up to more than 70%. After infusing processed ascites back into abdominal cavity, the pressure inside of peritoneum will descend and reabsorption route re-open. Thus protein concentration increases in abdominal cavity. Through dynamic exchange by viscus blood circulation protein is absorbed back into blood. Consequently, levels of albumin and total proteins in plasma increase, while CRE and BUN decrease. The treatment results into increased glomerular filtration rate (GFR), increased Na^+ content in urine, and decreased concentration of rennin, angiotensin, and aldosterone. Generally there will be no complication of electrolytes disturbance. Because of increased colloid osmotic pressure of plasma and increased effective circulating blood volume, the production of ascites is terminated and incidence of hepato-renal syndrome is rare. In addition, ultrafiltration and concentration will filter toxins out of ascites and enhance the content of complement C3 and number of macrophage cells. Therefore it decreases the risk of infection and spontaneous peritonitis.

For most of patients, ultrafiltration of ascites and peritoneal reinfusion could give satisfactory efficacy, shorter hospitalization period, and longer duration of life.

We use WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion System to treat 30 patients and obtain excellent clinical efficacy.

I. Subjects

Subjects of this clinical trail were enrolled exclusively form inpatients of our hospital who suffering with refractory ascites. All these patients responded poorly to routine treatment and were complicated with oliguria, anuria, and azotemia. The large amount of ascites resulted into obvious pressure symptoms, even umbilical hernia. The patients before treatment were considered as control group, and those post treatment as treated

group. Both groups had 23 males and 7 females with averaged age of 48.7 (ranged from 29 to 86).

II. Equipment, Materials and Methods

1. Equipment:

WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion System. There were two of the systems for each of these two hospitals, and verification period was 3 months.

2. Materials:

- (1) YT-100 hollow polyacrylonitrile fiber filter, with fiber hole diameter of 200 μ m, membrane area of 1.0m², and membrane hole diameter of 50,000 DW.
- (2) Polyethylene hemodialysis tubes.

3. Methods:

a. Preparation

- (1) Strict limitation in intake of sodium chloride (< 2g/d), and less strict limitation in ingestion of water.
- (2) Ceasing administration of diuretics more than 3 days before the operation.
- (3) Collecting 24 hours' urine before operation for examination of specific gravity, CRE, BUN, electrolytes and glucose.

- #### **b. Patient lay in horizontal position. Left-lower abdomen and right-middle abdomen were sterilized as normal, and then abdominal paracentesis was operated. Connect puncture needle with catheter. When puncturing, needle should be pushed ahead 1cm subcutaneously before it entered abdominal cavity, thus to avoid leakage. Additionally, the two needles should be apart properly to prevent the possibility of short circuit (as we know that this will affect the efficacy of ultrafiltration).**

Ascites was introduced from left-lower abdomen into artery catheter. Flow rate of positive pump was set at 150 – 250 ml/min. After transferred by peristaltic pump, ascites flew through filter and was ultrafiltered by vacuum pump, that is, water and medium and small molecules in it were filtered out. The concentrated ascitic fluid flew back to right-upper abdominal cavity through venous catheter. The whole circle was closed and sterile.

Total volume of ascites being ultrafiltered and reinfused may vary among 4000 – 12000 ml every time, and processing period may last 1.5 – 3.0 hours, or depending on targeted volume.

During processing, low molecular weight heparin was continuously infused into the artery end of tube systems (total dosage was 625 – 1250 U). At the end of treatment, antibiotics were injected into the venous end.

Wrist sphygmomanometer was applied to monitor heart rate and blood pressure during treatment.

4. Contraindications:

- (1) Severe heart diseases, electrolyte disturbance, or renal failure.
- (2) Obvious infection in abdominal skin.
- (3) Hepatic encephalopathy and hepatic coma had been classified as contraindications. However, there were reports that patients regained consciousness during reinfusion of ascites.
- (4) Recently hemorrhage of upper digestive tract and hemorrhage tendency were two relative contraindications.

5. Adverse events and managements:

Treatment by this system would normally bring no influence onto blood pressure and heart rate of patients. Occasionally, some patients may have adverse effects mentioned below:

- (1) Transient abdomen pain: this symptom was associated with decreased abdominal pressure and increased intestinal movements, and antispasmodics would relieve it.
- (2) Fever: this complication may be induced by cold stimulation during treatment and improper sterilization of reusable tube systems. Usually fever may recover spontaneously. As to those above 38°C, antibiotics could be used. Disposable filtration tubes may actually avoid the incidence of fever.
- (3) I° hepatic encephalopathy: this complication generally involved those with sub-clinical hepatic encephalopathy whose liver function had been severely damaged. Amine-deprivation treatment would be effective on this adverse effect.

6. Laboratory Examinations:

Blood was sampled on the day of treatment and the 3rd day after treatment to examine liver function (complex I) and renal function. Urine of the 3rd day after treatment was collected to determine parameters including specific gravity, CRE, BUN, electrolytes and glucose.

- (1) Renal function: CRE, BUN, electrolytes and glucose in blood.
- (2) Liver function complex I: TP, ALB.
- (3) Others: electrolytes, C3, and macrophages in ascites.

7. Criteria of Efficacy:

- 1) Significantly effective: significant relief in abdominal distension, relieved dyspnea, increased urine volume up to more than 500ml, improved appetite, and disappeared edema in lower limbs. With all the improvements mentioned above, patient had his ascites all gone or only a little remained, which lasting 3 months around.
- 2) Effective: patient had relieved abdominal distension, increased urine volume, and improved appetite. All these improvements lasted 1 month before ascites increased again.
- 3) Non-effective: patient had relieved abdominal distension, increased urine and improved appetite just for a short period. Half a month later ascites would regain up to the original level.

III. Results of Ultrafiltration & Reinfusion Treatment:

1. Symptoms and signs:

Table 1. Comparison of clinical symptoms and signs before and after treatment

	Body weight (kg)	Abdominal circumference (cm)	24 hours' urine volume (ml)
Before treatment	64.14±15.56	87.14±8.01	1250±152
After treatment	59.78±16.29	78.21±5.63	1875±170
P value	<0.05	<0.05	<0.05

Body weight decreased after ultrafiltration. So did abdominal circumference. Additionally, urine volume of 24 hours increased. After treatment symptom of dyspnea was relieved significantly.

2. Liver function:

Table 2. Comparison of liver function before and after treatment.

	TP	ALB
Before treatment	61.10±5.39	25.89±3.19
After treatment	65.89±7.03	29.87±4.00
P value	<0.05	<0.05

Compared with those before treatment, concentration of albumin and total protein in plasma increased after treatment, which was statistically significant.

3. Renal function:

Table 3. Comparison of renal function before and after treatment.

	CRE (μmol/L)	BUN (mmon/L)	K ⁺ (mmol/L)	Na ⁺ (mmol/L)	Cl ⁻ (mmol/L)
Before treatment	197±40.36	4.8±0.7	3.9±0.6	135.2±4.3	100.2±6.3
After treatment	130.82±31.62	5.0±0.9	4.2±1.8	136.7±5.1	101.5±3.4
P value	<0.05	>0.05	>0.05	>0.05	>0.05

Compared with those before ultrafiltration, concentration of BUN, K⁺, Na⁺ and Cl⁻ in plasma after treatment had no significant difference. While CRE level in blood decreased markedly. The treatment of ultrafiltration seemed play some good effects on renal function.

4. Observation of electrolytes in ascites before and after ultrafiltration-concentration:

Table 4. Comparison of electrolytes in ascites of 20 case / episode before and after treatment.

	K ⁺ (mmol/L)	Na ⁺ (mmol/L)	Cl ⁻ (mmol/L)
Before treatment	3.74±0.23	135.31±19.13	101.32±7.22
After treatment	3.69±0.39	134.45±16.67	98.49±8.87
P value	>0.05	>0.05	>0.05

Compared with those before ultrafiltration, contents of K⁺, Na⁺ and Cl⁻ in ascites after treatment had no significant difference.

5. Determination of complement C3 and macrophages in ascites before and after

ultrafiltration-concentration. Results were listed in Table 5.

Table 5. Comparison of complement C3 and macrophages in ascites before and after treatment.

	Complement C3 (X±S) (mg/100ml)	Number of macrophage (X±S) (/100ml)
Before treatment	20.14±13.79	12.17±14.11
After treatment	72.10±21.56	27.98±15.51
P value	<0.05	<0.05

Compared with those before ultrafiltration, contents of complement C3 and macrophages in ascites increased significantly after treatment, which had positive effects on prevention of infection in abdominal cavity.

6. Determination of Na⁺ excretion in 24 hour's urine. Results were listed in Table 6.

Table 6. Na excretion in 24 hour's urine

	Before treatment	After treatment	P value
Na ⁺ in 24h's urine	21.95±20.12	58.27±23.27	<0.05

After treatment, Na⁺ excretion in 24 hour's urine increased significantly, which indicating improved renal function and resulting into relieved clinical symptoms.

7. Efficacy:

Table 7. Efficacy: X² test

	Total number	Significantly effective	Effective	Non-effective
Patients	30	14	11	5
Percentage (%)	100	46.67	36.67	16.67
P value	/	<0.05	<0.05	<0.05

Percentage of patients with significantly effective response was 46.67%, percentage of those with effective response to treatment was 26.67%, and non-effective was 16.67%. X² test suggested that there is statistical significance between anterior and post treatment.

8. Side effects:

Patients with concentrated ascites reinfused back into their abdominal cavity showed no adverse effects during treatment. After then a few of them suffered transient abdominal pain, which relieved after administration of antispasmodics. 2 of 30 cases got slight fever (<37.5°C), and both of them recovered spontaneously the next day. No I° hepatic encephalopathy was observed.

IV. Discussion

1. After reinfusion of ascites, concentration of total protein and albumin increased, which was statistically significant. Refractory ascites was one of common symptoms, and there's no good management yet. Routine treatment of internal medicine had poor effects and complement of foreign protein may often be necessary. However, allergic reaction to foreign protein happened now and then. Moreover, they were expensive. As to all these shortcomings, ultrafiltration and concentration of ascites may be excellent alternatives. It also reduced the risk of infection when using blood products.
2. In patients with cirrhosis, blood pressure in capillary of portal circulation in hepatic sinusoid increased due to post-sinusoidal obstruction, which subsequently increasing blood content in

it and reducing systematic effective circulatory volume. Thus renal perfusion decreased and RAAS was activated, which led to retention of water and Na^+ . Many factors were involved in production of ascites, and symptoms of which included increased pressure intra-abdomen. Thus diaphragm was elevated to limit the movement of heart. Along with the decrease of cardiac output, perfusion of kidney was reduced, along with other humoral factors that may further activate RAAS to deteriorate the symptom of ascites. This vicious circle won't be terminated without medical management. The re-infusion of concentrated ascites resulted to significant reduction in body weight and abdominal circumference of patients. After the treatment patients had less creatinine in urine, and both urine volume and Na^+ excretion increased significantly also. Patients after treatment would have markedly increased albumin in plasma. Along with the relief of tension ascites, the circle mentioned above was terminated and RAAS was inhibited, which may have good influence to prevent hepato-renal syndrome.

3. As to patients with symptoms including severe dyspnoea, the treatment of re-infusing ultrafiltrated and concentrated ascites back into abdomen would relieve them immediately. Along with relieved abdominal distension and improved appetite patient may feel refreshed, also the duration of their hospitalization would be shortened. This treatment was quite safe and was effective in 83.33% patients. A large amount of water is filtered by the system, therefore large dose of diuretics was avoided, and thus adverse events of electrolytes disturbance complicated with diuretics would be avoided also. Therefore, the system is good enough to be recommended as a common measure to manage ascites.
4. The ultrafiltration-concentration may filter K^+ , Na^+ , Cl^- and BUN out of ascites, and result to increased concentration of complement C3 and macrophages, which may prevent abdominal infection.

V. Conclusion

Our study suggested that after ultrafiltration and concentration by WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion System (Beijing Wei Li Company), reinfusion of ascites could be an effective method to manage refractory ascites. After treatment patients would have decreased bodyweight, reduced abdominal circumference, increased 24 hours' urine volume, increased Na^+ excretion from urine, and significantly decreased creatinine and increased albumin and total protein in plasma. It is effective in 83.33% patients in clinical trial. This system is safe, reliable, and simple to operate. As an excellent measurement to control refractory ascites, it should be applied extensively.

the Earth Temple Hospital, Beijing

Clinical Trail Report: WLFHY-500 WeiLi Computerlized Ascites Dialytic Ultrafiltration & Reinfusion System

No. 302 Hospital of PLA

Ascites is one of the common symptoms of hepatic cirrhosis. We treated 30 cases with refractory ascites with WLFHY-500 WeiLi Computerlized Ascites Dialytic Ultrafiltration & Reinfusion System. After totally 51 cases / episodes of treatment we got excellent responses from these patients.

I. General Information

Subjects of this clinical trail were enrolled exclusively form inpatients of our hospital who suffering with hepatitis and cirrhosis complicated with ascites. Among 30 patients of treatment group, 26 were male and 4 female, with average age 45.6 (ranged from 25 to 63). Ascites of these subjects lasted 2.5 ~ 14 months. Circumference of abdomen varied 78 – 129 cm with average of 92.7 cm. The causes of ascites included hepatitis cirrhosis (23 patients, 38 cases / episodes), alcoholic cirrhosis (4 patients, 7 cases/ episodes), and Budd-Chiari syndrome (3 patients, 6 cases / episodes). All patients had poor responses to more than 2 weeks treatment of limited sodium intake and diuretics and got obvious sign of abdominal distension.

II. Materials and Methods

1. Materials:

WLFHY-500 WeiLi Computerlized Ascites Dialytic Ultrafiltration & Reinfusion System, which manufactured by Beijing WeiLi Inc.

2. Methods:

Operated in the same way as routine puncture, ascites was introduced from left lower abdomen into arterial catheter. Flow rate was controlled in the range of 150-250ml/min by positive pump. When passing through filter, thanks to vacuum pump ascites would lose water and medium and small molecules in it, which resulting into concentration. The concentrated ascitic fluid flew back to patient's right upper abdomen through venous catheter. The whole circle is closed and sterile. Total volume of ascites being ultrafiltered and reinfused may varies among 4000 – 12000 ml every time, and processing period lasted 1.5 – 3.0 hours, and interval between two processions should be 1 or 2 weeks.

3. Criteria of Efficacy:

- 1) Significantly effective: significant relief in abdominal distension, relieved dyspnea, increased urine volume up to more than 500ml, improved appetite, and disappeared edema in lower limbs. With all the

improvements mentioned above, patient had his ascites all gone or only a little remained, which lasting 3 months around.

- 2) Effective: patient had relieved abdominal distension, increased urine volume, and improved appetite. All these improvements lasted 1 month before ascites increased again.
- 3) Non-effective: patient had relieved abdominal distension, increased urine and improved appetite just for a short period. Half a month later ascites would regain up to the original level.

4. Laboratory Examination and Evaluation:

Ascites was sampled before and after treatment to determine the contents of electrolytes, protein, BUN, cholerythrin, endotoxin, macrophages and complement C3. Differences between groups before and after treatment were tested by students' t test and P values were gained. If P was <0.05 the treatment was evaluated as effective, P <0.01 was considered as significant effective, and P>0.05 as non-effective.

5. Verification Period

Two of WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion Systems were used in clinical practice during June 4, 2000 to September 2, 2000, and verification period was 3 months.

III. Results of Treatment by reinfusion of ultrafiltrated and Concentrated ascites

1. Symptoms and signs: See Table 1.

Table 1. Comparison of clinical symptoms and signs before and after treatment

	Body weight (kg)	Abdominal circumference (cm)	24 hours' urine volume (ml)
Before treatment	63.4±11.8	97.6±7.9	1160.9±250.5
After treatment	58.9±10.5	92.0±6.8	1860.8±210.8
P value	<0.05	<0.05	<0.05

All p values were <0.05, suggesting that ultrafiltration resulted into reduced body weight and decreased abdominal circumference. Additionally, urine volume of 24 hours increased. After treatment symptom of dyspnea was relieved significantly.

2. Changes of contents of electrolytes, protein, and cholerythrin in ascites after ultrafiltration: See Table 2.

Table 2. Comparison of electrolytes, protein and cholerythrin in ascites of 30 case / episode before and after treatment.

	K ⁺	Na ⁺	Cl ⁻	BUN	Total protein	Cholerythrin
	(mmol/L)	(mmol/L)	(mmol/L)	(mmon/L)	(g/l)	(μmol/L)
Before ultrafiltration	4.02	132.5	95.7	26.58	6.05	51.76
After ultrafiltration	3.97	134.8	96.23	16.24	30.46	153.69
P value	>0.05	>0.05	>0.05	>0.05	<0.01	<0.01

Compared with those before ultrafiltration, concentration of K⁺ and Na⁺ in ascites after treatment had no significant difference. However, BUN decreased slightly (P<0.05), and the concentration of total protein and cholerythrin increased 3-5 folds (P<0.01).

3. Determination of endotoxin in ascites of patients with hepatic ascites:

Microdetermination was used to measure the content of endotoxin in ascites before and after ultrafiltration in 23 patients with hepatitis cirrhosis complicated with ascites. (See Table 3)

Table 3. Observation of endotoxin content in ascites of 23 patients before and after ultrafiltration.

	Number of Positive response	Number of Negative response	Content of endotoxin (X±S) (pg/ml)
Before ultrafiltration	8	15	65.28±13.07
After ultrafiltration	2	21	17.54±12.78
P value			<0.01

Compared with the content of endotoxin in ascites before ultrafiltration, it decreased significantly after treatment (P<0.01), which indicating that many endotoxin would filter out of ascites during ultrafiltration.

4. Determination of complement C3 and macrophages in ascites before and after ultrafiltration: Results refer to Table 4.

Table 4. Determination of complement C3 and macrophages in ascites of 30 patients before and after ultrafiltration.

	Complement C3 (X±S) (mg/100ml)	Macrophage cells (X±S) (/100 ml)
Before ultrafiltration	30.54±12.79	15.50±8.04
After ultrafiltration	81.48±14.78	38.27±10.46
P value	<0.01	<0.05

The difference between contents of complement C3 in ascites before and after ultrafiltration was very significant (P<0.01). So did the number of macrophages (P<0.05). The markedly increased complement C3 and macrophages after ultrafiltration would help to prevent infection intra peritoneum.

5. Efficacy: Refer to Table 5.

Table 5. Efficacy: X² test

	Total number	Significantly effective	Effective	Non-effective
Patients	30	11	14	5
Percentage (%)	100	46.67	36.67	16.67
P value	/	<0.05	<0.05	<0.05

Effective rate was 83.34%, and X² test suggested that there is statistical significance between control and treated groups.

6. Adverse events:

Patients with concentrated ascites reinfused back into their abdominal cavity showed no adverse effects during treatment. After then a few of them suffered transient abdominal pain, which relieved after administration of antispasmodics. 2 of 30 cases got slight fever (<37.5°C), and both of them recovered spontaneously the next day. One patient, who with primarily peritonitis before ultrafiltration, had a temperature of 38°C after treatment. This patient recovered after 3 ~ 5 days of administration of antibiotics. There were no complications observed including decreased blood pressure, hepatic encephalopathy, and hemorrhage of digestive tract.

IV. Discussion

1. Ultrafiltration of ascites and peritoneal reinfusion could be used to treat refractory ascites caused by various reasons. It could relieve the symptoms resulted from large quantities of ascites including dyspnoea and abdominal distension. In our study the effective rate is 83.34%, that is, most of patients would gain relief quickly after the treatment. Along with pain relieved and symptoms disappeared, life quality may be elevated.
2. At later stage of hepatic cirrhosis liver function of patients will damaged severely, and their immunity were damaged also. In addition, the ability of body to eliminate endotoxins decrease. Infection and endotoxemia are two common complications. The ultrafiltration-concentration may filter K⁺, Na⁺, Cl⁻ and BUN out of ascites, and may filter part of endotoxin out. At the same time, it will result to increased concentration of total protein, complement C3 and macrophages, which may prevent abdominal infection and reduce endotoxemia.
3. Compared with ascites reinfusion intravenously, ultrafiltered ascites reinfusion peritoneal is safer. No contraindication is observed for the latter. Additionally, a large amount of water is filtered out by the system, therefore large dose of diuretics was avoided, and thus adverse events of electrolytes disturbance complicated with diuretics would be avoided also. Especially to those patients with increased BUN and creatinine and decreased volume of urine due to pressure of large amount of ascites, ultrafiltered ascites reinfusion peritoneal resulted into decreased BUN and creatinine in ascites and increased volume of urine, which may help to prevent the influence of hepato-renal syndrome.

4. WLFHY-500 WeiLi Computerized Ascites Dialytic Ultrafiltration & Reinfusion System (Beijing Wei Li Company) operate in a closed and sterile circulation, and is quite simple to operated. There is no adverse event during treatment with this system. After then a few of patients suffered transient abdominal pain related to increased intestinal movement, which relieved after administration of antispasmodics. 3 patients got slight fever (37.5°C), and all of them recovered spontaneously the next day. This may be induced by cold stimulation during treatment or improper sterilization of reusable tube systems. One patient, who with primarily peritonitis before ultrafiltration, had a temperature of 38°C after treatment. This patient recovered after 3 ~ 5 days of administration of antibiotics. There were no complications observed including decreased blood pressure, hepatic encephalopathy, and hemorrhage of digestive tract. Consequently, we concluded that the system manufactured by Beijing WeiLi Company is a safe, reliable, and simple methods in ascites ultrafiltration and peritoneal reinfusion to manage refractory ascites induced by various reasons.

No. 302 Hospital of PLA