

# *Refractory Ascites*

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# Ascites

- In medicine (gastroenterology), ascites (also known as peritoneal cavity fluid, peritoneal fluid excess, hydroperitoneum or more archaically as abdominal dropsy) is an accumulation of fluid in the peritoneal cavity. Although most commonly due to cirrhosis and severe liver disease, its presence can portend other significant medical problems. Diagnosis of the cause is usually with blood tests, an ultrasound scan of the abdomen, and direct removal of the fluid by needle or paracentesis (which may also be therapeutic). Treatment may be with medication (diuretics), paracentesis, or other treatments directed at the cause.

## *Refractory ascites*

is defined as **ascites** unresponsive to 400 mg of spironolactone or 30 mg of amiloride plus up to 120 mg of furosemide daily for two weeks.

## ■ Question

"Ascites in decompensated cirrhosis is a poor prognostic indicator, with a 50% 2-year survival, worsening significantly to 20% to 50% at 1 year when the ascites becomes refractory to medical therapy. We have many patients with refractory ascites at our institution; at what point in management is a patient considered to be resistant to medical therapy, and what algorithm is recommended for diuretic therapy?"

Second, in some studies bedrest has been shown to increase natriuresis in cirrhotic patients because it has been speculated that upright posture increases aldosterone levels, which is associated with sodium retention. What is your opinion on this and what do you recommend? Sodium retention is central to the formation of ascites and therefore a salt-restriction diet is essential, but do you recommend fluid restriction as well?

The term **refractory ascites** was introduced in the 1950s as a general term defining ascites that could not be satisfactorily managed by medical therapy; it was better defined approximately a decade later with the introduction of loop diuretics and spironolactone.

A proposed definition of **refractory ascites** is as follows: ascites that cannot be mobilized or the early recurrence of which (ie, after therapeutic paracenteses) cannot be satisfactorily prevented by medical therapy. It was then further proposed that refractory ascites includes 2 different subtypes:

1. diuretic-resistant ascites
2. diuretic-intractable ascites

1. **diuretic-resistant ascites** -- ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of lack of response to dietary sodium restriction and maximal doses of diuretics
2. **diuretic-intractable ascites** -- ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of the development of diuretic-induced complications that preclude the use of effective diuretic dosages.

## *DEFINITIONS*

For the correct diagnosis of true refractory ascites, the patient's condition should fulfill the following six criteria :



## *1-Diuretic-resistant ascites*

Failure of mobilization or the early recurrence of ascites which cannot be prevented because of a lack of response to sodium restriction and diuretic treatment is called diuretic-resistant ascites.

## *2-Diuretic-intractable ascites*

Failure of mobilization or the early recurrence of ascites which cannot be prevented because of the development of diuretic-induced complications that prevent the use of an effective diuretic dosage is called diuretic-

### *3-Treatment duration*

Patients must be on intensive diuretic therapy (spironolactone 400 mg/d and furosemide 160mg/d) for at least 1 wk and on a salt-restricted diet of less than 90 mmol/d.

### *4-Lack of response*

Mean weight loss of less than 0.8 kg over 4 d and urinary sodium output less than the sodium intake.

## *5-Early ascites recurrence*

There is an reappearance of grade 2 or 3 ascites (clinically detectable) within 4 wk of initial mobilization.

However,

it is important to notice that in patients with severe peripheral edema, reaccumulation of ascites within 2-3 d

of paracentesis must not be considered as early ascites recurrence because it represents a shift of interstitial fluid to the intraperitoneal space

## *6-Diuretic-induced complications*

Diuretic-induced hepatic encephalopathy is the development of encephalopathy in the absence of any other precipitating factor. Diuretic-induced renal impairment is indicated by an increase of serum creatinine by  $> 100\%$  to a value of  $> 2$  mg/dL in patients with ascites otherwise responding to treatment. Diuretic-induced hyponatremia is defined as a decrease of serum sodium by  $> 10$  mEq/L to a serum sodium of  $< 125$  mEq/L. Diuretic-induced hypo- or hyperkalemia is defined as a change in serum potassium to  $< 3$  mEq/L or  $> 6$  mEq/L despite appropriate measures. In addition to this, we should exclude dietary noncompliance (patient taking excess sodium in diet) and exclude the use of nonsteroidal antiinflammatory drugs (NSAIDs), which can induce renal vasoconstriction and diminish diuretic responsiveness

# *Treatment*

The ideal treatment of ascites should be effective in mobilization of ascites and prevention of recurrence, should improve patient's quality of life and survival, and should be acting directly on one or more steps in the pathogenesis of ascites and not just the mechanical removal of the fluid

- In a series of review articles, has popularized the standard algorithm used for the treatment of ascites.
- The initial treatment is restriction of dietary sodium intake to 88 mmol/day and oral diuretic therapy.
- The combination of spironolactone and furosemide is the most effective diuretic regimen. The typical starting daily dose is 100 mg of spironolactone and 40 mg of furosemide, with all medications taken once in the morning.
- The use of divided doses is not supported by pharmacokinetic data, and compliance is much better with a single daily dose. If there is no decrease in body weight or increase in urine sodium excretion after 3 days and up to 1 week, the doses of both drugs can be doubled to 200 mg/day of spironolactone and 80 mg/day of furosemide.

- The maximum daily doses are 400 mg of spironolactone and 160 mg of furosemide. An alternative strategy is to substitute amiloride for spironolactone at a starting dose of 10 mg/day, increasing to a maximum of 40 mg per day, but amiloride is more costly and this regimen is somewhat less effective than spironolactone and furosemide.

- If maximal doses of diuretics fail, the usual next step in the algorithm for managing refractory ascites is large-volume paracenteses.
- Procedure-related complications (ie, primarily bleeding) occur in less than 1% of cases. Although the literature remains undecided regarding its benefit, intravenous albumin (6-8 g per liter of fluid removed) is commonly used for plasma expansion after large-volume paracenteses.
- Another alternative when maximal doses of diuretics fail to control refractory ascites is transjugular intrahepatic portosystemic shunt (TIPS).



- Multiple studies show better control of refractory ascites with TIPS than with large-volume paracenteses, but without a survival benefit. However, TIPS cannot be used in patients with advanced, decompensated cirrhosis (eg, Child's class C), because shunting portal blood away from the liver often precipitates liver failure in this group of patients.
- Finally, any patient with refractory ascites should be evaluated for potential candidacy for liver transplantation.

- It is true that the supine position, or bedrest, reduces plasma renin concentrations and aldosterone levels. However, bedrest which has not been shown to promote more rapid natriuresis in the clinical setting predisposes patients to the formation of decubitus ulcers and is generally not practical.

- Sodium restriction is indeed an important cornerstone in the treatment of ascites, and the usual recommendation is to limit sodium intake to 88 mmol/day, which represents moderate sodium restriction.
- Diets with lower sodium content are not well tolerated. Many patients with cirrhosis and ascites have mild-to-moderate asymptomatic hyponatremia when they take fluid without restriction.
- It is generally accepted that fluid restriction is not necessary unless the serum sodium concentration drops below 120 mmol/L.

*Thank You*