


DIURETIC USE IN CIRRHOSIS

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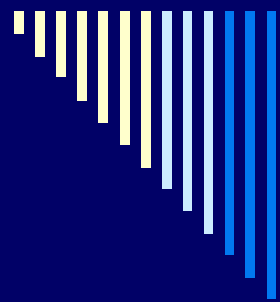
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Introduction:

- ❑ **Ascites is one of the most common complications of liver cirrhosis.**
- ❑ **The word “ascites” is derived from the Greek word “askos”, which means a bag or sack.**
- ❑ **Ascites occurs in about 50% of patients within 10 years of the diagnosis of cirrhosis.**
- ❑ **Cirrhotic patients who develop ascites have a probability of survival of 85% at 1 year and 56% at 5 years.**
- ❑ **International Ascites Club: Severity: grade 1,2 and 3. Or Complicated (SBP or HRS) , and uncomplicated and refractory.**



Ascitic Fluid

Portal Capillary

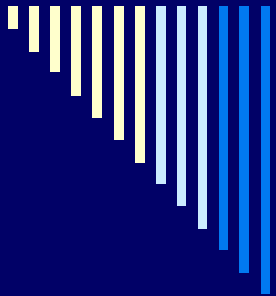
A.C.O.P.

S.C.O.P.

A.F.P.

P.C.P.

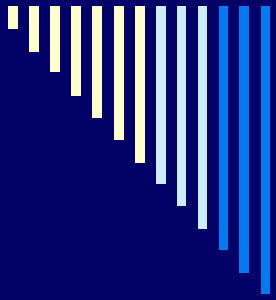
**Ascitic fluid circulates continuously
about 50% of fluid changes / hour**



Serum Ascites Albumin Gradient “SAAG”

**Serum Albumin level – Ascitic fluid Albumin
= Gradient gm/dl**

- * It correlates with portal pressure, the threshold is 1.1 gm/dl. If high gradient > 1.1 it is a transudate secondary to portal hypertension.**
- * Accuracy 97%.**



PATHOPHYSIOLOGY

CIRRHOSIS

Portal Hypertension

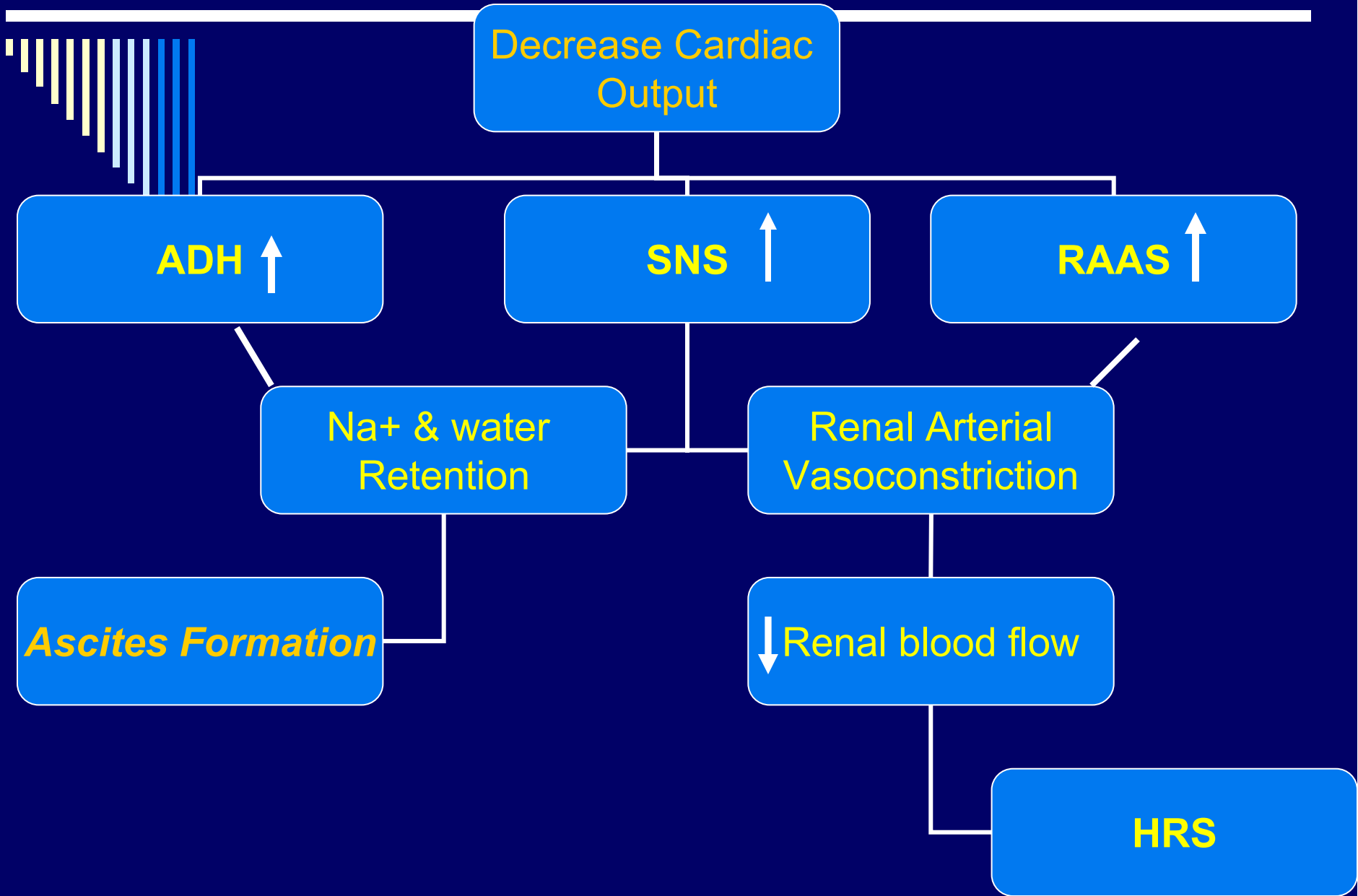
NO overproduction

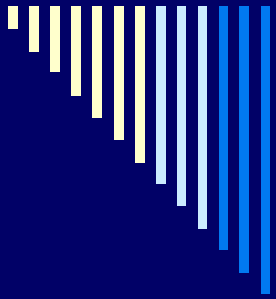
Splanchnic vascular & Peripheral Arterial Vasodilatation

Decrease Effective Blood Volume

↑ Splanchnic Lymph Production

Decrease Cardiac Output





- Derangement in the extracellular fluid volume regulatory mechanisms and ***SODIUM & WATER RETENTION*** is the main cause of ascites.
- So, most therapeutic modalities are directed on maintaining negative sodium balance, including salt restriction, bed rest and ***diuretics***.



MANAGEMENT:

- ***GOALS:*** Control of ascites, relief of ascites-related symptoms and prevent complications(SBP & HRS).
 - ***Number of modalities:***
 - bed rest.
 - diet modification.
 - diuretics.***
 - more intensive measurements: such as LVP, TIPS & PVS.
-



Bed Rest:

- Inhibits the neurohormonal system (**RAAS & SNS**) so it reduces plasma aldosterone level..... improves the response to diuretic therapy in cirrhotic.
 - Not recommended routinely.
-



Diet Modification:

- ***Sodium restriction:*** to achieve a negative sodium balance.
- Decrease salt intake in diet to 2 gm/day which equal to (88 mEq/day).
- Alone, efficacy is limited to 10% of patients.
- ***Water intake restriction:*** In cases of dilutional hyponatremia (serum Na < 130mEq/L).



DIURETIC THERAPY:

- ❑ Should not be postponed. It is recommended to start diuretic therapy immediately.
- ❑ Diuretic therapy, in addition to sodium restriction, is an effective therapeutic approach in 80-90% of cirrhotic patients.
- ❑ ***SPIRONOLACTONE*** alone or along with ***FUROSEMIDE*** (a loop diuretic) is the first-line therapy in persistent ascites.
- ❑ Initial dose 100 mg spironolactone + 40 mg furosemide. ***Maintain 100-40 ratio*** to preserve a normokalemic state.



Diuretic Therapy:

- Increase dose in a stepwise-fashion up to a **maximum dose** of 400 mg/day of spironolactone and to 160 mg/day of furosemide.
- How to monitor patient's response to diuretics???



Monitor Response:

- ***A) Daily weight loss:***
in absence of edema not more than 0.5 Kg/day. And not more than 1 Kg/day in edematous state.
- ***B) Side effects:*** gynecomastia or muscle cramps. Amiloride (K sparing diuretic 10-20 mg/day) as an alternative to spironolactone



□ **C) Urinary Sodium Concentration:**

- **24 hour urinary Na excretion.** If patient is not compliant with the diet, he will gain weight inspite of excreting $> 88\text{mEq Na/day}$. If it is $0\text{-}50\text{ mEq}$ Increase dose of diuretic.

Drawbacks!!!!.

- **Sodium in spot urine specimen:** easier and more convenient, lacks accuracy except if 0 mEq (lack of diuretic response) or $> 100\text{ mEq}$ (adequate response or patient is non compliant).

- **Furosemide-induced natriuresis:** IV 80 mg and measure urinary Na in the next 8 hours. Diuretic resistant if $< 50\text{ mEq/8 h}$.



When NOT to start Diuretics?:

If PATIENT:

- With active **variceal bleeding**.
 - Has Bacterial **infection** with hypotension.
 - His serum **creatinine** $> 2 \text{ mg } \%$ and rising steadily.
-



Patient Labeled Diuretic Resistant

- Who cannot increase Na output $>$ intake.
- Whom on 88 mEq Na daily intake + 400 mg spironolactone + 160 mg furosemide
 - * Don,t loose weight or ascitic fluid.

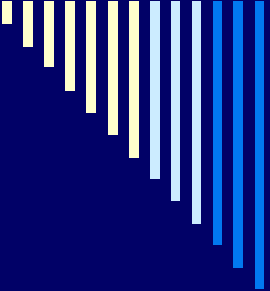
(EXCLUDE NSAID intake)

OR * Develop progressive azotemia(creatinine $>$ 2.4 mg%), hepatic encephalopathy or serious electrolyte imbalance(Na $<$ 120 mEq/L or K+ $>$ 5.5mEq/L).



AQUARETICS:

- ❑ **Vasopressin receptor antagonists that act on the distal tubule of the kidney to excrete solute-free water.**
- ❑ **Approved for hyponatremia due to SIADH. Evaluated for management of hyponatremia in cirrhosis & refractory ascites.**
- ❑ **Vasopressin receptors are V1a, V1b and V2.**

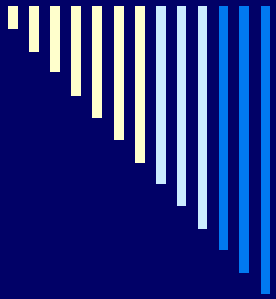
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- **Oral forms:** selective V2 (**Lixivaptan** and **Satavaptan**).
 - **IV form:** (**Conivaptan**) acts on V2 and V1a receptors and V1a mediates the vasoconstrictor response of vasopressin. So it cannot be used in ascites as it may cause variceal bleeding.
 - One study on 110 ascitic patients receiving satavaptan or placebo in addition to diuretics .

Those receiving satavaptan had significant decrease in abdominal girth and more weight reduction without significant side effects. (Genies et al, Hepatology 2008)



In Conclusion:

- Salt and water retention is the main mechanism in developing ascites in cirrhotic patients.**
- Salt restriction and diuretics are the cornerstone in treatment of ascites.**
- Spironolactone and Furosemide ratio must be kept during treatment.**
- Spot urine Na excretion is a reasonable way for monitoring response to diuretics.**
- Maximum dose must not be exceeded.**
- Aquaretics may have a future role in certain cases.**



THANK YOU

for your attention
