

High-Dose Diuretic as Treatment of Refractory Ascites Compared with Paracentesis: An Evidence Based Case Report

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Abstract: ***Introduction:** Cirrhosis hepatic is severe scarring in liver tissue caused by progression of chronic liver disease. Refractory ascites are seen in 5-10% in cirrhosis hepatic patients. The treatment of refractory ascites are diuretics and paracentesis. **Case illustration:** 50 years old male with refractory ascites caused by cirrhosis hepatic came to hospital with complaint heavy on breathing. We would like to investigate the efficacy between high-dose diuretics and paracentesis in treatment of our patient. **Method:** We search article in PubMed and Proquest, we found 2 eligible Randomized-Controlled Trial (RCT). We do critical appraisal using Center of Evidence-Based Medicine (CEBM) tool from Oxford University. **Result:** In two trial, the result are high-dose diuretic has more efficacy than paracentesis and there was higher incidence of Hepatic Encephalopathy (HE) and Spontaneous Bacterial Peritonitis (SBP) in paracentesis group. In High-dose diuretic group also show better Child-Pugh Score result. **Conclusion:** High-dose diuretics treatment is better than paracentesis in treatment of refractory ascites caused by cirrhosis hepatic.*

Keywords: Diuretic, Paracentesis, Refractory ascites

1. Introduction

Cirrhosis Hepatic (CH) is severe scarring in liver tissue caused by progression of chronic liver disease. Cirrhosis is more common in male than female with ratio 1,6:1. In Indonesia, CH because of hepatitis B is about 21,2 – 46,9% and hepatitis C is about 38,7-73,9%.¹ (papdi) The liver will loss its function and will cause many complicating events. In cirrhosis, we would found several conditions as ascites, esophageal varices, HE (hepatic encephalopathy), SBP (spontaneous bacterial peritonitis), hepatorenal syndrome, and many more.²(trial 3) Ascites is the most important findings in cirrhosis which there was accumulation of fluid in peritoneal cavity caused by increase of pressure in portal circulation. In patient with CH, ascites is defined as refractory when it can not be mobilized with standart dose of diuretic therapy.²

Refractory ascites are seen in 5-10% in CH patients. The mechanisms of refractory ascites are not fully understood. Some theory were [1] Peripheral arterial vasodilatation associated with portal hypertension induces a reduction in the effective blood volume, causing permanent activation of endogenous vasoconstrictive and anti-natriuretic mechanisms; [2] Refractory ascites is considered to occur as a result of extreme vascular underfilling with maximal activation of RAAS (Renin-angiotensin aldosterone system).^[3]

Treatment of ascites should be comprehensive, including: [1] Bed rest, this position will increasing perfusion to renal and glomerular filtration. This position will decrease RAAS level; [2] Diet, low sodium diet will help diuresis (40-60 meq/day); [3] Diuretic agent, diuretic that recommended is anti-aldosterone, which is spironolactone. This diuretic is potassium-sparing diuretic, works in distal tubulus and prevent sodium reabsorption. Loop diuretic is needed as

combination with spironolactone; [4] Paracentesis. The oldest form of therapy for ascites is a rapid and effective treatment. This procedure was abandoned after the introduction of modern diuretics because of its complication as SBP, hypovolemia, hyponatremia, HE. But nowadays, this procedure was recommended again with albumin substitution 6-8 gr/L.^{[1],[4]}

2. Case Illustration

Male 50 years has been diagnosed with cirrhosis hepatic from 1 years ago. He has been hospitalized 2 times in the last two months with complaint heavy on breathing. From the physical examination, his lung was in normal limit, examination obtained a moderate-severe ascites. From laboratory finding, his protein total was 6,1 g/dL, albumin level 1,9 g/dL, globulin level 4,2 g/dL, renal function was in normal limit, electrolyte was in normal limit. We considered the cause of his complaint was his ascites. His is on medication spironolactone 1 x 300 mg and furosemide 2 x 40 mg. We try to think about the best treatment for him, whether increasing his diuretic dose or do paracentesis. Question: In patient with refractory ascites, does high-dose diuretic is more effective than paracentesis? And what about the side effect of each treatment?

3. Method

We use PubMed and Proquest as search engines on 10th June 2018. We are using advanced search with keywords “paracentesis” AND “diuretic” AND “ascites” AND “cirrhosis”. Inclusion criteria were: [1] Clinical trial that comparing high-dose diuretic with paracentesis in refractory ascites treatment; [2] Article is available in english or Indonesian; [3] Available in free full text; [4] Article is not published more than 10 years before searching time. The eligible articles then being critical appraised by CEBM

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(Center of Evidence-Based Medicine) tool by Oxford University.

4. Result

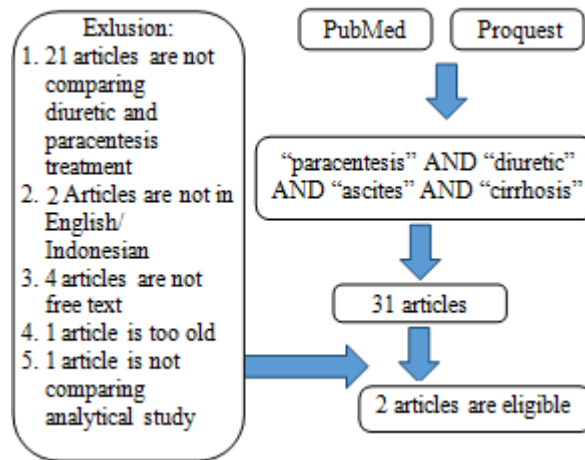


Figure 1: Our method to find article

Critical Appraisal

Study	Year	Sampel	Study design	Randomization	Similarity at start	Equal treatment	Intention to treat	Double blinded	Level of Evidence
Licata G, et al	2009	84	RCT	+	+	+	+	-	2
Yakar, et al	2016	78	RCT	+	+	+	+	-	2

Figure 2: Critical appraisal based on CEBM, Oxford University

5. Evaluation

Study	Patient and Method	Result	Conclusion
Licata G, et al 2009	84 patients with refractory ascites caused by cirrhosis hepatic (has been on treatment with spironolactone 400 mg/day + furosemide 160 mg/day), divided into 2 group. All the patients do not have acute renal failure, congestive heart failure, hepatocellular carcinoma, or any disease. Divided into 2 group. Group A: High-dose furosemide 250-1000 mg/day + 150 ml 1,4-4,6% NaCl Group B: Repeated paracentesis 4-6 L/day + albumin 8 gr/L	After treatment: <ul style="list-style-type: none"> •Group A has more diuresis than group B (p = < 0,001) •Group A shows lower child-pugh score than group B (p = < 0,04) •Group B has lower sodium level than group A (p = 0,04) •No significant different result in HE (Encephalopathy Hepatic), SBP (Spontaneous Bacterial Peritonitis) and worsening in renal function in both group 	High-dose furosemide + small-volume of hypertonic saline solutions is more effective compared with repeated paracentesis
Yakar T, et al 2016	78 patients with refractory ascites caused by cirrhosis hepatic (has been on treatment with spironolactone 400 mg/day + furosemide 160 mg/day), divided into 2 group. All the patients do not have acute renal failure, congestive heart failure, hepatocellular carcinoma, or any disease. Divided into 2 group. Group A: Spironolactone 100 mg/day + Furosemide 2 x 360–520 mg/day + Oral salt 2 x 3 gr/day (add on butter-milk) Group B: Repeated Large Volume Paracentesis (>5 L/day) + albumin 6 gr/L	After treatment: <ul style="list-style-type: none"> • Group A has more diuresis than group B (p = <0,001) • Group A shows lower child-pugh score than group B (p = <0,001) • Group B has lower sodium level than group A (p = <0,001) • Group B shows significant higher incidence of encephalopathy hepatic (p=0,017), spontaneous bacterial peritonitis (p=0,002), and worsening in renal function (p=0,049) 	Spironolactone + high-dose furosemide + oral salt seems possible and practical, and decline incidence of SBP, HE.

Figure 3: Evaluation of two studies

6. Discussion

From PubMed search engine, we find two articles that eligible. These two studies were Randomized Controlled

Trial from Licata G, et al and Yakar T, et al. The sampel condition from these two studies were similar, which are all the patient with refractory ascites because of cirrhosis,

without any renal disfunction, heart disfunction, hepatocellular carcinoma, or any disease.^{[2],[5]}

Study from Licata G, et al involved 84 subjects with cirrhosis and refractory ascites. The subjects were divided into two groups, group A received high-dose diuretic + hypertonic saline and group B received paracentesis procedure. From the result, group A has more efficacy than group B in treat refractory ascites, they said this result can happen because furosemide + Hypertonic saline are reducing plasma renin activity and serum aldosterone levels, rise in renal blood flow and glomerular filtration rate. The hypertonic saline related to volume expansion served to compensated the underfilling mechanism. The hypertonic solution can increase osmotic pressure and in the plasmatic volume determining the fast redistribution of fluid in the vascular compartment with result increase renal blood flow. This also induced increase of hydrostatic pressure which reduce reabsorption of sodium.^[5]

Study from Yakar T, et al involved 78 cirrhosis patients with refractory ascites, divided into two groups. Group A received high-dose diuretic + oral salt and group B received paracentesis. From the result, group A has more efficacy than group B. Group A has more diuresis than group B, lower incidence of hyponatremia, lower incidence of HE, SBP and worsening in renal disfunction. Group A also has lower score of child-pugh than group B. This result show that group A is more superior than group B. Yakar, et al said that oral salt ingestion increasing osmotic pressure and lead volume mobilization into vascular compartment and increasing the renal blood flow that stimulates renal perfusion. They said that paracentesis was effective too but have some disadvantages as HE and SBP.^[2]

7. Recommendation

We recommended the use of high-dose diuretic, either with small volume hypertonic saline solution or oral salt than repeated paracentesis in treating refractory ascites to minimalized the complication as HE, SBP, renal disfunction, and hyponatremia.

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